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Breeding disease resilient pigs

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Abstract

Animal breeding continues to play a role in improving the stability of farming systems by selecting resilient animals and developing methods of selection for disease resilience, disease resistance and disease tolerance. Routine veterinary observations on clinical and sub-clinical diseases as well as growth in challenging environmental conditions may be used as measures of disease resilience. However, disease resilience can only be measured reliably when a sufficient infection challenge is present in the standard farming system. Deliberately exposing a large number of animals to high infection levels to obtain more accurate measures of their disease resilience is not feasible due to welfare concerns and reduced profitability. Improvement in disease resistance and disease tolerance will lead to superior disease resilience. However, within-host infection levels have to be known for a reliable distinction between disease resistance and disease tolerance and this information is not expected to be available for farm animals. Genetic variation has been identified for direct measures of disease resistance, i.e. pathogen load, and indicators of disease resistance, i.e. susceptibility to disease and immune parameters. Selection strategies for direct measures of disease resistance (pathogen load) with beneficial health and welfare consequences for groups of animals lead to more robust environments that have lower levels of disease-causing organism and are less challenging for animals. Selection strategies for disease resistance with these consequences should be implemented in breeding programs. Multiple parameters including mean growth, mean pathogen load or mean of certain immune traits for groups of pigs as well as information on variation in air quality or heat load could be used to quantify the general infection challenge better. Variation in some of these environmental measures has already been observed in pig farms with good health and management procedures indicating that it is possible to select for disease resilience in commercial pig breeding programs.

Robust pig farms

The demand for pork continues to increase worldwide, and pig industries around the globe have concentrated on producing pork efficiently and cost-effectively. This focus has led to the development of highly productive farming systems for pigs that deliver pork at competitive prices. The continuous demand for pork further implies that pig farming systems have to be capable of maintaining productivity even when faced with internal or external challenges affecting grow-out conditions on farms. Such a farming system may be regarded as a robust pork production system.

The term robustness itself has been used in multiple disciplines often with different interpretation. In regard to agricultural systems, de Goede *et al.* (2013) concluded that agricultural systems are an illustration of ‘a robustness paradox’. This robustness paradox of agricultural systems arises from the need to maintain diversity and resilience to cope with unlikely events such as epidemics, while fulfilling market demands for a uniform and consistent product. The authors state that agricultural systems have become *robust, yet fragile* systems using the term introduced and discussed by Doyle (2010)). Agricultural systems are robust because they are able to maintain high performance when faced with *likely* challenges, arising from the usual seasonal fluctuations in climate or feed quality for example. Yet agricultural systems may be fragile when exposed to *rare* challenges. This may be the outbreak of a previously unknown disease with severe effects. Therefore, robustness of agricultural systems may be defined as a robustness *state* rather than a fixed feature of a system (de Goede *et al.*, 2013). The robustness state of an agricultural system was defined by its levels of stability and vulnerability. Stability of a system is characterised by reliable conditions, resilience, i.e. the ability to recover from disturbances, and non-sensitivity to challenges. Vulnerability on the other hand is characterised by its exposure to stressors, non-resilience to challenges and its sensitivity to challenges. Animal breeding continues to play a role in improving the stability of farming systems by contributing to more consistent performances of animals and reduced infection load as a result of selection for improved disease resilience, disease resistance and disease tolerance. The application of these strategies for pig breeding is described in this study.

Robust pigs

The eloquent description of robustness at the animal level provided by Knap (2005) is often used as the definition of robustness in pig breeding. Robust pigs were defined “as pigs that combine high production potential with resilience to external stressors, allowing for unproblematic expression of high production potential in a wide variety of environmental conditions”. The traits proposed for breeding robust pigs included low environmental sensitivity of genotypes and a range of traits describing survival and rebreeding success of sows. Since then, robustness has been defined as a central concept in reconciling productivity and feed efficiency with health, adaptation, welfare and reproduction (Phocas *et al.*, 2014). This extension of robustness to an encompassing concept implies that the term robustness itself has become quite unspecific and is less useful for specific applications in animal breeding unless it can be used to define different aspects of the robustness *state* of animals and of agricultural systems as proposed by de Goede *et al.* (2013). It is then possible to describe the robustness state of an animal through a range of traits that relate to the alternative strategies that an animal may employ to maintain productivity even in challenging situations. These strategies include non-sensitivity or tolerance to pathogenic and other environmental challenges and disease resistance, both of which lead to improved disease resilience.

Resilience

Disease resilience was defined by Albers *et al.* (1987) as the ability of a host to maintain a reasonable level of productivity when challenged by infection. Including productivity in the trait definition of resilience was motivated by the fact that such a resilience trait affects profitability of livestock production directly. Therefore, it might be more profitable to breed for low production losses due to infection rather than for high resistance to pathogen burden *per se* (Bisset and Morris, 1996). This approach focuses on reducing the effects of infection rather than reducing the infection itself following the earlier work by Clunies-Ross (1932) who had made the distinction between 'resistance to infection' and 'resistance to the effects of infection'.

When measures of productivity are used to distinguish between resilient and non-resilient pigs, sufficient infection challenge must be present in order to measure disease resilience and to observe genetic differences in disease resilience between animals (Fig. 1). If productivity is measured at a low infection challenge, animals are exhibiting predominantly their potential for high production rather than their ability to maintain productivity under infection challenge. This raises the question how much infection challenge has to occur for a meaningful measure of disease resilience. The minimum infection challenge necessary to distinguish between production potential and disease resilience reliably may differ for alternative traits. For example, productivity traits may require a higher infection challenge than traits describing health of animals for the purpose of quantifying disease resilience. Therefore, a measure of disease resilience should ideally include information about the amount of infection challenge that animals were exposed to. It should be noted that the exposure of animals to high infection levels is detrimental for the welfare of animals. Breeding programs that require permanent recording of a considerable volume of such records are non-sustainable because it is not acceptable to expose large numbers of animals deliberately to high infection challenges for the purpose of recording disease resilience. Whether it is acceptable to expose a small proportion of animals to high infection challenges for the purpose of genetic improvement of disease resilience that benefits a large population of animals is a question for the ethical debate.

Many animal breeding applications for disease resilience in sheep have focused on 'resistance to the effects of infection' because measures of productivity are readily available on farms (Bisset and Morris, 1996). However, this concept can easily be extended to include other traits recorded on farms that may provide a more direct measure of disease resilience such as animal survival rates, incidence of specific health problems, or requirements for medication. Often these traits may be readily available from veterinary management procedures which document specific medication of animals. In sheep breeding, animals were weighed repeatedly in order to determine the age at which a first drenching was required. The age at first drenching was then used as a resilience trait in selection lines (Bisset and Morris, 1996; Morris *et al.*, 2010). This disease-resilience trait was labour intensive which hindered adoption of this trait by industry.

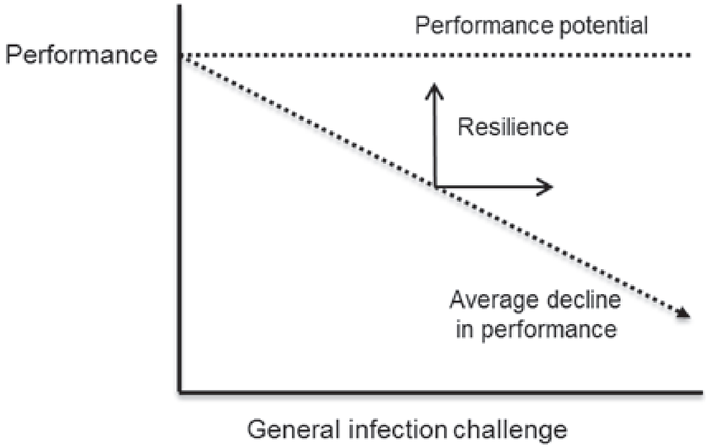

Figure 1. Resilience may be quantified by superior performance at a given infection challenge or by maintenance of performance with increasing infection challenge.

Veterinary records routinely collected on farms may be used for genetic improvement of disease resilience. Genetic variation was found for a simple disease incidence score based on routine observations on non-specific digestive disorders in a commercial rabbit population (Garreau *et al.*, 2008). This disease score has subsequently been implemented in commercial rabbit breeding programs in France (H. Garreau, personal communication). In pigs, time from the start of performance test until first diagnosis of a disease category was used by Henryon *et al.* (2001) to quantify genetic variation for clinical and sub-clinical diseases in pigs. Clinical and subclinical diseases were grouped into disease categories describing lameness, respiratory diseases or diarrhoea as well as reduced food consumption. Similar to Garreau *et al.* (2008), Henryon *et al.* (2001) regarded these clinical and subclinical disease traits as a measure of the degree of resistance because in their opinion a later diagnosis of a disease indicated a better resistance of a growing pig to that disease. It may be argued though, that these broad disease observations are in fact a measure of disease resilience because they measure the 'resistance to the effects of infection' and do not provide information about a specific pathogen load. It is noteworthy that genetic variation for these disease traits in pigs was identified under the good housing conditions of a central test station in Denmark using simple veterinary observations that may be recorded electronically as part of veterinary practice today. These results offer opportunities to develop alternative measurements of disease resilience for pig breeding programs.

Resilience and its association with resistance and tolerance

Animal breeding applications rely on appropriate genetic models and trait definitions for disease resilience to distinguish it from the associated concepts of disease resistance and disease tolerance. The conceptual illustration of the association between resilience, resistance and tolerance provided by Bishop (2012) was extended in Fig. 2 to demonstrate the favourable effects of improving disease resistance or disease tolerance on disease resilience. Disease resistance is the ability of a host to reduce its level of parasite or pathogen burden, while disease tolerance describes the decrease of performance with increasing levels of infection. Disease resilience is defined for a specific level of infection. A reduction in infection level due to increased resistance (A to A^+) improves resilience for a given tolerance level. Further, resilience may be improved by selecting genotypes with superior tolerance (B to B^+). This conceptual outline of the association between resilience, resistance and tolerance is helpful for developing new traits of disease resilience, disease resistance and disease tolerance for animal breeding applications. The pros and cons of using both disease resistance and disease tolerance for animal breeding have been discussed extensively by various authors in the book edited by Doeschl-Wilson and Kyriazakis (2012).

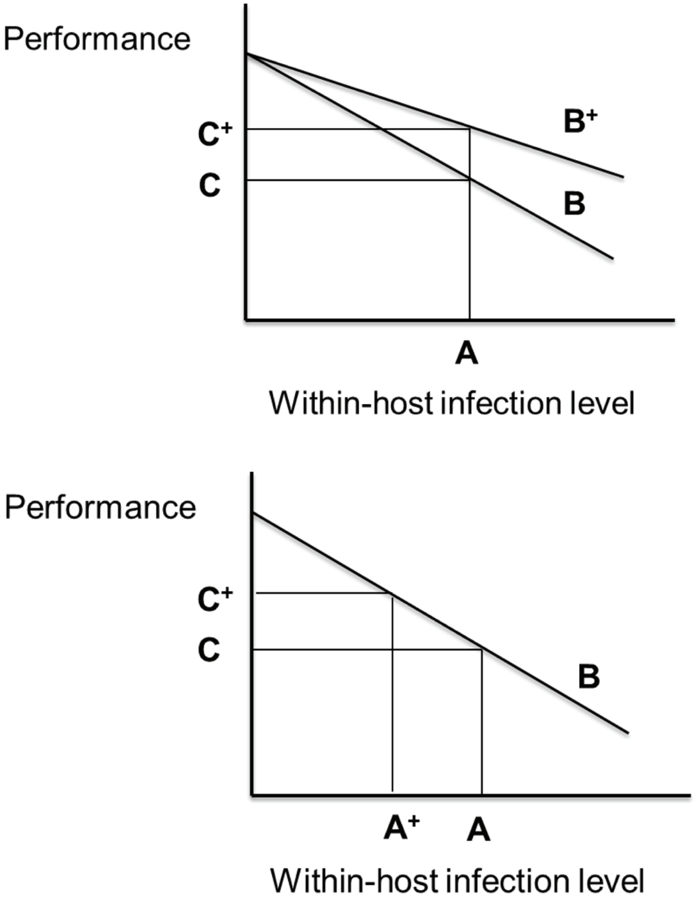

Figure 2. Resilience (C) is improved (C^+) due to a) increased resistance (A^+) or b) superior tolerance (B^+) of animals (extended from Bishop, 2012).

Resistance

Disease resistance is based on specific measures of parasite or pathogen burden. Direct measures of resistance relate to the intrinsic ability of animals to fight pathogens and are often based on accurate lab analyses of faecal egg count, viraemia or bacterial load to quantify the infection load due to nematodes, viruses or bacteria. It is therefore not surprising that genetic variation has been found for traits describing disease resistance. For example, the resistance trait of fecal egg count (FEC) was more heritable than the resilience measure of age at first drench in sheep (Morris *et al.*, 2010). In pigs, there is ample evidence for genetic variation in viral load of the porcine reproductive and respiratory virus (PRRSv; e.g. Lewis *et al.*, 2007; Lunney and Chen, 2010), which is regarded as the most important infectious disease threat in pigs. A large research effort is currently underway to establish the genetic basis of host response to PRRSv, which is further outlined by Doeschl-Wilson and Lough (2014, this publication).

The term disease resistance has generally been used in pig breeding when aspects of genetic improvement of the health status of pigs have been discussed by Rothschild (1998) and Crump (1999) in their reviews. Reduced susceptibility of pigs to infection, e.g. the animal's physiological response prevents the disease from establishing, is regarded as improved disease resistance. Genetic factors affecting susceptibility of pigs to atrophic rhinitis (a viral infection), *Escherichia coli* (a bacterium) and *Trichinella sprialis* (a macroparasite) were outlined in these reviews.

Disease resistance relies on an effective immune response of the host to infectious pathogens, and immune parameters may be used as indirect genetic clues for improved disease resistance. Multiple studies have demonstrated that genetic variation exists for a wide range of immune traits (e.g. Clapperton *et al.*, 2008, 2009; Flori *et al.*, 2011). These immunological measures are often described as being synonymous with disease resistance. However, higher levels of immune responses may not always lead to improved resistance, because different immune responses, including innate, cellular and humoral, are produced for different pathogens (Adamo, 2004). These immune parameters do affect the health status of animals though, and as such may provide information for economically important health traits. Genetic associations between immune and health traits are likely to be influenced by other challenging factors that animals may experience on farms. For example, immune response of pigs to disease challenge was affected by other environmental or social stressors (Salak-Johnson and McGlone, 2007) highlighting the need to account for as many interacting factors as possible in genetic models of immune traits. Despite these challenges, immune traits affect susceptibility and recovery of animals to infectious pathogens and provide information for genetic improvement of the health status of animals. The use of alternative immune traits for genetic improvement of disease resilience is outlined in more detail by Hine *et al.* (2014, this publication).

Selection for disease resistance may lead to more robust environments

Selection for direct measures of disease resistance can reduce pathogen burden on farms. This phenomenon was observed by sheep breeders who had selected sires for low FEC. The detailed epidemiological effects of selection for low FEC are impossible to quantify on farms, however, Bisset and Morris (1996) describe how farmers saw no advantage of low-FEC sires in comparison to sires selected for productivity alone, because all lambs shared the benefits of low pasture contamination. The review by Bishop (2012) lists further experimental studies that have demonstrated epidemiological benefits arising from populations of animals excreting fewer eggs. This observation provides a strong argument to implement selection strategies for improved disease resistance with beneficial health and welfare consequences for groups of animals in breeding programs, because selection for disease resistances leads indirectly to more robust environments that are less challenging for animals.

Tolerance

Disease tolerance may be quantified by change in performance with increasing pathogen burden. Genetic variation in tolerance implies that genotypes differ in their response to pathogen burden, which basically represents a genotype by environment interaction. Genetic variation in tolerance can be quantified with reaction norm models which describe the response of a genotype to varying environmental conditions. However, Bishop (2012) pointed out that "Geneticists believe they are measuring tolerance when in actual fact they are looking at a composite trait combining tolerance and resistance." This aspect was further explored by Doeschl-Wilson *et al.* (2012) who provided a mathematical framework to quantify a better measure of tolerance for an individual based on within-host pathogen burden. Such an approach requires information about a) repeated measures of host performance and pathogen burden over time for each animal, b) information about the performance potential of an animal in a pathogen-free environment and c) information about other factors influencing performance over time. While it may be possible to obtain sufficient data to fulfil b) and c) from farm data, repeated measures of host performance and pathogen burden for individual animals are currently not routinely available from commercial populations. Therefore, it may not be possible to distinguish between disease tolerance and disease resistance in practical breeding programs. Group measures of pathogen burden, however, do present an estimate of the overall infection burden prevalent on farm and may be used to develop new traits for disease resilience, which does not distinguish between disease tolerance and disease resistance.

How much infection challenge is required to quantify disease resilience?

Whether an animal is resilient or not can only be quantified if at least some animals on farms experience challenging conditions. It is therefore necessary to quantify the level of infection challenge for a more reliable measure of disease resilience. General environmental conditions on farms may vary between batches of pigs due to differences in climate, stocking densities, air quality or changing health status over time for example. These environmental stressors tend to act additively (e.g. Hyun *et al.*, 1998) and affect all animals housed as a group together. When it is known which pigs are grouped together, various characteristics of the group can be derived from data generally available from farms. This concept was used by Jones *et al.* (2011) who found that group characteristics like number of pigs and litters per group, mean flight time of pigs in each group and proportion of Duroc pigs in a group affected performance of individual pigs.

Differences between environments, however, may be gradual and may be described on a continuous scale describing an environmental trajectory. Such an approach was used by Schinckel (1999) to illustrate the response of genotypes to varying environmental conditions. The average growth rate of each environment was used to quantify differences in health status due to different weaning (segregated early weaning versus conventional weaning) and grow out (three-site versus continuous flow) practices. This combines the multiple, unspecific effects of alternative management strategies known to affect health status into one overall descriptor of the environment, based on the average growth rate of pigs exposed to the same management procedures.

This approach was used by Li and Hermesch (2014) as well as Gilbert *et al.* (2014) to quantify variation in environmental conditions observed on farms in Australia and France. Both studies found considerable variation in mean performance of groups of pigs for growth and backfat. In the Australian, study environmental conditions varied by 200 g/day for growth rate and by 6 mm for backfat between extreme contemporary groups defined as herd-birth-month groups across ten herds. Further, a considerable spread of environmental conditions within herds of 87 to 146 g/day for growth and 1.6 to 3.5 mm for backfat was found.

In comparison, estimates of environmental conditions observed in a research herd in France ranged by 110 g/day and by 6.88 mm for growth and backfat, respectively (Gilbert *et al.*, 2014). Pigs represented divergent selection lines for residual feed intake, and variation in estimates of contemporary groups was largest in later generations when more contemporary groups and more parities were available. Further, estimates of environmental descriptors had lowly negative correlations ranging from -0.08 to -0.24 between models, indicating that favourable environments for growth would also be favourable for backfat. Overall, these results are relevant for animal breeding because this variation in environmental conditions observed for nucleus herds with good health and management conditions offers opportunities to select for less environmentally sensitive animals within nucleus herds.

Growth as a proxy for health status

Growth rate is often used as a proxy for health status of animals because many sub-clinical diseases lead to reduced growth. For example, it was found that estimates of genetic correlations between growth traits observed in different environments decreased in a curvilinear fashion as the difference between environments increased (Fig. 3. from Li and Hermesch, 2013). A genetic correlation of less than 1 for growth rate defined as a separate trait in each environment indicates a genotype by environment interaction. A genetic correlation of 0.8 is generally regarded as biologically important for breeding programs due to re-ranking of animals across environments (Robertson, 1959). From Fig. 3, this would hold for lifetime growth rate in two environments beyond a 60 g/day difference of mean growth rate between those environments. This information is useful for developing traits that quantify disease resilience, because it indicates the difference in performance required to distinguish between productivity *per se* and the ability of animals to cope with environmental challenges, e.g. only animals raised in inferior environments with increased infection levels can express their level of disease resilience.

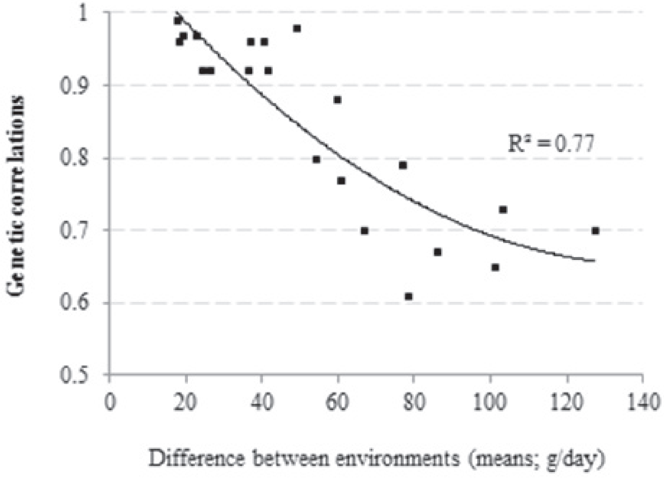

Figure 3.Genetic correlations for growth rate that was defined as a separate trait in each environment decline as the difference in mean growth rate between two envrionments increases (Li and Hermesch, 2013).

This raises the question how infection challenge should be quantified. Collins (2014, this publication) outlined how poor air quality increases the incidence of a number of diseases in pigs and reduces growth rate of pigs. It was suggested that monitoring air quality may provide a better indicator of pig health and growth than monitoring individual pathogen loads because air quality affects health and growth of pigs. Guy *et al.* (2012) emphasised the importance of accounting for other environmental challenges in genetic models for traits describing disease resistance and disease tolerance. It has been demonstrated in this chapter how improved disease resistance or disease tolerance leads to improved disease resilience. Further, traits describing disease resilience quantify the effects of infection load on performance. It is important to quantify infection load as accurately as possible for precise measures of disease resilience. Therefore, infection load may be based on environmental challenges such as poor air quality as well as specific pathogen loads measured for groups of animals. Mean levels of specific immune traits for groups of pigs provide additional information about infection challenge. Acute phase proteins in particular, have been proposed for health status surveillance of pigs at the herd level (Petersen *et al.*, 2004). Further research is required to develop procedures that combine multiple sources of information into a quantification of the overall infection load that is experienced by animals on farms. However, the variation in some of these environmental measures that has been observed within pig farms with good health and management procedures indicates that it is possible to select for disease resilience in commercial pig breeding programs.

Defining disease resilience traits

Disease resilience is only expressed when an infection challenge occurs. Therefore, disease resilience is a 2-dimensional trait that requires information about both performance of animals and infection challenge prevalent in a specific environment. The variation in infection challenge may be inferred from mean performance of groups of pigs in growth, health and immune traits as well as specific measures of pathogen load. Growth is often used as a proxy of health and growth in inferior environments with higher infection load may be used as a measure of disease resilience. First results indicate that environments should differ by at least 60 g/day in average performance in order to distinguish between growth as a measure of resilience (growth in inferior environments) and growth as a measure of performance potential (growth in superior environments). Other more direct measures of disease resilience may be based on veterinary records of clinical and sub-clinical diseases routinely observed on farms. Research is required to develop specific trait definitions of disease resilience based on the alternative strategies outlined in this study.

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