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Methodological aspects of the mapping of disease resistance loci in livestock

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Introduction

Animal diseases

Infectious diseases in livestock are mainly caused by bacteria, parasites or viruses. Their incidence in livestock animals is a major concern for animal breeders as well as for consumers. Different factors can explain this concern. Firstly, for the breeders, animal diseases induce high costs; the cost of the pharmaceutical treatments is generally high and can account for an important proportion of the production costs. Secondly, as the welfare of diseased animals is reduced, their production is also reduced. Thirdly, due to the intensive use of therapeutic agents (such as e.g. antibiotics, anthelmintics or insecticides), pathogens that are resistant to therapeutic agents are emerging; in this situation, the control of such pathogens is getting difficult. And fourthly, animal diseases can potentially represent a risk for the consumers as there exist pathogens that are adapted to both the human species and animal species.

In this context, a reduction in the use of antibiotics is consequently inevitable if one wants to avoid that the phenomenon gets out of control. An alternative to the use of therapeutic agents, is to increase the disease resistance of animals. Besides husbandry and management factors that are the most important factors to prevent the outbreak of diseases, disease resistance in animals can be achieved by two different ways: either by immuno prophylaxis (vaccines) or by genetic improvement. The present thesis focuses on the latter alternative.

Introduction

The genetic improvement of disease resistance can be achieved by two different ways: either by the selective breeding of more resistant animals based on their phenotypic value, or by the selection of animals on the presence or absence of some specific resistance genes in their genotype (i.e. marker assisted selection).

A prerequisite to the latter approach is the identification of the genes underlying genetic variation in terms of resistance. Owing to the recent advances in marker technology, the molecular dissection of heritable quantitative traits into their individual mendelian components or quantitative trait loci (QTL) is now possible.

Genetic tools

The combination of the marker information of animals with their phenotypic measurements requires sophisticated statistical tools, called QTL mapping methods. The efficiency of these methods to identify QTL depends among other on the respect of their underlying assumptions, and for example on the normality of the phenotypic distribution.

As evidenced in the present thesis, genetic resistance traits that are used to assess the resistance status of animals (such as bacteria counts, parasites counts, or antibody levels) are not always satisfying this assumption.

This thesis focuses therefore on the adequacy of the available QTL mapping methods to map QTL involved in the resistance of livestock animals when the underlying assumption of normality is not met.

Structure of the document

The chapters of this thesis are distributed in four different parts: (1) a first part describes the context of the study; (2) methodological aspects of the identification of disease resistance loci are treated in a second part; (3) in a third part, the results of QTL mapping analyses in chicken and sheep are presented; and (4) the conclusions from this thesis as well as the identified perspectives are given in a fourth part.

The Chapter 1 gives an overview of the **genetic basis of the resistance** to infectious diseases in livestock animals.

The Chapter 2 presents the underlying theory of **QTL mapping tests** in order to give the basis to understand the following methodological and applications chapters.

In Chapter 3, a bibliographical survey of the QTL mapping studies on the disease resistance in livestock is performed in order to identify typical classes of **resistance traits**.

The **objectives** of this thesis are then formulated in Chapter 4.

In Chapter 5, the **statistical power** of QTL mapping tests when analysing bacteria counts is assessed by means of simulations; methods are compared in terms of their efficiency to detect a QTL in simulated populations.

In Chapter 6, a modification of the **non-parametric** QTL mapping test is proposed to account for the specific statistical properties of disease resistance phenotypes based on a counting process.

The interest of combining **repeated measurements** of the same resistance trait in the context of parasitic diseases is then studied in Chapter 7.

Finally, the QTL mapping methodology is applied on two actual data sets, one in **chicken** (Chapter 8), and another one in **sheep** (Chapter 9).

Conclusions and perspectives are finally given in Chapter 10.