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Animal board invited review: Heritability of nitrogen use efficiency in fattening pigs: Current state and possible directions

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ABSTRACT

Pork, an important component of human nutrition worldwide, contributes considerably to anthropogenic nitrogen and greenhouse gas emissions. Reducing the environmental impact of pig production is therefore essential. This can be achieved through system-level strategies, such as optimising resource use, improving manure management and recycling leftovers from human food production, and at the individual animal level by maintaining pig health and fine-tuning dietary protein levels to individual requirements. Breeding, coupled with nutritional strategies, offers a lasting solution to improve nitrogen use efficiency (**NUE**) – the ratio of nitrogen retained in the body to nitrogen ingested. With a heritability as high as 0.54, incorporating NUE into breeding programmes appears promising. Nitrogen use efficiency involves multiple tissues and metabolic processes, and is influenced by the environment and individual animal characteristics, including its genetic background. Heritable genetic variation in NUE may therefore occur in many different processes, including the central nervous regulation of feed intake, the endocrine system, the gastrointestinal tract where digestion and absorption take place, and the composition of the gut microbiome. An animal's postabsorptive protein metabolism might also harbour important genetic variation, especially in the maintenance requirements of tissues and organs. Precise phenotyping, although challenging and costly, is essential for successful breeding. Various measurement techniques, such as imaging techniques and mechanistic models, are being explored for their potential in genetic analysis. Despite the difficulties in phenotyping, some studies have estimated the heritability and genetic correlations of NUE. These studies suggest that direct selection for NUE is more effective than indirect methods through feed efficiency. The complexity of NUE indicates a polygenic trait architecture, which has been confirmed by genome-wide association studies that have been unable to identify significant quantitative trait loci. Building sufficiently large reference populations to train genomic prediction models is an important next step. However, this will require the development of truly high-throughput phenotyping methods. In conclusion, breeding pigs with higher NUE is both feasible and necessary but will require increased efforts in high–throughput phenotyping and improved genome annotation.

Implications

With global concerns about nitrogen pollution, particularly in regions with high livestock densities, improving nitrogen use efficiency through genetic selection is emerging as a potential strategy to reduce the environmental footprint of pork production. This review summarises the evidence for a genetic basis for nitrogen use efficiency and shows that this trait is amenable to selection. It also outlines efforts to identify genetic variants associated with variation in nitrogen use efficiency. It acknowledges the challenges of phenotyping and identifying relevant genetic variants and suggests potential directions for breeding pigs with improved nitrogen use efficiency.

Introduction

Pork, a key component of global food security and nutrition, is one of the most consumed meats worldwide (Notarnicola et al., 2017; Parlasca and Qaim, 2022). Monogastric livestock (pigs and poultry) account for one-third of global anthropogenic nitrogen emissions (Cheng et al., 2022) and 2% of agricultural greenhouse gases (Lautrou et al., 2022). Although spreading pig manure on feed crop fields theoretically recycles nutrients, more than one-third of its nitrogen content is lost as ammonia, nitrate, or nitrous oxide (Lautrou et al., 2022), a potent greenhouse gas (Ruser and

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Schulz, 2015; Del Grosso et al., 2022). Its unbalanced nitrogen/phosphorus ratio contributes to the accumulation of phosphorus in the soil (Wienhold, 2005). These losses cause eutrophication, acidification and pollution of water and soil, ultimately reducing biodiversity (Galloway et al., 2008; de Vries et al., 2011). Intensive pig production in China, the European Union, and the United States, which together accounted for 78% of the total global production in 2023 (Foreign Agricultural Service, U.S. Department of Agriculture, 2024), generates large amounts of pig manure, often more than can be locally used to fertilise fields, as the majority of animal feed production takes place on another continent. Soy, for example, a preferred feed ingredient due to its favourable amino acid profile (Bracher, 2019; Wang et al., 2011) is predominantly produced in South America, where deforestation and land-use changes for intensive crop production lead to biodiversity loss and carbon sequestration problems (Foley et al., 2005; Graesser et al., 2018). This geographical separation of feed and pig production therefore leads to decoupled nutrient cycles and disrupted global nitrogen distribution (Erisman, 2004; Galloway et al., 2008). Foods of animal origin are inherently less nutrient efficient than plant-based foods (Foley et al., 2005; Beal et al., 2023), with important nitrogen losses in both crop and meat production. Monogastric animals exacerbate this inefficiency, as they consume about 2 kg of plant protein, often suitable for human consumption, to produce 1 kg of animal protein (Mottet et al., 2017a). This requires about 40% of the world's arable land for feed production (Cheng et al., 2022). Nitrogen compounds excreted in urine, which are estimated to account for up to 50% of the total nitrogen intake (Dourmad et al., 1999), are of major environmental concern due to their volatile form, which leads to their dispersion in the environment through leaching or run-off, contributing to eutrophication and the formation of particulate matter. Reducing the environmental impact of pig production is therefore crucial and can be addressed at both the system and individual animal levels.

Five strategies have been proposed to help align pork production with planetary boundaries and a growing human population. First, optimising the use of resources, such as land, feed, and water, and efficiently managing pig fattening and piglet production, are crucial in pork production (Mottet et al., 2017b; Van Zanten et al., 2019; Beal et al., 2023). Although intensification has increased efficiency over the last few decades, rising demand for pork meat has cancelled out the resulting savings in nitrogen emissions (Bouwman et al., 2011). Further intensification could reduce climate and land-use impacts but risk increasing zoonotic diseases and compromising animal welfare (Parlasca and Qaim, 2022). Second, reducing meat consumption in wealthier countries, while maintaining a balanced diet, may provide environmental benefits (Parlasca and Qaim, 2022; Beal et al., 2023). Third, increasing manure use as crop fertiliser, coupled with effective manure management to limit losses, could potentially meet over 80% of crop nitrogen and phosphorus requirements (Lautrou et al., 2022), up from the current 12% (Beal et al., 2023), by improving the circularity of the system. Fourth, reducing food waste, especially cereals, which account for 53% of global food waste (Lipinski et al., 2013) and require high nitrogen fertiliser inputs (Kim et al., 2014). Replacing cereals in pig feed with losses from human food production could conserve resources and mitigate land competition (Mottet et al., 2017a; Tretola et al., 2019; Van Zanten et al., 2019; Pinotti et al., 2021). Finally, using nutrient-efficient crops, adapting feeding strategies to local conditions and genetically selecting pigs (the latter will be the focus of this article) (Monteiro et al., 2016; Rauw et al., 2023; Kyriazakis, 2011) can improve the entire production system's nitrogen use efficiency (**NUE**) – the system's nitrogen output over the nitrogen input, thereby reducing nitrogen emissions.

Several strategies are key to improving NUE at the pig level, which is the amount of nitrogen retained in the whole body (or carcass) over the amount of nitrogen ingested. These include ensuring animal health, rearing intact boars where feasible, optimising carcass weight, fine-tuning dietary protein levels to individual requirements and utilising genetic selection. Healthy pigs with less chronic immune activation show faster growth and higher nitrogen retention (Williams et al., 1997). Omitting or delaying full castration, as can be achieved with immunocastration, allows male pigs to maintain their efficient metabolism longer before full castration (Millet et al., 2018). This method improves the NUE of male pigs because, unlike boars, barrows tend to consume more protein than they require (Millet et al., 2018). Further, slaughtering at lower weights can potentially reduce nitrogen emissions, as nitrogen excretion per kg BW increases with size (Shirali et al., 2012; Ruiz-Ascacibar et al., 2017). However, this approach needs to be carefully balanced to avoid increasing piglet production and thus the number of sows, another source of nitrogen excretion, to maintain the same level of pork production (Millet et al., 2018). Nutrition plays a critical role in improving NUE. A 1% reduction in dietary CP can decrease faecal nitrogen excretion and ammonia emissions by 10% and urinary nitrogen by 3% (Cappelaere et al., 2021). Precision feeding, which involves daily dietary adjustments to individual needs, can reduce lysine supply by 25%, nitrogen excretion by 40% and feed costs by 8% over the fattening period (Pomar and Remus, 2019).

Selective breeding, in addition to nutritional strategies, is a promising approach to permanently and cumulatively improve NUE. Despite the gradual nature of breeding, which likely results in only relatively modest increases in NUE per generation, the mitigation potential of every small improvement is significant, especially given the enormous scale of pork production worldwide, estimated at 120 million tonnes (Food and Agriculture Organization, 2022). The ideal scenario is to select pigs for optimal NUE on sustainable diets containing locally sourced ingredients of lower nutritional value, thereby minimising feed-food competition. This requires a departure from the common practice of over-supplying proteins in performance testing. Feeding pigs on protein-restricted diets (Stoll and Ruiz-Ascacibar, 2015), those that include energy-dense losses (Pinotti et al., 2021), or fibre-rich co-products rich in fibre from human food production (Lee et al., 2023; Déru et al., 2021; te Pas et al., 2021) would facilitate the selection of pigs better adapted to these constraints. Individual pigs differ in their ability to digest dietary proteins and in the efficiency of amino acid utilisation and recycling in the body, resulting in variation in NUE (Kyriazakis, 2011; Millet et al., 2018; Berghaus, 2022). Notably, NUE has shown considerable heritability, with estimates as high as 0.54 (Ewaoluwagbemiga et al., 2023a), as discussed in more detail below. This indicates that the inclusion of these traits in breeding programmes has the potential to contribute significantly to reducing the environmental impact of pig production.

Nitrogen use efficiency

Estimates or measurements of NUE depend on the growth stage, sex, breed and diet, among other factors, and therefore vary widely, making overall comparisons uninformative. Table 1 provides an overview of published NUE values of the whole body, presenting the diversity of available data concerning the sexes, major growth stages, common breeds and a wide range of diets. These values were obtained using a variety of methods, which are described in more detail below (in the Phenotyping NUE section). For all sexes and diets, NUE is highest in the starter period and lowest in the finisher period, with the grower period being

Table 1
Nitrogen use efficiency of the whole body in pigs.

Trait	Breed	Phase	Diet (protein content)	Sex	NUE %	Reference
NUE measured[1]	crossbred: Piétrain × (Landrace × Large White)	grower (60–65 kg BW)	77 different	barrows	40.4	Le Goff and Noblet (2001)
NUE measured[2]	Large White[3]	grower (47 kg BW) thermoneutral	standard	barrows	46.5	Renaudeau et al. (2013)
		32 °C week 1			34.1	
		32 °C week 2			34.6	
		32 °C week 3			37.4	
	Large White RFI+	grower; across 4 weeks of trial			34.1	
	Large White RFI-				44.8	
NUE measured[4]	crossbred: synthetic line	entire fattening period (25–105 kg BW)	3-phase[5]	gilts	37.0	Pomar et al. (2014)
			Multiphase (MP)[6]		40.0	
NUE measured[4]	crossbred; high-performance genotype	day 0–84	3-phase[5]	gilts & barrows	45.1	Andretta et al. (2016)
			MP110[7]		50.5	
			MP100[7]		52.8	
			MP90[7]		52.3	
			MP80[7]		56.7	
			overall	barrows	49.3	
				gilts	53.6	
NUE measured[4]	crossbred (including Piétrain)	grower (25–50 kg BW)	60% SIDLysR	barrows	52.0	Remus et al. (2020)
			70% SIDLysR		54.0	
			80% SIDLysR		56.0	
			90% SIDLysR		61.0	
			100% SIDLysR		65.0	
			110% SIDLysR		63.0	
		finisher (65–100 kg BW)	60% SIDLysR		40.0	
			70% SIDLysR		46.0	
			80% SIDLysR		46.0	
			90% SIDLysR		46.0	
			100% SIDLysR		49.0	
			110% SIDLysR		55.0	
NUE measured[8]	Large White dam line	entire fattening period (20–100 kg BW)	standard	boars	48.0	Based on data used in Kasper et al. (2020)
				gilts	44.6	
				barrows	44.3	
			protein-reduced[9]	boars	48.1	
				gilts	47.3	
				barrows	45.4	
		grower (40–60 kg BW)	standard	gilts, boars, barrows	49.1	
		finisher I (60–100 kg BW)			46.7	
		finisher II (100–140 kg BW)			43.3	
		grower (40–60 kg BW)	protein-reduced[9]		46.4	
		finisher I (60–100 kg BW)			47.2	
		finisher II (100–140 kg BW)			47.0	
NUE measured[1]	crossbred: synthetic boar × (Landrace × Large White)	14 weeks (low birthweight[10] pigs: 44.6 ± 4.5 kg, high birthweight pigs: 54.0 ± 3.5 kg)	standard	boars	63.8	Van der Peet-Schwering et al. (2020)
			protein-reduced		62.0	
NUE measured[1]	crossbred: synthetic boar × (Landrace × Large White)	day 104–125	standard	boars	52.7	Van der Peet-Schwering et al. (2021)
			protein-reduced[11]		55.8	
NUE measured[1]	crossbred: Landrace sows × Pietrain boars	starter (week 13)	standard	gilts	49.0	Berghaus et al. (2023)
				barrows	48.3	
		grower (week 16)		gilts	45.1	
				barrows	44.0	
NUE estimated[12]	Denmark	weaner	standard	NA	46.8	Dourmad et al. (1999)
		grower			36.8	
	France	weaner			44.9	
		grower			32.8	
	Netherlands	weaner			53.7	
		grower			33.4	
NUE estimated[13]	Landrace dam line	entire fattening period (35 – 110 kg)	standard	gilts & barrows	35.1	Saintilan et al. (2013)
	Large White dam line				37.1	
	Large White sire line				38.7	
	Pietran sire line				42.1	
NUE estimated[14]	hybrid sow × Piétrain boar	entire fattening period	standard	gilts, boars & barrows	46.0	Millet et al. (2018)

(continued on next page)

Table 1 (*continued*)

Trait	Breed	Phase	Diet (protein content)	Sex	NUE %	Reference
NUE estimated[15]	Crossbred: synthetic boar × (Landrace × Large White)	starter	standard[16] (corn and soybean meal)	boars	56.3	Verschuren (2021)
				gilts	53.9	
		grower		boars	51.1	
				gilts	48.1	
		finisher		boars	41.5	
				gilts	38.5	
		starter	standard[16] (wheat, barley and by-products)	boars	57.6	
				gilts	53.4	
		grower		boars	53.4	
				gilts	49.2	
		finisher		boars	45.5	
				gilts	42.6	

Abbreviations: NUE = nitrogen use efficiency; RFI = residual feed intake; SIDLysR = standardised ileal digestible lysine requirements; NA = not available.

[1] NUE measured in nitrogen balance trial in metabolic cage, collection of faeces and urine, weighing of feed refusals, chemical analyses of faeces, urine and feed.

[2] Respiration chamber, faeces and urine collection, chemical analyses of feed, weighing of feed refusals, nitrogen losses to the air measured.

[3] Divergent selection lines for RFI; NUE calculations across lines.

[4] Protein deposition from dual-energy X-ray absorptiometry lean measurements, feed intake from automated feeders. NUE calculated from Table 2 in Pomar 2014 (retained protein/protein intake) × 100.

[5] Phase 1: 100% feed A, phase 2: 63% feed A and 37% feed B, phase 3: 32% feed A and 68% feed B; calculated to meet the animals' requirements at the beginning of each feeding phase.

[6] Daily changes in proportions of feed A and B to meet nutritional requirements calculated for the group on that day.

[7] Blends of feeds A and B to match 110% (MP110), 100% (MP100), 90% (MP90), or 80% (MP80) of the estimated nutrient requirements of each individual pig.

[8] NUE measured as CP content of carcass from wet-chemistry analysis and CP intake via automated feeding stations.

[9] 80% CP content of standard.

[10] Littermates were chosen according to their birthweight: low and high birthweight pigs had birthweights of 1.11 ± 0.14 kg and 1.79 ± 0.14 kg, respectively.

[11] 70% CP content of standard.

[12] No description of N balance provided ("The situation in three European countries (Denmark, The Netherlands and France), as regards to nitrogen consumption, utilisation and losses in pig production, was evaluated and presented in the three previous country reports."). NUE calculated as nitrogen intake/retained in Table 3 inDourmad et al. (1999).

[13] NUE calculated as 100-N_r from Table 2 in Saintilan et al. (2013). N_r is the ratio of N excreted to N intake. Nitrogen intake estimated from total feed intake during the test period and the nitrogen content of pigs estimated from lean meat content and BW.

[14] NUE calculated from estimated N accretion from 8-110 kg live weight pig and estimated N input.

[15] NUE estimated from protein deposition using a Gompertz function (according to van Milgen et al., 2008) and CP intake via automated feeding stations.

[16] Diets differed mainly in fibre and fat content: corn-starch had lower fibre and fat content, wheat-barley had higher fibre and fat content.

intermediate. The lowest value was mentioned in a comparison of nitrogen balance in three countries, where no information on the estimation method was provided (Dourmad et al., 1999). Conversely, the highest NUE value was obtained in a study of crossbred barrows in the grower stage on a diet carefully designed to meet their specific nutritional requirements, and where NUE was precisely measured (Remus et al., 2020). Values of NUE at the carcass level are lower than on the whole body, since around half of the ingested protein is deposited in the organs (Merks et al., 2012). This is reflected in the average carcass NUE of 38% and a range of 34–40% (Table 2).

Tissues and processes involved in nitrogen use efficiency

Nitrogen use efficiency involves multiple tissues and metabolic processes, and is influenced by individual animal characteristics and the environment. Thus, similar to most relevant traits in livestock, NUE appears to be polygenic, with a large number of genetic variants across the genome, each contributing a small effect to the phenotype (Georges and Charlier, 2019). This has implications for breeding, which will be discussed later. How the ingested CP, and thus nitrogen, is digested, absorbed, and used by the body, built into muscle tissue, used to fight pathogens or synthesise peptide hormones and neurotransmitters, and recycled in the liver and kidneys, depends on the sex, genotype, growth stage and health status of the pig and its gut microbial communities, as well as on the external temperature, and the physical and chemical characteristics of the diet (Verschuren, 2021; Berghaus, 2022). These components of NUE do not act in isolation, but are interdependent. Thus, a pig can have high NUE as a result of small increases in performance in all of these processes, or large increases in one or a few components, such as muscle protein turnover or the ability to digest and absorb CP. Assuming that these processes are partly under genetic control, genetic selection can improve specific components or their ensemble.

Regulation of nutrient intake and utilisation

Basically, the size and therefore capacity of the stomach mechanically regulate food intake. Beyond this, the brain, in particular the hypothalamus, integrates neural, endocrine, and metabolic signals to regulate nutrient intake and utilisation according to the needs of the organism (Reyer et al., 2018). In particular, gut hormones and the cross-talk between the brain and the gut (gut-brain axis) are crucial for sensing and reacting to protein intake. The protein and energy content of a meal, hormone levels (e.g. insulin), growth factors (e.g. insulin-like growth factor 1 and fibroblast growth factor 21), glucocorticoids and hormones produced in the gastrointestinal tract (e.g. ghrelin, glucagon-like peptide 1, gastric inhibitory peptide, cholecystokinin, and peptide YY) interact to ensure that plasma amino acid levels remain remarkably constant (Murphy and Bloom, 2006; Reyer et al., 2018), even during protein deficiency (Bröer and Bröer, 2017). For instance, the peptide YY is produced in the intestines as a function of the protein content of a meal and leads to a decrease in appetite when high-protein diets are ingested (Bröer and Bröer, 2017). These processes mediate not only feed intake but also the secretions of gastric and pancreatic fluids and enzymes, nutrient transporters, gastric emptying, intestinal motility, and amino acid homeostasis in general (Bröer and Bröer, 2017; Reyer et al., 2018). It is likely that genetic variation underlies differences in the central nervous and hormonal control of nutrient intake and digestion, particularly through gut-brain signalling. This will then affect all subsequent

Table 2
Nitrogen use efficiency of the carcass in Swiss Large White pigs (dam line).

Trait	Phase	Diet (protein content)	Sex	NUE %	Reference
NUE measured[1]	entire fattening period (20–140 kg BW)	Standard	boars	37.7	Based on data used in Kasper et al. (2020)
			gilts	37.2	
			barrows	37.2	
		protein-reduced[2]	boars	37.8	
			gilts	39.6	
			barrows	38.2	
	grower (40–60 kg BW)	Standard	gilts, boars, barrows	39.6	
	finisher I (60–100 kg BW)			38.5	
	finisher II (100–140 kg BW)			36.2	
	grower (40–60 kg BW)	protein-reduced[2]		36.8	
	finisher I (60–100 kg BW)			38.9	
	finisher II (100–140 kg BW)			39.4	
NUE measured[3]	entire fattening period (20–100 kg BW)	Standard	gilts	38.3	Bee et al. (2021a)
			barrows	34.7	
NUE measured[3]	entire fattening period (20–100 kg BW)	Standard	gilts & barrows	33.8	Bee et al. (2021b)
		protein-reduced 1[4]		37.5	
		protein-reduced 2[5]		39.7	
		across diets	gilts	38.0	
			barrows	36.0	
NUE measured[3]	entire fattening period (20–100 kg BW)	mix[6]	gilts	39.6	Ewaoluwagbemiga et al. (2023a)[7]
			barrows	38.7	

Abbreviations: NUE = nitrogen use efficiency; NA = not available.

[1] NUE measured as CP content of carcass from wet-chemistry analysis and CP intake via automated feeding stations and wet-chemistry analysis.

[2] 80% CP content of standard.

[3] Protein deposition from dual-energy X-ray absorptiometry lean measurements, feed intake from automated feeders.

[4] Both grower and finisher diet protein-reduced (80% of standard).

[5] Only finisher diet protein-reduced (80% of standard).

[6] Mix of diets, mostly protein reduced (80% of standard).

[7] Contains data from Kasper 2020, Bee 2021a, Bee 2021b.

processes through effects on feed intake, enzyme secretion in the stomach and pancreas, amino acid transporter expression and peristalsis, ultimately influencing digestion, absorption, and metabolism in organs and tissues. For example, in Yorkshire pigs, variants in several genes associated with feed conversion rate (**FCR**) were proposed to cause differences in nutrient intake, digestion, and utilisation. A genetic variant within the *TPH2* gene is likely to affect serotonin expression in the hypothalamus and, consequently, intestinal motility (Miao et al., 2021). A variant within the *GRIP1* gene might modulate appetite through changes in gamma-aminobutyric acid and glutamate expression, and variants in the thyroid signalling pathway in the hypothalamus might lead to differential regulation of metabolism in muscle, liver and adipose tissue (Miao et al., 2021).

Digestion and absorption of proteins

The mechanical breakdown of the feed by the jaws determines the particle size, which can influence ileal digestibility. The rate of feed intake, and therefore the transit time of the digesta, also affects the ileal and faecal digestibility of nutrients and energy. Protein digestion begins in the stomach and the duodenum, where proteolytic enzymes break down proteins into smaller peptides and amino acids, and continues in the small intestine (Kurz and Seifert, 2021). The majority of amino acids and peptide absorption occurs before the distal ileum (Kyriazakis, 2011; Wielen et al., 2017) via intestinal peptide transporters and potentially tight junctions at the apical membrane of enterocytes (Bröer and Gauthier-Coles, 2022). This highly efficient process ensures the absorption of most amino acids in the intestinal lumen into enterocytes, where some amino acids are used for the maintenance of the gastro-intestinal system itself. From there, the remaining amino acids are transported through the basolateral membrane, and released into the portal vein, where they are transported to the peripheral tissues (Bröer and Gauthier-Coles, 2022). Undigested protein reaching the large intestine undergoes fermentation by the gut microbiota, which mainly benefits their own growth and metabolism (Blachier et al., 2022). However, it has been suggested that pigs, albeit to a much lesser degree than ruminants, can recycle nitrogen in the gut via the absorption of amino acids synthesised de novo from ammonia, urea, endogenous protein and complex carbohydrates by the microbiota (Fuller and Reeds, 1998). The site of absorption of microbiota-synthesised amino acids is mainly the small intestine. For example, more than 75% of the microbial lysine is absorbed in the small intestine (Torrallardona et al., 2003). Although colonocytes have a limited capacity to absorb amino acids after weaning (Blachier et al., 2022), studies indicate that some absorption occurs in the large intestine, although the extent remains uncertain and seems to be of minor importance to NUE (Fuller and Reeds, 1998; Metges, 2000; Torrallardona et al., 2003; Wielen et al., 2017; Shurson and Kerr, 2023). In the large intestine, urea nitrogen can be absorbed and deposited in muscle tissue (Mansilla et al., 2015). In pigs, 15–25% of dietary protein is not fully digested and absorbed (Noblet et al., 1989 in Kyriazakis, 2011) but is excreted in the faeces together with nitrogen-containing products of bacterial protein synthesis and endogenous substances, such as digestive enzymes, intestinal epithelium, and endogenous secretions (Le Goff and Noblet, 2001; Berghaus, 2022).

It has been suggested that digestive efficiency is heritable (Noblet et al., 2013; Déru et al., 2021; Martinsen et al., 2023). Kurz et al. (2022) reported inter-individual differences in enzyme activity and amino acid transporter expression in pigs. However, without data on feed intake and composition, which significantly affect enzyme expression and activity in the stomach and pancreas, it is uncertain whether these variations are genetically based. Evidence for genetic variation in absorption mechanisms in pigs is scarce, but could be inferred from other species. The intestinal morphology, especially villi height and width, as well as mucus depth, contributes to amino acid absorption and likely has a genetic basis in mice (Garside et al., 2023). In humans, the absorption of amino acids is generally not a limiting factor, in contrast to ileal digestibility (Trommelen et al., 2021). However, genetic variation in amino acid transporters have been implicated with genetic disorders of amino acid absorption in humans and other mammals (Palacín et al., 2005; Giacopo et al., 2013; Bröer and Fairweather, 2018) and could thus be relevant in the context of NUE. It would be worthwhile to investigate whether the same is true for pigs. However, if genetic selection were to increase the permeability of the small intestine through a decreased expression of tight junctions, there would be a risk that metabolites from microbes would be transferred into the bloodstream, leading to a systemic inflammatory state (i.e. leaky gut syndrome) (Hollander and Kaunitz, 2020). In pigs, Noblet et al. (2013) speculated that heritable variation in hindgut absorption of nitrogen contributes to differences in faecal CP digestibility.

The gut microbiome

The interaction of diet composition with gut microbiome composition influences faecal CP digestibility (Verschuren, 2021), as well as its postileal digestibility, the latter being largely due to the microbiome (Vigors et al., 2016; Sung et al., 2023). A significant pen × batch × diet effect was reported in Déru et al. (2021), indicating that the gut microbiome acquired in early life influences faecal CP digestibility. Inter-individual differences in the overall intestinal microbial composition (i.e. microbiability) that contribute to differences in the faecal digestibility of CP have been shown to be substantial (0.93 ± 0.10; Verschuren et al., 2020). Part of this variation is likely to be genetically determined (Maltecca et al., 2020). On high-fibre diets, 'unimproved breeds' show superior faecal CP digestibility than breeds optimised for low-fibre diets, which is likely due to enhanced microbial fermentation in the gut (Kyriazakis, 2011; Berghaus, 2022). A larger digestive tract may help digest and absorb nutrients from fibre-rich feeds by providing more surface area for absorption and harbouring the mucosal microbiome, and a longer transit time of the digesta allows for longer exposure to the activity of the luminal and mucosal microbiome. In particular, colon length and caecum size play a significant role in transit time and microbiome composition (Le Goff and Noblet, 2001; Kyriazakis, 2011). Fattening and selecting pigs on high−fibre diets is particularly relevant for breeding more sustainable pigs, as an increased capability to recycle and absorb nitrogen with the help of the microbiome can help reduce CP levels in pig feed, and facilitate the replacement of easily digestible soybean meal with high-fibre alternatives such as rapeseed meal. This could reduce long-distance transport and feed-food competition, as well as improve self-sufficiency, especially in European countries (Pérez de Nanclares et al., 2017; Berghaus, 2022).

Allocation of proteins to tissues and body functions

The postabsorption metabolism of amino acids in organs and tissues is another crucial NUE element, in which genetic variation can occur. Once absorbed, amino acids are distributed via the circulatory system and can be allocated to different body functions, such as growth and maintenance, for example the immune or endocrine system, the production of neurotransmitters and other regulatory components (Klindt et al., 2006; Kyriazakis, 2011; Bröer and Bröer, 2017). The maintenance requirements of the organism, including tissue turn-over and repair and defence against pathogens, have to be met, before proteins can be allocated to growth (Kyriazakis, 2011). Such a balance in the partitioning of proteins between these 'fitness' (i.e. maintenance) and 'productive' (i.e. growth) functions (Kyriazakis, 2011) is necessary, so that pigs' adaptive capacity (i.e. the ability to cope with stressors) and, thus, their welfare are not compromised by high lean growth production (Knap and Rauw, 2008). Since amino acids cannot be stored but are immediately used or excreted, the only free amino acids are found in blood plasma (Remus et al., 2021), where concentrations are kept within narrow limits (Bröer and Gauthier-Coles, 2022). Hence, if the amount of amino acids ingested exceeds maintenance and growth requirements, increased urinary nitrogen excretion offsets potential benefits (Harris et al., 2012; Renaudeau et al., 2013; Vigors et al., 2016; Mauch et al., 2018).

Maintenance. Even in the absence of growth and challenges, such as pathogens, nutrient deficiency, heat or other stressors, tissues must be constantly renewed. During this process, there is constant protein turnover to achieve a balance between autophagy and protein biosynthesis, regulated by the mTORC1 complex (Bröer and Bröer, 2017). Although amino acids are efficiently recycled in cells (estimated at 94% in pigs), the inevitable net loss through oxidation of amino acids via the urinary system is approximately 0.3% of the total body nitrogen (Whittemore et al., 2001; Berghaus, 2022); thus, they must be constantly replenished by intake. The rate of turnover of a tissue depends on its metabolic activity and the half-lives of its constituting proteins and can range from a few hours for enzymes to up to a year for structural proteins in skeletal muscle (Rolfs et al., 2021). The gastrointestinal system, with its high metabolic activity due to the continuous production of digestive enzymes and transporter proteins, uses already a considerable proportion of the absorbed amino acids for its own maintenance. Between 37 and 93% of the amino acids that make up the gastrointestinal tract are renewed every day, compared to 82% in the liver and only 9% in muscle (Ponter et al., 1994). Pig breeds differ in their maintenance requirements (Milgen et al., 1998), but this may be due to differences in body composition, protein intake and activity levels (Kyriazakis, 2011; Millet et al., 2018). Thus, there is a potential for genetic variation in maintenance requirements that could be exploited in selection (Kyriazakis, 2011; Shurson and Kerr, 2023), but the extent remains unclear.

Exposure to stressors, such as social or heat stress, immune challenges or injury, leads to a redirection of liver protein synthesis from structural proteins to acute-phase proteins. These play a critical role in fighting pathogens and promoting tissue repair (Cui et al., 2019). During infection with novel pathogens, protein resources are reallocated from lean tissue growth to the innate immune response, immunity build up and tissue repair (Kyriazakis and Sandberg, 2006). However, efficient pigs do not appear to be immune-compromised compared to less efficient pigs, on the contrary, they may be able to allocate resources more effectively by using different metabolic strategies (Dunkelberger et al., 2015, Merlot et al., 2016). In pigs divergently selected for residual feed intake (**RFI**), a disease challenge resulted in less growth impairment and earlier antibody level increase in low RFI (efficient) pigs than in high RFI pigs in a U.S. Yorkshire population (Dunkelberger et al., 2015) and similar average daily gain (**ADG**) in both lines. Further, there were indications of greater muscle protein accretion in low RFI pigs than in high RFI pigs during inflammation in a French Large White population (Merlot et al., 2016).

Chronic heat stress, in particular, is unfavourable for NUE (Renaudeau et al., 2013) (Table 1) because it diverts amino acids away from lean growth to tissue repair and the immune system (Pearce et al., 2013; Cui et al., 2019). Moreover, heat-stressed pigs reduce their feed intake and compensate for the negative energy balance by using amino acids as an energy source (Cui et al., 2019). Psychosocial stress, such as group mixing and crowding, has been shown to affect gut barrier and transporter function (albeit not amino acid transporters directly) and villi height, leading to reduced growth in pigs (Li et al., 2017), impaired gut-brain axis communication, and altered gut microbiome and gut motility in a range of mammalian species (Leigh et al., 2023). Further, psychosocial stress affects neuroendocrine regulation and immunity (Gimsa et al., 2018), diverting resources away from lean growth. Consequently, NUE could be indirectly improved by selecting for resilience and robustness, as pigs that are less susceptible to illness, heat or social stress will have reduced maintenance requirements and can allocate more amino acids to lean growth.

Growth. Provided that the diet contains sufficient energy and amino acids, growing pigs will allocate ingested amino acids in excess of maintenance requirements to muscle mass development until the animal's growth potential is reached. Beyond this point, any additional amino acids consumed that are not needed for maintenance, are deaminated and used for energy or glucose synthesis, and the resulting urea is excreted by the kidneys (Klindt et al., 2006; Kyriazakis, 2011). Thus, pigs whose genetic potential allows them to reach maturity at an older age will reduce the rate of protein accretion later than those that reach compositional maturity earlier (Fabian et al., 2003; Martínez-Ramírez et al., 2008) and will generally have higher NUE. This is the case for boars, which, on average, have a higher NUE than gilts, which, in turn, have a higher NUE than barrows (Ruiz-Ascacibar et al., 2017; Millet et al., 2018). Boars are also characterised by a higher proportion of lean mass both at and after maturity than barrows (Pauly et al., 2009), consequently requiring higher levels of amino acids for the maintenance of muscle tissue throughout their lives.

Under conditions of amino acid deficiency, however, the process can be reversed and amino acids in muscle can be repurposed to support essential functions, such as immune response and tissue repair, during periods of amino acid deficiency. This process is initiated by the mTORC1 complex, which activates metabolic pathways that degrade body proteins, primarily through autophagy (Bröer and Bröer, 2017). This metabolic flexibility is essential for pig fitness (Berghaus, 2022) because, in the absence of a reservoir of free amino acids, the body relies on the recycling of endogenous muscle proteins and should not be compromised in favour of higher production, despite the high energy cost and the potential to reduce NUE. Therefore, to ensure that only pigs that have the adaptive capacity to cope with limiting conditions are selected, it is advisable to select pigs in moderately demanding environments, such as those with limited protein supply and suboptimal hygiene. Otherwise, there is a risk of a reduced ability to cope with stressors, reduced resilience, and increased environmental sensitivity in typical agricultural settings (Knap and Rauw, 2008).

Phenotyping nitrogen use efficiency

The key to rapid and successful breeding is precise phenotypes, that is, measurements or estimates of the traits in an individual animal. The quality and statistical power of all downstream calculations, whether estimating genetic parameters or establishing a reference population for genomic selection, can be compromised by inaccurate phenotypes. Phenotyping NUE is notoriously difficult and laborious and, therefore, expensive. Metabolic chambers and cages are suitable for physiological and nutrient balance studies (Table 1), where small numbers of animals are sufficient but high accuracy of measurement of nitrogen intake and the amount of nitrogen excreted is required. However, to increase NUE through breeding, large numbers of animals need to be measured. To directly determine NUE when nitrogen balance studies are not feasible, accurate CP intakes are recorded over a period of time during which muscle tissue gain is determined. As the carcass is primarily used for human consumption, it seems reasonable to focus on phenotyping efforts at the carcass level rather than the whole body. Apart from the lower NUE values at the carcass level shown in Table 2 compared to Table 1, the difference is also apparent in the heritability estimates of NUE at the carcass and whole-body levels. For the same set of pigs, heritabilities of 0.36 and 0.41 were estimated for carcass and whole body, respectively, (Table 3) (Kasper et al., 2020), reflecting a higher environmental influence on carcass NUE than on whole-body NUE.

The aim of a phenotyping strategy should always be to reflect the trait as accurately as possible to achieve the desired result, and to attain a level of precision such that rank reversals of the estimated breeding values are avoided, which is unfortunately rarely investigated. The timing of phenotyping is important for accelerating genetic gain (Schmid et al., 2024). As discussed above, the heritability of NUE is higher in the starter and grower phases, but targeting the finisher phase with the highest feed consumption and nitrogen excretion will result in a higher total reduction of nitrogen excretions. Finally, the nutritional environment during phenotyping is likely to be pivotal. Ideally, phenotyping should take place in a production environment in which future pigs are expected to perform best, accompanied by diets that improve both pig and system NUE, such as high-fibre rapeseed co-products (Pérez de Nanclares et al., 2017).

Measuring nitrogen use efficiency

Studies estimating heritability using measured NUE based on input and retention at the level of the whole animal as a phenotype, rather than estimates of NUE or proxy traits, are rare for the reasons given above. Kasper et al. (2020) estimated a heritability of 0.41 using data from nutrition studies (Ruiz-Ascacibar et al., 2017; Bee et al., 2021a, b). The NUE of 294 pigs (gilts, boars and barrows) was measured by determining nitrogen intake by recording individual feed intake at automated feeder stations and by conducting wet-chemistry analysis of the nitrogen content in feed, empty body and carcass (Table 3). A follow-up experiment used an approach that was more amenable to a higher number of measurements, replacing wet chemical analysis of the body with scans of carcass halves using a dual X-ray absorptiometry (**DXA**) scanner (Ewaoluwagbemiga et al., 2023a). This method gives the lean content of the carcass, which can be converted into nitrogen content using a calibration equation, yielding high precision and low prediction error ($R^2 = 0.99$, rCV = 3.7%) (Kasper et al., 2021). It should be noted that, technically, the lean mass from the DXA method is estimated via a calibration equation, yet it is, in fact, very close to a measurement. The DXA method was used to phenotype 777 pigs (gilts and barrows) and the data were combined with those from Kasper et al. (2020), Bee et al. (2021a) and Bee et al. (2021b) to yield a heritability of 0.54 ± 0.1.

Estimation and prediction methods

With more and more experimental farms and test stations equipped with electronic feeders, it has become increasingly feasible to determine individual nitrogen uptake. However, it is still difficult to determine the body or carcass nitrogen content. Some studies used models or estimation methods to approximate the nitrogen content of pigs (Tables 1 and 3). Common to these studies is the assumption of an 'average' pig. While these assumptions are valuable for nutritional purposes, they mask the individual variation that is fundamental for estimating breeding values and linking genomic variation to trait variation. Saintilan et al. (2013) estimated nitrogen excretion as a proportion of nitrogen intake, which is comparable to NUE. Whereas the nitrogen intake of each pig was recorded by electronic feeders, the lean meat content – from which nitrogen deposition was calculated – was approximated via linear equations from the weights of cuts at dissection. This approach is still quite close to measuring NUE as described above; however, often, the weight of backfat, loin, and ham at dissection may not be available for the necessary large number of pigs. Heritability estimates ranged from 0.36 to 0.43, which is considerably lower than the abovementioned measurements of NUE.

Estimation methods may still have value if they do not average too crudely and allow for enough individual variation through sophisticated semi-mechanistic models (Verschuren, 2021). Verschuren (2021) measured individual nitrogen intake, and estimated protein deposition from BW gain by fitting a Gompertz function. However, this method still masks individual variation by assuming a constant relationship between BW and lean meat content. Thus, the heritability estimates obtained in this study, ranging from 0.21 to 0.27, were substantially lower than those reported in the studies described above (Saintilan et al., 2013; Kasper et al., 2020; Ewaoluwagbemiga et al., 2023a). Schmid et al. (2024) determined the daily nitrogen intake and BWs of single-housed pigs individually, but the nitrogen retention of each pig was extrapolated from a 10% sample, for which nitrogen balance data and blood metabolites were available (Berghaus et al., 2023). This could also lead to a loss of individual variation in these parameters, which might be reflected in the low heritabilities (Table 3). Predicting nitrogen digestibility from the faecal microbiome composition holds some promise but requires improvement (Verschuren et al., 2020), and there is a need to investigate whether it can also be used to predict NUE. Alternatively, NUE could be directly inferred from other traits, bypassing the need to determine both nitrogen intake and body nitrogen content. For instance, Ewaoluwagbemiga et al. (2021) attempted to predict NUE from feeding patterns collected by electronic feeders, but the precision was very low. However, combining feeding patterns with other information routinely available from production might help improve this method.

Component traits and proxies

Given the difficulties in measuring or even estimating NUE in a large number of animals, heritabilites are estimated for component traits or proxies instead. Table 3 lists a range of studies that estimated the heritability of faecal nitrogen digestibility with near-IR spectroscopy (Déru et al., 2021; Martinsen et al., 2023), protein deposition or lean or muscle growth rate (Stern et al., 1993; Chen et al., 2002, Gjerlaug-Enger et al., 2012; Shirali et al., 2014; Godinho et al., 2018), and nitrogen excretion either directly (Shirali et al., 2014) or as urea content in the blood (Klindt et al., 2006; Schmid et al., 2024). Component traits certainly reflect genetic potential in only a part of NUE, but not in the entire trait. The genetic potential for high protein digestibility may be counteracted by a reduced protein deposition capacity. Similarly, the rate of protein deposition will definitely be limited if only a low amount of protein is absorbed from the diet.

Faecal spot samples offer a simple method of phenotyping faecal digestibility but have limited temporal resolution. Heritability estimates can also be heavily influenced by diet type (e.g. Déru et al., 2021), and digestibility only captures one, albeit important, component of NUE. Muscle or lean tissue growth rates are of interest because they are endpoints of NUE and represent the tissue in which the effects of NUE are ultimately observed. The muscle growth rate was measured as the average daily growth of the muscle using computed tomography (Gjerlaug-Enger et al., 2012). The lean growth rate was approximated based on ultrasound measurements of muscle depth, weight gain, and slaughter yield (Stern et al., 1993) or estimated using a prediction equation (Chen et al., 2002). Similar traits in Table 3 are average daily protein deposition, estimated from water content using the deuterium dilution technique (Shirali et al., 2014), and protein deposition, estimated from BW and backfat thickness (Godinho et al., 2018). Heritabilities for these traits ranged from 0.14 to 0.46. Whereas heritability estimates in most breeds and under a standard diet were similar (ranging from 0.33 to 0.46), those obtained from pigs under a high fibre diet were lower (0.14–0.24) (Godinho et al., 2018), as was an estimate for Norwegian Landrace (h^2 = 0.19) on a standard diet. These particular findings of heritability estimates differing among diets and genetic backgrounds will be discussed below (Genetic correlations section).

Another component trait included in Table 3 was nitrogen excretion. Klindt et al. (2006) investigated the heritability of plasma urea nitrogen concentrations as an indicator of the efficiency of lean tissue growth and reported heritabilities between 0.16 and 0.35. Schmid et al. (2024) found considerable heritability (0.42 and 0.46) for blood urea nitrogen concentrations, an indicator of protein degradation levels. Blood urea nitrogen concentrations were moderately genetically correlated with NUE, questioning its suitability as a proxy. In summary, although precise methods are very difficult to implement on a large scale, proxies often yield lower estimates and thus allow for lower genetic gains. Furthermore, component traits focus on one component of NUE while neglecting the others, which could lead to unintended consequences in breeding, as will be discussed below.

Genetic parameters of nitrogen use efficiency

Heritability

Due to difficulties in phenotyping, only a few studies have estimated the heritability and genetic correlations of NUE and mapped quantitative trait loci (**QTL**). Furthermore, the comparability of these estimates is hampered by the fact that the phenotype varies between studies, that they are taken on the whole body or at the carcass level, and that different breeds, diets, age classes, and sexes have been included in the studies (Table 3). Despite the heterogeneity of the study designs, the 38 estimates gathered in Table 3 show that NUE and related traits are clearly heritable (mean h^2 = 0.34, range: 0.14–0.56) and are therefore promising targets for selection.

Breed differences

Differences between breeds are clearly evident in the NUE values presented in Table 1 from the only study that compares breeds (Saintilan et al., 2013). Nitrogen excretion was lowest in French Landrace, highest in Piétrain, and intermediate in Large White (Saintilan et al., 2013), indicating the influence of genetic background on NUE. For instance, the genetic background of Piétrain shows a distinct effect on NUE. This breed has been intensively selected for increased lean meat content, which has led to an increase in the frequency of a mutation in the *RYR1* (Halothane) gene (Gispert et al., 2007). While this mutation enhances lean growth, it also renders pigs susceptible to Porcine Stress Syndrome (Mitchell and Heffron, 1982; Ciepielewski et al., 2016) and negatively affects meat quality (Gispert et al., 2007; Bates et al., 2012). Interestingly, desirable performance with regard to lean growth, carcass and meat quality has been demonstrated even in Piétrain lines lacking the *RYR1* mutation (Plastow et al., 2005; Gispert et al., 2007). Heritabilities, however, did not differ remarkably between breeds for nitrogen excretion f(Saintilan et al., 2013) and lean growth rate (Chen et al., 2002); the estimates were intermediate and very similar between French and U.S. breeds. By contrast, Gjerlaug-Enger et al. (2012) reported a much lower heritability (and additive genetic variance) for muscle growth rate in Norwegian Landrace boars (h^2 = 0.19), a highly efficient breed with a long selection history, than in Duroc boars (h^2 = 0.43), which showed values more consistent with the other estimates.

Genomic regions associated with nitrogen use efficiency

The complexity of NUE described above – that is the involvement of various tissues and processes – suggests a polygenic trait architecture in which many genetic variants, distributed across the

Table 3
Heritability estimates of nitrogen use efficiency and related traits in pigs.

Trait	h^2	SE	n	Diet	Phase	Breed	Sex	*RYR1*	Level	Reference
NUE	0.41	NA	294	mix[1]	entire fattening period	Large White dam line	gilts, boars, barrows	free	carcass	Kasper et al. (2020)[2]
	0.36	NA							whole body	
NUE	0.54	0.1	1 071	mix[3]	entire fattening period	Large White dam line	gilts, boars, barrows	free	carcass	Ewaoluwagbemiga et al. (2023a)
NUE	0.22	NA	2 137	mix[4]	starter	crossbred	boars and gilts	NA	whole body	Verschuren (2021)
	0.27	NA			grower					
	0.21	NA			finisher					
NUE	0.29	0.08	508	standard	grower	crossbred	gilts and barrows	NA	whole body	Schmid et al. (2024)
	0.16	0.08			finisher					
N_r[5]	0.43	0.04	6 470	standard	entire fattening period	Landrace dam line	gilts and barrows	NA	whole body	Saintilan et al. (2013)
	0.37	0.03	10 694			Large White dam line				
	0.36	0.07	2 342			Large White sire line				
	0.41	0.06	2 448			Pietran sire line		yes		
PUN	0.35	0.15	511	standard	107 days	crossbred	gilts, boars, barrows	NA		Klindt et al. (2006)
	0.21	0.13			128 days					
	0.16	0.12			149 days					
BUN	0.42	0.09	508	standard	grower	crossbred	gilts and barrows	NA		Schmid et al. (2024)
	0.46	0.1			finisher					
TNE	0.32	0.21	315	standard	finisher	crossbred	gilts and barrows	yes[6]		Shirali et al. (2014)
PD	0.46	0.19								
PD	0.38	0.11	2 230	low fibre[7]	overall	Crossbred	boars and gilts	NA		Godinho et al. (2018)
	0.33	0.11			starter					
	0.37	0.11			grower					
	0.33	0.1			finisher					
	0.24	0.11		high fibre[8]	overall					
	0.14	0.09			starter					
	0.23	0.11			grower					
	0.23	0.1			finisher					
LTGR	0.39	0.09	2 885	high protein[9]	entire fattening period	Yorkshire	boars and gilts	free		Stern et al. (1993)
	0.35	0.08		low protein[9]						
LGR[10]	0.44[11]	0.01–0.02[12]	361 300	standard	all	Yorkshire	gilts, boars, barrows	NA		Chen et al. (2002)
	0.44[11]		154 833			Duroc				
	0.46[11]		99 311			Hampshire				
	0.39[11]		71 097			Landrace				
MG[13]	0.19	0.04	3 835	standard	all	Landrace	boars	free		Gjerlaug-Enger et al. (2012)
	0.43	0.05	3 139			Duroc				
DCN	0.27	0.12	1 242	standard	entire fattening period	Large White	boars	NA		Déru et al. (2021)
	0.56	0.15		high-fibre			boars			
ATTDn	0.20	NA	1 022	standard	entire fattening period	Duroc	boars	NA		Martinsen et al. (2023)

Abbreviations: h^2 = heritability; *RYR1* = tested for ryanodine receptor (Halothane) gene; NUE = nitrogen use efficiency; N_r = percent nitrogen excretion; PUN = plasma urea nitrogen concentration; BUN = blood urea nitrogen; TNE = total nitrogen excretion; PD = protein deposition; LTGR = lean tissue growth rate; MG = average daily muscle growth; LGR = lean growth rate; DCN = digestibility coefficient of nitrogen; ATTDn = apparent total tract digestibility of nitrogen; NA = not available.

[1] A part of the pigs was fed a standard diet and a part a protein-reduced diet; diet was included as a factor in the model.

[2] Data from Kasper et al. (2020) are included in Ewaoluwagbemiga (2023a).

[3] A small proportion of the pigs was fed a standard and most pigs a protein-reduced diet; diet was included as a factor in the model.

[4] A part of the pigs was fed a corn-soybean meal diet (lower fibre and fat content) and a part a wheat-barley diet (higher fibre and fat content); diet was included as a factor in the model.

[5] Ratio of N excreted over N intake. Nitrogen intake estimated from total feed intake during the test period and the nitrogen content of pigs estimated from lean meat content and BW.

[6] All grandsires were heterozygous at the *RYR1* locus.

[7] corn-starch (lower fibre and fat content).

[8] Wheat-barley (higher fibre and fat content).

[9] Two lines selected for high LTGR, one under diet with high and one with low protein content.

[10] Adjusted to 113.5 kg; predicted using equation in (National Pork Producers Council NPPC, 2000).

[11] Heritability estimates taken from model with litter effects but without maternal effects (Model 1 in Chen et al. (2002). Heritability estimates of a model including the maternal effect but not the litter effect (Model 2 in Chen et al. (2002)) were similar.

[12] Exact SEs were not given in Chen et al. (2002), but reported to range approximately from 0.01 to 0.02.

[13] Measured by computed tomography.

genome, individually contribute a very small effect to the phenotype (Boyle et al., 2017). To achieve sufficient statistical power, sample sizes in the tens of thousands are required. This presents a challenge to identifying the genes underlying the differences in NUE in a genome-wide association study (**GWAS**), with sample sizes that can realistically be achieved, given the difficulties of phenotyping. In addition, relevant loci are likely to be mediated by gene expression QTL (Gilad et al., 2008; Crespo-Piazuelo et al., 2023). Thus, not only differences in protein-coding genes but also in regulatory regions should be expected to contribute to variation in metabolic traits, such as NUE.

Shirali et al. (2013) genotyped 88 markers on 10 of the 18 chromosomes with reported or assumed contributions to lean and fat tissue traits and mapped QTL associated with nitrogen excretion and protein deposition in approximately 300 crossbred pigs. Of the 23 QTL identified for nitrogen excretion traits, 8 were significant for the entire fattening period, and 15 were specific to growth stages. The identification of different QTL for nitrogen excretion and protein deposition traits at different growth phases suggests that during the period of accelerated growth, other processes are prioritised than in periods of flattened growth (e.g. lean tissue growth vs reproduction). A QTL on Sus scrofa chromosome (**SSC**) 10, which was associated with nitrogen excretions in the grower phase, was ascribed to the grandfatherly Piétrain lineage (Shirali et al., 2013). On SSC9, a QTL was identified for the entire fattening period, and the authors interpreted this QTL as being particularly responsible for lean production, since this region was associated with an increase in feed intake, protein deposition and ADG. The same QTL, based on the same data, was also reported by Duthie et al. (2008) for protein deposition.

A recent study conducted a GWAS for NUE in around 500 individuals and used a similar cross of Landrace and Piétrain (Schmid et al., 2024). With approximately 50 Stoll, P., Ruiz-Ascacibar, I., 2015. Passen die Normen zu einer effizienten Aminosäurenversorgung der heutigen Schweinegenetik? Conference Proceedings ETH-Schriftenreihe zur Tierernährung, 13 May 2015, Zurich, Switzerland, pp. 33-38000 genomic variants, they identified 2 signals on SSC5 and 3 on SSC13 at a suggestive threshold ($P < 5 \times 10^{-5}$) for NUE exclusively in the grower phase and eight different signals on SSC6 in the finisher phase. Interestingly, suggestive single nucleotide polymorphisms (**SNP**s) for nitrogen intake, nitrogen retention and blood urea nitrogen concentrations did not overlap, except for some SNPs on SSC6 that were close to the suggestive threshold for nitrogen intake in the finisher phase. The studies of Shirali et al. (2013) and Schmid et al. (2024) both identified QTL on SSC13, but it is unclear if those truly overlap since different reference genomes were used. A signal on SSC6 was also present in both studies, and Shirali et al. (2013) speculated that the QTL on SSC6, which likely originates in the Piétrain grandpaternal breed, is unique for NUE. The signal identified by Schmid et al. (2024) on SSC5 could not be compared, since this chromosome was not investigated by Shirali et al. (2013).

Another study attempted to map QTL for NUE applied regional heritability mapping in addition to GWAS on over 1 000 Large White pigs (Ewaoluwagbemiga et al., 2023b). The genotype data were generated from low-pass (1x) whole-genome sequencing followed by imputation and consisted of approximately 15 million SNPs. Although no SNPs could be identified with GWAS for NUE, regional heritability mapping found a signal each on SSC2 and SSC9 at a suggestive threshold ($P < 9 \times 10^{-4}$). The pigs in this study had no Piétrain background, which might be a reason why there was no overlap with the QTL identified in Schmid et al.'s (2024) study. On the two chromosomes (SSC2 and SSC9), where suggestive QTL were located by Ewaoluwagbemiga et al. (2023b), Shirali et al. (2013) also detected signals for feed intake, protein deposition, and ADG. However, Ewaoluwagbemiga et al. (2023b) did not locate a signal on SSC9 for ADG, but a SNP for average daily feed intake was close to the false-discovery rate significance threshold according to GWAS.

Shirali et al. (2013) tested the associations of a small number of loci with the traits, which yielded significant QTL. However, no single SNP reached genome-wide significance in the two recent studies in which tens of thousands to millions of SNPs were tested (Ewaoluwagbemiga et al., 2023b; Schmid et al., 2024). This indicates that the genetic basis of NUE is indeed polygenic and suggests a high likelihood of false negatives, which impedes the identification of specific genes associated with NUE. Increasing sample sizes may improve detection but is often not feasible due to phenotyping difficulties. In such scenarios, incorporating weights based on functional relevance, based on a deeper biological understanding of NUE, into GWAS analyses may be particularly beneficial (Pérez-Enciso et al., 2015; Wolc and Dekkers, 2022).

Genetic correlations of nitrogen use efficiency

Between growth phases

Most of the genetic correlations of NUE or related traits reported between growth phases are clearly lower than unity (Klindt et al., 2006; Verschuren, 2021; Schmid et al., 2024), suggesting that the sets of genes underlying phenotypic differences in phases of exponential and decelerating growth overlap but are not identical. Whereas NUE during the starter and grower phases was genetically highly correlated ($r_G = 0.92$) in Verschuren (2021), the correlation between the grower and finisher phases was intermediate, while the correlation between the starter and finisher phases was rather low ($r_G = 0.47$ and 0.13, respectively, no SE reported). Schmid et al. (2024) also estimated a genetic correlation of only 0.71 ± 0.21 between the NUE of 40 kg and 60 kg pigs. The same pattern was found in a study that used plasma urea nitrogen concentration (Klindt et al., 2006), with only the genetic correlation between days 128 and 149 being high and clearly different from zero (0.92 ± 0.21) but not those between days 107 and 128 and between 107 and 149. This observation is in line with the findings that the majority of QTL identified for NUE or nitrogen excretion traits seem to be specific to the different growth phases (Shirali et al., 2013; Schmid et al., 2024) discussed above. Sometimes, this was reflected in the heritability estimate differences between growth phases. While the heritabilities across the starter, grower and finisher phases were similar in Verschuren (2021), they decreased with age in other studies (Klindt et al., 2006; Schmid et al., 2024), indicating an increasing influence of the environment in shaping NUE and related traits. However, the transition from one growth phase to the next is marked by a change in diet composition to ensure optimal nutrition for pigs at different ages and growth stages. Thus, the correlations between growth phases cannot be fully separated from correlations between diets or genotype-by-diet interactions (Schmid et al., 2024).

Among diets

Genetic correlations of NUE or related traits across diets that are clearly different from unity or markedly different genetic variance estimates between dietary groups indicate genotype-by-environment or, more specifically, genotype-by-feed (**G** × **F**) interactions. Déru et al. (2021) reported a genetic correlation of less than unity ($r_G = 0.85 \pm 0.21$) between two diets that differed substantially in fibre content, which provides some evidence that genotypes differ in their faecal digestibility response when exposed to varying dietary fibre content. The same study found substantially higher heritability (and additive genetic variance) of faecal nitrogen digestibility in the high-fibre treatment, suggesting that the high-fibre diet challenge revealed more variance in the pigs' ability to digest the feed. This opens up promising avenues for selecting pigs with higher NUE on high-fibre, low-input diets.

In another study, no evidence for G × F was found for protein deposition in Dutch crossbred pigs, since the genetic correlation between diets differing in fibre content was close to unity (r_G = 0.99 ± 0.15) (Godinho et al., 2018). This study also reported lower heritability in pigs receiving a diet with a higher fibre content (h^2 = 0.24) than those with a lower fibre content (h^2 = 0.38) (Godinho et al., 2018), which is opposite to Déru et al.'s (2021) findings. The stronger G × F effect on the faecal nitrogen digestibility coefficient than on protein deposition is certainly not surprising. This could be due to the different host genetic effects on microbiome composition. However, some of the negative effects of fibre on ileal nutrient digestibility and utilisation can be mitigated by other factors that make nutrients encased in fibre more accessible. These include chewing force, which can break down cell walls, and chyme viscosity and dynamics in the gastrointestinal tract (Schop et al., 2020). In general, only a few studies provided evidence of the presence of G × F at different protein levels by comparing breeds. However, especially with regard to the selection of pigs with high NUE, it would be important to evaluate the pigs' performance under various dietary conditions (te Pas et al., 2021) to select the animals that show the best performance in a particular (local) feeding regime. No evidence for a sire × feed interaction was found using Kasper et al.'s (2020) data, in which protein contents differed by 20% (Kasper, unpublished). In summary, the evidence suggests genotype-by-environment or G × F interactions in NUE-related traits, particularly with respect to faecal digestibility responses to different dietary fibre levels.

With growth performance

Genetic correlations with growth traits (Table 4) can indicate potential trade-offs in production. Ideally, NUE is positively correlated with growth, allowing for a shorter turnaround time and, consequently, a higher number of pigs produced per fattening unit. In the literature, the evidence for genetic correlations between these traits is inconclusive. Some studies suggest a lack of significant correlation, particularly in the early stages of growth (Verschuren, 2021; Schmid et al., 2024) or over the entire fattening period (Ewaoluwagbemiga et al., 2023a). Conversely, observations from later growth stages suggest a negative, albeit only intermediate, correlation between NUE and ADG (Verschuren, 2021; Schmid et al., 2024). For nitrogen excretion, there is contradicting evidence: plasma urea nitrogen concentrations were highly positively genetically correlated with ADG (Klindt et al., 2006). At the phenotypic level, there is considerable evidence for a positive correlation between urinary nitrogen and blood urea nitrogen (e.g. Zervas and Zijlstra, 2002; Kohn et al., 2005; Berghaus et al., 2023), indicating that high blood urea nitrogen concentrations reflect high nitrogen excretion. Furthermore, negative genetic correlations between NUE and blood urea nitrogen have recently been shown (Schmid et al., 2024). Thus, it appears that selecting for reduced excretion may lead to slower growth, especially in later growth phases (Klindt et al., 2006). By contrast, Saintilan et al. (2013) reported that nitrogen excretion was moderately negatively genetically correlated with ADG in three of four breeds; thus, selection for lower excretion would favourably affect ADG. Digestibility traits were not significantly correlated with ADG (Déru et al., 2021; Martinsen et al., 2023). Unsurprisingly, the lean tissue growth rate correlated highly positively with ADG (Stern et al., 1993) and highly negatively with days on feed (Chen et al., 2002). However, this effect might be driven primarily by the earlier growth phases, as intermediate genetic correlations were reported for birth to 25 kg live weight, whereas the values were near zero for 25 – 100 kg in Norwegian Landrace and Duroc (Gjerlaug-Enger et al., 2012). Together, it appears that pigs with a genetic disposition for higher NUE or lower nitrogen excretion may be expected to have slower growth rates in the finisher phase, which could lead to production and, thus, revenue losses.

With feed intake and feed conversion ratio

It would appear that, from an economic perspective, the optimal genetic correlation between NUE and feed intake is negative, as feed represents the majority of total pork production costs worldwide (Hoste and Benus, 2023). However, reduced feed intake poses a risk, particularly under stressful conditions, such as heat stress and disease, as it may compromise growth by diverting nutrients to immune function. This could significantly impair the pig's ability to cope with oxidative stress (Cui et al., 2019) and may contribute to compromised gut integrity, thus exacerbating immune stress (Pearce et al., 2013). Therefore, a negative genetic correlation between feed intake and NUE is unfavourable. However, a negative genetic correlation between NUE and FCR is desirable, so that nitrogen-use efficient pigs require less feed to produce 1 kg of bodyweight. Nitrogen use efficiency shows moderate negative genetic correlations with feed intake throughout the fattening period (Ewaoluwagbemiga et al., 2023a), as do nitrogen excretion (Saintilan et al., 2013; Shirali et al., 2014) and faecal nitrogen digestibility (Déru et al., 2021; Martinsen et al., 2023) (Table 4). This is particularly the case in the finishing phase, where the highest amount of feed is consumed (Verschuren, 2021; Schmid et al., 2024); therefore, the highest savings potential can be realised. Interestingly, the genetic correlations between nitrogen excretion and average daily feed intake or RFI differ among breeds (Saintilan et al., 2013).

Concerning FCR, the extent of the link with NUE is much less clear. For instance, Saintilan et al. (2013) estimated genetic correlations of nitrogen excretion with FCR that were close to unity. Interestingly, some studies report moderate to low negative correlations over the entire fattening period (Déru et al., 2021; Ewaoluwagbemiga et al., 2023a), or even no significant correlations in both the grower and finisher phases (Schmid et al., 2024). In Verschuren's (2021) study, genetic correlations of NUE with FCR differed highly between the growth phases, similar to average daily feed intake, with intermediate correlations in the starter phase that increased through the grower phase and almost doubled in the finisher phase. The muscle growth rate was significantly negatively genetically correlated with FCR in Duroc but not in Norwegian Landrace, an already highly feed-efficient breed (Gjerlaug-Enger et al., 2012). Therefore, breeding for increased NUE, nitrogen digestibility, or reduced nitrogen excretion can result in reduced feeding costs, not only because of the reduction in dietary protein but also because of the overall reduction in feed consumption. When breeding for increased NUE, it is essential to aim for stable feed intake to counter the potential adverse effects of nutrient deficiency, particularly under stressful conditions, during which reduced feed intake may exacerbate challenges.

With carcass composition

Genetic correlations with carcass traits (Table 4) provide information on expected changes in revenue when selecting for increased NUE. Backfat thickness is generally moderately negatively correlated with NUE (Ewaoluwagbemiga et al., 2023a) and faecal digestibility (Martinsen et al., 2023) and positively correlated with nitrogen excretion (Saintilan et al., 2013). The high positive genetic correlations of plasma urea nitrogen concentrations and backfat thickness in later growth phases reported by Klindt et al. (2006) can be explained by the ability to use amino acids as an energy source, leading to fat deposition and urea production, when amino acids are supplied in excess. Lean mass traits are genetically moderately positively correlated with NUE (loin muscle area; Ewaoluwagbemiga et al., 2023a) and, accordingly, in the

Table 4
Genetic correlations of nitrogen use efficiency and related traits with production, carcass and meat quality traits in pigs.

Trait	Item	ADG	ADFI	RFI	FCR	BFT	LMC	DP	L*	a*	b*	Reference
NUE	starter	0.11	−0.17		−0.47							Verschuren (2021)
	grower	−0.11	−0.50		−0.68							
	finisher	−0.43	−0.92		−0.90							
NUE	grower	−0.22 ± 0.22	−0.22 ± 0.20		0.02 ± 0.29[1]							Schmid et al. (2024)
	finisher	−0.37 ± 0.27	−0.42 ± 0.25		0.03 ± 0.42[1]							
NUE		−0.19 ± 0.19	−0.53 ± 0.14		−0.55 ± 0.14	−0.37 ± 0.16		0.28 ± 0.19[2] 0.31 ± 0.18[3]	0.06 ± 0.20	−0.27 ± 0.17	−0.31 ± 0.18	Ewaoluwagbemiga et al. (2023a)
LTGR	high protein	0.96 ± 0.01					0.51 ± 0.12					Stern et al. (1993)
	low protein	0.96 ± 0.01					−0.46 ± 0.12					
LGR[4]	Yorkshire	−0.84[5,6]				−0.32[7]						Chen et al. (2002)
	Duroc	−0.86[5,6]				−0.40[7]						
	Hampshire	−0.80[5,6]				−0.35[7]						
	Landrace	−0.83[5,6]				−0.41[7]						
MG[8]	Landrace, starter[9]	0.40 ± 0.11			−0.11 ± 0.12[11]							Gjerlaug-Enger et al. (2012)
	Landrace, grower & finisher[10]	−0.06 ± 0.12										
	Duroc, starter[9]	0.45 ± 0.07			−0.53 ± 0.07[11]							
	Duroc, grower & finisher[10]	0.07 ± 0.10										
PD				0.30 ± 0.29[12]								Shirali et al. (2014))
TNE				0.85 ± 0.11[12]								
PUN	day 107	−0.09 ± 0.29				0.23 ± 0.27[13]						Klindt et al. (2006)
	day 128	0.95 ± 0.30				0.87 ± 0.23[13]						
	day 149	0.81 ± 0.35				0.84 ± 0.28[13]						
N_r	Landrace	−0.46 ± 0.07	0.54 ± 0.06	0.41 ± 0.07	0.97 ± 0.01	0.48 ± 0.01	−0.64 ± 0.01	0.04 ± 0.02				Saintilan et al. (2013)
	Large White dam line	−0.29 ± 0.06	0.44 ± 0.05	0.38 ± 0.06	0.97 ± 0.01	0.43 ± 0.01	−0.55 ± 0.01	0.10 ± 0.01				
	Large White sire line	−0.05 ± 0.28	0.89 ± 0.07	0.57 ± 0.10	0.98 ± 0.01	0.42 ± 0.02	−0.53 ± 0.02	0.01 ± 0.02				
	Piétrain sire line	−0.32 ± 0.10	0.31 ± 0.10	0.83 ± 0.04	0.98 ± 0.01	0.22 ± 0.02	−0.32 ± 0.02	0.04 ± 0.02				
DCN		−0.15 ± 0.17	−0.53 ± 0.13	−0.54 ± 0.16	−0.24 ± 0.10	0.02 ± 0.15[14]	−0.08 ± 0.16	−0.49 ± 0.33[15]	−0.03 ± 0.24	−0.18 ± 0.15	−0.16 ± 0.20	Déru et al. (2021)
ATTDn		−0.11 ± 0.14[6]	−0.54 ± 0.11[16]			−0.31 ± 0.14	0.11 ± 0.13[17]					Martinsen et al. (2023)

Abbreviations: NUE = nitrogen use efficiency; LTGR = lean tissue growth rate; LGR = lean growth rate; MG = average daily growth of muscle; PD = protein deposition; PUN = plasma urea nitrogen; N_r = nitrogen excretion; TNE = total nitrogen excretion; DCN = digestibility coefficient of nitrogen; ATTDn = apparent total tract digestibility of nitrogen; ADG = average daily gain; ADFI = average daily feed intake; RFI = residual feed intake; FCR = feed conversion ratio; BFT = back fat thickness; LMC = lean meat content; DP = dressing percentage; L*, a*, b* = meat lightness, redness and yellowness, respectively, on the CIELAB colour space.

[1] Gain-to-feed ratio (the inverse of FCR).

[2] Warm dressing percentage.

[3] Cold dressing percentage.

[4] Adjusted to 113.5 kg; predicted using the equation in National Pork Producers Council (NPPC, 2000).

[5] Standard errors ranged from approximately 0.005–0.009 (Chen et al., 2002).

[6] Days on feed.

[7] Standard errors ranged from approximately 0.01–0.02 (Chen et al., 2002).

[8] Measured by computed tomography.

[9] Birth – 25 kg.

[10] 25 – 100 kg.

[11] Over entire fattening period.

[12] Residual energy intake.

[13] At 21 weeks.

[14] Backfat percentage.

[15] Carcass yield percentage.

[16] Feed consumption

[17] Loin depth.

opposite direction with nitrogen excretions (lean meat content; Saintilan et al., 2013). Carcass yield in terms of dressing percentage, however, has only weak favourable genetic correlations with NUE (Ewaoluwagbemiga et al., 2023a) and practically none with nitrogen excretions (Saintilan et al., 2013). The unfavourable genetic correlation of faecal nitrogen digestibility with carcass yield reported by Déru et al. (2021) might be explained by the larger digestive tracts of pigs with higher digestion ability, and thus a lower carcass yield at slaughter. In Stern et al.'s (1993) study, two lines selected for lean tissue growth rate for four generations showed opposite genetic correlations of lean tissue growth rate with carcass lean percentage. The line selected for lean tissue growth rate on a high-protein diet had a positive genetic correlation, whereas the line selected on a low-protein diet had a negative correlation. This was attributed to the fact that the line selected on the high-protein diet appeared to favour protein deposition, whereas the line selected on the low-protein diet was forced to increase feed intake to meet protein requirements, which could have resulted in increased fat deposition. Interestingly, the genetic background did not generally seem to lead to substantial differences in the genetic correlation estimates. In another study on lean growth rates, the genetic correlations with backfat thickness in four breeds were moderately negative and similar (Chen et al., 2002). In summary, it can be assumed that pigs with a higher genetic potential for NUE have reduced backfat thickness and higher lean mass, but it is not yet clear whether this leads to a higher yield at slaughter.

With meat quality

Finally, studies investigating the genetic correlations of NUE and related traits with meat quality are rare (Table 4). There is little evidence that pH or meat colour would be affected by genetically selecting for increased NUE or faecal nitrogen digestibility, as genetic correlations are low or not significant (Déru et al., 2021). However, meat redness and yellowness show low-to-moderate negative genetic correlations with NUE, which could lead to a reduction in the respective colour components (Ewaoluwagbemiga et al., 2023a). Consumer preferences regarding meat colour can vary widely between individuals or countries (Ngapo et al., 2007; Altmann et al., 2023), and its importance in purchasing decisions is unclear; it may not be important per se but could be used as a proxy for tenderness and juiciness (Altmann et al., 2023). Meat lightness, which has been reported to influence purchase decisions the most (Norman et al., 2003) and may be related to water-holding capacity (Gagaoua et al., 2023), was not significantly correlated with NUE (Ewaoluwagbemiga et al., 2023a). However, the water-holding capacity and the intramuscular fat content showed unfavourable genetic correlations with NUE (0.22 ± 0.19, 0.59 ± 0.15, and −0.39 ± 0.15 for drip loss, cooking loss and intramuscular fat content, respectively; Ewaoluwagbemiga et al., 2023a). Finally, there was no genetic correlation of NUE with shear force, indicating no conflict with meat tenderness (Ewaoluwagbemiga et al., 2023a). Taken together, genetically selecting for improved NUE might alter meat colour, but the effect on consumer acceptance is difficult to predict. However, the genetic improvement of NUE could lead to greater water loss and lower intramuscular fat content in the meat, which could be perceived negatively by customers.

Breeding for increased nitrogen use efficiency

From the above, it is clear that successful breeding for higher NUE is quite realistic. Studies investigating the heritability of NUE reported estimates of at least 0.14 but usually higher, up to 0.56. Genetic correlations with other traits are usually beneficial, or if not, they appear manageable. Although unintended negative consequences of breeding for higher NUE seem unlikely, they should be carefully monitored in future studies. Based on the evidence to date, there might be a slight risk of reduced growth performance (Saintilan et al., 2013; Déru et al., 2021; Verschuren, 2021; Martinsen et al., 2023; Ewaoluwagbemiga et al., 2023a; Schmid et al., 2024), which might be due to lower feed intake (Ewaoluwagbemiga et al., 2023a; Schmid et al., 2024) or increased maintenance requirements of the intestinal tract (Noblet et al., 1999; Déru et al., 2021). However, it can be assumed that breeding programmes can address this by giving appropriate weights to the traits in the selection indices. In addition, a limited CP content of the diet could result in increased lipid deposition that does not allow the pigs to realise their genetic potential for lean growth (Stern et al., 1993), but this can be countered with offering an adequate diet.

However, to date, NUE has not yet been directly targeted in pig breeding because of several major challenges. A primary challenge is phenotyping NUE, which is difficult and costly, as discussed above. It is also often argued that in general, breeding for increased performance automatically leads to increased NUE. However, as the genetic correlations of NUE with traits such as FCR and RFI are often considerably less than one, this is not necessarily the most effective approach, as discussed below. Breeding goals in commercial pig production, driven by market and societal factors (Knap, 2023), often lack financial incentives to reduce CP in feed, despite awareness of current unsustainable practices regarding nitrogen pollution and large-scale protein feed imports.

Indirect selection via feed efficiency and component traits

There is a logical overlap between NUE and FCR. The efficient conversion of dietary protein into lean mass is a key factor in achieving a lower FCR, with the remaining efficiency largely due to the conversion of energy into fat tissue. Over the last few decades, breeding for improved feed conversion and lean growth has indirectly improved NUE and considerably reduced manure volumes (Soleimani and Gilbert, 2021; Vonderohe et al., 2022). However, more targeted efforts to increase NUE are still needed as meat consumption continues to rise (Lassaletta et al., 2019). Direct selection for NUE has been shown to be more effective than indirect methods using FCR or RFI in poultry (de Verdal et al., 2011). It is assumed that selecting for a lower FCR or RFI will primarily improve energy efficiency rather than NUE, particularly under conditions where the diet provides non-limiting levels of CP (Millet et al., 2018). This is supported by Vigors et al.'s (2016) observations that a pig line selected for low RFI had a higher digestibility of gross energy, but not nitrogen, than a high RFI line in the ileum, where the majority of nutrient absorption occurs. Only when total tract nutrient digestibility was considered, did the low RFI line have a higher nitrogen digestibility than the high RFI line. The same study also reported a significantly higher relative gene expression of fatty acid and glucose transporters, but not of amino acid transporters in the jejunum of the low RFI line (Vigors et al., 2016).

As presented above, there is mixed evidence of a genetic relationship between NUE or related traits and FCR or RFI. One study reported near-unity genetic correlations of nitrogen excretions and FCR (Saintilan et al., 2013), suggesting that the traits are basically identical; however, other studies found moderate (Ewaoluwagbemiga et al., 2023a) or even no genetic correlations (Schmid et al., 2024). The genetic correlation between NUE and FCR seems to depend on the growth phase, with increasing absolute values with age (Verschuren, 2021). In accordance with this, it was observed that the overlap of QTL for total nitrogen excretion and FCR was greatest in the finisher phase (Shirali et al., 2013). In

Ewaoluwagbemiga et al. (2023b), there was little overlap in the potential QTL for the two traits. In addition, the proportion of genomic variance explained by every chromosome for NUE and FCR differs considerably, with the exception of SSC2 and SSC 6, which both contribute the most to NUE and FCR (Figs. 1 and 2 in Ewaoluwagbemiga, 2023). Interestingly, after SSC2, SSC10 explains most of the genomic variance for NUE but practically no variance for FCR. Taken together, it is difficult to predict whether improving overall feed efficiency will indirectly result in more nitrogen−efficient pigs.

Relying on selecting for component traits as proxies to improve NUE can increase the cost-efficiency of breeding programmes. However, this is likely to have shortcomings that need to be carefully considered. The genetic correlation between a proxy and a target trait is rarely perfect, and may change over the course of individual development as well as generations during selection. The ensuing discrepancies between the proxy and the target trait and their effects on animal performance, fertility, and health are often not well understood. This can potentially lead to suboptimal breeding decisions, as there is a risk of inadvertently selecting for undesirable traits associated with the proxy trait.

Focusing too much on one component of NUE at the expense of the other should also be avoided. For example, lean growth does not take into account feed intake, which is likely to increase as a result. Indeed, as Stern et al.'s 1993 findings show, compared to genetic potential, the genetic progress of the lean tissue growth rate was slower in a selection line on the low-protein diet than on the high-protein diet, as it limited lean growth and resulted in higher carcass fat content due to differences in feed consumption. Furthermore, due to strong selection over the last few decades, genetic variation in lean growth seems to be largely depleted (Gjerlaug-Enger et al., 2012; Shurson and Kerr, 2023). Selection of increased digestibility of CPs and amino acids is certainly promising, but does not guarantee a corresponding genetic gain in NUE, as the postabsorptive nutrient metabolism within organs and tissues may outweigh the effects of digestibility and play a crucial role in actual NUE differences (Windisch et al., 2016; Berghaus, 2022). Thus, if not accompanied by a corresponding increase in lean growth, nitrogen loss might be merely shifted from faeces to urine, which is more environmentally problematic (Déru et al., 2021).

Furthermore, the negative genetic correlation of faecal nitrogen digestibility with dressing percentage suggests that pigs may achieve high faecal digestibility by increasing gut size, thereby reducing carcass yield (Déru et al., 2021). Selecting for the desired outcome, NUE, directly should therefore be prioritised, as this promises to improve all components simultaneously, from reduced nitrogen uptake, improved ileal and total tract digestibility, especially of fibre-rich diets, increased protein deposition and possibly greater nitrogen recycling capacity. However, this could mask potential interactions between the component traits that could result in the genetic selection of single components in an unfavourable direction. As NUE is a ratio trait, determined by the proportion of nitrogen retained in the carcass to the total nitrogen intake, an increase in nitrogen retention (favourable) as well as a reduction of nitrogen intake (unfavourable) result in a higher trait value. In the practical implementation, a multitrait selection approach (Zetouni et al, 2017) should be applied, in which both retention and intake are selected to achieve the highest genetic gain for NUE.

Genomic selection

Genomic selection, in which breeding values are estimated based on genomic information (Meuwissen et al., 2001), has been successfully applied to other traits with similar genetic architectures (Georges and Charlier, 2019). Its application to NUE appears promising, since the genomic variants, despite failing to reach statistical significance, accounted for a large proportion of the pedigree-based heritability (Ewaoluwagbemiga et al., 2023b). Genomic selection would accelerate genetic progress, provided that sufficiently large high-quality reference populations can be established to train prediction models. For production traits in pigs, reference population sizes are typically several thousands to 80 000 (e.g. Ros-Freixedes et al., 2022), depending on how easily the trait can be measured. Of course, this would require advances in phenotyping, functional annotation of the pig genome, and the further development of models that allow the prioritisation of biologically meaningful variants. This progress is currently made in the Functional Annotation of ANimal Genomes framework (FAANG; Clark et al., 2020; Crespo-Piazuelo et al., 2023) as well as elsewhere (e.g. Groß et al., 2020; Wolc and Dekkers, 2022).

Outlook

Although research into the genetics of NUE has increased rapidly recently, there are some areas that need more attention. These include improving phenotyping, gaining more knowledge about G × F interactions and more generally about the physiology of NUE, and understanding the effects of selecting for NUE on health and welfare, as well as meat and carcass quality. Focusing selection on NUE would require to simplify phenotyping methods without compromising accuracy. Although electronic feeders facilitate the determination of feed intake, methods for high throughput assessment of whole body or carcass nitrogen content still need to be refined. DXA scanners offer precision; however, their throughput is limited (4–8 carcasses per hour), whereas during genetic evaluations, thousands of animals need to be assessed in a few days. Thus, it is clear that this approach is limited in its ability to generate the large sample sizes required for breeding value estimation or to establish a large reference population for genomic selection. This should prompt the consideration of alternative techniques such as AutoFOM^{TM}, an ultrasound method capable of scanning significantly more carcasses per hour (150–300 times) (Mohrmann et al., 2006). However, rigorous validation of AutoFOM^{TM} is required to ensure accurate estimation of lean meat content.

Further research is needed to determine the extent to which meat quality may be affected by selecting NUE to maintain quality standards and ensure a profitable economic return to producers. Intramuscular fat content, water retention, and meat colour could be adversely affected (Ewaoluwagbemiga et al., 2023a), which has also been reported in selecting for RFI and explained by changes in muscle fibre type (Saintilan et al., 2013). This may be the reason judges rated the meat of high NUE pigs as less juicy in sensory meat evaluation (Ewaoluwagbemiga et al., 2023a).

Genotype-by-feed interactions, as highlighted by recent studies (Godinho et al., 2018; te Pas et al., 2021), require extensive investigation, especially in the context of selecting pigs for diets aimed at reducing nitrogen emissions or addressing feed-food conflicts. Such diets, characterised by lower nutritional quality and higher fibre content or the partial substitution of cereals with losses from human food production, may induce different responses in NUE in different pig lines/genotypes. This variability could lead to significant shifts in performance rankings, as observed in studies testing diets with different CP content (Große-Brinkhaus et al., 2023), or hinder the realisation of genetic potential for feed efficiency under high-fibre diets, especially in pigs selected for low-fibre diets (Mauch et al., 2018).

A better understanding of the biology of NUE is crucial for accelerating genetic progress. First, knowledge of the physiological pathways in nitrogen metabolism will aid in selecting traits with significant genetic variation for breeding, although Kyriazakis

(2011) and Shurson and Kerr (2023) suggested that only digestibility and maintenance requirements harbour sufficient genetic variation suitable for this purpose. Second, unintended consequences that could be detrimental to the health and welfare of pigs could be better anticipated and monitored. For example, if increased nitrogen deposition in the form of lean mass leads to important increases in ADG, structural problems, particularly in breeding sows, can occur if bone growth cannot keep up, as it is the case with broilers (Hartcher and Lum, 2020). Third, understanding the physiology of NUE is key to improving the functional annotation of the genome and, thus, providing better and more comprehensive genomic resources for domestic pigs (Clark et al., 2020). As mentioned above, incorporating biological information into genomic selection can accelerate genetic gains (Pérez-Enciso et al., 2015) and aid the identification of associated QTL in GWAS (Wolc and Dekkers, 2022). Fourth, nutritional modelling will benefit from a deeper understanding of the "average animal" (Millet et al., 2018), and more knowledge about the interplay of the gut microbiome and host genetics is crucial for improving faecal digestibility (Verschuren et al., 2020). Lastly, there might be potential applications for using pig nitrogen metabolism as an easily traceable model for human nutrition, where nutrient intake and metabolism are much more difficult to monitor.

Finally, from the perspective of resource allocation theory, the reduced ability to cope with stress in high-performing pigs is a concern (Knap and Rauw, 2008). Pigs selected for faster growth in nutrient-limiting environments are expected to be more affected by pathogens (Kyriazakis, 2011), but immune challenge studies on divergently selected RFI lines discussed above suggest the opposite (Dunkelberger et al., 2015; Merlot et al., 2016). Saintilan et al. (2013) highlighted physiological differences in divergently selected RFI lines, suggesting reduced energy requirements for maintenance in low-RFI pigs, potentially affecting physical activity and social interactions. Dietary CP restriction combined with reduced hygiene standards has been associated with increased rates of damaging behaviour (Meer et al., 2017), possibly due to the activation of the immune system concurrent with reduced protein intake. However, little evidence of a phenotypic association of an increase in problematic behaviours, that could indicate low-–stress resilience, was observed with NUE in pigs on a CP-restricted diet (Roch et al., 2023), which requires further investigation at the genetic level. Taken together, balanced breeding programmes are essential for maintaining fitness and robustness in pigs in the context of NUE (Knap, 2023).

Conclusion

In this review, I highlight the importance of improving NUE in pigs through selective breeding as a key strategy to reduce the environmental impact of pork production. Nitrogen use efficiency is a heritable trait that is genetically favourably correlated with feed efficiency. No major trade-offs with other traits are expected, except for some minor unfavourable genetic correlations with growth performance and some meat quality traits, which appear to be manageable. The complexity of NUE, influenced by several genetic and environmental factors, makes phenotyping challenging. However, this remains essential for selection, as it appears that direct selection for NUE may be more effective than current indirect methods, such as focusing on FCR or RFI. Furthermore, merely improving a single component of NUE, such as digestibility, without simultaneously improving other components, such as lean growth, may not effectively improve NUE at the organism level. Developing balanced breeding strategies involves an integrated approach that considers environmental sustainability, animal welfare, and market demands. This requires a deeper understanding of component traits, such as postabsorptive amino acid metabolism and the interplay between the gut microbiome, diet quality, and N recycling, and how NUE performance can be maintained during stressful situations, such as rising temperatures, social stress and immune challenges. Genetic selection of pigs in environments where they need to perform well in terms of NUE, for instance on sustainable diets with low nutritional value, is crucial. The development of high-throughput phenotyping strategies, improved genetic resources and more sensitive genomic prediction models is underway and will provide interesting results and valuable tools in the coming years. These developments are essential in addressing nitrogen pollution and ensuring sustainable pork production in the face of growing environmental and societal challenges.

Ethics approval

Not applicable.

Data and model availability statement

Not applicable. Information can be made available from the authors upon request.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author used DeepL and ChatGPT4 to improve style and grammar. After using this tool/service, the author reviewed and edited the content as needed. Thus, the author takes full responsibility for the content of the publication.

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Declaration of interest

None.

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