

Computational methods for EEG recordings during periodic sensory stimulation

Dounia Mulders

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Dissertation committee:

Prof. Michel Verleysen (advisor)	UCLouvain, Belgium
Prof. André Mouraux (advisor)	UCLouvain, Belgium
Prof. Jean-Pierre Raskin (chairperson)	UCLouvain, Belgium
Prof. François-Xavier Standaert (secretary)	UCLouvain, Belgium
Prof. Susana Ferrao Santos	UCLouvain, Belgium
Prof. Thomas Weiss	Jena University, Germany
Prof. Matthias Treder	Cardiff University, United Kingdom

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Abstract

UNDERSTANDING how the human brain processes sensory stimuli remains a challenging issue in neuroscience. For this purpose, scalp electroencephalography (EEG) is of particular interest to directly record brain activity non-invasively with a high temporal resolution while the subject is exposed to sensory stimulation. In particular, brief sensory stimuli can elicit event-related potentials (ERPs) recorded on the EEG which have been extensively considered in clinical and research studies. However, much less is known about the dynamics of brain responses and subsequent perception evoked by longer-lasting, tonic stimulation. In order to extract the stimulus-evoked activity from background noise, phasic responses can be highlighted through time or frequency averaging across trials, among others. At the opposite, it is far more difficult to tease out tonic responses from background activity without any temporal cues along long time intervals.

In this context, this thesis considers periodic stimulation to better link the brain responses to their input tonic stimulus. Indeed, this offers several advantages, as the periodic modulation of a sensory stimulus elicits synchronized periodic activity in the neuronal populations responding to the stimulus, referred to as a steady-state response (SSR). In the frequency domain, the stimulus-evoked activity concentrates at the frequency of stimulation and its harmonics, and can thus hopefully be isolated from non-stimulus-related activity. In the time domain, the known periodicity also conveniently enables highlighting the dynamics of the elicited responses, i.e. the shape of their time course. In this dissertation, the approach is designed and implemented to study thermosensation, a sense which is of crucial importance to allow proper thermoregulation, to identify textures and to assess potential threats arising from noxious heat or cold stimuli. The EEG responses and perception elicited by warm and cool stimuli whose intensities are slowly and periodically modulated are recorded and analyzed. The baseband EEG responses as well as ongoing oscillations in physiological frequency bands are

described in the time, frequency and time-frequency domains.

Despite the numerous advantages of periodic stimulation, their benefits remain conditioned to a sufficient signal-to-noise ratio (SNR) of the analyzed responses. Unfortunately, EEG recordings typically exhibit a very low SNR, harming their direct exploitation in a large number of applications. For this reason, one needs to develop, compare and assess dedicated signal processing techniques to faithfully identify the stimulus-related activity. This thesis therefore proposes and compares methods to extract periodic components from multidimensional recordings. These approaches consist in (1) spatial filters maximizing the periodicity of the extracted components from a multidimensional signal, (2) spatial filters optimizing the specificity of such periodic components to classes of multidimensional signals and (3) tensor factorization schemes to highlight the most periodic components through unsupervised algorithms. Simulations illustrate how the SNR of SSRs can be significantly enhanced to help enabling the use of periodic stimulation in practical contexts.

More generally, this dissertation contributes to improving the design, selection and relevance of computational schemes to analyze periodic signals, especially in neuroscience contexts.

Author's publications

THE content of several chapters in this dissertation has been published in scientific articles. These articles are listed hereunder and their links with this dissertation are indicated.

Journal article

- [1] Mulders, D., de Bodt, C., Lejeune, N., Courtin, A., Liberati, G., Verleysen, M., & Mouraux, A. (2020). Dynamics of the perception and EEG signals triggered by tonic warm and cool stimulation. *PLoS One*, DOI: 10.1371/journal.pone.0231698.

- Part I corresponds to the content of this paper.

Conference proceedings (peer-reviewed)

- [2] Mulders, D., de Bodt, C., Lejeune, N., Lee, J. A., Mouraux, A., & Verleysen, M. (2019). Tensor factorization to extract patterns in multimodal EEG data. In *ESANN* (pp. 601-606).

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- [3] Mulders, D., de Bodt, C., Lejeune, N., Mouraux, A., & Verleysen, M. (2018). Linear Periodic Discriminant Analysis of Multidimensional Signals. In *ICONIP* (pp. 476-487, vol. 6).

- Chapter 10 describes this paper.

- [4] Mulders, D., de Bodt, C., Lejeune, N., Mouraux, A., & Verleysen, M. (2018). Spatial filtering of EEG signals to identify periodic brain activity patterns. In *LVA/ICA* (pp. 524-533).

- Chapter 9 describes this paper.

Other works and collaborations resulted in additional scientific publications whose content is not discussed in this thesis. These articles are listed below.

Journal articles

- [5] de Bodt, C., Mulders, D., Verleysen, M., & Lee, J. A. (2020). Fast Multi-scale Neighbor Embedding. *IEEE Transactions on Neural Networks and Learning Systems*. Under review.
- [6] Courtin, A., Mulders, D., Liberati, G., & Mouraux, A. (2020). EEG frequency tagging using different target temperatures and slopes to disclose brain responses elicited by the activation of C-warm receptors, C-fibre polymodal nociceptors, A-fibre cold receptors and C-fibre cold nociceptors in humans. *NeuroImage*. Under review.
- [7] Mulders, D., de Bodt, C., Bjelland, J., Pentland, A. S., Verleysen, M., & de Montjoye, Y.-A. (2019). Inference of Node Attributes from Social Network Assortativity. *Neural Computing and Applications*, DOI: 10.1007/s00521-018-03967-z.
- [8] de Bodt, C., Mulders, D., Verleysen, M., & Lee, J. A. (2019). Nonlinear Dimensionality Reduction with Missing Data using Parametric Multiple Imputations. *IEEE Transactions on Neural Networks and Learning Systems*, 30(4), 1166-1179.
- [9] Chemin, B., Huang, G., Mulders, D., & Mouraux, A. (2018). EEG time-warping to study non-strictly-periodic EEG signals related to the production of rhythmic movements. *Journal of neuroscience methods*, 308, 106-115.
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Conference proceedings (peer-reviewed)

- [11] de Bodt, C., Mulders, D., López-Sánchez, D., Verleysen, M., & Lee, J. A. (2019). Class-aware t -SNE: *cat*-SNE. In *ESANN* (pp. 409-414).
- [12] de Bodt, C., Mulders, D., Verleysen, M., & Lee, J. A. (2018). Extensive assessment of Barnes-Hut t -SNE. In *ESANN* (pp. 135-140).
- [13] de Bodt, C., Mulders, D., Verleysen, M., & Lee, J. A. (2018). Perplexity-free t -SNE and twice Student tt -SNE. In *ESANN* (pp. 123-128).
- [14] Mulders, D., de Bodt, C., Bjelland, J., Pentland, A. S., Verleysen, M., & de Montjoye, Y.-A. (2017). Improving Individual Predictions using Social Networks Assortativity. In *WSOM+* (pp. 127-134). IEEE.
- [15] Mulders, D., de Bodt, C., Verleysen, M., Bjelland, J., Pentland, A. S., & de Montjoye, Y.-A. (2017). Improving Individual Predictions using Social Networks Assortativity. In *Benelearn* (pp. 134-136).
- [16] Mulders, D., Liberati, G., Mouraux, A., & Verleysen, M. (2017). Characterizing Resting Brain Activity to Predict the Amplitude of Pain-Evoked Potentials in the Human Insula. In *Benelearn* (pp. 89-91).

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Chapter 1

Introduction

A fundamental challenge in neuroscience consists in understanding how does the brain process sensory stimuli [17]. A sensory stimulus applied to an individual is first transduced through dedicated receptors before being encoded with action potentials and finally conveyed toward the cortex [18]. In order to study the links between the activity of complex neuronal networks and the human perception of external events from different modalities (such as vision, audition, touch, . . .), sensory stimulation can be applied to subjects while recording their brain activity. On the one hand, the brain recording technique must somehow reveal the function implemented by the neuronal assemblies. Therefore, non-(or slightly) invasive functional neuroimaging or electrophysiological approaches can be considered, such as functional magnetic resonance imaging (fMRI), positron-emission tomography (PET), magnetoencephalography (MEG) or electroencephalography (EEG) [19, 20, 21]. On the other hand, the physical characteristics of the employed stimulus, such as its intensity and duration, can be chosen in order to reveal diverse aspects of the sensory information processing. In particular, given that most sensory receptors can be slowly or quickly adapting [18], brief (lasting less than one second) or longer-lasting (lasting several seconds or minutes) stimulation can be considered to disentangle and analyze the brain responses elicited by the activation of different receptors. While brief stimulation allows to highlight clear and sharp stimulus-evoked responses thanks to time

and/or frequency averaging across repetitions [22, 23, 24], employing longer stimulation requires to vary their intensity in order to be able to relate the recorded brain activity to the input stimulus and thereby to identify and characterize the stimulus-evoked components. The stimulus intensity variations can be of different natures. For instance, random variations in the stimulus intensity (or perceived intensity) already allow to correlate the time course of recorded brain activity with the time course of the intensity (or of tonic perception) [25, 26, 27]. However, to ease the identification of the elicited responses and hence consider more robust experimental settings, the intensity variations can be chosen to be more regular. In particular, periodically-modulated stimuli can elicit synchronized periodic activity in the neuronal populations responding to the stimulus, known as a steady-state response (SSR) [28, 29, 30]. The SSR can easily be isolated from background noise in the frequency domain based on its known periodicity. In addition, the regularity of the stimulation also eases the identification of the evoked responses along time, for instance through time averaging across cycles. This approach is sometimes referred to as frequency tagging and is illustrated in Fig. 1.1.

In this context, this thesis generally aims at (1) characterizing SSRs related to sustained cool and warm stimulation and (2) providing methods to guide the extraction of periodic components within multidimensional signals. The dissertation is divided in two main parts which are introduced below.

The first part employs periodic intensity modulations to study the perception and EEG responses elicited by tonic cool and warm stimulation. Thermosensation is crucial for humans to probe the environment and detect threats arising from noxious heat or cold. To study the links between activation of some populations of thermoreceptors, elicited brain activity and subsequent human thermal perception, numerous previous works focused on the responses evoked by brief thermal pulses [24, 31, 32, 33, 34], reflecting activity generated by quickly-adapting thermoreceptors. At the opposite, much less is known about the responses elicited by tonic thermoreceptors. Indeed, only few studies attempted to characterize the dynamics of brain activity elicited by long-lasting heat stimuli [25, 35]. Over the last years, EEG frequency tagging using long-lasting periodic radiant heat stimulation has been proposed as a means to study the cortical processes underlying tonic heat perception [35]. This approach allows to exploit the high temporal resolution of the EEG signals thanks to stimuli with temporal structure, easing the identification of stimulus-evoked activity [36]. In this part, this approach is extended using a contact thermode to generate both heat- and cold-evoked SSRs and thereby study the dynamics of tonic thermal perception. Furthermore, we characterize the tem-

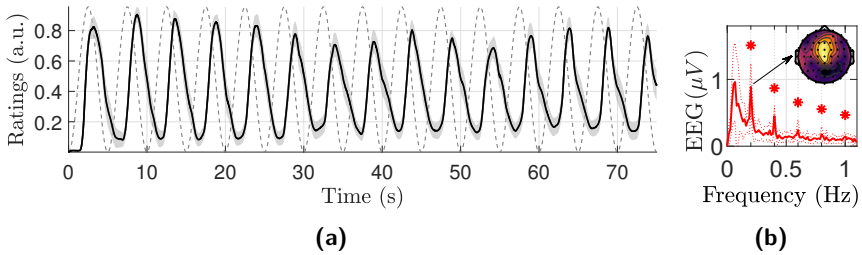


Fig. 1.1 Illustration of the principle of frequency tagging. When a periodic stimulus, in this example a sinusoid at 0.2 Hz, is applied to a subject, both its rated perception (a) and the brain response (b) from the neuronal populations responding to the stimulus are expected to oscillate at the same frequency. This knowledge can therefore guide the identification of the stimulus-evoked responses both in the time and frequency domains. In (a), the stimulation time course is indicated with dashed lines and the shaded areas indicate intervals of one standard deviation around the mean perceived intensity across several subjects. In (b), periodic brain responses are recorded with EEG and the dotted lines show intervals of one standard deviation around the mean spectrum across subjects, at fronto-central electrode FCz. The periodic brain responses are not likely to be strictly sinusoidal and can therefore have power at the fundamental frequency of 0.2 Hz and its harmonics. Asterisks indicate significant enhancements of power at these frequencies compared to baseline. The amplitude at 0.2 Hz across all scalp channels is depicted on the topography.

poral dynamics of the elicited responses, relate these dynamics to perception, and assess the effects of displacing the stimulated skin surface to gain insight on the heat- and cold-sensitive afferents conveying these responses. Two experiments were conducted on healthy volunteers. In both experiments, noxious heat and innocuous cool stimuli were applied during 75 seconds to the forearm using a Peltier-based contact thermode, with intensities varying sinusoidally at 0.2 Hz (see Fig. 1.1a). Displacement of the thermal stimulation on the skin surface was achieved by independently controlling the Peltier elements of the thermal probe. Continuous intensity ratings to sustained heat and cold stimulation were obtained in the first experiment with 14 subjects, and the EEG was recorded in the second experiment on 15 subjects. Both contact heat and cool stimulation elicited periodic EEG responses and percepts. Compared to heat stimulation, the responses to cool stimulation had a lower magnitude and shorter latency. All responses tended to habituate along time, and this response attenuation was most pronounced for cool compared to warm stimulation, and for stimulation delivered using a fixed surface compared to a variable surface.

This part therefore presents an approach to envision the perception and brain responses to periodic stimulation and thereby opens numerous perspectives for future basic and clinical studies aiming to characterize the dynamics of tonic sensory perception and to probe the responses elicited by the activation of different kinds of sensory afferents.

The second part then develops, compares and assesses computational tools to bring out periodic components from multidimensional signals. These methods hence aim at enhancing the signal-to-noise ratio (SNR) of periodic responses. This part is naturally motivated by applications in neuroscience, to study sensory perception using periodic stimulation as presented above. However, the extraction of periodic components is also of prior importance in order to design brain-computer interfaces (BCIs) [37, 38]. Indeed, numerous neuromuscular diseases impair voluntary muscular control of affected patients without altering their cognitive functions. These disorders hence highly prevent interactions with conventional devices, such as a touch screen, a mouse or a keyboard. To improve the quality of life of such patients, BCIs are communication systems aiming to translate recorded brain activity into motor commands that can help patients to control a computer or a prosthesis, for instance. Brain signals are often recorded with EEG. Then, one of the widely considered BCI paradigms relies on the presentation to the patient of visual stimuli flickering at different frequencies, and eliciting steady-state visual evoked potentials (SSVEPs) [39, 40, 41, 42, 43, 44].

For interpreting elicited periodic responses as well as to build BCI systems

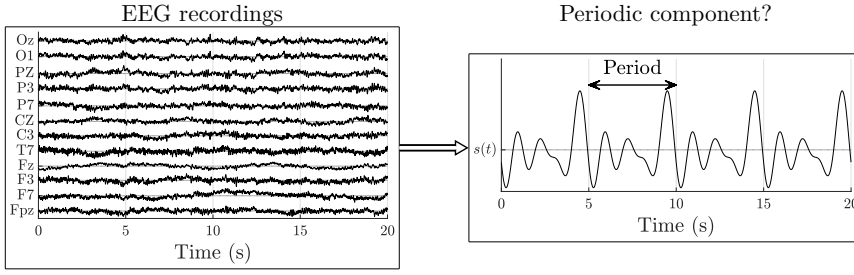


Fig. 1.2 Illustration of the extraction of a periodic component, denoted by $s(t)$, from multidimensional recordings such as EEG signals. The principle is to develop methods enabling to highlight periodic unidimensional signals, as depicted in the right panel, contained in the raw recordings of the left panel. Within the left panel, labels along the y-axis indicate channel names.

in situations when the SNR is limited or based on single trial recordings, mathematical tools are required in order to best isolate the periodic activity from the background noise in multidimensional signals, as illustrated in Fig. 1.2. Indeed, noise components can hinder both the temporal structure and the spatial distribution of latent periodic components, misleading their interpretations and analyses [45]. In this setting, this part aims at designing spatial filters to improve the interpretation of periodic components, such as the thermal SSRs recorded in Part I. More precisely, the goal is first to characterize single-class periodic responses by enhancing their SNR with linear spatial filtering methods. These filters can uncover proper time courses and topographic patterns of the SSRs [46, 47]. The considered methods take into account the periodicity of the activity to highlight. Then, these techniques are extended to handle pairs of signals from two classes and extract periodic sources which are specific to one among the two classes [48]. This allows to obtain class-specific features of SSRs. Spatial filters are optimized to discriminate as much as possible the two classes of signals, while accounting for the periodicity of the analyzed responses. Finally, an unsupervised alternative to the two aforementioned approaches is considered, based on the factorization of tensors [49, 50]. This is particularly suited in situations when the amount of available data is limited to compute and validate the extracted components or when the interpretation of the spatial patterns is of prior importance. The tensor model allows to robustly improve the SNR of periodic responses for different model sizes, and to extract spatial patterns and time courses present in several subjects.

This thesis dissertation is structured as follows. First, two introductory chapters set the general frame of the thesis. In particular, background aspects of electroencephalography and thermal perception in humans are presented in Chapter 2. Likewise, methods to extract features from multidimensional signals such as the EEG are introduced in Chapter 3. In particular, spatial filtering approaches and time-frequency decompositions are defined. Then, Part I explains how periodic thermal stimulation can be employed to help characterizing tonic perception in humans. This part is first introduced in Chapter 4. Next, two distinct experiments conducted on healthy subjects and their outcomes are detailed. Chapter 5 describes the first experiment which assesses the subjective perception of the stimulation, while Chapter 6 presents the second experiment in which EEG recordings are obtained on subjects exposed to the same periodic thermal stimuli. The links between the results from these two experiments are finally discussed in Chapter 7. Afterward, Part II considers the extraction of periodic components in multidimensional signals such as EEG through supervised filtering methods and tensor factorization approaches. The extraction of periodic components from a single data set is explained in Chapter 9 and these techniques are extended in Chapter 10 to find periodic components specific to one among two multidimensional signals. Then, an unsupervised alternative to these methods is considered in Chapter 11 based on tensor factorization. This part is concluded in Chapter 12, where the applicability of the presented methods is discussed. Finally, Part III discusses more generally the approaches studied in the context of this thesis and sketches future perspectives.

Chapter 2

Neurophysiological background

THE perception of thermal stimuli results from the activation of thermosensitive afferents eliciting neuronal activity ascending to the brain through spinal tracts [51, 52, 53]. In humans, the non-invasive study of thermosensation typically involves applying a thermal stimulus while recording brain activity, through electroencephalography (EEG), magnetoencephalography (MEG), or functional imaging techniques such as functional magnetic resonance imaging (fMRI) or positron-emission tomography (PET). In this chapter, we therefore start by summarizing the main neuronal pathways involved in thermosensation in Section 2.1. Then, the basic principle of recording neuronal activity through EEG is explained in Section 2.2, as it is the brain recording technique employed in this thesis.

2.1 Thermal perception

Cutaneous thermosensation contributes to maintaining core body temperature, to the discrimination of manipulated object properties based on its thermal characteristics and, importantly, to the detection of potentially harmful cold and heat stimuli [54, 55]. The qualitatively-different sensations elicited by thermal stimuli,

ranging from innocuous to noxious depending on the stimulus intensity, result from the activation of a variety of cold- and heat-sensitive afferents. These fibers have so-called free nerve endings located in the epidermis, as illustrated in Fig. 2.1a.

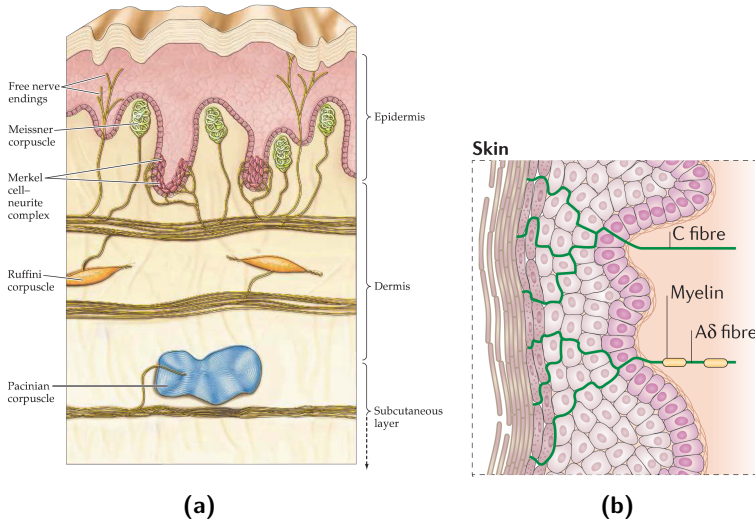


Fig. 2.1 (a) Illustration of the free nerve endings of thermosensitive fibers. Reproduced from [18]. (b) There are two classes of afferents mediating the perception of temperatures: thinly myelinated A δ and unmyelinated C fibers. Reproduced from [55].

Thermosensitive afferents are thinly myelinated A δ fibers and unmyelinated C fibers, as shown in Fig. 2.1b, having conduction velocities in the range of 3 – 30 m/s and around 1 m/s [56], respectively. Naturally, these distinct conduction velocities induce distinct latencies of perception. In the case of a painful stimulus, for instance a noxious thermal stimulus, typical sensations elicited by the activity of both kinds of fibers can be easily identified. Indeed, two widely recognized categories of pain perception are (1) an early, short-lasting and pricking ‘first-pain’, followed by (2) a later, longer-lasting and more diffuse ‘second pain’ (Fig. 2.2) [57, 58]. These two sensations are mediated by A δ and C fibers respectively.

Thermoreceptors can be further classified according to the types of stimuli to which they respond, and the way they respond to these stimuli [59]. A given thermosensitive afferent can be activated by a particular range of temperatures and, in the case of a polymodal nociceptor, can also be activated by mechanical or chemical stimuli [54, 60]. For instance, most C fibers appear to be polymodal [18]. Besides, when thermal stimuli are maintained over time, the response of ther-

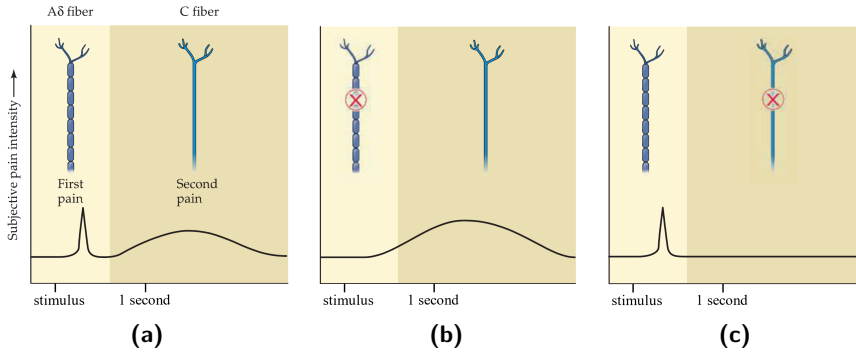


Fig. 2.2 Two categories of pain perception. (a) The ‘first pain’ and ‘second pain’ sensations are respectively mediated by A δ and C fibers. This is exemplified by the selective blockade, illustrated with red crosses in the figure, of (b) A δ and (c) C afferents. Adapted from [18].

moreceptors can adapt either quickly or slowly [54, 59, 61]. Furthermore, repeated activation of the same receptors can induce activity-dependent slowing, which is most pronounced in C fibers, but also varies across different types of C fiber afferents [62, 63]. The molecular basis for thermal transduction by thermoreceptors involves, at least, a diversity of cold- and heat-sensitive Transient Receptor Potential (TRP) ion channels [55]. In this view, the types of receptors expressed by each thermosensitive afferent determine its sensitivity to a particular range of temperatures, as indicated in Fig. 2.3.

After being transduced within the free nerve endings, the thermal information is conveyed as action potentials to the brain through spinal tracts. The neuronal pathways conveying temperature, as well as nociceptive, information from the periphery to the brain constitute the anterolateral system. Ascending neuronal routes of this system elicit activity in a widespread array of brain regions, sometimes called the ‘pain matrix’, primarily within the contralateral hemisphere to the stimulation side [51, 65, 66]. These regions are illustrated in Fig. 2.4. Although it is widely accepted that thermal, especially noxious, information is processed through the coordinated activity of several neuronal populations distributed across the whole brain, the exact sequence and causality among these triggered brain activities are still debated [67, 68, 69].

Importantly, the thermal information which is conveyed to the brain does not only depend on the input stimulus and its transduction, but it can also be largely regulated (i.e. enhanced or inhibited) through descending modulatory

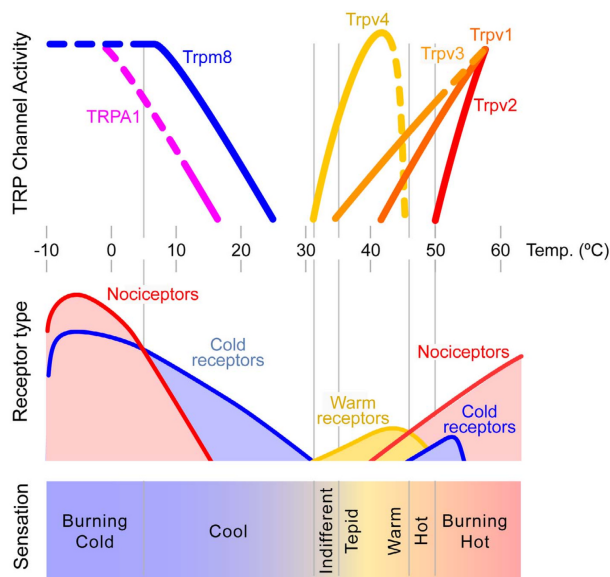


Fig. 2.3 Several TRP channels are present on some A δ and C fibers and are, at least partly, responsible for transducing thermal stimuli. Different classes of these ion channels are sensitive to different ranges of temperatures. Reproduced from [64].

pathways [70]. The bottom-up and top-down systems mediating thermosensation are illustrated in Fig. 2.5. In addition, neuronal circuits within the spinal cord can also potentially modify the transmission of thermal inputs from the periphery to the brain, thereby affecting the resulting perception [71].

Interestingly, the anterolateral system is responsible for mediating multidimensional sensory experiences: pain perception, in particular, includes sensory-discriminative, affective-motivational and cognitive-evaluative components [72]. Therefore, the complex brain activity elicited by thermal or noxious stimulation may be partly categorized depending on the preferential encoding of one of these components. In this view, parallel pathways could likely process different components of the thermal feelings [18, 52]. In particular, the sensory-discriminative components of thermal, innocuous or not, information would be primarily conveyed through the spinothalamic tract [18, 52]. This tract mostly targets the primary sensory (S1) and motor (M1) cortices, the granular part of the insula and some portions of the cingulate cortex, as shown in Fig. 2.5a [67, 52, 53]. Besides, the affective-motivational components would likely emerge from activity in brain areas related to the limbic system, through pathways such as the spinoparabrachial or spinoreticular tracts [73, 53, 52].

2.2 Electroencephalography (EEG)

Electroencephalography (EEG) consists in non-invasively recording electrical activity from the brain by placing electrodes on the scalp and then amplifying the obtained voltages, as illustrated in Figs. 2.6 and 2.7. The first recording of this kind on a human was performed in 1929 by Hans Berger [74]. Since then, EEG has been widely employed both by clinicians and researchers to study numerous brain processes related to perception or cognition, and also to identify biomarkers of some neurological disorders, such as epilepsy [75]. The electrical potentials recorded with EEG are thought to mainly result from synchronized postsynaptic potentials within cortical pyramidal neurons whose apical dendrites are perpendicular to the cortical surface, and not from action potentials [76, 77, 78].

This non-invasive technique allows to analyze fine time dynamics of brain activity evoked by an external or internal stimulus, with a temporal resolution of the millisecond order, at the expense of a rather low spatial resolution compared to functional neuroimaging techniques such as PET or fMRI [19]. Indeed, EEG electrodes are rather remote from the neurons, and electrical currents are attenuated by the bone and the meningeal envelopes [18]. This low spatial resolution makes it difficult to identify and tease out the brain sources eliciting the recorded elec-

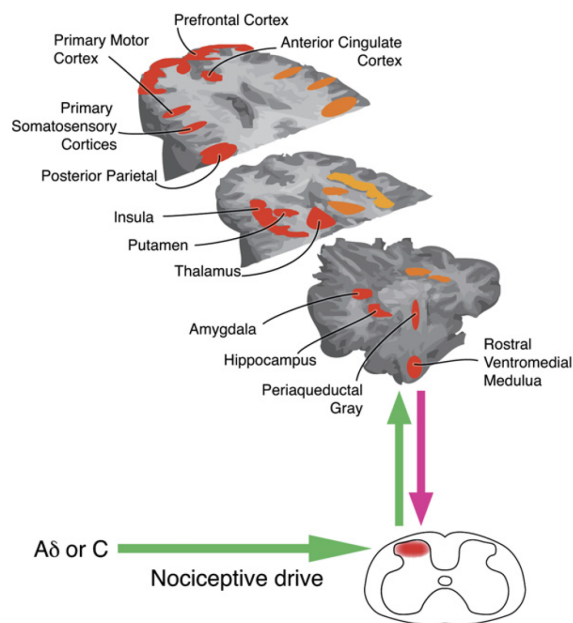


Fig. 2.4 A large and widespread array of brain areas, sometimes called the ‘pain matrix’, can be activated following a nociceptive stimulation. Increased activations are indicated in orange, contralateral to the stimulation side. Green arrows represent ascending nociceptive information, and the pink arrow shows descending modulatory pathways. Reproduced from [51].

trical activity on the scalp and therefore motivates the design of so-called source localization techniques [79]. Nevertheless, features of the EEG signals can still be compared on the scalp across experimental or clinical conditions, without necessarily knowing with certainty their underlying brain sources, in order to attribute functional roles to the recorded waves [75].

The high time resolution of EEG recordings allows to study its features in the frequency domain in addition to the time domain. For this purpose, reference physiological frequency bands have been defined, which have progressively been associated with particular functions or neurophysiological mechanisms [21]. From lower to higher frequencies, these bands and some of the functions they are assumed to reflect are defined as follows [80, 18, 23]:

- delta (< 4 Hz) oscillations: mostly increase during slow sleep, but can also indicate cerebral dysfunction if their power is abnormally elevated.
- theta (4-8 Hz) oscillations: increase just before sleep, and can also indicate cerebral dysfunction if their power is abnormally elevated.
- alpha (8-12 Hz) oscillations: are often seen as an awake resting indicator. For instance, their power increases over posterior regions when the subject closes the eyes.
- beta (12-30 Hz) oscillations: are mostly present during active cognitive conditions and could serve the functional coupling of remote brain areas.
- gamma (> 30 Hz) oscillations: are thought to play a role in cortical synchronization and multisensory integration.

Naturally, nothing prevents to consider different frequency bands or to analyze the entire EEG spectrum. However, these ones being largely employed in the literature, they are assumed to implement specific neuronal processes (evoked by a stimulus and/or spontaneous) [81, 21] and they allow to easily compare outcomes across studies. An example of EEG signal at one electrode and its components filtered in these frequency bands are shown in Fig. 2.8.

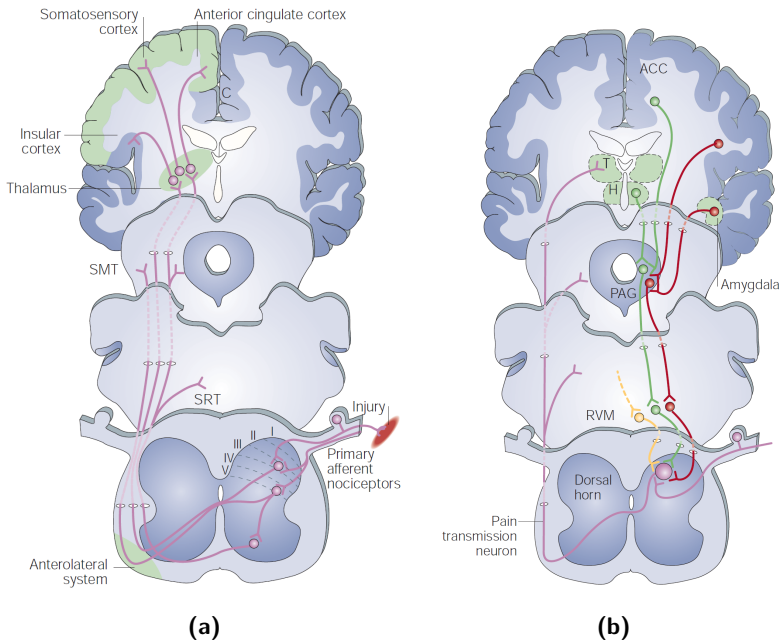


Fig. 2.5 Nociceptive circuits mediating painful and temperature sensations. (a) Ascending pathways, conveying thermal information from the periphery to the cortex through the activation of $A\delta$ and C fibers. (b) Descending modulatory pathways influencing the perceptive information within the spinal cord. This top-down circuit can be activated by external stimuli or motivational factors. Pink neurons transmit ascending information. Green, red and yellow neurons represent inhibitory, facilitatory and state-dependent controls respectively. SMT: spinomesencephalic tract, SRT: spinoreticular tract, RVM: rostral ventromedial medulla, PAG: periaqueductal grey, H: hypothalamus, T: thalamus, ACC: anterior cingulate cortex. Reproduced from [70].

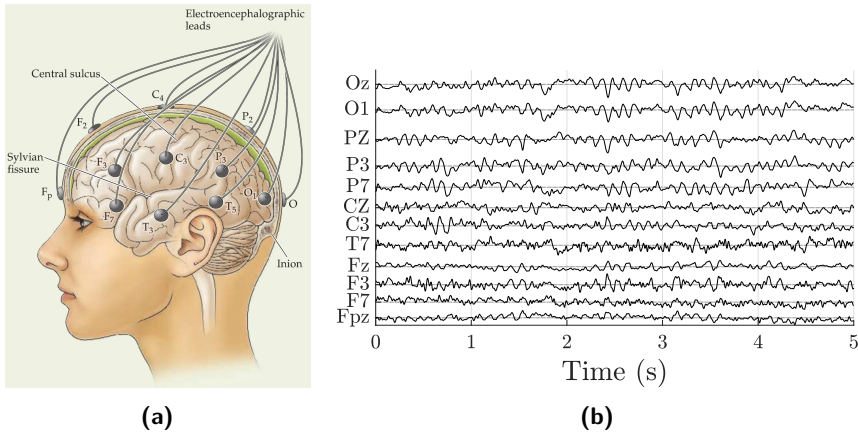


Fig. 2.6 (a) Electroencephalography (EEG) consists in placing recording electrodes on the scalp and then amplifying the recorded signals. Reproduced from [18]. (b) Examples of the amplitudes (μV) of EEG recordings over a short time interval.

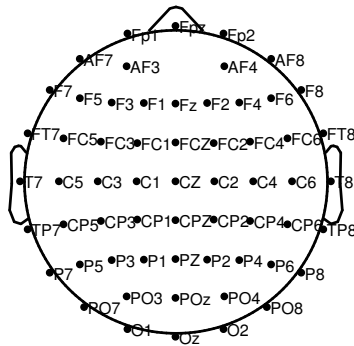


Fig. 2.7 Electrode names of an EEG cap according to the international 10/10 system.

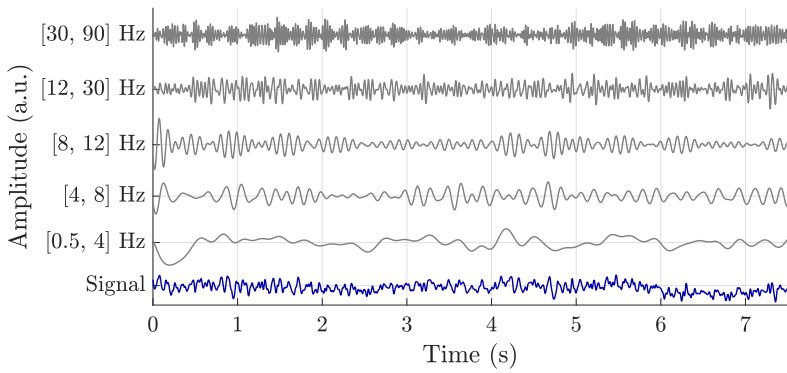


Fig. 2.8 A segment of EEG signal (bottom row) with its components in the physiological frequency bands delta (δ : 0.5-4 Hz), theta (θ : 4-8 Hz), alpha (α : 8-12 Hz), beta (β : 12-30 Hz) and gamma (γ : 30-90 Hz). The amplitudes are normalized per frequency band. a.u.: arbitrary units.

Chapter 3

Signal processing background

MULTIDIMENSIONAL signals are encountered in numerous contexts. Typical examples include audio and video data sets, as well as neuroimaging time series such as the EEG as described in Section 2.2. In all these cases, signals are recorded over several captors, sensors or channels, which naturally provide substantially more information than a single sensor. Depending on the applications, the objective can be to classify such signals (e.g. to build a Brain-Computer Interface (BCI) using EEG recordings) or to interpret them, and therefore to gain insights into the underlying processes that generated the observed data [82]. Although multidimensional signals contain very rich information to tackle such tasks, they are inherently complex to handle in practical context as they are noisy, high-dimensional and their components are often interdependent. These properties require to design dedicated mathematical tools in order to extract, highlight and exploit the content of interest in the data [83]. Indeed, the noise may hinder the identification of patterns and decrease the classification performances. In addition, the curse of dimensionality has many negative impacts on standard data analyses [84, 82] and interdependent features can both (1) reduce the selection and accuracy of classifiers and (2) mislead data and model interpretations [85].

In this setting, this chapter introduces standard tools to extract relevant features from multidimensional signals and thereby enhance their usability. From a general point of view, these signals can be characterized spatially (namely, across

channels), spectrally or temporally. Chapter 8 therefore defines the basic principles of spatial filtering and focuses on a widely employed approach which is called Common Spatial Patterns (CSP) to illustrate how linear spatial filters can be optimized. Such methods are designed to provide spatial filters, spatial patterns and associated time courses of components optimizing the ratio of variance between two signals according to diverse applications requirements. This chapter especially introduces the methods studied in Chapters 9 and 10 and is therefore detailed in the second part of the thesis. Besides, Section 3.1 provides a short overview of time-frequency decompositions for one-dimensional signals. In particular, properties of continuous wavelet transforms (CWTs) and short-time Fourier transforms (STFTs) are compared for data exploration purposes. This background section introduces the time-frequency analyses performed in Chapter 6.

3.1 Time-frequency analyses

This section now presents common tools to study the dynamics of one-dimensional signals. As mentioned before, a signal can primarily be characterized along time or based on its frequency content. When the process generating the signal is nonstationary however, the frequency content can change along time. Electrical activity from the brain recorded through EEG is a typical example of signals generated by a nonstationary process. In such cases, the frequency content of the signals is better characterized as a function of time. This section hence introduces two popular methods providing a time-frequency characterization of a signal, namely the short-time Fourier transform (STFT) and the continuous wavelet transform (CWT).

The basic principle of any (time-)frequency decomposition is to measure the similarity between the input signal and some reference oscillating waveforms through inner products. For a given signal of fixed length and sampling frequency, there is always a trade-off to choose between the time and frequency resolutions achieved by a decomposition (by resolution, it is meant the smallest interval, either in time or frequency, that can be resolved with the transform). On the one hand, using sinusoidal reference waveforms leads to the Fourier transform (FT), which has a maximal frequency resolution and a minimal time resolution, since the spectrum is computed for the whole time segment available. On the other hand, reference sinusoids can be modulated to have a limited support in time, for instance using bell-shaped functions such as Gaussian, Hann or Hamming windows. Intuitively, this allows improving the time resolution, at the expense of the frequency resolution which can only get worse as the sinusoids are truncated.

This reduction of the support of the reference waveforms can be performed either by using a fixed time window, or by keeping the same number of oscillations for all explored frequencies, leading respectively to the STFT and the CWT. In more general contexts, the CWT is not necessarily computed using modulated sinusoids, it can also use different reference waveform shapes with a limited support. However, considering modulated sinusoids is particularly suited to illustrate time-frequency components of signals [86, 87, 88].

Let us now define these concepts mathematically and then illustrate some properties of the STFT and CWT.

The short-time Fourier transform (STFT) of a signal x at time τ and frequency f using a full-length Gaussian window is defined as:

$$\Psi_x(\tau, f) = \int_{t=-\infty}^{+\infty} x(t) \cdot e^{\frac{-(t-\tau)^2}{2 \cdot (L_w/6)^2}} \cdot e^{-2\pi j f(t-\tau)} dt. \quad (3.1)$$

The width parameter L_w of the Gaussian window $e^{\frac{-(t-\tau)^2}{2 \cdot (L_w/6)^2}}$ determines the time support of the modulated complex exponential, which is fixed for all frequencies f .

The continuous wavelet transform (CWT) of a signal x at time τ and frequency f using a mother wavelet denoted by $\psi(t)$ corresponds to the inner product $\langle x(t), \sqrt{\frac{f}{f_0}} \cdot \psi(\frac{f}{f_0}(t - \tau)) \rangle$, with f_0 the wavelet center frequency, namely:

$$\Psi_x^w(\tau, f) = \int_{t=-\infty}^{+\infty} x(t) \cdot \sqrt{\frac{f}{f_0}} \cdot \psi^*\left(\frac{f}{f_0}(t - \tau)\right) dt. \quad (3.2)$$

At (τ, f) , the wavelet whose inner product with the input signal x is computed is denoted by

$$\psi_{\tau, f}(t) := \sqrt{\frac{f}{f_0}} \cdot \psi\left(\frac{f}{f_0} \cdot (t - \tau)\right). \quad (3.3)$$

Contrarily to the STFT, the time support (i.e. width) of the wavelet therefore adapts to each considered frequency: the mother wavelet is dilated at lower frequencies and contracted at higher frequencies to keep a fixed number of periods $(1/f)$ for each explored frequency (f) . A popular choice for $\psi(t)$ is the complex Morlet wavelet, although there exist numerous other options such as the Mexican hat, Haar wavelet, Shannon wavelet, Meyer wavelet, ... The

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complex Morlet wavelet is presented here as it leads to the same transform as the STFT with a Gaussian window like in (3.1) for a given frequency and window width. Indeed, it also consists in a complex exponential (like for the FT) modulated by a Gaussian function:

$$\psi(t) = \frac{1}{\sqrt{\pi f_b}} \cdot e^{\frac{-t^2}{f_b}} \cdot e^{2\pi j f_0 t}. \quad (3.4)$$

The bandwidth parameter f_b and the wavelet center frequency f_0 jointly determine the number of oscillations of the wavelet, which is fixed for all frequencies and hence leads to improved time resolution at higher frequencies [86, 87].

As indicated above, at each considered frequency f and time τ , the wavelet whose similarity with the input signal is computed can be written

$$\psi_{\tau,f}(t) = \sqrt{\frac{f}{f_0}} \cdot \frac{1}{\sqrt{\pi f_b}} \cdot e^{\frac{-(t-\tau)^2 \cdot f^2}{f_0^2 \cdot f_b}} \cdot e^{2\pi j f(t-\tau)}. \quad (3.5)$$

The time and frequency resolutions depend on the support of $\psi_{\tau,f}(t)$ along time and frequency. These two supports are computed hereunder.

The time support of $\psi_{\tau,f}(t)$ is determined by the Gaussian window $e^{\frac{-(t-\tau)^2 \cdot f^2}{f_0^2 \cdot f_b}}$ in (3.5). Assuming that the support extends until three standard deviations from the mean (i.e. until this function reaches 1% of its maximal amplitude), the support width is given in seconds by

$$t_r(f) := 2 \cdot \sqrt{4.5 \cdot f_b} \cdot \frac{f_0}{f} = \frac{N_O}{f}, \quad (3.6)$$

with $N_O := 2 \cdot \sqrt{4.5 \cdot f_b} \cdot f_0$ the number of oscillations of the wavelet.

The frequency support of $\psi_{\tau,f}(t)$ can be obtained by computing its Fourier Transform (FT), denoted by $\Psi_{\tau,f}(s)$:

$$\begin{aligned} \Psi_{\tau,f}(s) &= \int_{-\infty}^{\infty} \sqrt{\frac{f}{f_0}} \cdot \frac{1}{\sqrt{\pi f_b}} \cdot e^{\frac{-(t-\tau)^2 \cdot f^2}{f_0^2 \cdot f_b}} \cdot e^{2\pi j f(t-\tau)} \cdot e^{-2\pi j s t} dt \\ &= \sqrt{\frac{f}{f_0}} \cdot \frac{1}{\sqrt{\pi f_b}} \cdot e^{-2\pi j s \tau} \cdot \int_{-\infty}^{\infty} e^{\frac{-t^2 \cdot f^2}{f_0^2 \cdot f_b}} \cdot e^{-2\pi j t(s-f)} dt \end{aligned}$$

$$\begin{aligned}
&= \sqrt{\frac{f}{f_0}} \cdot \frac{1}{\sqrt{\pi f_b}} \cdot e^{-2\pi j s \tau} \cdot \\
&\int_{-\infty}^{\infty} e^{\frac{-f^2}{f_0^2 \cdot f_b} \left(t^2 + 2tj\pi(s-f) \frac{f_0^2 f_b}{f^2} + (j\pi(s-f) \frac{f_0^2 f_b}{f^2})^2 \right)} \cdot e^{-\pi^2 (s-f)^2 \frac{f_0^2 f_b}{f^2}} dt \\
&= \sqrt{\frac{f}{f_0}} \cdot \frac{1}{\sqrt{\pi f_b}} \cdot e^{-2\pi j s \tau} \cdot e^{-\pi^2 (s-f)^2 \frac{f_0^2 f_b}{f^2}} \cdot \\
&\underbrace{\int_{-\infty}^{\infty} e^{\frac{-f^2}{f_0^2 \cdot f_b} \left(t + j\pi(s-f) \frac{f_0^2 f_b}{f^2} \right)^2} dt}_{= \sqrt{\pi f_b (f_0/f)^2}, \text{ integral of a Gaussian function}} \\
&= \sqrt{\frac{f_0}{f}} \cdot e^{-2\pi j s \tau} \cdot e^{-\pi^2 (s-f)^2 \frac{f_0^2 f_b}{f^2}} \tag{3.7}
\end{aligned}$$

In the frequency domain, the width of the wavelet is hence controlled by the Gaussian window $e^{-\pi^2 (s-f)^2 \frac{f_0^2 f_b}{f^2}}$ in (3.7). Similarly as in the time domain, the frequency support width in Hz develops as

$$f_r(f) := 2 \cdot \sqrt{\frac{4.5}{\pi \cdot f_b}} \cdot \frac{f}{f_0} = \frac{18}{\pi \cdot N_O} \cdot f, \tag{3.8}$$

and is therefore proportional to the considered frequency.

As explained above, the time and frequency resolutions of the CWT are adapted to each frequency, while they are kept fixed for the STFT as the Gaussian window has a fixed width. Therefore, the choice of one of these two transforms to analyze a given signal can be made knowing that

- the CWT is very well suited to localize signal peaks in time, thanks to its enhanced time resolution at higher frequencies.
- When the time interval of interest is known by the user and constant across the explored frequencies (as it will be the case in Part I for instance), the STFT is more convenient than the CWT. Indeed, the time resolution is fixed across frequencies and can therefore be chosen according to the time interval of interest.

These properties are illustrated in Fig. 3.1. A random periodic signal of fundamental frequency 0.2 Hz has been defined as the sum of cosine functions at frequencies

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$\{k \cdot 0.2\}_{k=1}^5$ Hz with random phases. The signal is shown in the bottom insets of Fig. 3.1 and its CWT and STFT are displayed in Figs. 3.1a and 3.1b respectively.

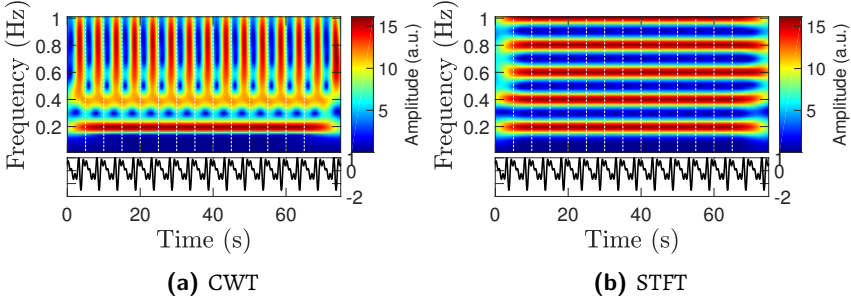


Fig. 3.1 Time-frequency analyses of a random periodic signal during 75 seconds, computed with (a) a continuous wavelet transform (CWT) and (b) a short-time Fourier transform (STFT). The signal is constructed by summing cosines at frequencies $\{k \cdot 0.2\}_{k=1}^5$ Hz with random phases. For the CWT, the bandwidth parameter $f_b = 0.05$ and the wavelet center frequency $f_0 = 5.27$, leading to 5 wavelet oscillations. The same number of oscillations is considered for the STFT at 0.2 Hz.

The ideal combination of time and frequency resolutions depends on the considered signals and aims. Also, the STFT and the CWT have been presented above in a unified framework using the same Gaussian windowing, which is well suited to highlight time-frequency components from signals such as the EEG [86, 87, 88]. However, there exist numerous variants of these transforms which can be obtained by adapting the window shape in the STFT and the wavelet functions in the CWT and which can be better suited for some applications.

PART I

Characterizing tonic thermal perception

THIS part investigates the dynamics of perception and EEG responses elicited by thermal, both warm and cool, stimulation. For this purpose, intensity ratings and EEG signals are collected on healthy subjects exposed to warm and cool stimuli whose intensities are slowly and periodically modulated along time. The average and dynamical evolutions of these recordings are extensively investigated, on the one hand to provide, for the first time, a description of the responses elicited by periodic contact thermal stimulation and on the other hand to guide future analyses of similar recordings obtained during periodic stimulation. This part is structured as follows:

- Chapter 4 details the study objectives, and how they are related to state-of-the-art approaches in neuroscience.
 - Chapter 5 describes the first experiment in which subjective intensity ratings are collected and analyzed.
 - Chapter 6 reports the setting and outcomes of the second experiment in which EEG signals are recorded.
 - Chapter 7 discusses all the results and establishes links with previous studies.
-

Chapter 4

Background

As mentioned in Chapter 2, thermosensation is mediated by a variety of cold- and heat-sensitive thinly myelinated A δ and unmyelinated C fiber afferents. Each class of fibers express various cold- and heat-sensitive receptors allowing to transduce the thermal stimulation [55].

Despite remarkable advances in the understanding of how thermoreceptors respond to thermal stimuli [55, 60], the links between activation of some populations of these receptors, elicited brain activity and subsequent human thermal perception are not yet fully elucidated. In order to delineate these links, there is a need to characterize and compare perception and brain responses to a large variety of thermal stimuli, by varying their features such as their intensity and duration.

Several studies already aimed at preferentially activating specific types of thermosensitive afferents, mainly using electroencephalography (EEG) and the recording of event-related brain potentials (ERPs) [33]. For example, brief high-intensity laser heat stimuli applied onto the skin generate laser-evoked brain potentials (LEPs) that are thought to mainly result from the activation of one class of polymodal nociceptors: so-called 'Type 2' (quickly-adapting) mechano- and heat-sensitive A δ fiber nociceptors (AMH-2) [89, 90]. Although such stimuli are also expected to activate quickly-adapting C fiber thermonociceptors, co-activation of these unmyelinated afferents does not elicit any evident brain activity compatible with their slow conduction velocities [91, 66]. Conversely, similar short-lasting laser

heat stimuli with a lower intensity can elicit LEPs whose latencies are compatible with the conduction of unmyelinated C fibers, probably because such stimuli selectively activate heat-sensitive C fiber thermonociceptors having a lower thermal activation threshold than AMH-2, such as quickly-adapting mechano- and heat-sensitive C fiber nociceptors (CMH) or C fiber warm receptors [92]. More recently, it was shown that rapid innocuous cooling of the skin elicits cool-evoked brain potentials whose short latencies are compatible with the activation of cool-sensitive A δ fiber afferents [93, 94, 34].

Because the responses elicited by very transient thermal stimuli can be expected to predominantly reflect activity generated by quickly-adapting thermoreceptors responding vigorously to rapid changes in skin temperature, not much is known about the brain responses elicited by tonic thermoreceptors. Mainly using functional magnetic resonance imaging (fMRI) [95, 26, 96] or positron-emission tomography (PET) [97, 98], some previous studies characterized the brain activity elicited by long-lasting heat stimuli inducing tonic heat pain over several seconds. However, the low temporal resolution of fMRI and PET makes it difficult to tease out brain activity elicited by quickly-adapting thermonociceptors responding at the onset of the thermal stimulus from activity elicited by slowly-adapting thermonociceptors responding gradually and in a sustained fashion over time. Other studies have attempted to identify sustained changes in ongoing oscillatory activity related to the perception of tonic pain using EEG [99, 25, 100, 101, 102]. One interesting approach that was attempted using both EEG and fMRI is to introduce random variations in the intensity of the eliciting stimulus (or exploit the spontaneous pain fluctuations) in order to relate the time course or temporal structure of the measured brain activity (e.g. fluctuations in the fMRI-BOLD (blood-oxygen-level dependent) signal, or fluctuations in the magnitude of ongoing EEG oscillations) with the time course or temporal structure of tonic pain perception over time [25, 26, 27]. Lately, Colon et al. proposed a new method to characterize the cortical processes related to tonic heat perception, based on ‘EEG frequency tagging’ using long-lasting sinusoidal heat stimulation of the skin [35]. Periodic modulation of a sensory stimulus can be expected to elicit synchronized periodic activity in the neuronal populations responding to the stimulus, sometimes referred to as a steady-state response (SSR) [30]. Unlike ERPs, SSRs are thus sustained over time. In the frequency domain, the stimulus-evoked ‘frequency-tagged’ activity concentrates at the frequency of stimulation and its harmonics, and is thus easy to isolate from non-stimulus-related activity. In the time domain, the known periodicity also allows highlighting the dynamics of the elicited responses. The recording of SSRs with EEG is proposed to complement the classical approach of recording ERPs [103, 104, 36]. Most importantly, depending on the frequency of stimulation

and, possibly, the shape of the periodic stimulus, periodic thermal stimulation can be expected to preferentially activate different types of thermoreceptors. For example, periodic radiant heat stimulation of the skin to 50°C at a very slow oscillation frequency of 0.2 Hz was shown to generate a periodic EEG response predominantly conveyed by unmyelinated C fibers [35].

In the present study, using a novel contact thermal stimulator that allows generating well-controlled cooling and warming ramps [94], we characterize for the first time SSRs related to the sustained periodic activation of cool-sensitive afferents, compare these responses to the SSRs elicited by periodic noxious heat stimulation, and relate the temporal dynamics of the elicited SSRs to the temporal dynamics of the stimulus-induced cold and heat sensations. As explained above, sustained or repeated stimulation of thermoreceptors can be expected to induce some amount of peripheral habituation [31] and/or activity-dependent slowing. In addition, central mechanisms can also affect the perception and brain responses to sustained stimuli [105]. In particular, sensitization mechanisms, wind-up or temporal summation [106, 107] could lead to enhanced responses along time, while habituation mechanisms or more abrupt phenomena such as offset-analgesia [108] could decrease the observed responses. Therefore, taking advantage of the fact that the thermal stimulator allows separately controlling five different zones of the probe contacting the skin, we also assessed the effect of displacing the stimulated skin area across the stimulation cycles. All stimuli consisted in a sinusoidal temperature profile oscillating at 0.2 Hz between a neutral temperature of 31°C and either 14°C (cool stimulation) or 48°C (heat stimulation). The amplitude of the cool and heat stimuli was thus identical ($\Delta = 17^\circ\text{C}$), but the cool stimulation was expected to generate activity within cool-sensitive afferents whereas the heat stimulation was expected to generate activity within heat-sensitive nociceptors. In a first experiment, we collected continuous subjective intensity ratings from healthy subjects exposed to the warm and cool stimuli applied to a fixed or varying area of the skin along the stimulation cycles. In a second experiment, we recorded the EEG of healthy subjects exposed to the same stimuli, allowing to confront the observed EEG features with subjective perception. The baseband EEG responses and ongoing oscillations in physiological frequency bands were analyzed in the time, frequency and time-frequency domains.

Chapter 5

Experiment 1: time course of heat and cool perception

5.1 Participants

Fourteen healthy volunteers took part in Experiment 1 (5 men and 9 women, aged 24-35 years). All participants were right-handed and did not suffer from any neurological disorder. The study was approved by the local ethics committee (Comité d’Ethique Hospitalo-Facultaire de l’Université catholique de Louvain, B403201316436) and all participants gave written informed consent.

5.2 Contact thermal stimulation

All the stimuli considered in this study were delivered using a prototype contact thermal stimulator (TCS-II) made of micro Peltier elements whose temperature can be varied at rates of up to 300°C/s (QST Lab, Strasbourg, France). The stimulation probe weighs 440 g and has a flat 30-mm diameter surface which is applied against the skin and contains 15 micro Peltier elements, as indicated in Fig. 5.2. The Peltier elements are organized in five zones of around 24 mm^2 . The tempera-

5 | Experiment 1: time course of heat and cool perception

ture is controlled independently in each zone, allowing to vary the stimulated skin surface without displacing the stimulation probe. The temperature of the probe is negligibly affected by the subject's skin temperature [94].

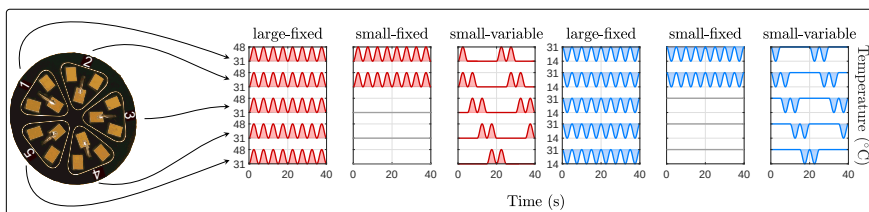


Fig. 5.1 Stimulation employed. Stimulation surface of the Thermal Cutaneous Stimulator (TCS) employed and stimulation temperature profiles considered in Experiment 1, depicted in red (or blue) for the warm (or cool) stimuli and truncated to 40 seconds for readability.

All stimuli consisted in 15 periods of 0.2 Hz sinusoidal cooling (between 31 and 14°C) or warming (between 31 and 48°C) of the skin. Each stimulus thus lasted 75 seconds (15 cycles of 5 seconds). The maximal warm temperature of 48°C was chosen such as to recruit the largest amount of heat-sensitive thermnociceptors while avoiding burn lesions due to stimulus duration [61]. The frequency of 0.2 Hz was selected because previous studies showed that, at this frequency, radiant heat stimuli generate clear SSRs related to the activation of heat-sensitive C fiber afferents [35]. The same frequency, stimulus duration and amplitude of temperature variation were used for cool stimulation, such as to allow a direct comparison of heat and cool-evoked SSRs.

The goal of this first experiment was to assess the time course of the perception elicited by long-lasting periodic cool and warm stimuli oscillating at a frequency of 0.2 Hz. In order to study the effect of displacing the stimulation on the skin surface, three types of stimulation profiles were used for both warm and cool stimulation: (1) synchronous activation of all five zones of the probe (large-fixed), (2) two fixed zones during the entire stimulation (small-fixed), and (3) two alternating zones per cycle (small-variable). We chose to stimulate using 2/5 zones of the probe because the sensation elicited by activating only one zone was very weak. The temperature profiles are illustrated in Fig. 5.1.

5.3 Methods

Two epochs were delivered for each of the six conditions (illustrated in Fig. 5.1), in a randomized order across participants and with self-paced inter-stimulus intervals, on either the right or left volar forearm. The stimulated arm was resting on a soft surface with the volar side upwards. The probe was manually displaced after each 75-s stimulus to avoid trial-to-trial habituation or sensitization. Due to technical problems, one participant could not receive the stimuli from the cool large-fixed condition.

During stimulation, the subject was asked to continuously rate the perceived thermal intensity on a visual analog scale (VAS). The participant had to displace a 10 cm vertical slider with the contralateral hand. The extremities of the slider were defined as lowest and highest intensities that can be imagined. The continuous ratings were digitized at 1000 Hz with an analog/digital converter (USB-6343, National Instruments, Texas) and the two epochs of each condition were then averaged. Furthermore, at the end of each 75-s stimulus, subjects were asked to describe the quality of the sensation by selecting one or more descriptors from the following list: 'not perceived', 'light touch', 'touch', 'tingling', 'pricking', 'warm', 'hot', 'burning', 'cool', 'cold' and 'humid' [89]. These reports lead to an average inter-stimulus interval of 50 seconds and the experiment lasted approximately 20 minutes.

To study the time courses of the intensity ratings and how they were affected by the temperature (warm or cool) and the way the stimulation probe was employed, some features were extracted and analyzed as follows. For all statistical tests mentioned, significance level was set to 5%. When multiple comparisons were performed, this level was adapted with the Holm-Bonferroni correction, as detailed in what follows.

Average features. For each intensity rating waveform, per subject and type of stimulus, the point of maximum rating was identified in each of the 15 stimulation cycles. These maximum ratings and their latencies relative to the stimulation cycle (0 second corresponding to when the temperature change relative to baseline was maximal) were averaged across stimulation periods. These two measures were then compared across stimulation conditions using a two-way repeated measures ANOVA with the factors temperature (cool or warm) and surface (large-fixed, small-fixed, small-variable). The numbers of degrees of freedom of the F -distributions were adapted with the Huynh-Feldt correction when the condition of sphericity was violated (according to Mauchly's test for sphericity) [109, 110]. Whenever the effect of one of the

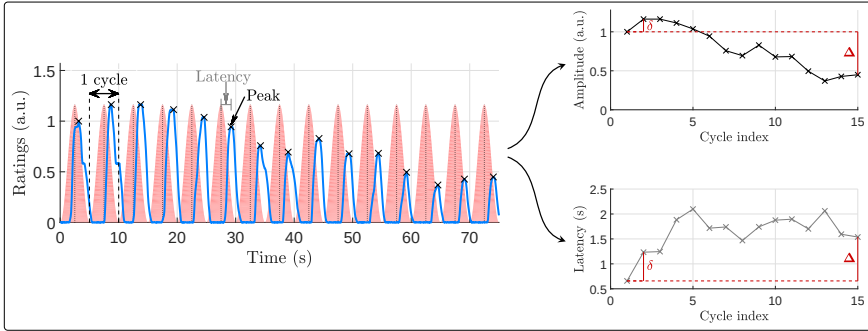


Fig. 5.2 Example of intensity ratings collected. Example of intensity ratings from one subject during one stimulus (warm large-fixed). The temperature waveform is shaded in red and the blue curve is the intensity rating. In each cycle of 5 seconds, the amplitude of the rating peak and its latency compared to the corresponding temperature peak were computed. (Right panels) Definition of the first and final differences, denoted respectively by δ and Δ , of the rating peaks amplitudes and latencies along the cycles.

factors was significant, post-hoc paired sample *t*-tests were conducted with Holm-Bonferroni correction [111]. Furthermore, for each type of stimulus, the relative delay between the maximum intensity rating and stimulation was assessed by comparing the average latencies of maximum rating against zero using one-sample *t*-tests.

Temporal dynamics of heat and cool perception across stimulation cycles. Each rating time course was then normalized such that the maximum and minimum ratings during the first stimulation cycle corresponded to 0 and 1 respectively, as illustrated in Fig. 5.2. This allowed characterizing the temporal dynamics of intensity ratings along the stimulation cycles without being affected by initial differences in rating amplitude across conditions. These waveforms normalized to the ratings of the first stimulation cycle were used to extract the maximum rating of each stimulation cycle (expressed relative to the rating of the first stimulation cycle) and its latency. Within these normalized ratings, if the intensity of the stimulus-evoked sensation tended to increase (resp. decrease) across stimulation cycles, this would result in maximum ratings becoming greater (resp. smaller) than 1. Since the evolution of the intensity of a long-lasting sensation is typically nonlinear, with an early strong decrease (or increase) rate when habituation (or sensitization, respectively) occurs [105, 112, 113, 106], the changes in maximum

ratings and in latencies of the maximum ratings across stimulation cycles were characterized both between the first and the second cycle (to assess immediate changes in perception already occurring after the first cycle), and between the first and the last cycle (to assess global changes in perception occurring across the 15 cycles). The immediate and global changes in rating intensities and latencies, denoted respectively by δ and Δ , are illustrated in Fig. 5.2. These quantities were compared across stimulation conditions using two-way repeated measures ANOVAs with the factors ‘temperature’ (cool or warm) and ‘surface’ (large-fixed, small-fixed or small-variable) as within-subject fixed factors. Post-hoc paired *t*-tests were conducted when justified. In addition, one sample *t*-tests were employed to assess the significance of each of these changes against 0.

Other features of the percept elicited by periodic cool and warm stimulation were assessed, such as the minimum ratings of intensity across stimulation cycles and the amplitude of the cyclic variation in ratings of intensity. These are reported as Supplementary Material.

5.4 Results

The time courses of the percepts elicited by the different warm and cool stimuli and averaged across the stimulation cycles are shown in Fig. 5.3a. The grand average time courses along the cycles are depicted in Fig. 5.4a. In the latter figure, the maximum amplitude within the first stimulation cycle does not necessarily reach 1 although the ratings were normalized, because the extrema are not perfectly time-locked across subjects. The outcomes of the ANOVAs assessing the effects of stimulation temperature and surface on intensity ratings are summarized in Table 5.1. Subsequent post-hoc comparisons are illustrated in Figs. 5.3 and 5.4 and the results are detailed hereunder.

Average features. The intensity of the percept elicited by periodic warm stimulation was greater than the intensity of the percept elicited by periodic cool stimulation, regardless of the stimulation surface employed (Fig. 5.3b and ‘Mean peak’ in Table 5.1). The latency of the sensation elicited by cool stimulation was significantly shorter than the latency of the sensation elicited by warm stimulation (Fig. 5.3c and ‘Mean latency’ in Table 5.1). Furthermore, for cool stimulation, the average intensity of the percept was lower when stimuli were delivered using a fixed surface as compared to a variable surface (small-fixed vs. small-variable; Fig. 5.3b and Table 5.1). Cool

Table 5.1 ANOVAs for the features of the intensity ratings. Outcomes for the main effects and interactions from the repeated measures ANOVA performed for the average (two first rows) and dynamical (four last rows) features of the intensity ratings. Partial eta squared (η_p^2) are indicated for the effect sizes and the p -values smaller than the significance level of 0.05 are in bold.

	Temperature			Surface			Temperature*Surface			
	F	Prob>F	η_p^2	F	Prob>F	η_p^2	F	Prob>F	η_p^2	
Mean	Mean peak (a.u.)	25.294	0.000	0.658	14.537	0.000	0.517	3.569	0.043	0.222
	Mean latency (s)	46.763	0.000	0.781	8.040	0.013	0.378	6.724	0.005	0.350
Early	δ Peak (%)	8.606	0.011	0.395	0.237	0.790	0.017	1.016	0.377	0.075
	δ Latency (s)	14.313	0.002	0.516	10.398	0.000	0.438	10.515	0.000	0.457
Global	Δ Peak (%)	6.058	0.028	0.314	10.107	0.001	0.428	0.558	0.579	0.043
	Δ Latency (s)	3.291	0.092	0.200	0.009	0.951	0.001	1.360	0.275	0.098

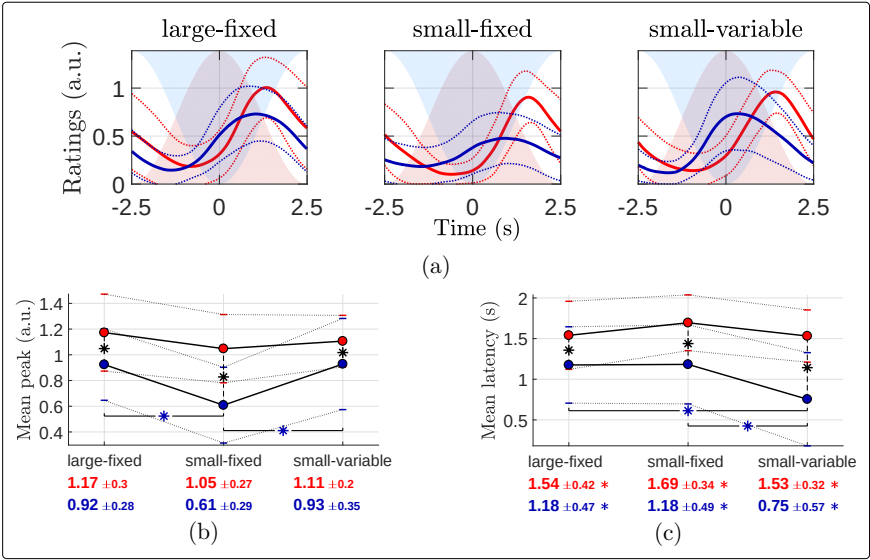


Fig. 5.3 Intensity ratings averaged across stimulation cycles. (a) Group-level average ($\pm$ standard deviation in dotted) time courses of the intensity ratings averaged across stimulation cycles, in (light) red and (dark) blue for the warm and cool conditions respectively. The stimulation temperatures are shaded. (b-c) Pairwise comparisons of (b) the mean peak intensity rating and (c) the mean peak intensity latency. The red (resp. blue) dots show the mean features for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. These means and standard deviations are also reported below the plots with the corresponding color. Each asterisk in the plot indicates a significant difference according to paired samples t -tests with Holm-Bonferroni correction. The asterisk is red, blue (horizontally) or black (vertically) respectively when the two compared conditions are warm, cool or different. In (c), an asterisk besides an x-axis tick label shows that the corresponding mean feature is significantly different from 0 based on one sample t -tests with Holm-Bonferroni correction.

stimulation using a fixed surface also increased the latency of the maximum rating as compared to stimulation using a variable surface (small-fixed vs. small-variable; Fig. 5.3c and Table 5.1).

Temporal dynamics of heat and cool perception across stimulation cycles. Both for cool and warm stimulation, and regardless of whether stimulation was applied using a fixed vs. a variable surface, the amplitude of the cyclic variations in ratings induced by the periodic stimulus tended to decrease along

5 | Experiment 1: time course of heat and cool perception

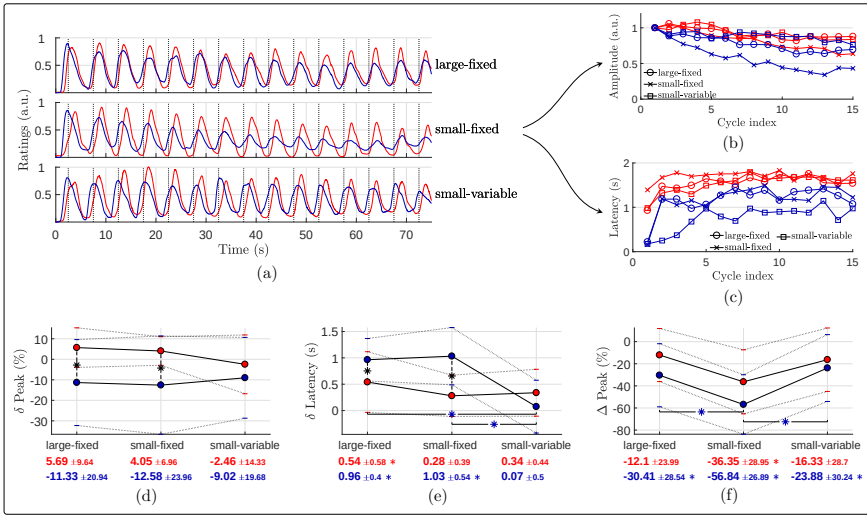


Fig. 5.4 Intensity ratings dynamics. (a) Group-level average intensity ratings along the cycles, in (light) red and (dark) blue for the warm and cool conditions respectively. The vertical dotted lines indicate the times of extreme temperature (2.5 s after the beginning of each stimulation cycle). From each normalized individual time course, the rating peaks and their latencies within each cycle are extracted, their grand average being illustrated in (b) and (c). (d-e-f) Pairwise comparisons of (d) the early change in peak intensity rating, (e) the early change in peak latency and (f) the global change in peak intensity rating. Early and global changes are computed from the first to the second and last cycles respectively. The red (resp. blue) dots show the mean features for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. These means and standard deviations are also reported below the plots with the corresponding color. Each asterisk in the plot indicates a significant difference according to paired samples t -tests with Holm-Bonferroni correction, in red, blue (horizontally) or black (vertically) respectively when the two compared conditions are warm, cool or different. An asterisk besides an x-axis tick label shows that the corresponding mean feature is significantly different from 0 based on one sample t -tests with Holm-Bonferroni correction.

the stimulation cycles (Fig. 5.4b, the exact reductions and their significance being indicated at the bottom of Fig. 5.4f). This habituation of perception appeared to be stronger for cool stimulation as compared to warm stimulation, especially when stimulation was delivered using a fixed surface. The individual time courses of the rating peaks and their latencies are reported

in Figs. 5.5 and 5.6 respectively.

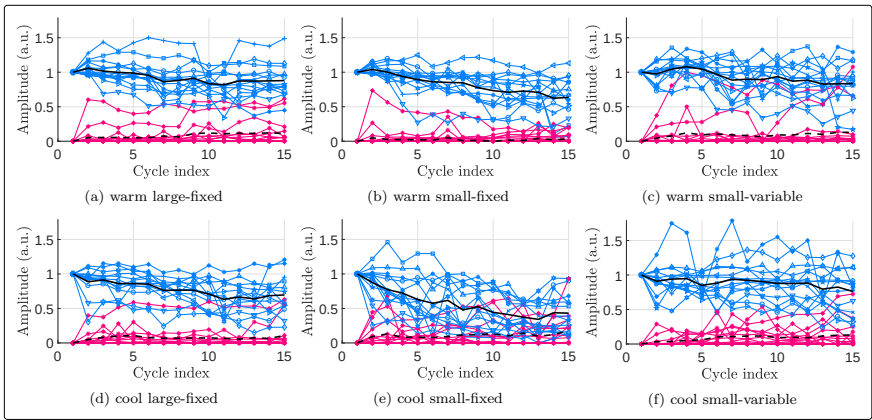


Fig. 5.5 Individual rating peaks and troughs across cycles. The amplitude of the rating peaks as a function of the cycle index is depicted in blue, for the warm (top row) and cool (bottom row) stimulation. Each curve is normalized by the first peak amplitude. The grand average is in black. The pink curves indicate the minimum rating amplitudes reported between the corresponding peaks (the dotted black lines being their averages).

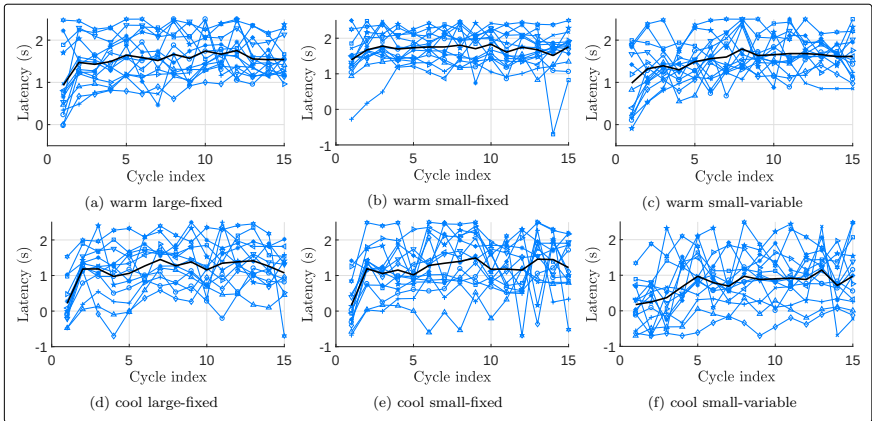


Fig. 5.6 Individual latencies of the rating peaks across cycles. Latency between the temperature and rating peaks as a function of the cycle index, for the warm (top row) and cool (bottom row) stimulation. The grand average is in black.

Immediate changes in perception occurring after the first stimulation cycle. As shown in Fig. 5.4d, there was no marked change in the intensity of the percept elicited by warm stimulation between the first and the second stimulation cycle. In contrast, maximum ratings of the intensity of the percept elicited by cool stimulation tended to decrease from the first to the second stimulation cycle, especially for stimuli delivered using a fixed surface. The ANOVA revealed significant main effect of temperature (cool vs. warm) on the change in rating between the first and second cycle of stimulation, but no main effect of stimulation surface (fixed vs. variable), and no interaction between the two factors (' δ Peak' in Table 5.1). The latency of the maximum rating of intensity of perception also differed between the first and the second stimulation cycle. The ANOVA showed a main effect of temperature, a main effect of stimulation surface, and an interaction between the two factors (' δ Latency' in Table 5.1). Post-hoc comparisons showed that all rating latencies increased in the second compared to the first cycle, and that this increase was larger for cool compared to warm stimulation when the stimulation surface was fixed (Fig. 5.4e).

Global changes in perception occurring after 15 stimulation cycles. The ANOVA comparing the changes in intensity ratings between the first and the last stimulation cycle revealed significant effects of both temperature and surface (' Δ Peak' in Table 5.1). Paired comparisons showed that, for cool stimulation, the global decrease in perception was stronger when stimulation was delivered using a fixed surface as compared to a variable surface (Fig. 5.4f). The decrease in perception across the stimulation cycles was also greater for cool compared to warm stimulation, although the differences were not significant. The ANOVA comparing the changes in rating latencies did not show any significant effect (' Δ Latency' in Table 5.1).

The results of the ANOVA and post-hoc tests for the additional quantities that were compared are reported in Table 5.2 and Fig. 5.7. There was no significant effect of the temperature nor the surface on the minimum intensity ratings, and the effects on the amplitudes of the cyclic variations (rating ranges) were similar to the ones of the rating peaks reported above.

Quality of the sensations elicited by heat and cool stimulation. The descriptors chosen to describe sensation quality are shown in Fig. 5.8. Periodic heat stimulation was most often described as 'warm', 'hot', 'burning' or 'pricking'. Periodic cool stimulation was most often described as 'cool', 'cold' or 'humid'.

Table 5.2 ANOVAs for the remaining features (troughs and ranges) of the intensity ratings. Outcomes for the main effects and interactions from the repeated measures ANOVA performed for the last average (two first rows) and dynamical (four last rows) features of the intensity ratings. Partial eta squared (η_p^2) are indicated for the effect sizes and the p -values smaller than the significance level of 0.05 are in bold. These results concerning the rating troughs and ranges are separated from the previous ones given in Table 5.1 as there was no significant effect for the rating troughs, and the effects for the rating ranges were similar to the ones for the rating peaks.

	Temperature			Surface			Temperature*Surface		
	F	Prob>F	η_p^2	F	Prob>F	η_p^2	F	Prob>F	η_p^2
Mean									
Mean trough (a.u.)	0.030	0.865	0.002	0.345	0.711	0.025	2.496	0.050	0.166
Mean range (a.u.)	24.059	0.000	0.647	15.223	0.000	0.529	7.875	0.002	0.386
δ Trough (%)	0.081	0.780	0.006	0.912	0.589	0.064	1.027	0.218	0.076
δ Range (%)	7.926	0.014	0.376	0.315	0.683	0.023	1.720	0.200	0.121
Δ Trough (%)	0.877	0.366	0.062	0.147	0.606	0.011	1.728	0.210	0.121
Δ Range (%)	7.241	0.018	0.356	9.128	0.001	0.406	2.920	0.073	0.189

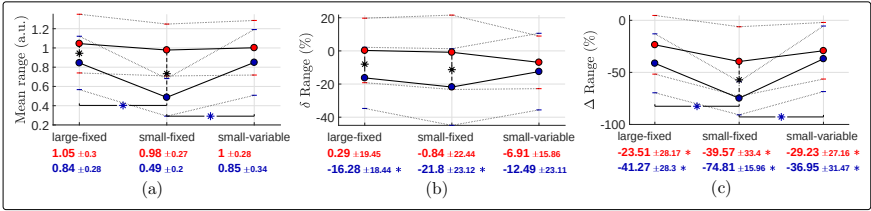


Fig. 5.7 Post-hoc comparisons of the amplitudes of the cyclic variations in intensity ratings. Pairwise comparisons for the effects of the temperature and surface (a) on the rating range averaged across cycles, (b) on the early difference of rating range and (c) on the global difference of rating range across cycles. The dots colored in red (resp. blue) show the mean features in the warm (resp. cool) conditions. These means (with the standard deviations) are also indicated below the plots with the same color. Each asterisk in the plot indicates a significant difference according to paired sample *t*-tests with Holm-Bonferroni correction, in red, blue or black respectively when the two compared conditions are warm, cool or different. In (b,c), an asterisk besides an x-axis tick label shows that the corresponding mean feature is significantly different from 0 based on one sample *t*-tests with Holm-Bonferroni correction. These comparisons of the rating ranges are similar to the ones of the rating peaks presented in Fig. 5.4.

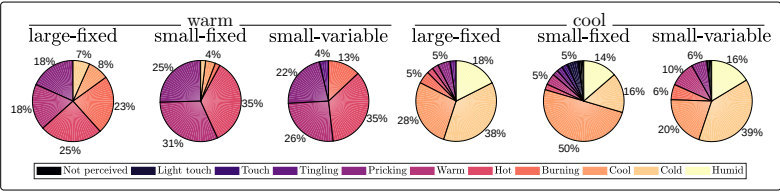


Fig. 5.8 Quality of the percepts. Reported quality of the percepts from all the subjects and for each condition. The proportions below 3% are not indicated for clarity.

5.5 Discussion

Both sinusoidal contact heat stimulation and sinusoidal contact cold stimulation at 0.2 Hz elicit a sensation whose intensity varies periodically over time.

The variations of skin area to which the thermal stimuli were applied did improve the perception, but they were not sufficient to avoid some clear adaptation of the responses. This adaptation occurred for the cool and warm stimuli, but was stronger and earlier in the former case, especially with a fixed stimulation area.

Indeed, the temperature (warm vs. cool) affected the early and global dynamics of the intensity ratings, with an overall enhanced steadiness, namely with less habituation, for the warm compared to the cool stimuli. Besides, and coherently, slightly varying the stimulation surface mostly improved the cool perception along the cycles, both early in terms of the latencies and globally in terms of the perception intensity.

Interestingly, the latency of the peak of cool perception across stimulation cycles was markedly affected by varying the stimulated skin area, with an important increase of latency occurring after the first stimulation cycle when the surface was kept fixed. This phenomenon could be explained by activity-dependent slowing [62] and/or peripheral adaptation of cool-sensitive receptors, leading to an increase in their threshold [106].

Chapter 6

Experiment 2: electroencephalographic recordings

6.1 Participants

Fifteen healthy volunteers took part in Experiment 2 (6 men and 9 women, aged 21-34 years). All participants were right-handed and did not suffer from any neurological disorder. The study was approved by the local ethics committee (Comité d’Ethique Hospitalo-Facultaire de l’Université catholique de Louvain, B403201316436) and all participants gave written informed consent.

6.2 Contact thermal stimulation

All the stimuli considered were delivered using the contact thermal stimulator (TCS-II) described in Section 5.2.

Such as in Experiment 1, each stimulus lasted 75 seconds (15 periods of a 0.2 Hz sinusoidal waveform). For this second experiment, four temperature profiles

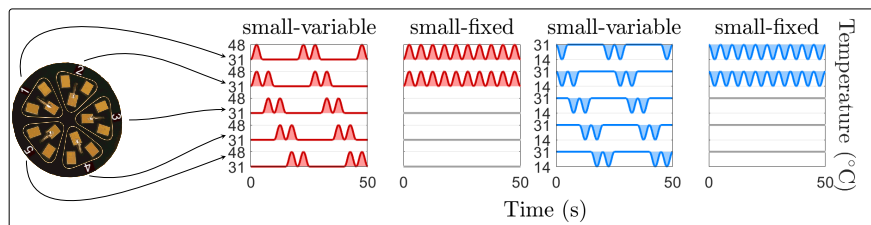


Fig. 6.1 Stimulation employed. Stimulation surface of the Thermal Cutaneous Stimulator (TCS) employed and stimulation temperature profiles considered in Experiment 2, depicted in red (or blue) for the warm (or cool) stimuli and truncated to 50 seconds for readability.

were tested: small-surface cool (between 31 and 14°C) and heat (between 31 and 48°C) stimuli delivered using two zones of the contact probe at either a fixed or variable skin location, as illustrated in Fig. 6.1.

6.3 Methods

In this second experiment, the EEG was recorded while participants were exposed to cool-variable, cool-fixed, warm-variable and warm-fixed stimulation. Participants were seated with their right forearm resting on a soft surface, with the volar side upwards. They were instructed to keep their gaze fixed at eye level. All stimuli were delivered to the right volar forearm. Each type of stimulus was repeated 12 times, presented in a randomized order. Inter-stimulus interval was self-paced by the experimenter and varied between 10 and 20 seconds. The TCS-II probe was manually displaced after each stimulus. The entire recording session lasted approximately 1h30. Such as in experiment 1, a significance level of 5% was used for all statistical tests, and the Holm-Bonferroni method was used to correct for multiple comparisons.

EEG recording and preprocessing. The EEG was recorded using 64 Ag-AgCl electrodes, whose impedances were kept below 10k Ω , placed on the scalp according to the international 10/10 system (WaveGuard 64-channel cap; Advanced Neuro Technologies). Signals were amplified and digitized at 1000 Hz, with an average reference. The EEG recordings were analyzed offline using Matlab R2017a (The MathWorks), and the preprocessing was performed using Letswave 6 (<http://letswave.org>) [114]. All signals were high-pass filtered above 0.05 Hz to remove slow drifts with a 4th order zero-phase

Butterworth filter, and power line noise was removed with a 50 Hz notch filter. The epochs were defined by segmenting the EEG from 0 to 75 seconds after each stimulation onset. Each epoch was then centered, and stereotyped artifacts (eye movements or blinks and muscle artifacts) were removed using an Independent Component Analysis (ICA) decomposition [115]. For each subject, the full rank data matrix was decomposed using 63 independent components [116]. Epochs containing large artifacts were finally rejected by visual inspection, leading to exclude an average ($\pm$ standard deviation) of 0.6 ± 0.74 , 0.8 ± 1.21 , 0.73 ± 0.88 and 1.2 ± 1.15 epochs for the conditions warm-fixed, warm-variable, cool-fixed and cool-variable, respectively.

Frequency domain analysis. Average waveforms were computed for each subject and condition. Since the stimulation was periodic, a periodic stimulus-evoked response was expected. This response was not likely to be a perfect linear mapping of the applied sinusoidal stimulation intensity, but could be any periodic signal with the same fundamental period of 5 seconds. The power of such a periodic signal is concentrated at its fundamental frequency of 0.2 Hz and its harmonics (0.4, 0.6, 0.8, ... Hz) [9, 117]. To identify the presence of a stimulus-evoked EEG response, the Fourier Transform (FT) of each 75-s average waveform was hence computed per subject, stimulation condition and electrode with a frequency resolution of 0.013 Hz. The significance of the signal amplitude at the stimulation frequency and its first harmonics was then assessed. To do so, the noise level at each frequency of interest (FOI) was estimated using the average amplitude at eight neighboring frequencies (located at $\pm\{0.027, 0.04, 0.053, 0.066\}$ Hz around each FOI) and was removed from the spectrum, resulting in *noise-subtracted (NS) amplitudes* [103, 117]. The significance of the NS amplitudes at the FOI $f_k = k \cdot 0.2$ Hz, for $k = 1, \dots, 5$, was then tested using one sample t -tests against 0. The electrode where the NS component at 0.2 Hz was the largest on average across conditions was then selected for the next analyses. Then, the NS amplitudes at the stimulation frequency were compared across stimulation conditions using a two-way repeated measures ANOVA with the factors ‘temperature’ (cool or warm) and ‘surface’ (fixed or variable). Post-hoc paired t -tests were conducted when justified.

Time domain analysis. The 75-s average waveforms were further segmented in 15 periods of 5 seconds and averaged to analyze the stimulus-induced periodic EEG waveform and assess its latency across the different conditions. Response latency was defined as the difference between the peak of the EEG response and the latency of maximum temperature change. Latencies were

compared across conditions using a two-way repeated measures ANOVA with the factors ‘temperature’ (cool or warm) and ‘surface’ (fixed or variable). Paired t -tests were used for post-hoc comparisons. Furthermore, for each type of stimulus, the relative delay between the EEG response and stimulation was assessed using one-sample t -tests against 0.

Time-frequency analysis. As each stimulus lasted 75 seconds, the stimulus-evoked EEG signals cannot be assumed to be strictly stationary along such a long time interval. In addition, the SSRs are also mixed with a bunch of other signals generated by non-stationary brain and external processes, leading to a relatively low SNR of stimulus-evoked responses along time. Time-frequency analysis of the standardized recordings averaged across the epochs were therefore considered in order to highlight the temporal dynamics of the EEG components at 0.2 Hz. Short-time Fourier transforms (STFTs) were employed to characterize the frequency content of the recordings at frequencies ranging from 0.02 Hz to 1 Hz in steps of 0.02 Hz. The STFT was preferred to a continuous wavelet transform as the time resolution of interest was determined by the stimulation period, and was therefore fixed across frequencies. By analogy with the complex Morlet wavelet which is appropriate to characterize time-frequency components of EEG signals [86, 87, 88], the STFT was implemented using a full-length Gaussian window. The employed STFT of a signal x is hence defined as

$$\Psi_x(\tau, f) = \int_{t=-\infty}^{+\infty} x(t) \cdot \exp\left(\frac{-(t-\tau)^2}{2 \cdot (L_w/6)^2}\right) \cdot \exp(-2\pi j f(t-\tau)) dt. \quad (6.1)$$

The width parameter L_w determines the number of oscillations of the modulated complex exponential, which was fixed to 5 with $L_w = 5$, as suggested in [32, 118] to reach a good time-frequency resolution for the frequency of interest of 0.2 Hz. The STFT of the EEG recordings at the electrode with maximal SSR was computed for each subject and condition.

In order to assess the magnitude of the EEG response elicited by the periodic thermal stimuli along time, the STFT amplitudes $|\Psi_x(\tau, f)|$ (per subject and condition) were first noise-subtracted. The noise at each frequency along time was estimated, similarly to the Fourier transform, by computing the mean amplitude of the STFT at four neighboring frequencies, located at $\pm\{0.04, 0.06\}$ Hz around the considered one. Within these noise-subtracted time-frequency maps $\Psi_x^{NS}(\tau, f)$, the sum of the STFT amplitudes at the

frequency of stimulation and its four first harmonics,

$$\sum_{k=1}^5 \Psi_x^{\text{NS}}(\tau, k \cdot 0.2), \quad (6.2)$$

was used as a measure of the time course of the EEG response elicited by the periodic stimuli. The amplitude of this component at 0.2 Hz, which should not be significantly different from 0 when there is no stimulus-related activity, was compared against 0 with one sample *t*-tests along time. The global response amplitude was then defined as the area under the curve (AUC) of this component. This AUC was compared across temperatures (cool or warm) and surfaces (fixed or variable) with a repeated measures ANOVA and post-hoc paired *t*-tests.

Finally, to further assess the habituation of the components at 0.2 Hz across cycles, we computed the noise-subtracted FT amplitude at 0.2 Hz by progressively removing an increasing number of periods at the beginning of the signals, while keeping the signal length fixed with zero-padding. One sample *t*-tests with Holm-Bonferroni correction were used to assess the significance of the noise-subtracted amplitudes at 0.2 Hz for each number of initial cycles removed, allowing to highlight whether EEG responses at 0.2 Hz maintained after a few cycles, even if their amplitude was reduced.

Modulation of ongoing oscillations. Periodic sensory stimulation can also be expected to induce a periodic modulation of the magnitude of ongoing EEG oscillations [35, 119]. In order to assess whether periodic 0.2 Hz cool and warm stimulation delivered using a fixed or variable surface induced a periodic modulation of ongoing EEG oscillations within different frequency bands, we estimated the signal envelopes within theta (4-8 Hz), alpha (8-12 Hz), beta (12-30 Hz) and gamma (30-50 Hz) frequency bands, as follows. First, we band-pass filtered all the unaveraged EEG epochs within each of these bands using a 4th order zero-phase Butterworth filter and then computed the envelopes of these signals as the norms of the corresponding analytic signals that were obtained through Hilbert transforms. These envelopes were then studied in the same way as the original signals, following the procedures described above. The signal envelopes were averaged across trials, the FTs were computed and the electrode with the largest NS amplitude at 0.2 Hz was selected. Then, the signals were averaged across each stimulation cycle and STFTs were computed. The gamma range was chosen so as to avoid considering the 50 Hz frequency around the center of the band, in which

case the low-frequency modulations of this band would have been hindered by the 50 Hz notch filter [120].

6.4 Results

Frequency domain analysis. The EEG frequency spectra at electrode FCz obtained during warm and cool stimulation using a fixed or variable surface are shown in Fig. 6.2a. The periodicity was the largest on average at this electrode. For cool stimulation, a significant but small response was observed at the frequency of stimulation (0.2 Hz) when stimulation was delivered using a variable surface, and no response was observed when stimulation was delivered using a fixed surface. For warm stimulation, a markedly greater response was observed, both when delivered using a fixed surface and when delivered using a variable surface. The increase was significant at the frequency of stimulation (0.2 Hz) and the three following harmonics (0.4, 0.6 and 0.8 Hz). The ANOVA conducted on the noise-subtracted amplitude at 0.2 Hz revealed main effects of temperature and surface (Table 6.1). Post-hoc comparisons showed that the periodic EEG response was greater for warm vs. cool stimulation, and greater for stimulation using a variable vs. fixed surface (Fig. 6.2b).

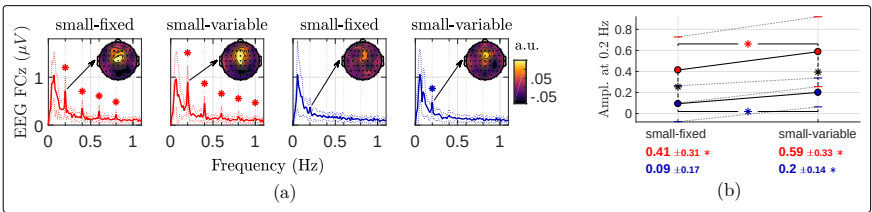


Fig. 6.2 EEG frequency analysis. (a) Group-level average ($\pm$ standard deviation in dotted) Fourier transforms of the EEG signals at electrode FCz. A star indicates significance of the noise-subtracted peak at $\{k \cdot 0.2\}_{k=1}^5$ Hz (t -tests against 0). The scalp maps show the distributions of the noise-subtracted amplitudes at 0.2 Hz. (b) Pairwise comparisons of the noise-subtracted EEG amplitudes at 0.2 Hz at electrode FCz. The red (resp. blue) dots show the mean amplitudes for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. These means and standard deviations are also reported below the plots with the corresponding color. Each asterisk in the plot indicates a significant difference according to paired samples t -tests, in red, blue (horizontally) or black (vertically) respectively when the two compared conditions are warm, cool or different.

Table 6.1 ANOVAs for the features of the EEG signals. Outcomes of the ANOVA performed to assess the main effects of the temperature and surface and their interaction on the EEG signals at FCz. Partial eta squared (η_p^2) are indicated for the effect sizes and the p -values smaller than the significance level of 0.05 are in bold.

	Temperature			Surface			Temperature*Surface		
	F	Prob>F	η_p^2	F	Prob>F	η_p^2	F	Prob>F	η_p^2
Ampl. at 0.2 Hz	23.690	0.000	0.629	10.905	0.005	0.438	0.894	0.360	0.060
Mean lat. (s)	25.926	0.000	0.649	0.042	0.841	0.003	0.271	0.611	0.019
AUC at 0.2 Hz (a.u.)	27.969	0.000	0.666	8.982	0.010	0.391	0.119	0.735	0.008

Group-level average scalp topographies of the noise-subtracted amplitudes at 0.2 Hz are shown in Fig. 6.2a. In all conditions in which stimulation elicited a significant periodic EEG response, its topography was maximal over fronto-central electrodes, and symmetrically distributed over the two hemispheres.

Time domain analysis. The EEG signals averaged across all stimulation cycles are depicted in Fig. 6.3a. At electrode FCz, the EEG response elicited by warm stimulation consisted in a positive wave peaking approximately 1 second after the peak of heat stimulation. For cool stimulation the response also appeared to consist of a positive wave, but its amplitude was much smaller than for warm stimulation, especially when stimulation was delivered using a fixed surface. The peak latency of the response to cool stimulation was also much shorter than the peak latency of the response to heat stimulation (Fig. 6.3b; Table 6.1).

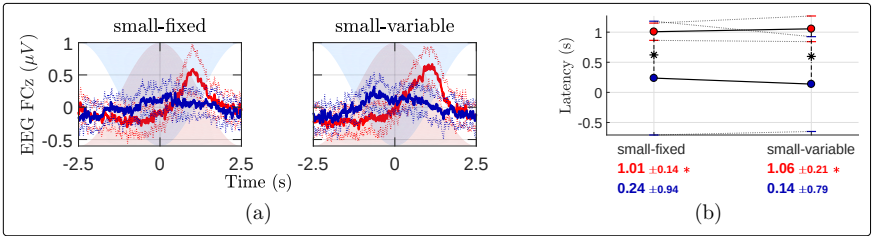


Fig. 6.3 EEG averaged across stimulation cycles. (a) Group-level average ($\pm$ standard deviation in dotted) time courses of the EEG signals at electrode FCz averaged across stimulation cycles, in (light) red and (dark) blue for the warm and cool conditions respectively. The stimulation temperatures are shaded. (b) Pairwise comparisons of the latencies of the EEG peaks compared to the temperature peaks. The red (resp. blue) dots show the mean latencies for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. These means and standard deviations are also reported below the plots with the corresponding color. Each asterisk in the plot indicates a significant difference across temperature according to paired samples t -tests. An asterisk besides an x-axis tick label shows that the corresponding mean latency is significantly different from 0 based on one sample t -tests with Holm-Bonferroni correction.

Time-frequency analysis. The STFT of the signals revealed a marked decrease of the components at 0.2 Hz in all conditions, which appeared to be greater for stimulation delivered using a fixed surface (Fig. 6.4). This decrease was particularly strong and early for cool stimulation, as highlighted by the time

course of the stimulus-evoked components at 0.2 Hz (bottom insets). The ANOVA performed on the AUC of these components (used as a measure of global response amplitude: the larger and the more persistent the elicited activity, the larger the AUC) confirmed that the elicited response was indeed stronger for the warm compared to the cool stimulation (Fig. 6.5a and Table 6.1). Although not statistically significantly, using a variable surface induced a larger AUC than using a fixed surface. Besides, the noise-subtracted amplitudes of the FT at 0.2 Hz (Fig. 6.5b) indicated that there was a significant periodic EEG response at FCz until 7 (or 12) periods were removed in the warm condition with a variable (or fixed, respectively) surface. Also, the periodicity remained significant for the cool condition with a variable surface when up to 3 cycles were removed, showing that a stimulus-evoked response persisted for at least a few cycles.

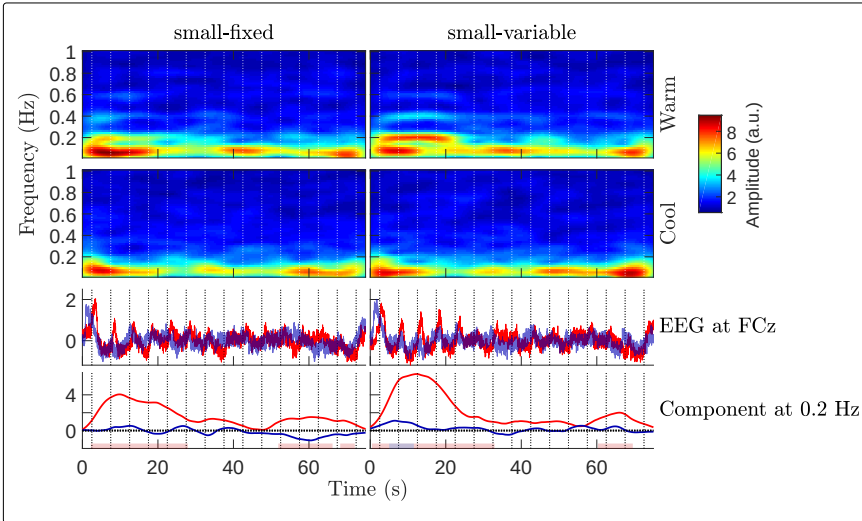


Fig. 6.4 EEG time-frequency analysis Amplitude of the STFT of the EEG signals at FCz, averaged across subjects. The first (resp. second) row of bottom insets displays the grand average time courses (resp. the stimulus-evoked EEG components at 0.2 Hz, estimated as the sum of the noise-subtracted STFT amplitudes at $\{k \cdot 0.2\}_{k=1}^5$ Hz), in red and blue for the warm and cool conditions. The temperature peaks in each cycle are indicated with vertical dotted lines. The shaded horizontal bars at the bottom of the figure show, for each of the four conditions, the significant time clusters where the depicted noise-subtracted amplitude at 0.2 Hz is significantly greater than 0 (t -tests against 0).

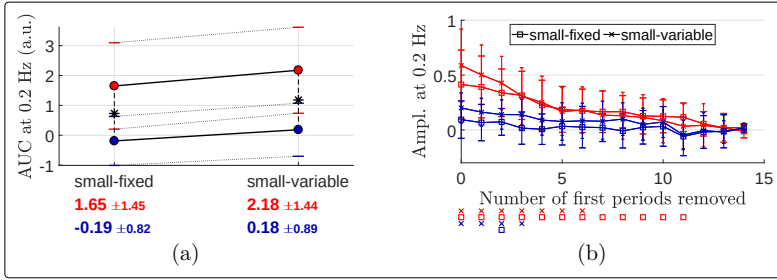


Fig. 6.5 Habituation of the EEG components at 0.2 Hz. (a) Effects of the stimulation temperature and surface on the AUC of the stimulus-evoked EEG component at 0.2 Hz at FCz, estimated as the sum of the noise-subtracted STFT amplitudes at $\{k \cdot 0.2\}_{k=1}^5$ Hz. The red (resp. blue) dots show the mean amplitudes for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. These means and standard deviations are also reported below the plots with the corresponding color. Each asterisk in the plot indicates a significant difference across temperature according to paired samples t -tests. (b) Noise-subtracted amplitudes of the Fourier transforms at 0.2 Hz at FCz as a function of the number of periods removed at the beginning of the EEG signals. The error bars show the standard deviations across subjects, with larger caps when the surface is fixed than when it is variable. For each number of periods removed along the x -axis, a marker drawn below the plot indicates that the noise-subtracted amplitude in the associated condition (with the same color and marker) and for this abscissa is significantly different from 0, according to one-sample t -tests with Holm-Bonferroni correction.

Modulation of ongoing oscillations. Warm stimulation induced a periodic modulation (reduction) of the power of alpha- and beta-band oscillations, associated with a scalp topography maximal over centro-parietal areas contralateral to the stimulated arm (especially at C3), as illustrated in panels (a) and (b) of Figs. 6.7 and 6.8. Like for the baseband signal, the cool stimulation elicited similar modulations, but with smaller magnitudes and shorter latencies. All responses tended to decrease along the stimulation cycles, especially with a fixed stimulated surface (see Figs. 6.7c, 6.7e, 6.8c and 6.8e). There was no consistent and significant modulation of theta and gamma power. The results of the analysis of these envelopes are provided in Figs. 6.6 and 6.9.

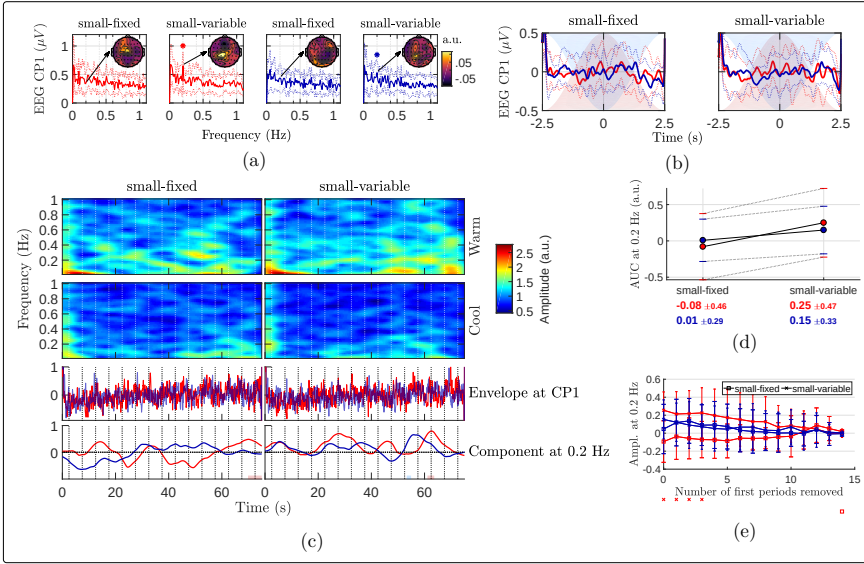


Fig. 6.6 Signal envelopes in the theta frequency band (4-8 Hz). (a) Fourier transforms of the envelopes averaged over the epochs (grand mean $\pm$ standard deviation) at electrode CP1. A star indicates significance of the noise-subtracted peak at $\{k \cdot 0.2\}_{k=1}^5$ Hz (t -tests against 0). The scalp maps show the distributions of the noise-subtracted amplitudes at 0.2 Hz. (b) Envelopes averaged across stimulation periods (grand mean $\pm$ standard deviation). (c) Grand mean STFT of the average signals at CP1 and (d) pairwise comparisons of the AUC of the stimulus-evoked envelope components at 0.2 Hz. The red (resp. blue) dots show the mean AUCs for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. Each asterisk in the plot indicates a significant difference according to paired samples t -tests, in red, blue or black respectively when the two compared conditions are warm, cool or different. (e) Noise-subtracted amplitudes of the Fourier transforms at 0.2 Hz at CP1 as a function of the number of periods removed at the beginning of the envelopes. The error bars show the standard deviations across subjects, with larger caps when the surface is fixed than when it is variable. For each number of periods removed along the x -axis, a marker drawn below the plot indicates that the noise-subtracted amplitude in the associated condition (with the same color and marker) and for this abscissa is significantly different from 0, according to one-sample t -tests with Holm-Bonferroni correction.

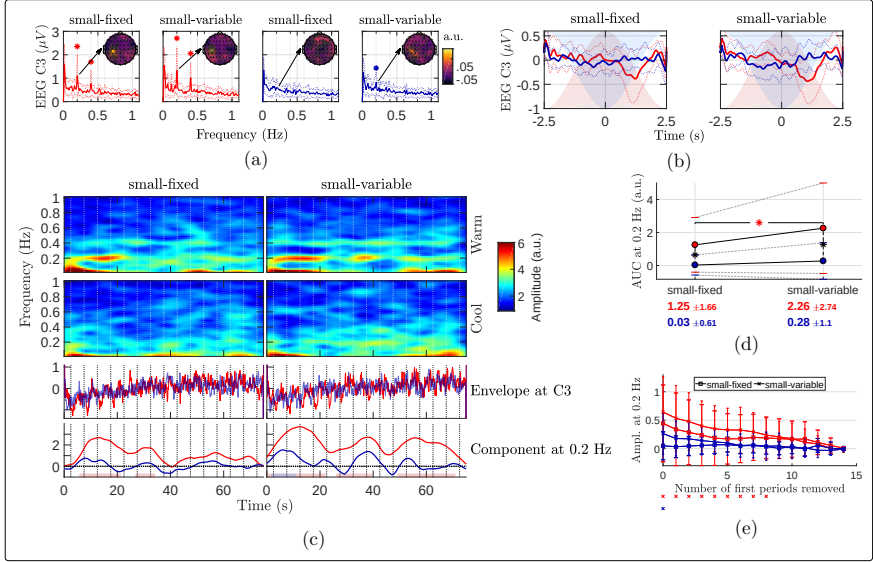


Fig. 6.7 Signal envelopes in the alpha frequency band (8-12 Hz). (a) Fourier transforms of the envelopes averaged over the epochs (grand mean $\pm$ standard deviation) at electrode C3. A star indicates significance of the noise-subtracted peak at $\{k \cdot 0.2\}_{k=1}^5$ Hz (t -tests against 0). The scalp maps show the distributions of the noise-subtracted amplitudes at 0.2 Hz. (b) Envelopes averaged across stimulation periods (grand mean $\pm$ standard deviation). (c) Grand mean STFT of the average signals at C3 and (d) pairwise comparisons of the AUC of the stimulus-evoked envelope components at 0.2 Hz. The red (resp. blue) dots show the mean AUCs for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. Each asterisk in the plot indicates a significant difference according to paired samples t -tests, in red, blue or black respectively when the two compared conditions are warm, cool or different. (e) Noise-subtracted amplitudes of the Fourier transforms at 0.2 Hz at C3 as a function of the number of periods removed at the beginning of the envelopes. The error bars show the standard deviations across subjects, with larger caps when the surface is fixed than when it is variable. For each number of periods removed along the x -axis, a marker drawn below the plot indicates that the noise-subtracted amplitude in the associated condition (with the same color and marker) and for this abscissa is significantly different from 0, according to one-sample t -tests with Holm-Bonferroni correction.

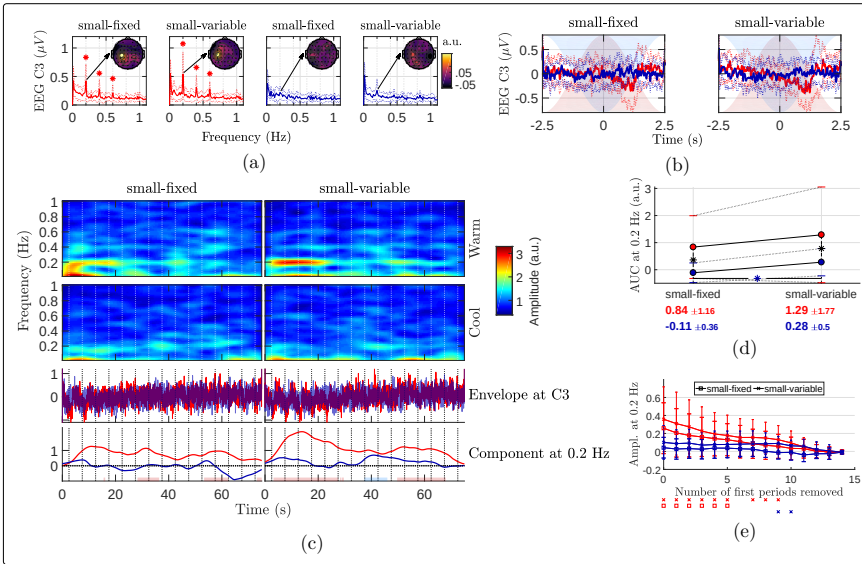


Fig. 6.8 Signal envelopes in the beta frequency band (12-30 Hz). (a) Fourier transforms of the envelopes averaged over the epochs (grand mean $\pm$ standard deviation) at electrode C3. A star indicates significance of the noise-subtracted peak at $\{k \cdot 0.2\}_{k=1}^5$ Hz (t-tests against 0). The scalp maps show the distributions of the noise-subtracted amplitudes at 0.2 Hz. (b) Envelopes averaged across stimulation periods (grand mean $\pm$ standard deviation). (c) Grand mean STFT of the average signals at C3 and (d) pairwise comparisons of the AUC of the stimulus-evoked envelope components at 0.2 Hz. The red (resp. blue) dots show the mean AUCs for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. Each asterisk in the plot indicates a significant difference according to paired samples t -tests, in red, blue or black respectively when the two compared conditions are warm, cool or different. (e) Noise-subtracted amplitudes of the Fourier transforms at 0.2 Hz at C3 as a function of the number of periods removed at the beginning of the envelopes. The error bars show the standard deviations across subjects, with larger caps when the surface is fixed than when it is variable. For each number of periods removed along the x -axis, a marker drawn below the plot indicates that the noise-subtracted amplitude in the associated condition (with the same color and marker) and for this abscissa is significantly different from 0, according to one-sample t -tests with Holm-Bonferroni correction.

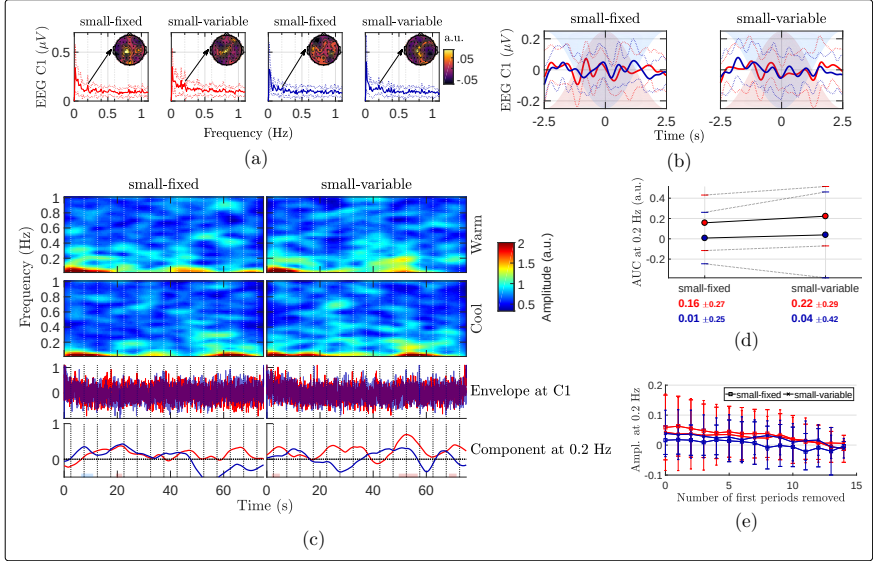


Fig. 6.9 Signal envelopes in the gamma frequency band (30-50 Hz). (a) Fourier transforms of the envelopes averaged over the epochs (grand mean $\pm$ standard deviation) at electrode C1. A star indicates significance of the noise-subtracted peak at $\{k \cdot 0.2\}_{k=1}^5$ Hz (t -tests against 0). The scalp maps show the distributions of the noise-subtracted amplitudes at 0.2 Hz. (b) Envelopes averaged across epochs that were first low-pass filtered below 2 Hz to be able to identify the nature of the periodic modulations and then averaged across stimulation periods (grand mean $\pm$ standard deviation). (c) Grand mean STFT of the average signals at C1 and (d) pairwise comparisons of the AUC of the stimulus-evoked envelope components at 0.2 Hz. The red (resp. blue) dots show the mean AUCs for the warm (resp. cool) stimulation, the standard deviations being indicated with horizontal bars. Each asterisk in the plot indicates a significant difference according to paired samples t -tests, in red, blue or black respectively when the two compared conditions are warm, cool or different. (e) Noise-subtracted amplitudes of the Fourier transforms at 0.2 Hz at C1 as a function of the number of periods removed at the beginning of the envelopes. The error bars show the standard deviations across subjects, with larger caps when the surface is fixed than when it is variable. For each number of periods removed along the x -axis, a marker drawn below the plot indicates that the noise-subtracted amplitude in the associated condition (with the same color and marker) and for this abscissa is significantly different from 0, according to one-sample t -tests with Holm-Bonferroni correction.

6.5 Discussion

Sinusoidal contact heat stimulation and sinusoidal contact cold stimulation at 0.2 Hz elicit a periodic EEG response at 0.2 Hz and its harmonics, although the EEG response elicited by cool stimulation is of much lower magnitude than the EEG response elicited by warm stimulation.

Consistency with laser stimulation. In previous studies using laser heat stimulation, we showed that slowly and sinusoidally heating the skin between baseline and 50°C at a frequency of 0.2 Hz elicits a periodic EEG response mainly driven by the activation of unmyelinated C fibers [35]. Indeed, selectively blocking the conduction of myelinated fibers did not alter the elicited SSRs. In the present study, periodic contact heat stimulation at 0.2 Hz elicited a similar SSR, maximal at the scalp vertex and symmetrically distributed over the two hemispheres. Furthermore, such as in Colon et al., periodic contact heat stimulation at 0.2 Hz elicited a periodic modulation of ongoing oscillations, with a scalp topography maximal over parietal regions contralateral to the stimulated limb.

EEG responses evoked by cool stimulation. Innocuous periodic cooling of the skin at the same frequency also elicited a periodic EEG response. However, as compared to periodic heat stimulation, the magnitude of cool-evoked SSRs was markedly lower. This suggests that, at 0.2 Hz, the periodic activity generated by the activation of cool-sensitive afferents using contact cooling of the skin is not as strong as the periodic activity generated by the activation of heat-sensitive afferents. Besides, the cool SSRs could also be influenced by the periodic suppression of spontaneous tonic activity within warm-sensitive afferents [121, 60].

Modulation of ongoing oscillations. The temporal structure of periodic stimuli nicely allows to assess the presence of modulations of ongoing oscillations and to study their time dynamics. Our analyses showed that the periodic warm stimuli negatively modulated ongoing alpha and beta oscillations in contralateral centroparietal areas. The periodic cool stimuli induced similar reductions of ongoing oscillations, with however smaller magnitudes and shorter latencies. These modulations closely resembled the baseband SSRs in terms of latency and reversed shape. These features are compatible with previous studies suggesting that tonic (cold or heat) pain could be accompanied by a reduction of alpha and beta power maximal over contralateral sensorimotor areas [99, 122, 102, 101, 25]. Such reduction of alpha (and sometimes beta) activity is also similarly observed following

transient painful stimuli [123, 101, 124]. In this case, it is commonly referred to as alpha event-related desynchronization (α -ERD) [24]. The α -ERD is typically observed over the contralateral sensorimotor cortex and in occipital areas [123]. This reduction of alpha (and beta) power, probably originating from sensorimotor areas, is therefore common to both tonic and brief painful stimuli, and it likely encodes stimulus intensity [125, 25]. Coherently with this hypothesis, non-painful cool stimulation also significantly reduced alpha and beta powers in our study, with a smaller magnitude correlating with the smaller perceived intensity, with shorter latencies and with stronger habituation, as for the baseband responses. Habituation also tended to be enhanced when the stimulated skin surface was kept fixed.

Besides, we did not observe a consistent and significant modulation of gamma power, although an enhancement of gamma power during tonic painful stimulation had been reported in prefrontal regions [25] or widespread across the scalp [101], and could be specific to tonic pain perception [123]. The absence of a clear gamma modulation in our study could be explained by (1) the limited duration of our stimuli (75 seconds), (2) the overall habituation of the responses and/or (3) the large difference between the stimulation period (5 seconds) and the short time scales on which gamma oscillations evolve.

Relations with imaging studies. The contralateral centro-parietal modulations of alpha and beta oscillations described above likely originate, at least partly, from the contralateral sensorimotor cortex [25]. Besides, the scalp topography of the EEG responses at 0.2 Hz, maximal over fronto-central electrodes and symmetrically distributed over the two hemispheres, could rather result from brain activity originating from the anterior cingulate cortex and/or the operculo-insular cortices [103]. Our findings are therefore compatible with functional neuroimaging studies showing that experimental tonic pain is accompanied by an increase in cerebral blood flow (CBF) in a large network of brain areas including the cingulate, primary and secondary somatosensory, prefrontal and insular cortices [95, 53, 96, 126, 26]. The fact that the magnitude of the phase-locked stimulus-evoked responses at 0.2 Hz and the modulations of ongoing oscillations had different scalp topographies further suggests that the widespread increases in CBF could be linked to distinct EEG features, such as a reduction of alpha-band oscillations in somatosensory areas and a phase-locked response from the insular and/or cingulate cortices. Further studies will be needed to functionally characterize all the components of the EEG responses and to better relate them to the brain structures highlighted in fMRI studies.

Chapter 7

Discussion

THE objective of this study was to compare the perception and EEG responses elicited by long-lasting warm and cool stimuli frequency-tagged by slowly and periodically varying their intensity over time at a frequency of 0.2 Hz, and applied either to the same patch of skin or to a varying patch of skin along the stimulation periods.

Links between perception and EEG responses. Although the perceptual ratings and EEG recordings have different natures and signal-to-noise ratios, some of their properties can be linked. On average, the magnitudes of both the periodic percept (Fig. 5.3b) and the EEG response at 0.2 Hz (Figs. 6.2b and 6.5a) were larger for warm than cool stimulation, and also larger when the surface was variable compared to fixed in the cool case. In the warm case, only the stimulus-evoked EEG response was increased by using a variable surface. Yet, the significant main effect of the surface on the global rating changes (without significant temperature - surface interaction, see Table 5.1) indicates that the warm perception also decreased more with a fixed surface than with a variable one. Then, the EEG and rating latencies were smaller for cool than warm stimuli (Figs. 5.3c and 6.3b). In terms of perception, varying the stimulated skin surface increased the latencies for cool stimuli while such difference was not observed with the EEG. However, the EEG latency for cool stimuli delivered on a fixed surface was not very reliable since the periodic response

was not significant. The intensity ratings and EEG recordings can be less accurately compared in terms of dynamics, as the maximum rated intensity and its latency could be extracted during each stimulation cycle whereas a clear stimulus-evoked EEG response could not be identified for each cycle. Nevertheless, the global and early changes in intensity rating (Fig. 5.4) show that habituation of the perception was stronger and earlier for the cool stimuli, especially with a fixed stimulation area. Likewise, the amplitude at 0.2 Hz became non-significant sooner for the cool than the warm stimulation as the first cycles were removed from the EEG signals (Fig. 6.5b), with no significant periodic response at all for a cool fixed stimulation. All these large similarities between the perceptual outcomes and EEG features hence suggest that the EEG responses were mostly correlated with perception.

Habituation of perception and EEG responses. Both heat- and cool-evoked responses tended to attenuate along the stimulation cycles. Possible explanations for this response attenuation are receptor fatigue or adaptation at peripheral level and/or habituation processes or alternative phenomena occurring at the level of the central nervous system [105, 108]. This response attenuation could explain why both heat-evoked and cool-evoked SSRs tend to be of smaller magnitude than the SSRs typically elicited by other types of stimuli, such as vibrotactile, visual or auditory stimuli [30, 127, 128]. The finding that attenuation of the EEG response and perception over time is stronger for cool as compared to heat stimulation could be explained by (1) peripheral mechanisms differentially affecting the responsiveness of heat vs. cool-sensitive afferents and/or (2) central mechanisms specific to the painful nature of the heat stimuli compared to the cool ones. However, further supporting a contribution of peripheral mechanisms is the observation that the response attenuation was less pronounced when the stimulated skin area was varied along the stimulation cycles, i.e. when different free nerve endings were exposed to heat or cold across the stimulation cycles [105]. Notably, when Colon et al. recorded heat-evoked SSRs using infrared laser stimulation, the laser beam was displaced between each stimulation cycle such that stimulation was never repeated at the same skin area over the entire duration of the periodic stimulus [35]. Using such stimuli, no habituation of perception or SSRs was observed, suggesting a limited contribution of central habituation. Therefore, the reduced steadiness of the EEG responses when the warm stimulation is applied on a fixed skin location further suggests that rather quickly-adapting fibers were, at least partly, responsible for the EEG responses elicited by the first cycles of warm stimulation [129, 61].

Differences in latency of the responses. Another marked difference between the responses elicited by periodic heat and cool stimulation was a difference in la-

tency. Regarding the time course of perception, the periodic variations of the intensity of heat perception were delayed by approximately 0.8 seconds as compared to the periodic variations of the intensity of cool perception. A similar delay of approximately 0.8 seconds was observed when comparing the time course of heat- and cool-evoked SSRs. These differences in response latency should be interpreted with caution, as they could be explained by at least three factors. First, these differences could be related to differences in peripheral conduction times, considering that the responses elicited by sinusoidal heating of the skin at 0.2 Hz are predominantly related to the activation of slowly-conducting unmyelinated C fibers [35], whereas cool stimuli might be mostly conveyed by faster-conducting thinly-myelinated A δ -fibers [60, 54]. However, the observed latency differences could also be explained by differences in timings of peak discharge frequency and in relative activation thresholds. Single-unit recordings in monkeys have shown that C fiber thermnociceptors can be either quickly adapting (QC) or slowly adapting (SC) [59, 61]. Exposed to a step increase of temperature from baseline to 49°C maintained during 30 seconds, QCs respond vividly at the onset of the stimulus with a peak discharge occurring approximately 0.4 s after stimulation onset, and then rapidly adapt. Conversely, SCs respond more gradually to the step increase in skin temperature, with a peak discharge approximately 2 seconds after stimulation onset, and then tend to maintain a tonic level of activity during the entire stimulus duration. Besides, the thermal activation threshold of QCs and SCs have been shown to be around 41°C and 46°C, respectively [61]. The response properties of cool-sensitive free nerve endings have not been characterized as extensively [60, 54]. Humans are able to detect transient decreases in skin temperature of as little as 0.2-0.5°C [130], and to respond sharply at the onset of the stimulus [131]. Therefore, when cooling the skin progressively from baseline to 14°C, activation of cool-sensitive afferents may be expected to occur earlier than the activation of QC and/or SC fibers when the skin was progressively heated to 48°C, both because thermal activation threshold was reached earlier in the stimulation cycle for cool stimulation as compared to heat stimulation, and because cool-sensitive afferents may be expected to reach peak discharge rate earlier than C fibers [61, 131]. As a consequence, the responses to cool stimulation sometimes peaked earlier than the temperature itself.

Scope of the study and future works. This study compared long-lasting warm and cool stimulation. The presented results naturally depend on the selected frequency of stimulation, the waveform shape and the temperature delta, and varying these parameters may lead to different outcomes, as different populations of afferent fibers could be selectively activated and/or deactivated [59]. In this part,

the stimulus-induced activations of afferents were mainly discussed since literature results suggest that they should mostly determine the elicited responses [60]. However, these responses can also be affected by other stimulus-induced changes within the afferents, as studies have shown that some thermonociceptors (e.g. warm-sensitive C fibers) may maintain a tonic activity at rest, whose suppression by a (e.g. cool) stimulus could contribute to the elicited (e.g. cool) sensations and brain responses [121, 60].

Besides, while the stimulus duration (75 seconds) was limited compared to usual constant tonic thermal stimulation, the proposed approach enables studying the responses elicited by particular stimulation waveforms (e.g. lasting 5 seconds in the present work). Finally, given the habituation observed in our recordings and the relatively weak SSR, future studies will improve the functional characterization of the elicited brain responses across all the scalp channels, including the modulations of ongoing oscillations, for instance by testing painful and non-painful heat and cold stimuli and comparing the timing and localization of the obtained responses [124].

PART II

Extracting periodic components from multidimensional recordings

THIS part investigates whether and how spatial filtering can be employed to extract periodic components from multidimensional recordings. For this purpose, different methods and approaches are proposed and tested on simulated signals as well as on the data described in Part I, Chapter 6. This part is structured as follows:

- Chapter 8 introduces the principle of linear spatial filtering.
 - Chapter 9 details and compares spatial filters for periodicity maximization.
 - Chapter 10 proposes spatial filters to extract discriminative periodic components.
 - Chapter 11 shows how unsupervised tensor factorizations can be employed to extract periodic components.
 - Chapter 12 discusses the considered methods and in particular their applicability in practical contexts.
-

Chapter 8

Background: linear spatial filtering

THIS chapter defines spatial filtering and presents a widely employed approach of this kind used in classification settings, which is called Common Spatial Patterns (CSP). This technique computes spatial patterns and associated time courses of the most discriminant components among two classes of signals. The formulation of the objective function as well as its analytic solution are very much related to the ones that will be studied in Chapters 9 and 10.

It can be noted that this chapter does not provide a complete overview of existing spatial filtering approaches, but instead focuses on a cornerstone technique of this kind, thereby introducing the main concepts of such methods.

8.1 Common Spatial Patterns (CSP)

Linear spatial filtering consists in computing a linear combination of the components of an input multidimensional signal $\mathbf{x}(t) \in \mathbb{R}^C$, with C the number of channels, as

$$s(t) := \mathbf{w}^T \mathbf{x}(t), \tag{8.1}$$

where $\mathbf{w} \in \mathbb{R}^C$ is called a spatial filter [47] (unless stated otherwise, all vectors employed are column vectors). The filtered signal $s(t)$ can be seen as a virtual, surrogate or latent channel [48]. In practical settings, the filter $\mathbf{w}$ is obtained using training samples according to a selected criterion expressing the application needs regarding the structure or origin of $s(t)$. This approach is very popular to estimate brain sources from scalp recordings [79, 132], whose features can then be used in classification contexts [133, 46, 48]. This section explains the principle of the powerful spatial filtering technique called Common Spatial Patterns (CSP) in a two-class problem and shows how the optimal filters can be computed analytically. There exists a large number and variants of spatial filtering approaches which are suited for single-class or multi-class problems, and which can be model-based or fully data-driven. Independent Component Analysis (ICA), to only cite one, is a very well known example of data-driven filtering method which is largely employed in neurophysiology [134, 135, 136]. CSP is chosen here for its simplicity and because it introduces the techniques presented in Chapters 9 and 10.

Based on signals from two classes $\mathbf{x}_1(t)$ and $\mathbf{x}_2(t) \in \mathbb{R}^C$, with zero-mean along time, CSP aims at finding a linear filter $\mathbf{w}$ which maximizes the ratio of variance of the filtered signals $s_1(t) := \mathbf{w}^T \mathbf{x}_1(t)$ and $s_2(t) := \mathbf{w}^T \mathbf{x}_2(t)$ [133, 137, 138]. In other words, it computes the filter which maximizes the signal power in the first class compared to the second one as follows:

$$\mathbf{w}_{\text{csp}} = \arg \max_{\mathbf{w}} \left\{ F_{\text{csp}}(\mathbf{w}) = \frac{\sum_t (s_1(t))^2}{\sum_t (s_2(t))^2} = \frac{\mathbf{w}^T C_1 \mathbf{w}}{\mathbf{w}^T C_2 \mathbf{w}} \right\}, \quad (8.2)$$

where $C_i = \mathbb{E}_t \{ \mathbf{x}_i(t) \mathbf{x}_i(t)^T \} \in \mathbb{R}^{C \times C}$ for $i \in \{1, 2\}$. This approach is data-driven as the filter $\mathbf{w}$ is not constrained and no generative model is assumed. Alternatively, (8.2) can also be minimized to obtain the filtered components with maximal power in the second class instead of the first one. Once an optimal filter is found by optimizing $F_{\text{csp}}(\mathbf{w})$, a second filter can be found, leading to an optimal component in the orthogonal subspace of the first one, and a matrix $\mathbf{W} \in \mathbb{R}^{C \times C}$ is hence recursively built, whose columns are the filters ranked in decreasing order of specificity for class 1.

Regarding the solution of (8.2), it can be noted that $F_{\text{csp}}(\mathbf{w})$ is a generalized Rayleigh quotient. More generally, given two square and symmetric matrices $\mathbf{A}$ and $\mathbf{B} \in \mathbb{R}^{C \times C}$, $\mathbf{B}$ being positive definite, the generalized Rayleigh quotient of a vector $\mathbf{x} \in \mathbb{R}^C$ is defined as

$$R_G(\mathbf{x}) = \frac{\mathbf{x}^T \mathbf{A} \mathbf{x}}{\mathbf{x}^T \mathbf{B} \mathbf{x}}. \quad (8.3)$$

Besides, it is said that $\mathbf{x}_i \in \mathbb{C}_0^n$ and $\lambda_i \in \mathbb{C}$ are respectively generalized eigenvector and eigenvalue for the matrix pair $(\mathbf{A}, \mathbf{B})$ if they satisfy the equation

$$\mathbf{A}\mathbf{x}_i = \lambda_i \mathbf{B}\mathbf{x}_i. \quad (8.4)$$

In matrix form, when C generalized eigenvectors can be found, this leads to the Generalized Eigenvalue Decomposition (GEVD)

$$\mathbf{A}\mathbf{X} = \mathbf{B}\mathbf{X}\mathbf{\Lambda}, \quad (8.5)$$

where $\mathbf{X} \in \mathbb{C}^{C \times C}$ contains the generalized eigenvectors and $\mathbf{\Lambda} \in \mathbb{C}^{C \times C}$ is the diagonal matrix of generalized eigenvalues.

It is easy to show that $R_G(\mathbf{x})$ admits as stationary values the generalized eigenvalues of the matrix pair $(\mathbf{A}, \mathbf{B})$, with the corresponding arguments being the generalized eigenvectors:

$$\begin{aligned} \nabla R_G(\mathbf{x}) &= \frac{2(\mathbf{A}\mathbf{x} - R_G(\mathbf{x})\mathbf{B}\mathbf{x})}{\mathbf{x}^T \mathbf{B}\mathbf{x}} \\ &= 0 \Leftrightarrow \mathbf{x} \text{ is a generalized eigenvector of } (\mathbf{A}, \mathbf{B}) \end{aligned} \quad (8.6)$$

As a consequence, the generalized eigenvectors associated with the smallest and largest generalized eigenvalues of $(\mathbf{A}, \mathbf{B})$ minimize and maximize $R_G(\mathbf{x})$ respectively.

Concerning the existence of generalized eigenvectors leading to a generalized eigenvalue decomposition (GEVD), it can be shown ([139]) that if $\mathbf{A}$ and $\mathbf{B}$ are symmetric and $\mathbf{B}$ is positive definite then there exists a non-singular matrix $\mathbf{X} \in \mathbb{R}^{C \times C}$ such that

$$\mathbf{X}^T \mathbf{A} \mathbf{X} = \text{diag}(\lambda_1, \dots, \lambda_C) \quad \& \quad \mathbf{X}^T \mathbf{B} \mathbf{X} = \mathbf{I}_C. \quad (8.7)$$

The columns of $\mathbf{X}$ are hence generalized eigenvectors for $(\mathbf{A}, \mathbf{B})$. It may be noted that if non-symmetric matrices $\mathbf{A}$ and $\mathbf{B}$ are considered in the optimization of a generalized Rayleigh quotient, the obtained GEVD is not guaranteed to be real (similarly as for the eigenvalue decomposition).

Once the filters are optimized, features can be defined for subsequent classification, such as $\log(\mathbf{w}^T \mathbf{C} \mathbf{w})$, with $\mathbf{C}$ the covariance matrix of the test signal [133, 140, 141, 142].

CSP has found numerous applications thanks to the generality of its objective function in order to maximize the variance of the filtered signal along time seg-

ments of interest, thereby enhancing the signal-to-noise ratio of these segments. This technique has been successfully employed to differentiate brain states based on EEG recordings, for instance to detect abnormalities [133], to identify the direction of imaginary movements of the arms in BCI systems [141, 143] or to detect the presence of epileptic activity [137]. Unless a sufficient amount of training data is available [46, 45], CSP is known to be sensitive to noise and outliers and can therefore be prone to overfitting [144, 143]. That is why several regularization schemes have been developed to improve its classification performances, by adapting either the considered covariance matrices or directly the objective function [143, 144, 145].

Chapter 9

Spatial filtering to maximize periodicity

LONG-LASTING periodic sensory stimulation is increasingly used in neuroscience to study, using electroencephalography (EEG), the cortical processes underlying perception in different modalities. This kind of stimulation can elicit synchronized periodic activity at the stimulation frequency in neuronal populations responding to the stimulus, referred to as a steady-state response (SSR). While the frequency analysis of EEG recordings is particularly well suited to capture this activity, as illustrated in Part I, it is limited by the intrinsic noisy nature of EEG signals and the low signal-to-noise ratio (SNR) of some responses. This chapter therefore compares and adapts spatial filtering methods for periodicity maximization to enhance the SNR of periodic EEG responses, a key condition to generalize their use as a research or clinical tool. This approach uncovers both temporal dynamics and spatial topographic patterns of SSRs, and is validated using the EEG data from 15 healthy subjects exposed to periodic cool and warm stimuli that are described in Chapter 6.

9.1 Introduction

Understanding the neural mechanisms underlying human perception of stimuli from different modalities, such as visual, auditory, tactile or nociceptive, is a challenging issue in neuroscience. In this context, scalp electroencephalography (EEG) is particularly suited to record brain activity, as it is non-invasive and directly measures neuronal activity with a high temporal resolution of the millisecond order. Meanwhile, most studies consider brief sensory stimuli, lasting less than one second and eliciting well-known event-related potentials (ERPs) [24]. However, the recording of neural responses to long-lasting periodic stimulation is increasingly proposed in several works as an alternative to probe sensory perception [146], since it reveals new aspects of the sensory information processing [103]. Such long-lasting stimuli indeed induce a periodic activity at the stimulation frequency in some neuronal populations. This so-called steady-state response (SSR) can usually be recorded with multichannel EEG.

One of the main advantages of the aforementioned periodic stimuli is that the signal-to-noise ratio (SNR) of the SSR is usually higher in the frequency domain compared to the time domain. Therefore, most neuroscience works up to now use frequency analyses to highlight the SSR features. The EEG time course and frequency transform at some specific electrodes can be studied, as well as the distribution across the scalp of the signal amplitude at the stimulation frequency. Although these approaches provide direct measures of the signal periodicity, their efficiency is limited when the SNR is low. For instance, this is the case with nociceptive SSRs generated from infrared laser stimulation [35]. In the meantime, whereas linear filtering methods have been successfully developed in the context of brain-computer interfaces (BCI) to classify steady-state visually evoked-potentials (SSVEP) [41, 39], they were surprisingly not yet adapted to extract, interpret and characterize the EEG activity related to different periodic stimuli. Indeed, while the optimized filters can lead to high classification accuracies, their spatial patterns may also refine the analysis of SSRs.

In this context, this chapter compares filtering methods maximizing the periodicity of the extracted components to study and, more importantly, interpret the cortical processing of periodic stimuli. The filters are constrained to be linear, thereby defining meaningful topographic patterns of the associated components. Besides, the objective is to extract periodic components which are not strictly sinusoidal, namely whose spectral content is not necessarily concentrated around a single narrow frequency band [147, 45]. We propose to adapt four spatial filtering methods to enhance the SNR of SSRs. The two first methods are derived from a

measure of periodicity in the time domain, first introduced by Saul and Allen [148]. This approach, called Periodic Component Analysis (π CA), was initially used to extract periodic components from speech signals. Variants have been developed, handling for instance non-strictly periodic signals such as the electrocardiogram [149]. A third method is based on Canonical Correlation Analysis (CCA) between the multichannel EEG signals and a relevant reference periodic signal [41]. Finally, the last method directly optimizes the spectral concentration of the filtered signals at the fundamental stimulation frequency and its harmonics.

The rest of this chapter is organized as follows. Section 9.2 defines the compared methods in the context of our application. Section 9.3 presents empirical results validating the proposed methods on an EEG data set collected on 15 healthy subjects. Finally, Sect. 9.4 concludes and presents further perspectives.

9.2 Methods

This section introduces four methods aiming at extracting periodic components by filtering a noisy multidimensional signal $\mathbf{x}(t) \in \mathbb{R}^C$, assumed to have a zero-mean (i.e. $\sum_t \mathbf{x}(t) = 0$). Since the ultimate goal is to interpret the links between these components and the original signals, the spatial filters are constrained to be linear and will be denoted by vectors $\mathbf{w} \in \mathbb{R}^C$. These filters are optimized to define a maximally periodic component

$$s(t) := \mathbf{w}^T \mathbf{x}(t) \quad (9.1)$$

of fundamental frequency f_* and corresponding fundamental period $T_* = 1/f_*$. Once an optimal filter is found by optimizing a cost function F , a second optimal filter can be found, leading to a component in the orthogonal subspace of the first one. A matrix $W \in \mathbb{R}^{C \times d}$ is hence recursively built, whose columns are the filters ranked in decreasing order of periodicity of the filtered components as measured by F , which determines $d \leq C$. Pseudo-inverting the matrix $W^T \in \mathbb{R}^{d \times C}$ then estimates patterns of activity of the extracted components. Each filtered signal indeed has a fixed projection across the components of $\mathbf{x}$: writing the linear forward model as $\mathbf{x}(t) = A\mathbf{z}(t)$, with $\mathbf{z}(t) \in \mathbb{R}^{d \times 1}$ the periodic *sources*, estimates $W^T \approx A^{-1}$ are derived; the first column of $(W^T)^{-1}$ approximates the spatial pattern of the first estimated source signal $\mathbf{z}_1(t)$ [137].

9.2.1 Periodic Component Analysis

Periodic Component Analysis (π CA) [148] defines an optimal linear filter by minimizing a scale-invariant periodicity measure of the filtered signal $s(t) = \mathbf{w}^T \mathbf{x}(t)$:

$$\mathbf{w}_{\pi 1} = \arg \min_{\mathbf{w}} \left\{ F_{\pi 1}(\mathbf{w}) = \frac{\sum_t (s(t + T_*) - s(t))^2}{\sum_t (s(t))^2} = \frac{\mathbf{w}^T R_{\mathbf{x}}(T_*) \mathbf{w}}{\mathbf{w}^T C_{\mathbf{x}}(0) \mathbf{w}} \right\}, \quad (9.2)$$

where

$$R_{\mathbf{x}}(T_*) := \mathbb{E}_t \{ (\mathbf{x}(t + T_*) - \mathbf{x}(t)) (\mathbf{x}(t + T_*) - \mathbf{x}(t))^T \} \quad (9.3)$$

and

$$C_{\mathbf{x}}(\tau) = \mathbb{E}_t \{ \mathbf{x}(t + \tau) \mathbf{x}(t)^T \} \quad (9.4)$$

The minimization of this generalized Rayleigh quotient is solved by the generalized eigenvalue decomposition (GEVD) of the matrix pair $(R_{\mathbf{x}}(T_*), C_{\mathbf{x}}(0))$. These two matrices being symmetric, the matrix of generalized eigenvectors W sorted in increasing order of magnitude of the associated generalized eigenvalues gives the components $W^T \mathbf{x}(t)$ ranked in decreasing order of periodicity [139].

9.2.2 Periodic Component Analysis Variant

Another periodicity measure can alternatively be optimized as:

$$\mathbf{w}_{\pi 2} = \arg \max_{\mathbf{w}} \left\{ F_{\pi 2}(\mathbf{w}) = \frac{\sum_t s(t + T_*) \cdot s(t)}{\sum_t (s(t))^2} = \frac{\mathbf{w}^T C_{\mathbf{x}}(T_*) \mathbf{w}}{\mathbf{w}^T C_{\mathbf{x}}(0) \mathbf{w}} \right\}. \quad (9.5)$$

This defines a variant [149] of π CA, denoted here by π CA₂. This problem can be similarly solved by a GEVD of the matrices $(C_{\mathbf{x}}(T_*), C_{\mathbf{x}}(0))$. It is noteworthy that whenever $C_{\mathbf{x}}(T_*)$ is symmetric, $R_{\mathbf{x}}(T_*) = 2 \cdot (C_{\mathbf{x}}(0) - C_{\mathbf{x}}(T_*))$ and (9.5) is hence equivalent to (9.2). For any real-world signal $\mathbf{x}$ however, $C_{\mathbf{x}}(T_*)$ is unlikely to be symmetric. Therefore (9.2) and (9.5) will typically not define the same filters.

9.2.3 Canonical Correlation Analysis

Another approach to extract periodic components from a multidimensional signal is based on Canonical Correlation Analysis (CCA) [150]. The principle is to maximize the correlation between a filtered signal and a linear combination of the components of a reference signal $\mathbf{y}(t)$, with the same length as $\mathbf{x}$. In our setting, the components of $\mathbf{y}$ are defined from the Fourier series of a periodic signal of fundamental frequency f_* : $\mathbf{y}(t) = (\sin(2\pi f_* t) \cos(2\pi f_* t) \sin(2\pi 2f_* t) \dots \sin(2\pi N_h f_* t) \cos(2\pi N_h f_* t))^T$, where N_h is a parameter indicating the number

of accounted harmonics [41]. The CCA optimization problem is

$$(\mathbf{w}_{\pi 3}, \mathbf{w}_{\pi 3-y}) = \arg \max_{\mathbf{w}, \mathbf{w}_y} \left\{ F_{\pi 3}(\mathbf{w}, \mathbf{w}_y) = \frac{\mathbf{w}^T C_{\mathbf{x};\mathbf{y}} \mathbf{w}_y}{\sqrt{\mathbf{w}^T C_{\mathbf{x}}(0) \mathbf{w} \cdot \mathbf{w}_y^T C_{\mathbf{y}}(0) \mathbf{w}_y}} \right\}, \quad (9.6)$$

where

$$C_{\mathbf{x};\mathbf{y}} = \mathbb{E}_t \{ \mathbf{x}(t) \mathbf{y}(t)^T \}. \quad (9.7)$$

Only the optimal filter $\mathbf{w}_{\pi 3}$ is interesting in our context. The filter $\mathbf{w}_{\pi 3-y}$ being also optimized, (9.6) amounts finding the filtered signal $\mathbf{w}_{\pi 3}^T \mathbf{x}(t)$ which is maximally correlated with an arbitrary periodic signal whose frequency content is limited to $N_h f_*$. The solution to (9.6) is obtained by diagonalizing $C_{\mathbf{x};\mathbf{y}}$, $C_{\mathbf{x}}(0)$ and $C_{\mathbf{y}}(0)$ using only two matrices W and W_y with the filters in their columns [151].

9.2.4 Spectral Contrast Maximization

Spectral contrast maximization (SCM) consists in maximizing the magnitude of some frequency components of the filtered signal, with respect to the whole spectrum energy [152]. It is recommended when the searched components are more easily separable in the frequency domain, i.e. when the frequency band to amplify is known a priori. Let $S(f) := \mathcal{F}_f \{s(t)\} = \mathbf{w}^T \mathcal{F}_f \{\mathbf{x}(t)\} = \mathbf{w}^T X(f)$ denotes the Fourier transform of the filtered signal at frequency f . The optimal SCM filter is then defined as

$$\mathbf{w}_{\pi 4} = \arg \max_{\mathbf{w}} \left\{ F_{\pi 4}(\mathbf{w}) = \frac{\mathbb{E}_{f \in \nu} \{|S(f)|^2\}}{\mathbb{E}_{f \in \mu} \{|S(f)|^2\}} = \frac{\mathbf{w}^T S_{\mathbf{x}} \mathbf{w}}{\mathbf{w}^T C_{\mathbf{x}}(0) \mathbf{w}} \right\}, \quad (9.8)$$

with

$$\nu := \{\pm f_*, \pm 2f_*, \dots, \pm N_h f_*\} \quad (9.9)$$

the set of considered frequencies, μ the whole frequency range (the Nyquist band for discrete signals),

$$S_{\mathbf{x}} := \mathbb{E}_{f \in \nu} \{X(f) X(f)^*\} \quad (9.10)$$

and using the Parseval's identity at the denominator [120]. The set ν contains negative frequencies to ensure the realness of the cross-spectrum matrix $S_{\mathbf{x}}$. Again, N_h is the number of harmonics to consider, including the fundamental frequency. This problem is solved using the GEVD of $(S_{\mathbf{x}}, C_{\mathbf{x}}(0))$.

Although the two last methods are formulated differently, they are intrinsically related. Indeed, CCA maximizes the correlation of the filtered signal with an arbi-

trary sum of sines and cosines at the harmonic frequencies, while SCM maximizes the Fourier amplitudes of the filtered signal at the same frequencies. In both cases, normalization ensures a scale-invariance of the solutions.

9.3 Processing EEG Signals

The comparison of the performances of the methods introduced in Sect. 9.2 is conducted on the EEG data set described in Chapter 6, whose definition is first summarized in Sect. 9.3.1 with some notations. Section 9.3.2 defines the quality criterion employed to quantitatively compare the methods, and Sect. 9.3.3 presents the results.

9.3.1 Experimental setting

We recorded scalp EEG on $N = 15$ healthy subjects to whom we applied sinusoidal stimulation with a thermal cutaneous stimulator (TCS) in 4 different conditions, as shown in Fig. 9.1: warm and cool with either a fixed or a variable active surface along the stimulation cycles. Five distinct zones of the TCS stimulation surface could indeed be controlled independently. Each stimulus consisted in a 0.2 Hz sinusoidal waveform lasting 15 periods (i.e. 75 seconds) and was applied to the right forearm. Each subject received 12 trials from each condition, leading to 48 trials in total presented in a randomized order. To reduce artifacts, these 12 trials are time-locked averaged for each condition before computing and applying the filters. The EEG was sampled at 1000Hz and recorded using 64 electrodes placed on the scalp according to the international 10/10 system. All signals were high-pass filtered above 0.05 Hz to remove slow drifts (4th order zero-phase Butterworth filter).

9.3.2 Quality Measure

In order to assess the quality of an extracted component, we define a periodicity measure for a given unidimensional signal $y(t)$ and fundamental frequency f_* . First, since each frequency amplitude $|Y(f)|$ is affected by some background noise, the average amplitude at 10 neighboring frequencies (5 higher and 5 lower) is removed from each frequency amplitude [103], resulting in a *noise-subtracted spectrum* $Y_{NS}(f) \in \mathbb{R}$. Then, the periodicity measure is defined as

$$M_\pi(y) = 100 \cdot \frac{\sum_{k=1}^{\lfloor f_s/(2 \cdot f_*) \rfloor} Y_{NS}(k \cdot f_*)}{\sum_f |Y(f)|}, \quad (9.11)$$

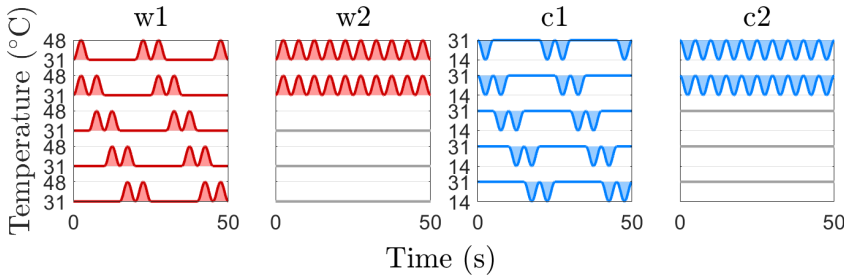


Fig. 9.1 Stimulation temperature profiles (only two thirds of the whole stimulus length of 75 seconds are shown for readability). Each row corresponds to the temperature of one of the five zones of the stimulator. w1 and w2 (resp. c1 and c2) indicate the two warm (resp. cool) conditions with a variable and fixed stimulation surface respectively.

with f_s the sampling frequency. In addition to accounting for the background noise, this measure is normalized with respect to the total signal amplitude. A positive (resp. negative) M_π suggests that the spectrum amplitude of y contains local maxima (resp. minima) on average at the harmonics $k \cdot f_\star$. It is noteworthy that the components extracted using the methods from Sect. 9.2 should maximize this measure. Meanwhile, these methods are constrained to produce a linear filtering of the original signals, thereby providing topographical patterns of the extracted components which can be interpreted.

9.3.3 Periodic Components Extraction

Before analyzing the results obtained with the methods described in Sect. 9.2, we can observe whether the periodic components are visible in the raw EEG signals. The topographies of the Fourier transforms at $f_\star = 0.2$ Hz, shown in Fig. 9.2, suggest that the periodic components seem to be most prominent at centro-frontal electrodes (see Fig. 9.2b). The periodicity of the EEG signal at electrode FCZ, where the periodicity is the largest on average across conditions, will hence be compared to the periodicity of filtered signals. The EEG time courses averaged over the stimulation periods as well as the spectra at this electrode are shown in Figs. 9.3 and 9.4 for all subjects. In both figures, the periodicity is visible for the warm conditions, while it is less clear for the cool ones, especially when the stimulation surface is fixed (condition c2). The average over the periods highlights more easily the periodic structure in the EEG, and in particular gives an estimate of the latency between the temperature and EEG peaks. The fact that the EEG peak in condition

c1 appears earlier than the temperature peak is discussed in Chapter 7.

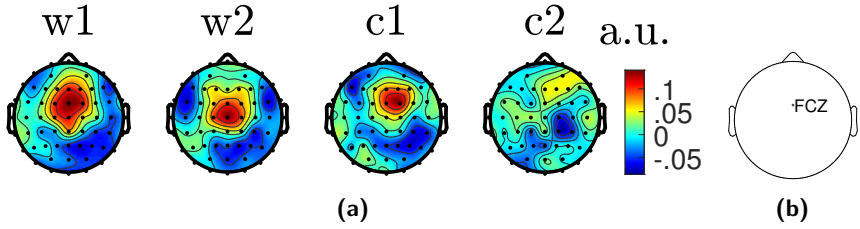


Fig. 9.2 Scalp topographies of (a) the group-level average noise-subtracted spectrum amplitudes at $f_{\star} = 0.2$ Hz and (b) the position of the FCZ electrode.

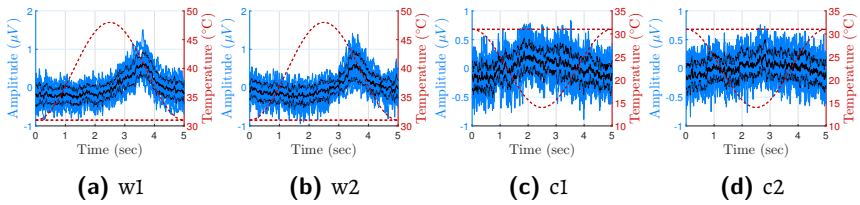


Fig. 9.3 EEG time courses averaged over the stimulation periods, at electrode FCZ for all 4 conditions. There is one curve per subject and the group-level average is in bold, with intervals of $\pm$ one standard deviation around the mean delimited with dotted lines. Dashed lines indicate the stimulation temperature.

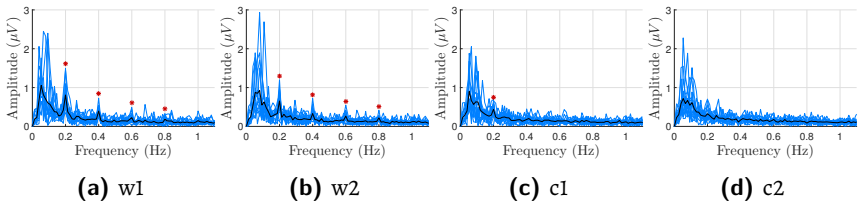


Fig. 9.4 EEG frequency spectrum at electrode FCZ for each subject and the 4 conditions. The group-level average is in bold. A star indicates significance of the noise-subtracted peaks (Sect. 9.3.2) at $k \cdot f_{\star} = k \cdot 0.2$ Hz (paired t -tests vs 0).

Performances of the periodicity-maximization methods are given in Table 9.1. First, the filter obtained from πCA_2 , $w_{\pi 2}$, outperforms the performances reached by $w_{\pi 1}$. Importantly, all filtering methods lead to a filtered signal with an improved periodicity compared to the raw EEG signal at FCZ, even when this raw signal is hardly periodic, such as for condition c2 for instance, which corresponds to

cool stimulation with a fixed stimulation surface. Two values of the parameter N_h are shown for CCA and SCM, chosen according to an analysis of the method performances as a function of N_h . This analysis revealed a saturating increase of the performances which was consistent for all the conditions: as long as N_h is chosen higher than approximately 8, M_π has almost reached a plateau. The results of this table also indicate that:

- The SS responses obtained when stimulating the forearm with a variable surface (conditions w1 and c1) exhibit a more pronounced periodicity compared to the stimuli applied with a fixed surface (w2 and c2). The periodicity measure indeed shows this difference for almost all the filtered and raw signals.
- CCA and SCM extract the same periodic components (for all signals). This is not very surprising regarding the similarity between these two methods that was discussed in Sect. 9.2; a deeper algorithmic comparison is left for future works.
- Performances of CCA and SCM are improved when the number of harmonics is increased, for all conditions. This further motivates the idea of extracting periodic non sinusoidal components instead of analyzing raw EEG frequency spectra or narrow-band signals [147, 45]: a single spatial pattern can regroup information from several harmonics.

The spatial patterns and filters obtained with the best filtering method (SCM with $N_h = 10$) are shown in Fig. 9.5. These spatial patterns indicate the distribution of the most periodic component across the scalp. Besides, the spatial filters have more intricate scalp topographies than their associated patterns as they need to cancel the other interfering (noise) components [47]. In addition, the associated component time courses, averaged over the stimulation periods, and their Fourier transforms are given in Figs. 9.6 and 9.7, the y-scales of the latter differing from Fig. 9.4. These two last figures show the high periodicity of the filtered signals. This is in striking contrast with the raw signals at FCZ, especially for condition c2 depicted in Fig. 9.3d (with its spectrum in Fig. 9.4d), where no clear periodicity was visible. However, all methods rank, according to M_π , the components for each condition (i.e. the entries in each column of Table 9.1) in almost the same order as the FCZ signals (i.e. first column of Table 9.1), which encourages the valid interpretation of the filtered signal. Further validation will be conducted to ensure that the periodic amplified activity indeed reflects stimulation-related patterns. The average curves from Fig. 9.6 are also interesting as they show the time lag between the temperature peaks and the extracted part of the SSR. In particular,

Table 9.1 Mean(std) for the 15 subjects of the periodicity measure M_π of the components extracted with the periodicity-maximization methods of Sect. 9.2: periodic component analysis (π CA), its variant (π CA₂), canonical correlation analysis (CCA) and spectral contrast maximization (SCM). For each stimulation type (row), the best performances are in bold and the corresponding signals are statistically significantly more periodic than the other ones of the same row. Significance is computed with paired t -tests and is adjusted for multiple comparisons using the Holm-Bonferroni correction.

	FCZ Signal	π CA	π CA ₂	CCA		SCM	
				$N_h = 1$	$N_h = 10$	$N_h = 1$	$N_h = 10$
w1	1.02(0.49)	1.60(1.72)	2.61(1.46)	2.84(1.20)	3.04(1.15)	2.84(1.20)	3.04(1.15)
w2	0.80(0.51)	1.50(1.65)	2.16(1.46)	2.70(0.96)	2.93(1.01)	2.70(0.96)	2.93(1.01)
c1	0.19(0.24)	0.39(0.40)	1.29(0.70)	1.99(0.56)	2.17(0.57)	1.99(0.56)	2.17(0.57)
c2	0.06(0.31)	0.44(0.51)	0.93(0.59)	1.88(0.41)	2.03(0.47)	1.88(0.41)	2.03(0.47)

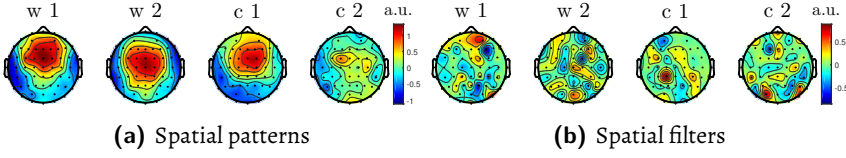


Fig. 9.5 Group-level average spatial patterns and spatial filters (defined at the beginning of Sect. 9.2) of the first component extracted with SCM ($N_h = 10$).

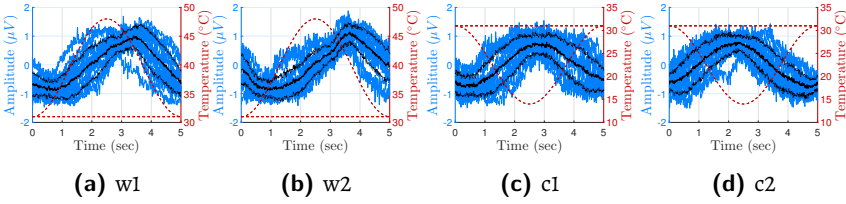


Fig. 9.6 Average over the stimulation periods of the optimal component extracted with SCM ($N_h = 10$). There is one curve per subject and the group-level average is in bold, with intervals of $\pm$ one standard deviation around the mean delimited with dotted lines. Dashed lines indicate the stimulation temperature.

we observe a longer time lag for both warm conditions compared to the cool ones. This is in accordance with the fact that cool stimuli activate thinly-myelinated A δ fibers [93], while the employed warm periodic stimuli most probably activate unmyelinated C fibers with slower conduction velocities [35].

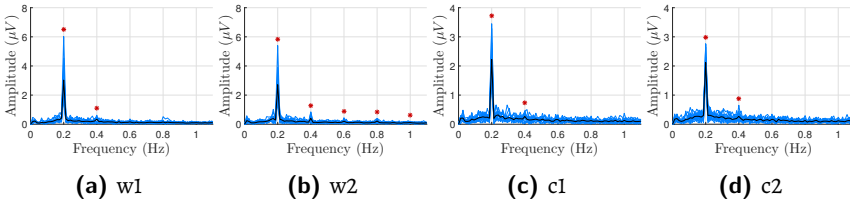


Fig. 9.7 Frequency spectrum of the components extracted with SCM ($N_h = 10$) for each subject. The group-level average is in bold. A star indicates significance of the noise-subtracted peaks (Sect. 9.3.2) at $k \cdot 0.2$ Hz (paired t -tests vs 0).

9.4 Conclusions and Perspectives

This chapter suggests employing spatial filters to enhance the SNR of EEG responses elicited by periodic sensory stimulation. Four approaches are detailed and compared on an EEG data set recorded on 15 healthy subjects exposed to four different kinds of long lasting sinusoidal thermal stimuli. We show that these methods are able to extract periodic components from signals which do not necessarily exhibit a pronounced temporal periodicity. The estimated spatial activity patterns as well as the component time courses can hence characterize the steady-state responses.

As to further perspectives, the filtering methods considered in this work have been applied to the EEG signals averaged over the trials, enhancing their phase-locked components. Studying the periodic responses on a trial-basis, possibly using tensor methods, would enable determining whether and to which extent phase variability across trials affects the observed SSR. Another line of work is related to the analysis of the multiple suboptimal components, in terms of periodicity, extracted by the linear filters defined in Sect 9.2. Whereas this chapter focuses on the periodicity and spatial patterns of the optimal component identified by each method, it is very likely that the linear space spanned by the spatial patterns reflecting stimulation-related activity is more than one-dimensional in the studied EEG data. The considered linear filters moreover cannot compensate some phase changes across channels reflecting the propagation of the SSR within brain regions. This hence suggests analyzing the links between the time dynamics of different filtered components and their spatial localization on the scalp.

Chapter 10

Spatial filtering to extract specific periodic components

EXTRACTING relevant information from noisy multidimensional signals has tremendous impacts in numerous applications, ranging from audio separation to electrophysiological recording analysis. Linear filters are often considered to reconstruct and interpret the latent sources generating the data. Known properties of the sources can be used to guide their separation. In neuroscience, the cortical processes underlying perception in different modalities (visual, auditory, ...) is often studied using electroencephalography (EEG) during periodic stimulation, eliciting periodic activity in neural sources, some of which being specific to the considered modality. Whereas current approaches extract sources either periodic or discriminative, none of them accounts for both aspects at once. This chapter proposes several methods extracting periodic sources specific between two classes, hence termed as Linear Periodic Discriminant Analysis methods. They are validated on synthetic data and EEG recordings of subjects to whom periodic stimulation from two modalities is applied. The methods enable uncovering modality-specific periodic responses.

10.1 Introduction

Multidimensional signals are encountered in a broad range of situations including music editing, speech recognition or physiological monitoring. In many cases, such observed signals result from the noisy mixing of several components or sources of interest [153]. So-called source separation algorithms are therefore considered to recover the latent sources. The mixing is often linearly approximated, allowing an easy interpretation of the sources in the original sensor space. Independent Component Analysis (ICA) methods are probably the most well-known approaches to this kind of problems, only relying on the minimal assumption of independence between the source signals [134]. ICA has proven to be very useful in many contexts, including the extraction of single speech signal from mixed recordings [136] or artifacts removal from electrophysiological signals [135]. In several applications however, specific structures of the latent sources are expected, which can be used to guide the definition of source separation algorithms. In audio signal processing for instance, diverse forms of guidance have already been considered, using either priors on the mixing processes or the temporal dynamics of the sources [154]. Such temporal structures are also exploited in the study of biological signals, for instance to enhance periodic components of a given multidimensional signal [4]. Other works have extended this kind of methods to extract quasi-periodic signals such as the electrocardiogram [149].

In this line, structured, and in particular periodic, signals also often arise in neuroscience. For instance, periodic stimulation is increasingly proposed to probe sensory perception in humans [146]. This kind of stimulus elicit a periodic activity at the stimulation frequency in some neural populations, known as a steady-state response (SSR), which can be partly recorded with electroencephalography (EEG). Each source contributing to the SSR associated to stimuli from one modality (e.g. visual, auditory, tactile,...) can be common to several studied modalities, or specific to a particular one. As an example, if cool and warm periodic stimuli are applied to a subject, part of the SSR can be expected to be common to the two classes, warm and cool, since both stimuli share some characteristics (they both activate the spinothalamic system). To study the specific cortical processing of each class of stimulus however, one is more interested in finding the most discriminant components of the SSR. Although linear filtering methods aiming to extract either periodic or discriminant components exist and are well-documented in the literature, the optimization of filters defining periodic components which are specific to one class of signals among two has surprisingly not yet been studied. Such a method would better capture the mechanisms governing specific sensory

perception in humans, thereby helping to understand and subsequently diagnose sensory disorders. In this context, this chapter presents methods to extract such sources. The approach is inspired, on the one hand, by the source separation methods aiming to maximize periodicity of the extracted components [4] and, on the other hand, by the Common Spatial Pattern (CSP) algorithm largely studied and adapted in Brain-Computer Interfacing (BCI) researches [48, 143]. The specific periodic components are obtained by optimizing interpretable linear filters, hence the name of the presented approach: Linear Periodic Discriminant Analysis (LPDA). Several objective functions are proposed, compared and assessed on synthetic and real data. In particular, results on both simulated and real data are convincing, the presented methods enabling the discovery of modality-specific periodic structures. Our methodology, combining periodicity and discrimination maximization, outperforms state-of-the-art approaches accounting for one of both aspects at once.

The chapter is organized as follows. Section 10.2 introduces and motivates the definition of several LPDA objective functions. Experiments are conducted in Sect. 10.3, both on synthetic and EEG data. Section 10.4 finally concludes the work.

10.2 Linear Periodic Discriminant Analysis Methods

This section defines and justifies the proposed approaches to extract periodic components specific to one among two multidimensional signals, belonging to two different classes. The zero-mean (over time) signals from the first and second classes, respectively denoted by $\mathbf{x}_1(t)$ and $\mathbf{x}_2(t) \in \mathbb{R}^C$, are assumed to result from the linear mixing of latent periodic sources. For instance, they can be C -channel EEG signals recorded on one subject in two different conditions, e.g. exposed to periodic warm vs. cool stimulation. The sources, of period T_* and fundamental frequency $f_* = 1/T_*$ for both classes 1 and 2, can either be common to both signals or specific to $\mathbf{x}_1$ or $\mathbf{x}_2$. This leads to the noiseless latent model

$$\mathbf{x}_i(t) = A_u \mathbf{z}_u(t) + A_{s,i} \mathbf{z}_{s,i}(t), \quad (10.1)$$

where $i \in \{1, 2\}$ and s (resp. u) indexes the *specific* (resp. *unspecific*) mixing matrices $A_{s,i} \in \mathbb{R}^{C \times N_{s,i}}$ (resp. $A_u \in \mathbb{R}^{C \times N_u}$) and periodic sources $\mathbf{z}_{s,i}(t) \in \mathbb{R}^{N_{s,i}}$ (resp. $\mathbf{z}_u(t) \in \mathbb{R}^{N_u}$), $N_{s,i}$ (resp. N_u) being the number of specific (resp. unspecific) sources. In practice, different sources of noise will also affect the observed signals.

10 | Spatial filtering to extract specific periodic components

Also, each specific source has a distinct level of specificity expressed by its variance. For convenience, the sources in a vector are ordered in decreasing order of specificity; for instance, $\mathbf{z}_{s,1}^1(t)$ is the most specific source for class 1, where the exponent indicates the component of the vector $\mathbf{z}_{s,1}(t)$. Each column of a mixing matrix A is a spatial pattern of the associated source [137]. Under this framework, both the specific spatial patterns $A_{s,i}$ and the specific source time courses $\mathbf{z}_{s,i}(t)$ should be recovered using $\mathbf{x}_1$ and $\mathbf{x}_2$. To this end, spatial filters $\mathbf{w} \in \mathbb{R}^C$ are optimized to obtain filtered signals

$$s_i(t) := \mathbf{w}^T \mathbf{x}_i(t) \quad (10.2)$$

such that $s_1(t) \approx \mathbf{z}_{s,1}^1(t)$. Similarly, the filters can be optimized for class 2 to obtain $s_2(t) \approx \mathbf{z}_{s,2}^1(t)$ instead. Once a first optimal filter $\mathbf{w}_1$ for class i is found by optimizing a cost function F , a second optimal filter can be obtained, leading to a component in the orthogonal subspace of the first one. A matrix $W \in \mathbb{R}^{C \times C}$ is hence recursively built, whose columns $\mathbf{w}_k$ are the filters ranked according to F . The first $N_{s,i}$ columns of the pseudo-inverse of W^T then estimate the spatial patterns of the extracted components for class i : $[(W^T)^{-1}](:, 1 : N_{s,i}) = \widehat{A}_{s,i}$.

In order to obtain optimized filters, one must first define relevant cost functions characterizing the class-specific periodicity of the filtered signals. In the following, we propose several such objective functions, based on generalized Rayleigh quotients capturing periodicity differences, to obtain the filters for the specific activity of class 1, without loss of generality; both classes can be swapped to obtain the specific activity of class 2.

- **Method 1 (M1).** Periodic Component Analysis [148, 4] aims to extract periodic sources from a single data set based on the periodicity measure

$$\frac{\sum_t (s(t + T_\star) - s(t))^2}{\sum_t (s(t))^2} \quad (10.3)$$

of the signal $s(t)$. In the studied two-classes setting, a ratio of periodicity inspired by this measure can be optimized to find components $s_i(t) = \mathbf{w}^T \mathbf{x}_i(t)$, being periodic in class 1 and not necessarily in class 2:

$$\mathbf{w}_1 = \arg \min_{\mathbf{w}} \left\{ F_1(\mathbf{w}) = \frac{\sum_t (s_1(t + T_\star) - s_1(t))^2}{\sum_t (s_2(t + T_\star) - s_2(t))^2} = \frac{\mathbf{w}^T R_1(T_\star) \mathbf{w}}{\mathbf{w}^T R_2(T_\star) \mathbf{w}} \right\}, \quad (10.4)$$

where

$$R_i(T_\star) = \mathbb{E}_t \{ (\mathbf{x}_i(t + T_\star) - \mathbf{x}_i(t)) (\mathbf{x}_i(t + T_\star) - \mathbf{x}_i(t))^T \}. \quad (10.5)$$

It can be noted that $F_1(\mathbf{w}) \geq 0$ and that $F_1(\mathbf{w}) = 0$ for a perfectly periodic signal $s_1(t)$. However, $F_1(\mathbf{w}) = 0$ as well when $s_1(t) = 0$ even though a flat signal may probably not be related to the sources of interest. This objective should hence be used with caution when some channels are correlated, in which case $s_1(t)$ could be 0.

- **M2.** Alternatively, the periodicity of the filtered signals can be emphasized by a simple averaging over the fundamental periods:

$$s_{\mu i}(t) := \frac{1}{K} \cdot \sum_{k=0}^{K-1} s_i(t + kT_*) := \mathbf{w}^T \mathbf{x}_{\mu i}(t), \quad (10.6)$$

with K the number of periods in the available signals. As in the CSP algorithm [48], the variance ratio of these averaged signals can be optimized as

$$\mathbf{w}_1 = \arg \max_{\mathbf{w}} \left\{ F_2(\mathbf{w}) = \frac{\sum_t (s_{\mu 1}(t))^2}{\sum_t (s_{\mu 2}(t))^2} = \frac{\mathbf{w}^T C_{\mu 1} \mathbf{w}}{\mathbf{w}^T C_{\mu 2} \mathbf{w}} \right\}, \quad (10.7)$$

where $C_{\mu i} = \mathbb{E}_t \{ \mathbf{x}_{\mu i}(t) \mathbf{x}_{\mu i}(t)^T \}$.

- **M3.** Another approach is based on Canonical Correlation Analysis (CCA), which was already proposed to extract periodic components [41]. In the present work however, the method maximizes the correlation between the differences of the filtered signals in both classes and an arbitrary periodic signal $\mathbf{w}_y^T \mathbf{y}(t)$ of the same length as s_i . This periodic signal is defined from the Fourier series of a periodic signal of fundamental frequency f_* : $\mathbf{y}(t) = (\sin(2\pi f_* t) \cos(2\pi f_* t) \sin(2\pi 2f_* t) \dots \sin(2\pi N_h f_* t) \cos(2\pi N_h f_* t))^T$, where N_h indicates the number of accounted harmonics. Since the correlation $\mathbb{E}_t \{ \mathbf{w}^T (\mathbf{x}_1(t) - \mathbf{x}_2(t)) \mathbf{y}(t)^T \mathbf{w}_y \}$ must be maximized with scale invariance, the optimization problem is formulated as

$$(\mathbf{w}_1, \mathbf{w}_{1,y}) = \arg \max_{\mathbf{w}, \mathbf{w}_y} \left\{ F_3(\mathbf{w}, \mathbf{w}_y) = \frac{\mathbf{w}^T (C_{1;y} - C_{2;y}) \mathbf{w}_y}{\sqrt{\mathbf{w}^T C_{12} \mathbf{w} \cdot \mathbf{w}_y^T C_y \mathbf{w}_y}} \right\}, \quad (10.8)$$

where $C_{i;y} = \mathbb{E}_t \{ \mathbf{x}_i(t) \mathbf{y}(t)^T \}$, $C_{12} = \mathbb{E}_t \{ (\mathbf{x}_1(t) - \mathbf{x}_2(t)) (\mathbf{x}_1(t) - \mathbf{x}_2(t))^T \}$ and $C_y = \mathbb{E}_t \{ \mathbf{y}(t) \mathbf{y}(t)^T \}$. This method is only well suited when the common activity is assumed to be highly similar (in terms of amplitude and phase) in both classes, leading to its cancellation through the point-by-point difference

$$\mathbf{x}_1(t) - \mathbf{x}_2(t).$$

- **M4.** Inspired by the Spectral Contrast Maximization (SCM) approach [152], the ratio of spectral content at the fundamental frequency f_* and its harmonics in both classes can be optimized. With $S_i(f) := \mathcal{F}_f\{s_i(t)\} = \mathbf{w}^T \mathcal{F}_f\{\mathbf{x}_i(t)\} = \mathbf{w}^T X_i(f)$ the Fourier transform of the filtered signals at frequency f , a fourth objective can be formulated in the following way:

$$\mathbf{w}_1 = \arg \max_{\mathbf{w}} \left\{ F_4(\mathbf{w}) = \frac{\mathbb{E}_{f \in \nu} \{|S_1(f)|^2\}}{\mathbb{E}_{f \in \nu} \{|S_2(f)|^2\}} = \frac{\mathbf{w}^T S_{\mathbf{x}_1} \mathbf{w}}{\mathbf{w}^T S_{\mathbf{x}_2} \mathbf{w}} \right\}, \quad (10.9)$$

with $\nu := \{\pm f_*, \pm 2f_*, \dots, \pm N_h f_*\}$ the set of frequencies of interest and $S_{\mathbf{x}_i} := \mathbb{E}_{f \in \nu} \{X_i(f) X_i(f)^*\}$. This objective is expected to be maximized by concentrating the frequency content of $s_1(t)$ to these frequencies. It should however be stressed that it can also be maximized if its denominator tends toward 0 while keeping the numerator bounded.

- **M5.** The quantity $\sum_t (s_i(t + T_*) - s_i(t))^2$ is used in (10.4) to describe the periodicity of the signal $s_i(t)$. An alternative periodicity measure which can be considered is $\sum_t s_i(t + T_*) \cdot s_i(t)$ [149], leading to the optimization problem

$$\begin{aligned} \mathbf{w}_1 &= \arg \max_{\mathbf{w}} F_5(\mathbf{w}), \text{ with} & (10.10) \\ F_5(\mathbf{w}) &= \frac{\sum_t s_1(t + T_*) \cdot s_1(t) - s_2(t + T_*) \cdot s_2(t)}{\sum_t (s_1(t))^2 + (s_2(t))^2} \\ &= \frac{\mathbf{w}^T (C_1(T_*) - C_2(T_*)) \mathbf{w}}{\mathbf{w}^T (C_1(0) + C_2(0)) \mathbf{w}}, \end{aligned}$$

where $C_i(\tau) = \mathbb{E}_t \{\mathbf{x}_i(t + \tau) \mathbf{x}_i(t)^T\}$. Note that a difference of periodicity between the two classes is considered instead of a ratio similar to (10.4), because the matrices $C_i(T_*)$ are not necessarily positive definite contrarily to $R_i(T_*)$.

- **M6.** Another variant of (10.4) can be defined using a difference instead of a ratio of periodicity. A distinct normalization ensures the scale-invariance of the filters:

$$\mathbf{w}_1 = \arg \min_{\mathbf{w}} \left\{ F_6(\mathbf{w}) = \frac{\mathbf{w}^T (R_1(T_*) - R_2(T_*)) \mathbf{w}}{\mathbf{w}^T (C_1(0) + C_2(0)) \mathbf{w}} \right\}. \quad (10.11)$$

- **M7.** A similar change can be applied to (10.9), leading to a last formulation:

$$\mathbf{w}_1 = \arg \max_{\mathbf{w}} \left\{ F_7(\mathbf{w}) = \frac{\mathbf{w}^T (S_{\mathbf{x}_1} - S_{\mathbf{x}_2}) \mathbf{w}}{\mathbf{w}^T (C_1(0) + C_2(0)) \mathbf{w}} \right\}. \quad (10.12)$$

All the objective functions above, except the third one, are expressed as generalized Rayleigh quotients of the form

$$\frac{\mathbf{w}^T \mathbf{A} \mathbf{w}}{\mathbf{w}^T \mathbf{B} \mathbf{w}} \quad (10.13)$$

and can be solved by the generalized eigenvalue decomposition (GEVD) of the matrix pair $(\mathbf{A}, \mathbf{B})$, yielding a set of filters $\{\mathbf{w}_k\}_{k=1}^C$ corresponding to the generalized eigenvectors ranked in decreasing or increasing order of cost function values, depending on whether the objective function is maximized or minimized. When $\mathbf{A}$ is symmetric and $\mathbf{B}$ positive-definite, the decomposition is real and hence interpretable [139]. The formulation (10.8) is also solved analytically, as for classical CCA [151].

It is here assumed that the filters are ranked in decreasing order of specificity for class 1, hence with $\mathbf{w}_1$ being the most specific filter for class 1. The successive extracted sources are denoted by

$$s_i^k(t) := \mathbf{w}_k^T \mathbf{x}_i(t). \quad (10.14)$$

10.3 Experimental Results

This section assesses the methods introduced in Sect. 10.2. Their behavior and performances are first studied and compared in Sect. 10.3.1 on synthetic data, for which the latent sources are known. Then, preliminary results on the real EEG data set from chapter 6 are presented in Sect. 10.3.2, for which the specific patterns are obtained. As to the quality assessment, different criteria are proposed in Sect. 10.3.1.

10.3.1 Synthetic Data

As stated in Sect. 10.1, the studied methods aim to extract class-specific periodic components from two multidimensional signals. Therefore, synthetic data are generated by linearly mixing specific and common components for the two classes, with additional noise. Denoting by $X_i(t) \in \mathbb{R}^C$ the simulated data from class i at time sample t , $Z_{u,i}(t) \in \mathbb{R}^{N_u}$ and $Z_{s,i}(t) \in \mathbb{R}^{N_s}$ the common (i.e. unspecific

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to the class) and specific periodic factors respectively, for $i \in \{1, 2\}$, data are simulated according to the model

$$X_i(t) = \underbrace{A_u \cdot Z_{u,i}(t)}_{\text{periodic interference}} + \underbrace{A_s \cdot Z_{s,i}(t)}_{\text{signal}} + \underbrace{N_i(t)}_{\text{noise}}, \quad (10.15)$$

with the common and specific mixing matrices $A_u \in \mathbb{R}^{C \times N_u}$ and $A_s \in \mathbb{R}^{C \times N_s}$, $N_i(t) \in \mathbb{R}^C$ being additive random noise. The common activity can be seen as interferences in this problem. Although the mixing matrices are common to both classes, the factor (or source) time courses are not. In particular:

- the specific factors $Z_{s,1}$ and $Z_{s,2}$ are mutually independent, with distinct specificity levels expressed by their variances which are proportional to $(N_s - 1, N_s - 2, \dots, 1, 0)$ and $(0, 1, \dots, N_s - 2, N_s - 1)$ [138]. These sources are ordered in decreasing order of specificity for class 1, the first (resp. last) $\lfloor \frac{N_s}{2} \rfloor$ being specific to class 1 (resp. 2). If $N_s = 1$, there is no specific factor for class 2.
- The common factors $Z_{u,i}$ are equal in both classes, up to an arbitrary time lag, as the common activity can have distinct latencies, e.g. due to differences in fiber conduction velocities in the case of EEG signals.

For each simulation, the entries of the mixing matrices are uniformly distributed in $[0, 1]$ and the factors are random periodic signals of period T_* . However, since the performances of the optimized filters highly depend on the relative position in $\mathbb{R}^C$ of the columns of A_u with respect to the ones of A_s , the columns of A_s can be altered to reach some pre-defined angles with respect to the ones of A_u .

Regarding the assessment, different types of metrics can be considered.

- The reconstruction quality of the mixing matrix is evaluated using the canonical angle (CA) between the subspace spanned by the columns of A_s and its estimate $\widehat{A_s}$ computed from the optimized filters. The CA is the maximum angle found between orthogonal bases of these subspaces [139], and is therefore invariant to permutation and scaling of the columns of each matrix. Focusing on the most discriminant periodic source, the angle between the first true and estimated spatial patterns ($A_s^1 := A_s(:, 1)$ and $\widehat{A_s}^1 := \widehat{A_s}(:, 1)$) is also evaluated.
- The time-correlation $\text{corr}(s_1^1(t), \mathbf{z}_{s,1}^1(t))$ between the first true and estimated sources, $\mathbf{z}_{s,1}^1(t)$ being the first component of $\mathbf{z}_{s,1}(t)$, is insensitive to the

pseudo-inversion required to obtain the spatial patterns from the optimized filters.

- The periodicity difference between $s_1^1(t)$ and $s_2^1(t)$ assesses the relevance of the first filter $\mathbf{w}_1$ in terms of periodicity and discrimination. The following measure is employed to quantify the periodicity of a signal $y(t) \in \mathbb{R}$ at a frequency $f_\star$, as explained in Sect. 9.3.2:

$$M_\pi(y) = 100 \cdot \frac{\sum_{k=1}^{\lfloor f_s/(2 \cdot f_\star) \rfloor} Y_{NS}(k \cdot f_\star)}{\sum_f |Y(f)|}, \quad (10.16)$$

where f_s is the sampling frequency, $Y(f) = \mathcal{F}_f \{y(t)\}$ and Y_{NS} is the *noise-subtracted spectrum*. At frequency f , $Y_{NS}(f) \in \mathbb{R}$ is obtained by subtracting the average amplitude at 10 neighboring frequencies (5 higher and 5 lower) from the frequency amplitude $|Y(f)|$. Additional details are provided in [103, 4]. The components extracted using the methods from Sect. 10.2 should maximize $M_\pi(s_1^1) - M_\pi(s_2^1)$, while providing topographical patterns of the extracted components which can be interpreted thanks to the linear filtering. Only this criterion can be used on real data as it does not rely on the ‘true’ sources.

In the following, each signal is generated with $C = 20$ channels, a sampling rate of 500 Hz, $f_\star = 0.5$ Hz and a duration of 20 seconds. The signal variances are defined over the channels and time samples [152]. Denoting $\sigma_u^2 := \text{var}(A_u \cdot \mathbf{z}_{u,i}(t))$, $\sigma_s^2 := \text{var}(A_s \cdot \mathbf{z}_{s,i}(t))$ and $\sigma_N^2 := \text{var}(\mathbf{n}_i(t))$, the two first quantities control the signal-to-interference ratio (SIR), while the signal-to-noise ratio (in dB) is defined as

$$\text{SNR} = 10 \cdot \log_{10}(\sigma_s^2 / \sigma_N^2). \quad (10.17)$$

In order to simulate realistic EEG data, which are studied in Sect. 10.3.2, pink additive noise is chosen for $N_i(t)$, i.e. with a frequency power spectrum proportional to $1/f$ [155]. Unless stated otherwise, there are $N_u = 10$ unspecific factors and the SIR is fixed with $\sigma_u = 1$ and $\sigma_s = 1$. The canonical angles between A_u and A_s are $\geq 70^\circ$ and there is a time lag of 0.3 seconds between $Z_{u,1}(t)$ and $Z_{u,2}(t)$. The performances of the methods are commented with either 1 or 4 specific pattern(s) and then with varying unspecific activity according to N_u and σ_u .

- The performances of the methods with $N_s = 1$ specific factor are depicted in Figs. 10.1a to 10.1d. The angular position of the first specific pattern A_s^1 is also compared to the C -length vector of the Fourier frequency coefficients

of the mixed signals at f_* in Fig. 10.1a (curve labeled ‘FFT’). Although this pattern is usually employed in neuroscience studies to describe the periodic cortical activity elicited by periodic stimuli, it can be highly different from the spatial pattern of the source of interest. All the quality measures considered indicate the superiority of M7 to recover the specific pattern, followed by M2 and M5. Comparing Figs. 10.1b and 10.1c indicates that M3 probably amplifies common instead of specific activity, leading to both high $M_\pi(s_1^1)$ and $M_\pi(s_2^1)$. As this method uses a point-by-point difference between the two classes of signals, it is sensitive to a non-zero time lag between the common activity in both data sets.

- When $N_s = 4$, the results in Figs. 10.1e to 10.1h confirm the overall previous conclusions. The canonical angles between all the true and estimated specific patterns shown in Fig. 10.1f are larger than the angles computed only using the most specific pattern (Fig. 10.1e), indicating that the methods indeed recover more easily the first specific pattern. All methods are affected by the increased number of specific sources, and this effect is more pronounced for M1.
- The effects of σ_u and N_u on the M7 performances (the seemingly most efficient method) are shown in Fig. 10.2. For a fixed SIR, the number of common factors N_u only affects the performances when the SNR gets closer to 0, leading to better recovered spatial patterns as N_u increases. On the other hand, increasing σ_u deteriorates the recovery of the most specific pattern, especially when $N_s = 4$. Let us note that, unlike the angle, the correlation between the first true and estimated sources is almost independent of N_u and σ_u (see Figs. 10.2b, 10.2d, 10.2f and 10.2h), suggesting that increasing N_u or σ_u does not affect the first optimal filter but rather the following ones, which in turn influences the first pattern after inverting the filter matrix.

The results presented in this section are obtained on data with 20 channels. Similar conclusions can be drawn with different dimensions, although on average all the angles tend to increase with the dimension, as a consequence of the curse of dimensionality [156]. Results are also similar with different canonical angles between A_u and A_s , with overall decreasing performances when they tend to be small as it becomes impossible for a filter to be orthogonal to the interference patterns A_u . M2 is especially affected by the reduction of these angles, while M5 and M7 are more robust.

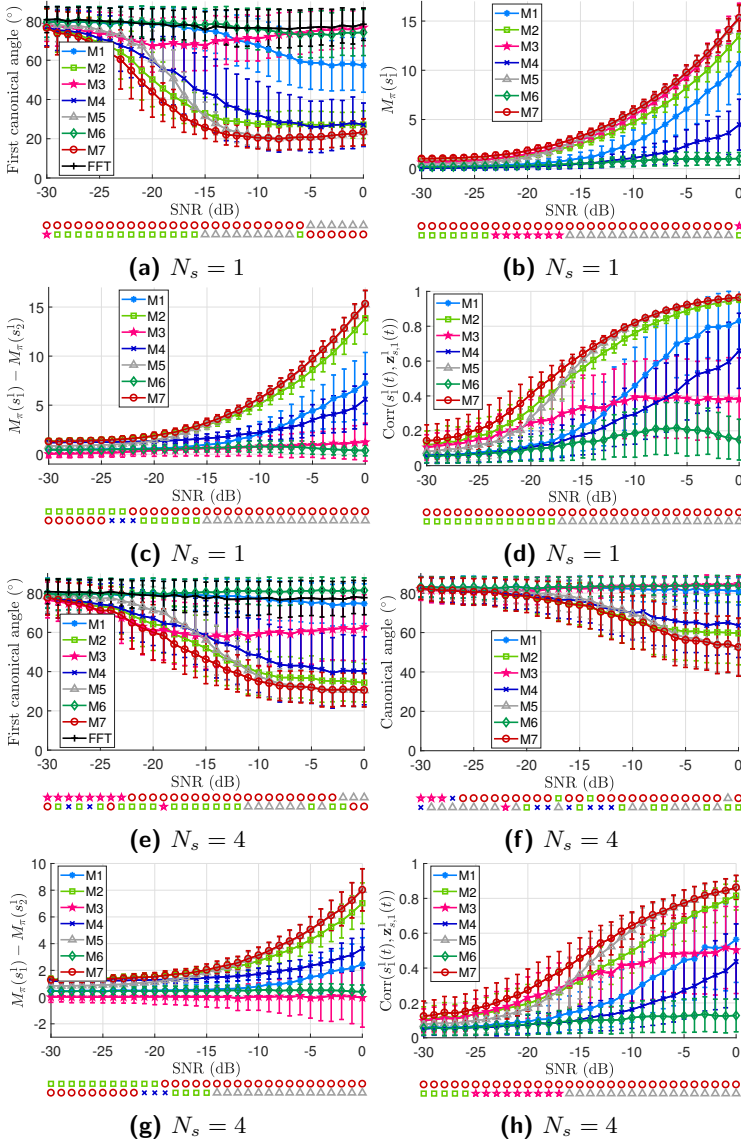


Fig. 10.1 Methods performances (mean $\pm$ std of 500 runs) on synthetic data as a function of the SNR. The two rows of markers below each figure indicate (1) the best method on average for each SNR and (2) the best method which is significantly outperformed by the best one (t -tests, Holm-Bonferroni corrected).

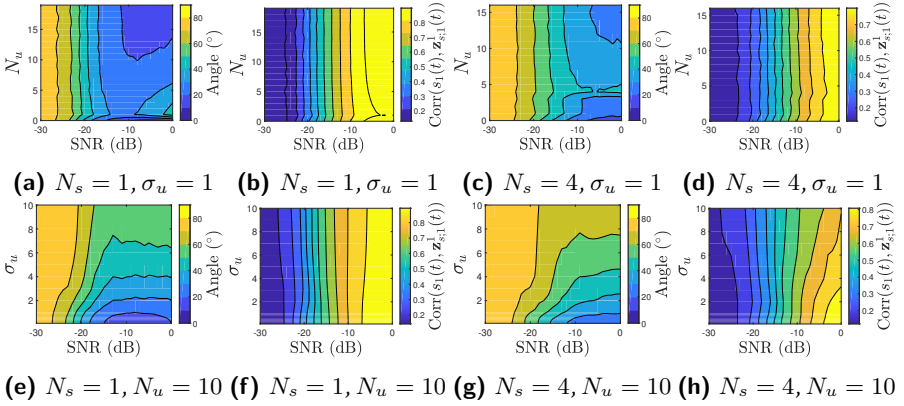


Fig. 10.2 Angle between the first specific true and estimated patterns (a, c, e, g) and correlation between the true and estimated most specific sources (b, d, f, h), for M7 on synthetic data as a function of the SNR and either N_u (a-d) or σ_u (e-h). Results are averaged over 500 signal generations and $\sigma_s = 1$.

10.3.2 Electroencephalogram (EEG) Data

This section shows brief results of the LPDA methods and of state-of-the-art filters on the EEG data set of Chapter 6, which was recorded on 15 healthy subjects to whom periodic stimulation from four classes was applied: painful warm or non-painful cool, each applied on a variable or fixed skin surface (denoted resp. by w1, w2, c1 and c2). Each subject received each kind of stimulus with a frequency $f_\star = 0.2$ Hz and a duration $T = 75$ seconds (15 cycles). From a neuroscientific point of view, interest lies in finding the specific components of the condition w1 compared to c1 and w2 compared to c2. It would allow to disentangle the neural processing of warm and cool stimuli, thereby providing cues on the specific brain responses to painful stimuli.

As to the compared methods, to the best of our knowledge, there is no existing approach optimizing both the periodicity and the specificity of an extracted component at once. The results of our methods are hence compared to one method maximizing the periodicity (SCM [4]), another one optimizing the discrimination (CSP [143]) and Principal Component Analysis (PCA), a widely used non-guided filtering method.

LPDA methods are applied on the EEG data of each subject to obtain, for each ordered pair of conditions among $\{w1-c1, w2-c2, c1-w1, c2-w2\}$, the most specific source for the first condition of the pair and its associated spatial pattern and filter. Each optimal filter w_1 can be applied to both signals of the pair to obtain

$s_1^1(t)$ and $s_2^1(t)$. Table 10.1 confirms the superiority of method M7, followed by M5, in terms of difference of periodicity in any two compared classes, as it was observed on synthetic data, with the periodicity measure (10.16). M2, M3 and M6 results are of the same order of magnitude as the ones of M4. Except for M7, the standard deviations are roughly of the same order as the mean results, indicating a high variability across subjects. It should be stressed that the performances of all methods vary coherently with respect to the subjects since M7 always statistically significantly outperforms the other schemes. These results are encouraging as they show that periodic components specific to one class can be extracted, M7 overcoming the three baselines. Further validations should be undertaken to disentangle physiologically interpretable patterns from potentially slightly overfitted results.

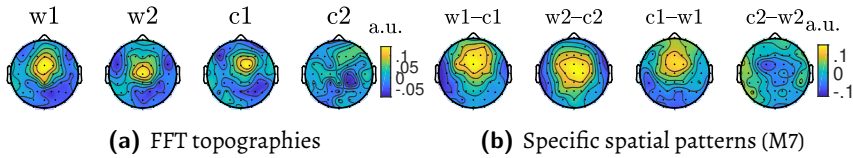


Fig. 10.3 Group-level average spatial patterns of (a) the frequency amplitudes at $f_* = 0.2$ Hz and (b) the most specific components extracted by M7 ($N_h = 10$) for the first class in each pair.

Finally, Fig. 10.3 shows the spatial pattern of the frequency spectrum at f_* , usually analyzed in neuroscience, and the most specific spatial pattern extracted for each class of signals. The specific patterns of the two warm conditions are relatively similar but different from those of the cool conditions. The specific warm patterns have a larger central positive cluster than the corresponding FFT topographies, while the specific cool patterns are more diffuse, reflecting a larger inter-subjects variability. Cold receptors being known to habituate rapidly to repeated stimuli [94], this could affect the stability of the SSR.

10.4 Conclusions and Perspectives

This chapter proposes several linear filtering methods for multidimensional signals aiming to extract periodic components which are specific to one class among two. Seven objective functions are defined, combining discrimination and periodicity maximization in simple formulations. The methods are discussed and their results compared on synthetic data sets, allowing to study their behavior and reliability in a controlled context. They are also applied on real EEG recordings to highlight

modality-specific spatial patterns of brain activity elicited by periodic cool and warm stimulation. The results are encouraging, as the extracted patterns are consistent with the nature of the considered stimuli and indeed exhibit a markedly increased periodicity for the considered class.

Further investigations will be carried regarding the proper validation of the extracted specific patterns to enable their fair interpretation in the neuroscience context. This validation is however not trivial due to the very limited number of trials available for each subject and condition. While the current results are assessed by quantifying the difference of periodicity between each compared pair of modalities, the discriminative power of the filters could also be analyzed.

Table 10.1 For each pair of conditions (in row), mean(std) for the 15 subjects of the difference of periodicity M_π (10.16) between the filtered signals in both conditions using the most specific filter for the first condition of the pair. The best performances per row are in bold. Non-italic characters indicate that the corresponding signal is significantly less periodic than the best one of the same row (paired t-tests with Holm-Bonferroni correction). For M4 and M7, $N_h = 10$.

	LPDA methods				Baseline methods		
	M1	M4	M5	M7	SCM	CSP	SVD
w1-c1	0.55(0.42)	0.35(0.43)	0.55(0.94)	3.25(1.04)	2.84(1.08)	0.25(0.56)	0.22(0.32)
w2-c2	0.31(0.46)	0.09(0.15)	0.68(1.23)	3.25(1.05)	2.98(0.98)	0.15(0.29)	0.17(0.37)
c1-w1	0.10(0.53)	0.30(0.27)	0.31(0.39)	2.43(0.67)	1.59(0.86)	-0.12(0.28)	-0.19(0.28)
c2-w2	0.11(0.46)	0.19(0.14)	0.42(0.47)	2.44(0.55)	1.78(0.69)	-0.01(0.36)	-0.12(0.43)

Chapter 11

Tensor factorization

NOISY multi-way data sets are ubiquitous in many domains. In neuroscience, electroencephalogram (EEG) data are recorded during periodic stimulation from different sensory modalities, leading to steady-state (SS) recordings with at least four ways: the channels, the time, the subjects and the modalities. Improving the signal-to-noise ratio (SNR) of the SS responses is crucial to enable their practical use. Supervised spatial filtering methods can be considered for this purpose to relevantly guide the extraction of specific activity patterns. Nevertheless, such approaches are difficult to validate with few subjects and can process at most two data ways simultaneously, the remaining ones being either averaged or considered independently despite their dependencies. This chapter hence designs unsupervised tensor factorization models to enable identifying meaningful underlying structures characterized in all ways of multimodal SS data. We show on EEG recordings from 15 subjects that such factorizations faithfully reveal consistent spatial topographies, time courses with enhanced SNR and subject variations of the periodic brain activity.

11.1 Introduction

Noisy multi-way data sets are encountered in numerous machine learning and signal processing applications, including audio and image processing, biomedical studies, chemometrics and social sciences [50, 157]. In neuroscience in particular, neurophysiological recordings such as the electroencephalogram (EEG) naturally span more than two dimensions, including the channels, the time, the frequency and the subjects. The analysis of such data usually requires to isolate the underlying hidden patterns of interest from the noise activity [153]. For instance, to study the cortical processing of sensory stimuli, EEG can be recorded during periodic stimulation from different modalities (visual, auditory, etc.). This kind of stimulation can elicit periodic activity at the stimulation frequency in neuronal populations responding to the stimulus, referred to as a steady-state response (SSR). In this setting, guided (i.e. supervised) spatial filtering methods can be considered to uncover the temporal and spatial patterns of the SSR by maximizing the periodicity of the extracted components [4, 149, 45, 147]. These approaches are particularly relevant when the hidden activity of interest has a specific structure, such as the periodicity, which can be directly optimized. Nevertheless, the structure optimization requires a careful validation of the obtained patterns, which is not straightforward, especially when the number of subjects is limited [45]. In addition, such approaches are defined on two-way arrays although the studied data usually are higher-order tensors, requiring to either average some results over the subjects or process pairs of ways independently. Finally, interpreting the underlying activity entails inverting the filters to obtain source patterns [47], which may lead to irrelevant patterns when few filters are computed.

On the other hand, unsupervised tensor factorization (TF) models circumvent the three aforementioned shortcomings of the supervised spatial filtering approaches to extract SSRs from noisy EEG. Indeed, their unsupervised nature eases their validation and they account for all data ways at once, without the need for any inversion. Surprisingly, despite numerous successful applications of TFs [50, 158, 49], including on EEG data mainly to identify space-time-frequency atoms of some waveforms [159, 160, 161, 162], higher-order tensors have not yet been considered for the SSR analysis. In this chapter, we therefore analyze whether and how TF can enhance the SNR of the SSR observed on raw EEG. Using EEG data from 15 healthy subjects exposed to periodic stimuli from four modalities, we first create a tensor with three modes, namely the subjects, the channels and the time for all modalities, to capture common spatial and varying time patterns across modalities. Second, we employ the canonical polyadic (CP) model to factor this

tensor, successfully enhancing the SNR of the SSR while preserving the specific temporal dynamics for each modality and extracting spatial and temporal patterns involved in all the subjects. Finally, a sensitivity analysis of the periodicity gain over the raw mean signals with respect to the number of tensor factors reveals significant improvements, even with as few as two factors.

This chapter is organized as follows. Section 11.2 introduces the studied EEG data. Then, terminology and common tensor factorization models are described in Sect. 11.3. The TF model is detailed in Sect. 11.4 and the obtained results are commented in Sect. 11.5. Section 11.6 concludes the work and sketches perspectives.

11.2 Electroencephalogram (EEG) data

To study the perception of long-lasting periodic thermal stimuli, we recorded scalp EEG on $N = 15$ healthy subjects to whom we applied, with a thermode, sinusoidal stimulation from $M = 4$ modalities: warm and cool, each applied on a variable or fixed skin surface along the stimulation cycles, respectively denoted by w1, w2, c1 and c2. The EEG was sampled at $f_s = 1000$ Hz and recorded using $C = 64$ electrodes (i.e. channels). The subjects received each kind of stimulus with a frequency $f_\star = 0.2$ Hz and a duration of 75 seconds ($15/f_\star$). Additional data descriptions are provided in Chapter 6. The EEG time courses and their Fourier transforms are illustrated in Sect. 11.5 with some tensor factors.

The activity of interest in these data is the SSR reflecting the stimulus processing in the brain, which is assumed to be periodic, with fundamental frequency $f_\star$. To assess and compare further results, we hence quantify the periodicity of a unidimensional signal $y(t)$, whose frequency transform is denoted by $Y(f)$, as

$$M_\pi(y) = 100 \cdot \frac{\sum_{k=1}^{\lfloor f_s/(2 \cdot f_\star) \rfloor} Y_{NS}(k \cdot f_\star)}{\sum_f |Y(f)|}, \quad (11.1)$$

with $Y_{NS}(f)$ the *noise-subtracted* frequency amplitude at frequency f , obtained by subtracting the average amplitude at 10 neighboring frequencies (5 higher and 5 lower) from $|Y(f)|$ [4]. If y is (resp. not) periodic, $M_\pi(y)$ will be positive (resp. tend towards 0). According to one-sample t -tests with 5% confidence, M_π indicates a significant periodicity, on average over the subjects, for the raw signals of the conditions w1, w2 and c1, at the fronto-central electrode named FCZ, where the periodicity is the highest. In condition c2, neither M_π nor $Y_{NS}(k \cdot f_\star)$ for any k are significantly greater than 0 at FCZ.

11.3 Terminology

This section shortly presents some definitions and common notations adopted when dealing with real tensors. These concepts are then employed in the next section for defining the tensor model proposed in this chapter. The goal is therefore not to give a formal and exhaustive description of existing tensor decompositions and their properties, but rather to introduce the key concepts necessary to employ such decompositions in practical contexts. For further details, the reader can refer to different existing works such as [49, 50].

A tensor is a multidimensional array [49], namely a function of a fixed number D of indices $(i_1, i_2, \dots, i_D)$ [158]. It is therefore naturally first characterized by its number of **dimensions**, which are often called **modes** or **ways**. This number of dimensions, D , is the tensor **order**. It follows that, with the size of each mode denoted by $I_i \in \mathbb{N} \setminus \{0\} \forall i$,

- a vector $\mathbf{a} \in \mathbb{R}^{I_1}$ is a first-order tensor,
- a matrix $\mathbf{A} \in \mathbb{R}^{I_1 \times I_2}$ is a second-order tensor,
- a three-way array $\mathcal{A} \in \mathbb{R}^{I_1 \times I_2 \times I_3}$ is a third-order tensor and
- the order D can continue increasing for multi-way arrays $\mathcal{A} \in \mathbb{R}^{I_1 \times \dots \times I_D}$, also called higher-order tensors as soon as $D \geq 3$.

For an arbitrary tensor of order D denoted by $\mathcal{A} \in \mathbb{R}^{I_1 \times \dots \times I_D}$, its **size** is given by $(I_1, \dots, I_D)$.

Data containing more than two ways can therefore be represented with tensors. Similarly as with data stored in matrices, analyzing and understanding the content of these data entails finding a data decomposition, or factorization, leading to the identification of hidden patterns. By analogy, this amounts to identifying the molecules constituting a given material based on a compound sample. The tensor rank is first defined hereunder, and then two most-used such decompositions for higher-order tensors are presented.

A tensor $\mathcal{A} \in \mathbb{R}^{I_1 \times \dots \times I_D}$ is **rank-one** if and only if it can be expressed as the outer product of D nonzero vectors $\mathbf{u}_i \in \mathbb{R}^{I_i}$ for each $i \in \{1, \dots, D\}$ as

$$\mathcal{A} = \mathbf{u}_1 \circ \dots \circ \mathbf{u}_D, \quad (11.2)$$

where $\circ$ denotes the vector outer product [49].

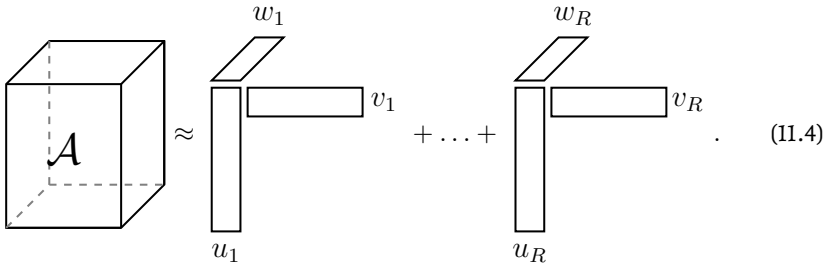
The **rank** of a tensor $\mathcal{A}$, noted $\text{rank}(\mathcal{A})$, is the minimum number of rank-one tensors whose sum equals $\mathcal{A}$ [49]. It can be noted that the tensor rank is generally

not bounded by the tensor dimensions (each I_i), at the opposite of the matrix rank. In fact, computing the rank of an arbitrary higher-order tensor is NP-hard [163]. Also, although the concept of matrix rank can be uniquely defined in several ways (as the dimension of the column or row space, among others), there exists at least one other definition of rank for higher-order tensors, which is the n -**rank** for each dimension n , which can be different for each n and which is not equivalent to the above one [164]. In what follows, third-order tensors are considered for illustration purposes and for simplicity, although the presented decompositions extend to higher-order tensors as well.

The notion of tensor rank leads us to the definition of a first popular tensor factorization, which is called the **Canonical Polyadic (CP) model** [165], Parallel Factor Analysis (PARAFAC) [166, 159] or Canonical Decomposition (CANDECOMP) [167]. It consists in approximating a tensor $\mathcal{A} \in \mathbb{R}^{I_1 \times I_2 \times I_3}$ as a sum of R rank-one tensors, for a given number of factors $R \in \mathbb{N} \setminus \{0\}$, optimally in the least squares sense [168]. The factorization can therefore be written as

$$\mathcal{A} \approx \sum_{r=1}^R u_r \circ v_r \circ w_r, \quad (11.3)$$

with $u_r \in \mathbb{R}^{I_1}$, $v_r \in \mathbb{R}^{I_2}$ and $w_r \in \mathbb{R}^{I_3}$. It can further be illustrated as



$$\mathcal{A} \approx \begin{matrix} w_1 \\ \text{---} \\ \text{---} \\ u_1 \end{matrix} v_1 + \dots + \begin{matrix} w_R \\ \text{---} \\ \text{---} \\ u_R \end{matrix} v_R. \quad (11.4)$$

The smallest number of components of an exact (i.e. with equality in (11.3)) CP decomposition corresponds to the tensor rank. When this decomposition is exact and $R = \text{rank}(\mathcal{A})$, it is called the **rank decomposition** [49]. An important property of the CP factorization is that it is unique (up to scaling and permutations of the factors) under mild conditions [169]. These conditions are satisfied for most higher-order tensors, while it is rarely the case for matrices, unless additional constraints such as orthogonality of the factors along each dimension are imposed, leading to the widely employed Singular Value Decomposition (SVD) [170].

The CP model is not the only decomposition of higher-order tensors into sim-

pler components. For instance, a very general factorization is the **Block Term Decomposition (BTD)** [171, 172, 173]. Before defining this decomposition, let us introduce the n -mode product for tensor multiplication by a matrix along mode n [49].

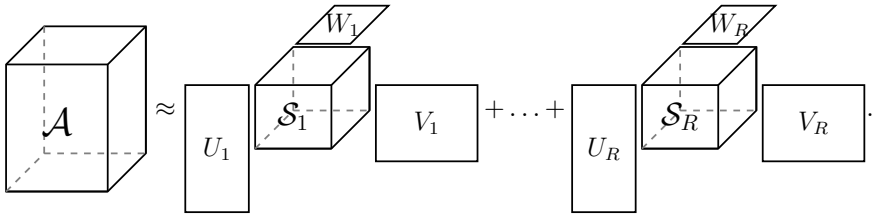
The n -mode (matrix) product of a tensor $\mathcal{A} \in \mathbb{R}^{I_1 \times I_2 \times \dots \times I_D}$ with a matrix $\mathbf{U} \in \mathbb{R}^{J \times I_n}$ is denoted by $\mathcal{A} \cdot_n \mathbf{U}$ and is of size $(I_1, \dots, I_{n-1}, J, I_{n+1}, \dots, I_D)$. Elementwise, it gives

$$(\mathcal{A} \cdot_n \mathbf{U})_{i_1 \dots i_{n-1} j i_{n+1} \dots i_D} = \sum_{i_n=1}^{I_n} a_{i_1 \dots i_D} u_{j i_n}. \quad (11.5)$$

For a given number of factors $R \in \mathbb{N} \setminus \{0\}$, a BTD has the form

$$\mathcal{A} \approx \sum_{r=1}^R \mathcal{S}_r \cdot_1 \mathbf{U}_r \cdot_2 \mathbf{V}_r \cdot_3 \mathbf{W}_r, \quad (11.6)$$

with $\mathcal{A} \in \mathbb{R}^{I_1 \times I_2 \times I_3}$, $\mathbf{U}_r \in \mathbb{R}^{I_1 \times R_1}$, $\mathbf{V}_r \in \mathbb{R}^{I_2 \times R_2}$, $\mathbf{W}_r \in \mathbb{R}^{I_3 \times R_3}$ and $\mathcal{S}_r \in \mathbb{R}^{R_1 \times R_2 \times R_3}$. Such decomposition can be illustrated as



$$\mathcal{A} \approx \mathbf{U}_1 \mathcal{S}_1 \mathbf{V}_1 + \dots + \mathbf{U}_R \mathcal{S}_R \mathbf{V}_R. \quad (11.7)$$

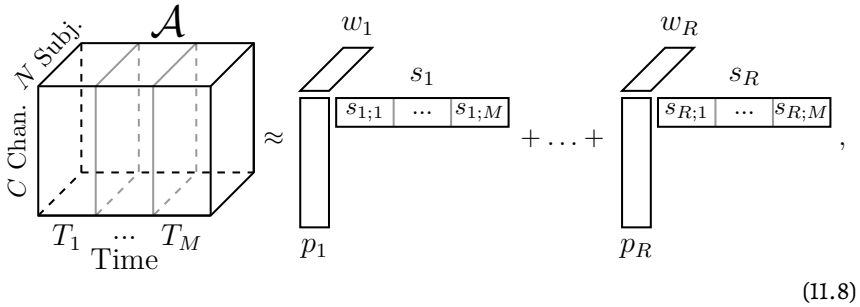
The number of columns of the matrices $\mathbf{U}_r$, $\mathbf{V}_r$ and $\mathbf{W}_r$ (resp. R_1 , R_2 and R_3) are additional hyper-parameters of the model. In the particular case when $R = 1$, the BTD corresponds to a **Tucker decomposition** [171]. As for the CP model, BTDs can also be shown to be unique under mild conditions [171]. The choice of a tensor factorization, and therefore the constraints on the structure of each factor, depends on the application needs [172].

11.4 Methods

This section aims to construct a tensor containing the data described in Sect. 11.2 and whose factorization emphasizes the SSR. Since the stimuli from all four conditions activate the spinothalamic tract, they are expected to elicit brain activities

with similar spatial topographies, but with possibly distinct time courses, at least partly due to the different conduction velocities of the activated afferent fibers. In addition, the identified SSR should be common to (almost) all subjects, possibly in distinct proportions.

Consequently, let us first define a three-way array $\mathcal{A} \in \mathbb{R}^{C \times T \times N}$, where $T := \sum_{i=1}^M T_i$ and T_i is the number of time samples for condition i , $i \in \{1, \dots, M\}$. The time samples for the M modalities are hence stacked along the second dimension of $\mathcal{A}$. We then consider the canonical polyadic (CP, also known as CANDECOMP or PARAFAC) model to factorize $\mathcal{A}$ [162]. For a given number of factors R , it computes the sum of R rank-1 tensors which best approximates $\mathcal{A}$ in the least squares sense [168]. The factorization can be expressed as $\mathcal{A} \approx \sum_{r=1}^R p_r \circ s_r \circ w_r$, where $\circ$ denotes the vector outer product, $p_r \in \mathbb{R}^C$ the spatial patterns, $s_r \in \mathbb{R}^T$ the factor time courses (i.e. temporal patterns) and $w_r \in \mathbb{R}^N$ the subject weightings. This decomposition can be illustrated as



$$\mathcal{A} \approx \sum_{r=1}^R p_r \circ s_r \circ w_r, \quad (11.8)$$

where the segment $s_{r;i}$ is the time course for the modality i in the r^{th} factor. All ways of the data set can hence be analyzed in a single factorization with shared spatial and distinct temporal patterns for all modalities. Each w_r (i.e. mode-3 fiber) indicates the between-subject variations. Indeed, in accordance with the above intuition, each frontal slice (i.e. matrix for a fixed third index) in (11.8) is defined through the same spatial and temporal patterns pairs, but with different proportions according to the mode-3 fibers (i.e. weightings across subjects). As the periodicity of the time courses drives our interest in the factors of this decomposition, they are sorted in decreasing order of the value $\max_i M_\pi(s_{r;i})$, such that s_1 contains the most periodic time course from one modality.

The fast and scalable algorithm CP-OPT, using the L-BFGS optimization method, is employed to compute the CP models for various R values [168]. It is implemented in the open-source Tensor Toolbox [174].

11.5 Results

This section presents how model (11.8) can extract periodic time courses as a function of the number R of factors and illustrates the three-way patterns obtained on the EEG data set described in Sect. 11.2. The factor time courses $s_{r;i}$, and their periodicity in particular, are compared to the raw EEG recordings at electrode FCZ, since they depict the highest periodicity and would hence be the analyzed signals if no factorization was employed [45]. The significance level of the statistical tests is set to 5%.

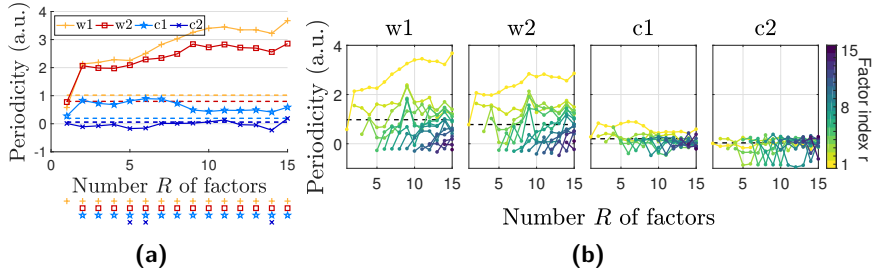


Fig. 11.1 Periodicity measure M_π of (a) the first temporal patterns $s_{1;i}$ of the tensor decomposition and of (b) all patterns $s_{r;i}$ as a function of the number R of factors. i indexes the condition (w1, w2, c1 and c2), and r indicates the factor index in the decomposition. The dotted horizontal lines indicate the periodicity at FCZ, averaged over the subjects for each condition. In (a), a marker below the plot for a given R indicates that the periodicity of the pattern represented with the same marker is significantly different from the mean periodicity at FCZ (one-sample t -tests, Holm-Bonferroni corrected).

The number R of factors considered in the CP approximation needs to be determined. Intuitively, too small R would not enable separating the noise from the periodic activity of interest (e.g. if $R = 1$, the whole EEG activity needs to be approximated in the sole factor), whereas too large R could tend to spread this activity among several factors. The periodicity of the temporal patterns $s_{1;i}$ are reported in Fig. 11.1a, with one color and marker for each modality i . For all $R \geq 2$, the periodicity of the extracted pattern is significantly larger than the one of the signal at FCZ for all conditions except c2. The absence of periodicity gain for all R for condition c2 suggests that there is indeed no periodic response for this condition, as the periodicity at FCZ was not significant in Sect. 11.2. Also, Fig. 11.1b indicates the periodicity of $s_{r;i}$ for all $r = 1, \dots, R$, the factors being ordered in decreasing order of $\max_i M_\pi(s_{r;i})$. It can be noted that the first time course

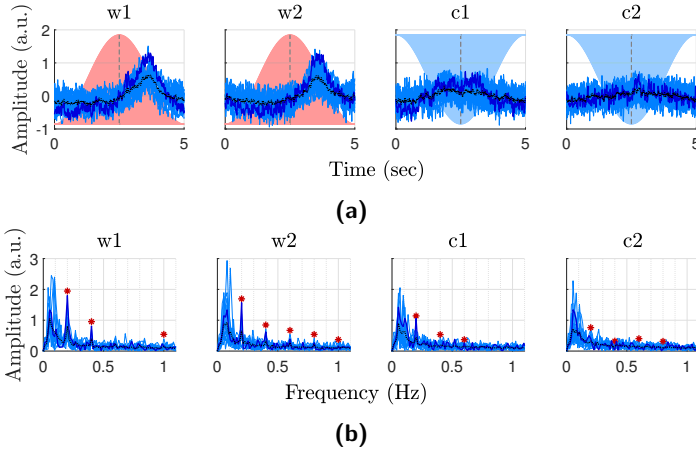


Fig. 11.2 (a) Time courses averaged over the cycles and (b) frequency transforms of the first factors $s_{1;i}$ when $R = 6$ (dark blue lines), and of the EEG at FCZ (subject-level curves in blue and mean curves over the subjects in black and dotted). The stimulation temperatures are shaded and a star indicates a significant difference between the amplitudes at FCZ and of $s_{1;i}$ at $k \cdot f_*$ (one-sample t -tests).

$s_{1;i}$ is the most periodic for all three first conditions i and all R , suggesting that employing shared spatial patterns for the conditions is indeed relevant.

Fig. 11.2 illustrates $s_{1;i}$ extracted when $R = 6$ compared to the signals at the single electrode FCZ. One can observe that considering all the channels and subjects at once in the CP model improves the SNR of the periodic components, while preserving their temporal dynamics, especially the latencies of the peaks.

Finally, Fig. 11.3 depicts the first spatial patterns $\{p_i\}_{i=1}^3$ and subject weightings $\{w_i\}_{i=1}^3$ obtained when $R = 6$. The first extracted topography is consistent with the nature of the considered stimuli [4] and w_1 indicates that the first spatio-temporal factor is reflected in all subjects with well-balanced proportions, whereas the second and third factors appear to be more subject-specific.

11.6 Conclusion

This chapter shows that tensor approximations can be employed to enhance the SNR of some EEG responses. In particular, we found a relevant spatial pattern shared by four modalities and associated with modality-specific periodic time courses, reflecting the SSR of all subjects. Employing unsupervised tensor factor-

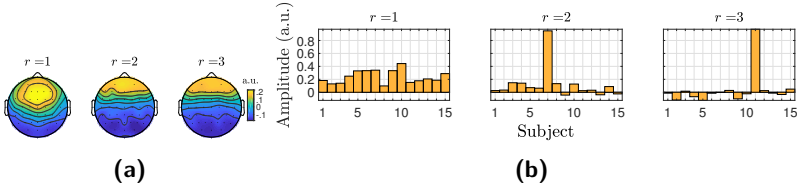


Fig. 11.3 First three (a) spatial patterns p_1 , p_2 and p_3 and (b) between-subject weightings w_1 , w_2 and w_3 , when $R = 6$ (r being the factor index).

izations enables (1) avoiding overfitting a given criterion, (2) highlighting temporal activity patterns from all subjects with a higher SNR than the raw mean signals and (3) considering all the modes of a multi-way data set at once, without requiring further averaging nor data selection. These encouraging results motivate further works to study the model fitting and its robustness as a function of both the model and the sample sizes and to enlarge its application.

Chapter 12

Discussion and applicability

THE goal of this part is to determine how periodic components can be extracted from multidimensional signals such as EEG recordings $X(t) \in \mathbb{R}^C$. In this setting, a linear latent model of the form

$$X(t) = \underbrace{\mathbf{A} \cdot Z(t)}_{\text{signal}} + \underbrace{N(t)}_{\text{noise}} \quad (12.1)$$

is first assumed to generate the observed data, with $Z(t) \in \mathbb{R}^{N_s}$ the latent factor activity, assumed to be periodic of period T_* , $\mathbf{A} \in \mathbb{R}^{C \times N_s}$ the mixing matrix, whose columns are the spatial patterns of the periodic components and $N(t) \in \mathbb{R}^C$ additive noise. No specific assumption is made on the nature of the latter noise, which can consist in structured interferences and/or colored channel noise for instance.

In order to identify the latent factor $Z(t)$ and their spatial patterns $\mathbf{A}$, four objective functions are defined in Section 9.2. All formulations lead to spatial filters of observed multidimensional signals optimizing the periodicity of the extracted components, thereby providing interpretable estimates of the time courses and spatial patterns of hidden periodic sources [46]. It is shown on experimental recordings that all four methods can enhance the periodicity of the signals compared to

the maximum periodicity of the raw signals $X(t)$. However, although the form of all the formulations may look similar, all approaches are not equivalent. In particular, the optimality criteria (9.2) and (9.5) have a different nature than (9.6) and (9.8). On the one hand, πCA and πCA_2 ((9.2) and (9.5) respectively) lead to filtered components such that each period along their time course is maximally similar to the previous one. The periodicity optimized is therefore rather ‘local’. On the other hand, the CCA-based and SCM methods ((9.6) and (9.8)) optimize the periodicity of the filtered component with a measure computed along the whole time segment available, using sinusoidal functions. The periodicity optimized is in this case more ‘global’. As a consequence, πCA and πCA_2 may be more influenced by non-stationarities in the hidden components of interest, such as amplitude modulations. These differences may, at least partly, explain the lower performances of these two approaches on experimental data, given that the periodicity of the extracted components is only assessed globally. The knowledge of this difference may be helpful to guide the choice of one of the filtering methods in a given application, depending on whether non-stationarities should rather be preserved or ignored [44].

Besides, it can be noted that the studied filtering techniques provide outcomes which partly overfit the optimized criterion, given that they are ‘guided’ and not blind [45]. As a consequence, the absolute periodicity of the extracted components cannot be used to claim that the analyzed data contain periodic sources. Instead, filters could be optimized using data from all conditions and then the periodicity could be compared across conditions.

In a second step, the extraction of periodic components specific to one signal among two is considered. This problem is motivated by the fact that brain activity elicited by a stimulus, possibly periodic, of a given modality (e.g. heat, cold, visual, auditory, ...) can be made up of multimodal components, i.e. components that are similarly elicited by several stimulation modalities, and specific components to a particular modality [175, 176]. In this case, the latent model of interest contains signals $X_i(t) \in \mathbb{R}^C$ from two different classes indexed by $i \in \{1, 2\}$ and can be written as

$$X_i(t) = \underbrace{\mathbf{A}_u \cdot Z_{u,i}(t)}_{\substack{\text{periodic} \\ \text{interference}}} + \underbrace{\mathbf{A}_s \cdot Z_{s,i}(t)}_{\text{signal}} + \underbrace{N_i(t)}_{\text{noise}}, \quad (12.2)$$

with the common (i.e. unspecific to the class, or multimodal) and specific mixing matrices $\mathbf{A}_u \in \mathbb{R}^{C \times N_u}$ and $\mathbf{A}_s \in \mathbb{R}^{C \times N_s}$, $Z_{u,i}(t) \in \mathbb{R}^{N_u}$ and $Z_{s,i}(t) \in \mathbb{R}^{N_s}$ the common and specific periodic factors respectively, and $N_i(t) \in \mathbb{R}^C$ being additive random noise. The common activity can be seen as interferences in this problem and is such that $Z_{u,1}(t) = Z_{u,2}(t - \tau)$ for an arbitrary time lag τ . Meanwhile, the specific time courses are independent in both classes: $Z_{s,1}(t) \perp\!\!\!\perp Z_{s,2}(t)$, with decreasing (resp. increasing) variances in class 1 (resp. 2), as in Section 10.3.1 [138].

With this latent model, the objective is now to identify the specific factors $Z_{s,i}(t)$ and their spatial patterns $\mathbf{A}_s$ through spatial filtering. For this purpose, seven objective functions are defined in Section 10.2 based on the combination of (1) discrimination criteria and (2) periodicity maximization techniques suited for problem (12.1). The performances of these methods are assessed on simulated data in order to compare the behaviors of the different approaches. Interestingly, these simulations show that some of the optimized spatial filters are systematically better suited than others to recover the latent periodic activity of interest.

Finally, an unsupervised alternative to the two aforementioned approaches is also considered. To this aim, a three-way tensor is built to account for all the data dimensions at once. The data set is then approximated, through the CP model, as a sum of rank-one factors. This decomposition is chosen as the spatio-temporal factors of interest reflecting the stimulus central processing should be present in all subjects, possibly with distinct proportions. Each factor directly highlights the spatial patterns and associated time courses of the periodic activity, as well as the subject variations. It can be noted that this powerful approach requires to order the computed factors based on a chosen criterion, which is the periodicity of the time course in the present case.

PART III

Conclusions

Chapter 13

Conclusions

THE goal of this thesis is to propose, develop and compare computational tools for the analysis of periodic components in multidimensional signals. Latent periodic components are especially interesting in neuroscience, in the context of BCI applications or to study sensory perception of a periodically-modulated stimulus using scalp EEG recordings [29, 36, 44]. EEG signals are popular in these contexts as they provide a measure of overall brain activity in a non-invasive way and with a temporal resolution of the millisecond order [21].

The first part of this dissertation shows how periodic stimulation can indeed be helpful in neuroscience to study long-lasting perception and brain responses. It focuses on the characterization of such responses to sustained warm and cool stimulation in the time, frequency and time-frequency domains and therefore demonstrates how the regular structure of periodic stimuli guides the identification of the stimulus-evoked responses to several extents. Then, the second part proposes pattern extraction methods to improve the SNR of latent periodic sources. Spatial filtering and tensor factorization techniques are assessed on simulated data and the real EEG recordings described in Part I. The approaches enable obtaining the most periodic hidden factors in single-class or two-class contexts, revealing their spatial distributions across the scalp and their time courses. At the opposite of classical frequency analyses focusing on the spatial distribution of one frequency component at a time, typically at the fundamental frequency,

filtering and factorization approaches automatically combine the contribution of all the harmonics to the periodic responses, which are non necessarily strictly sinusoidal in practical settings [28]. The considered approaches are particularly suited in situations when the periodic response of interest has a weak amplitude, hindering its proper identification through frequency and time analyses [45]. The contributions of these two parts are summarized and commented below, and some perspectives are suggested.

13.1 Characterization of thermal perception

Part I studies how periodic thermal stimulation can be employed to characterize tonic perception. Although there exists a large variety of thermosensitive afferents [54, 60, 55], the responses resulting from the activation of only a small subset of these fibers have been widely studied. For instance, classical laser-evoked potentials are thought to mainly result from the selective activation of quickly adapting A δ fibers, AMH-2 [89, 90]. At the opposite, much less is known about physiological perception and brain responses elicited by the activation of tonic thermoreceptors compared to phasic ones [119]. Previous works exploited the random variations in the intensity of the eliciting stimulus or the spontaneous pain fluctuations to be able to relate the brain activity of interest to the applied long-lasting thermal stimulus [25, 26, 27]. This technique enables correlating the time course of an input stimulus to recorded brain signals, thereby identifying the linear stimulus-evoked responses. However, the brain responses evoked by an external stimulation are not likely to result from a perfect linear mapping of the stimulus intensity.

Therefore, inspired by these approaches, we propose to employ periodically modulated stimuli to further explore tonic thermosensation. Although the signal-to-noise ratio of stimulus-evoked responses in the EEG can be very low (especially concerning weak tonic activity), the periodicity of the stimulus can relevantly guide the extraction of the stimulus-evoked components which can result from any nonlinear mapping of the applied stimulus intensity [28]. This guidance takes place both in the frequency domain, where the useful activity concentrates at the frequency of stimulation and its harmonics, and in the time domain, where the known period allows identifying the structure of the stimulus-evoked component. In this setting, this part explores the dynamics of perception and brain responses evoked by long-lasting cool and warm stimuli applied with a contact thermode. It is shown that both sinusoidal contact heat stimulation and sinusoidal contact

cold stimulation at 0.2 Hz elicit a sensation whose intensity varies periodically over time. Furthermore, both stimuli elicit a periodic EEG response at 0.2 Hz and its harmonics, although the EEG response elicited by cool stimulation is of much lower magnitude than the EEG response elicited by warm stimulation. The latencies of the perception and EEG responses elicited by cool stimulation are, on average, shorter than those elicited by warm stimulation. This latency difference is most pronounced during the first cycle of stimulation. Both the perception and the EEG responses to warm and cool stimulation tend to habituate over time. This habituation is stronger for cool stimulation as compared to warm stimulation. Response habituation is less pronounced when stimuli are delivered using a variable surface as compared to a fixed surface [1].

Although peripheral habituation (a.k.a. receptor fatigue) can partly account for the decrease in amplitude of the recorded responses, the predictability of the stimulation waves induced by their periodic structure along time and across spatial locations is also likely to increase responses habituation [175, 177, 178]. Indeed, whereas robust sensory event-related potentials (ERPs) can be recorded when long and variable inter-stimulus intervals (ISIs) are considered, employing short and constant ISIs leads to strong habituation of the brain responses [177, 178]. Bioadaptive stimulation, which consists in adjusting the stimulus intensity based on subjective ratings in order to compensate responses habituation, could be considered in an attempt to obtain more stable responses [179]. However, this would not be suited for a sinusoidal stimulus at 0.2 Hz reaching an initial peak temperature around 48°C, as it would not be feasible to increase the stimulation temperature without burning the subject.

In addition to characterizing tonic perception of contact thermal stimuli, this part underscores different ways through which periodic stimulation can be helpful to study both phase-locked and non phase-locked stimulus-evoked responses. A first line of research to complement this study therefore consists in describing how these responses are affected by varying the stimulus features such as the waveform shape, its modulation, amplitude and frequency in order to (1) improve the functional characterization of the elicited responses and (2) gain insights into the populations of afferents evoking the brain responses. In particular, the responses to periodic painful heat, painful cold, non-painful warm and non-painful cool could be analyzed to highlight components which could specifically encode pain. Also, tonic thermal illusions, such as the thermal grill illusion [180, 181, 182], could also be evoked with periodic stimulation to characterize features of their central processing.

13.2 Extraction of periodic components

Part II aims to develop methods to extract periodic components from multidimensional signals such as the EEG. It hence first introduces and compares four spatial filtering methods aiming to maximize the periodicity of the filtered components [148, 149, 41, 152]. Then these approaches are combined with discrimination objective functions [46] in order to find the periodic components which are specific to one class of signals among two. Interestingly, simulations show that some formulations are systematically better suited than others to recover the hidden patterns of interest. Finally, it is shown that an unsupervised factorization also allows improving the SNR of periodic components across different modalities and subjects. All these techniques estimate the spatial patterns and time courses of the periodic sources. Although the topography of the signal amplitude at the fundamental frequency is often considered to describe the spatial distribution of some elicited periodic brain activity [45], Chapter 10 shows that this vector can be very different from the actual spatial pattern of the source of interest. This is especially the case when periodic interferences occur, which can correspond to multimodal periodic activity for instance [175, 176].

The supervised spatial filtering methods are very attractive as they directly rank the components according to the criterion which is optimized [137]. At the opposite, in most blind source separation algorithms, the identification of sources of interest is performed in two steps, with first the computation of the sources and second the ordering and selection of the useful components. Yet, the direct supervision also implies that the validation of the outcomes is fundamental for these methods, especially when the aim is to interpret the extracted patterns. Validations are easily conducted in classification contexts with clearly defined quality criteria through cross-validation [41, 133], whereas for exploratory analyses, randomization procedures can be considered to determine the significance of the obtained sources [183, 184]. Indeed, supervised spatial filters naturally overfit the criterion they are optimizing and would therefore extract periodic components even if they were applied to pure noise. As a consequence, the absolute periodicity of such extracted sources cannot serve as a proof of the presence of a periodic component within a data set. Instead, the filters can be optimized using data from mixed conditions and the resulting periodicity can be compared across experimental conditions [45]. While this dissertation focused on the comparisons and analyses of the spatial filtering methods, the assessment of these methods can be completed to several extents. On the one hand, the methods could be further compared on simulated data with controlled latent periodic sources. In particular, the behavior of the

approaches in the over- or underdetermined cases has not been formally studied yet [185]. On the other hand and in light of the simulation outcomes, the techniques should be tested on diverse real recordings.

Concerning the tensor factorization (TF) approach, it allows to consider all data ways at once in a unique unsupervised decomposition. As a consequence, there is no permutation and sign indeterminacies which are inherent to all filtering approaches applied subject-wise [45]. Indeed, a single time course is extracted per factor and is associated with subject weightings. As to future perspectives, for the analysis of similar data as the ones considered in this dissertation, four-way tensors could be built with an additional mode corresponding to the epochs, if the number of available epochs is kept fixed across participants. If it is not the case, the single trials data could also be represented by concatenating the trials along the subject dimension of a three-way array. In both cases, this would allow to observe the evolution of the periodic components across repetitions of the stimuli and thereby to characterize the habituation or sensitization across trials [106, 112, 113]. In addition, such models could be employed to illustrate the non phase-locked components. Besides, the chances of overfitting are reduced with an unsupervised model compared to the supervised filtering. Still, the obtained factors are ordered based on a chosen criterion, which is the periodicity in this work. Therefore, the approach can be seen as a supervised extraction of patterns as well, with the difference that the optimization is conducted on a restricted set delineated by the extracted factors. However, considering all the data ways at once automatically provides reassuring elements: the subject weightings indicate whether the found components are indeed relevant for the studied subjects sample. Statistical tests can easily be conducted to determine which components are present in all subjects and which are not.

Neither the spatial filtering methods nor the TF models impose orthogonality constraints on the obtained filters or factors [139, 186]. The extracted components are hence as general as possible, except that several spatial filters lead to successive sources which are decorrelated. Therefore, the choice of a supervised or unsupervised approach depends on the application needs. For instance, one would favor the supervised methods in order to maximize classification performances such as to build BCIs, while unsupervised techniques would be preferred for their greater flexibility when the structure of the patterns have to be interpreted.

Finally, a last perspective consists in further bridging the two parts of this dissertation. Indeed, the pattern extraction approaches proposed in Part II can be employed to ease the analysis of diverse practical data sets containing periodic components. It would therefore be interesting to compare the different methods

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on several data sets, driven by the practitioners aims, either in the context of BCI systems or to study sensory perception of different modalities.

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List of symbols and acronyms

Acronyms

BCI	Brain-Computer Interface (p. 17)
CCA	Canonical Correlation Analysis (p. 72)
CSP	Common Spatial Patterns (p. 65)
CWT	Continuous wavelet transform (p. 18)
EEG	Electroencephalography (p. 1)
ERP	Event-related potential (p. 25)
fMRI	Functional magnetic resonance imaging (p. 26)
FT	Fourier transform (p. 18)
GEVD	Generalized Eigenvalue Decomposition (p. 67)
PET	Positron-emission tomography (p. 7)
π CA	Periodic Component Analysis (p. 72)
SCM	Spectral contrast maximization (p. 73)
SNR	Signal-to-Noise Ratio (p. 70)
SSR	Steady-State Response (p. 26)
STFT	Short-time Fourier transform (p. 18)
TCS	Thermal Cutaneous Stimulator (p. 29)
TF	Tensor Factorization (p. 98)

Vectors, matrices and tensors

$\mathbf{W}$ _____ Deterministic matrix (p. 71)

$\mathcal{A}$ _____ Deterministic tensor (with at least three ways or modes) (p. 100)

d _____ Deterministic scalar value (p. 71)

$\mathbf{x}$ _____ Deterministic column vector (p. 65)

X _____ Random variable (scalar or vector) (p. 87)

Operators

$\mathbb{E}_t$ _____ Expectation along time (p. 72)

$\mathcal{F}_f$ _____ Fourier transform at frequency f (p. 73)

Sets

$\mathbb{C}$ _____ Complex numbers (p. 67)

$\mathbb{N}$ _____ Nonnegative integers (natural numbers) (p. 100)

$\mathbb{R}$ _____ Real numbers (p. 65)

Problem variables

$\mathbf{x}(t)$ _____ Multidimensional input signal (p. 65)

$f_\star$ _____ Fundamental frequency (p. 71)

$T_\star$ _____ Fundamental period (p. 71)

C _____ Number of channels (p. 65)

M _____ Number of modalities (p. 99)

N _____ Number of subjects (p. 74)

T _____ Number of time steps (p. 103)

M_π _____ Periodicity measure (p. 74)

$\mathbf{w}$ _____ Linear spatial filter (p. 66)

$s(t)$ _____ Filtered signal (p. 65)

t _____ Time (p. 65)

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