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Report 765

Masterplan for the development of nutrient based dynamic mechanistic response models for pigs and poultry

March 2014

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Editing
Communication Services

Wageningen UR Livestock Research and Central Veterinary Institute of Wageningen UR, both part of Stichting Dienst Landbouwkundig Onderzoek (DLO Foundation), together with the Department of Animal Sciences of Wageningen University comprises the Animal Sciences Group of Wageningen UR (University & Research centre).

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Abstract
The masterplan describes the development of new nutrient based dynamic mechanistic response models for pigs and poultry predicting the animal's performance, the retention of nutrients in the body and in "end products", and the output of non-retained nutrients in the environment. The plan has been developed in the framework of the Public Private Partnership Feed4Foodure (F4F) in the Netherlands.

Keywords
Modelling, animal responses to nutrients, animal performance, pigs, poultry.

Reference
ISSN 1570 - 8616

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“Masterplan for the development of nutrient based dynamic mechanistic response models for pigs and poultry” is part of the PPS Feed4Foodure BOnr – 31.03-005-001

Preface

The present masterplan describes the development of new nutrient based dynamic mechanistic response models for pigs and poultry. The plan has been developed in the framework of the Public Private Partnership Feed4Foodure (F4F) in the Netherlands and the part of the research line “More with less” within F4F. The authors thank the members of the project team for their valuable contributions to the development of the plan. The execution of the plan will start in 2014.

The authors

Summary

The present masterplan describes the development of new nutrient based dynamic mechanistic response models for pigs and poultry predicting the animal's performance, the retention of nutrients in the body and in "end products" such as eggs and the output of non-retained nutrients in the environment. Development of the models for growing pigs, reproductive sows, broilers and laying hens is estimated to take a period of eight years (2014-2021), the former being dependent of the availability of adequate funding. The plan has been developed in the framework of the Public Private Partnership Feed4Foodure (F4F) in the Netherlands in which stakeholders in the private domain, the Ministry of Economic affairs in The Netherlands and research institutes and universities collaborate.

The plan describes the state of the art with regard to modelling of animal responses and animal performance in dependence of feed and nutrient intake and digestion and describes the objectives for the development of new nutrient based response models for pigs and poultry which are to be developed within the F4F programme. The execution of the plan foresees in the development of new dynamic mechanistic response models for pigs and poultry predicting the animal's performance and retention of nutrients and output of non-retained nutrients based on the composition and characteristics of feed ingredients and the diet, intake of the diet, digestive processing of nutrients in the gastrointestinal tract and metabolic transformation and retention of nutrients taking into account dietary physico-chemical, animal and environmental variables. The masterplan further describes the conceptual outline of the foreseen new models as well as the availability of data required for model development and the way how the evaluation and implementation of the models are foreseen.

In the execution of the plan, first attention will be given to the development of nutrient response models for growing pigs and broilers. In the first part, the focus will be on modelling of the digestive process up to the absorption of nutrients by the intestinal tissues, whereas in the second part attention will focus on the modelling of post-absorptive nutrient utilization, including the interactions with the environment. The models will be developed for answering strategic questions in feed evaluation and feeding strategies in practice, for research, for identification of gaps of knowledge in processes related to nutrient processing (hydrolysis and absorption) in the gastro-intestinal tract and in the post-absorptive metabolism.

Application of the models will allow the pig and poultry production sectors to more precisely adjust diet composition and feeding strategy to the (desired) response of production animals in terms of producing high quality human food and minimizing environmental nutrient losses under a variety of conditions as encountered on farms in the Netherlands.

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1 Introduction

Systems for the characterization of the nutritive value of feeds and feed ingredients for livestock are used as tools to optimise diets and dietary allocations for livestock production. They are the primary means to translate knowledge obtained in nutritional research into practice. In the future, these systems need to predict and manage not only animal performance, but also the efficiency of production, product quality and safety, environmental impact, and animal health and welfare. Increasingly, these systems become vital tools for meeting the twin challenges of climate change and global feed and food security, and for recognising that this has to be accomplished with (local) feed resources that are not in competition with human food.

Current feed evaluation systems used in animal nutrition are based on the concept of “feeding value” of feed ingredients and diets and nutritional requirements for individual nutrients of target animal species. Different European countries have developed or adopted feeding systems to account for local conditions. Requirement-based feeding systems ignore the fact that the animal responds to the nutrient supply in a dynamic way, and that this response needs to be considered in a multi-facetted manner in terms of animal performance, emissions into the environment, tissue and product composition, and animal health and behaviour.

Dynamic mechanistic models predict the output of an animal or group of animals based on a certain input of nutrients and characteristics of the animal system. Currently available models are often based on empirical relationships between input and output and ignore underlying physiological concepts and mechanisms. Dynamic mechanistic models are helpful tools to evaluate responses of animals to changes in dietary composition and feeding strategies and identify critical factors in nutrient efficiency based on given characteristics of the animal in a certain environment. Such models are less suitable for optimizing diets in the economic context, i.c. optimizing ingredient composition against a set of nutrient and ingredient constraints for a minimum cost price, as is applied in the feed industry by the use of linear programming.

The aim of the present masterplan is to describe the development of dynamic mechanistic models for predicting the response of pigs and poultry on a given or dynamic input of nutrients via the diet. In the first part of the execution of the plan the focus will be on the development of models for growing pigs and broilers. The conceptual basis of these models can also be used for the development of models for other categories of pigs (e.g. gestating and lactating sows) and poultry (laying hens and breeders) at a later stage.

The models will focus on two important components of the conversion of dietary nutrients into end products of animal origin. The first refers to digestion of feed and absorption nutrients in the gastrointestinal (GI) tract and the second part to post absorptive metabolism of nutrients and their deposition in “end product(s)”.

The use of these models will contribute to the identification of options for further minimizing the losses of nutrients in animal production and contribute towards a more sustainable animal production.

The present master plan describes the various phases and actions within phases which have to be taken in order to obtain further defined response based models for pigs and poultry. For dairy cows, the development of components for such a model has started in The Netherlands more than 10 years ago. At the initiation of the development of the latter also a master plan was presented (Gerrits et al., 2000).

The present masterplan covers the development of nutrient based response models for pigs (growing pigs and gestating/lactating sows) and poultry (broilers and laying hens). In time, it is proposed to start with the development of the nutrient based response models for growing pigs and broilers. The choice is based on the volumes of animal feeds produced in The Netherlands for the various animal categories and on estimates for the overall relative increase in nutrient utilization by the use of the models by the stakeholders.

In Table 1 the annual production of compound feed for monogastric animals in The Netherlands is presented as well as estimates for the potential relative improvement in nutrient utilization by the use of the response models for different animal categories. It is clear that the highest volume of compound feed within the category pigs is produced for growing pigs. Within the category poultry the volumes of compound feed are almost similar between broilers and laying hens, including pullets. Based on the estimated effects in terms of quantitative improvement of nutrient utilization in The Netherlands by the development and application of the new response based models for different animal categories, the focus in the first part of the execution of the masterplan will be on the development of models for growing pigs and broilers. Similar models will be developed for other categories of pigs and poultry using the same conceptual framework in a later stage.

Table 1 Industrial production of compound feed in The Netherlands in 2009 and expected impact on improvement of nutrient utilization as a result of the application of nutrient based dynamic mechanistic response models per animal category.

	Feed production (MMT/yr)[1]	Improvement (%)	Savings in feed (MMT/yr)	Relative effect (%)[2]
Pigs	**6.017**			
Piglets	0.802	6	0.048	14.2
Growing pigs	3.926	4	0.157	46.3
Breeding pigs	1.289	3	0.039	11.4
Poultry	**3.333**			
Broilers	1.439	4	0.058	17.0
Layers and pullets	1.894	2	0.038	11.2

[1]Source: FEFAC (from Hoste and Bolhuis, 2010).
[2]Percentage relative to the total effect for all pig and poultry categories (=100%).

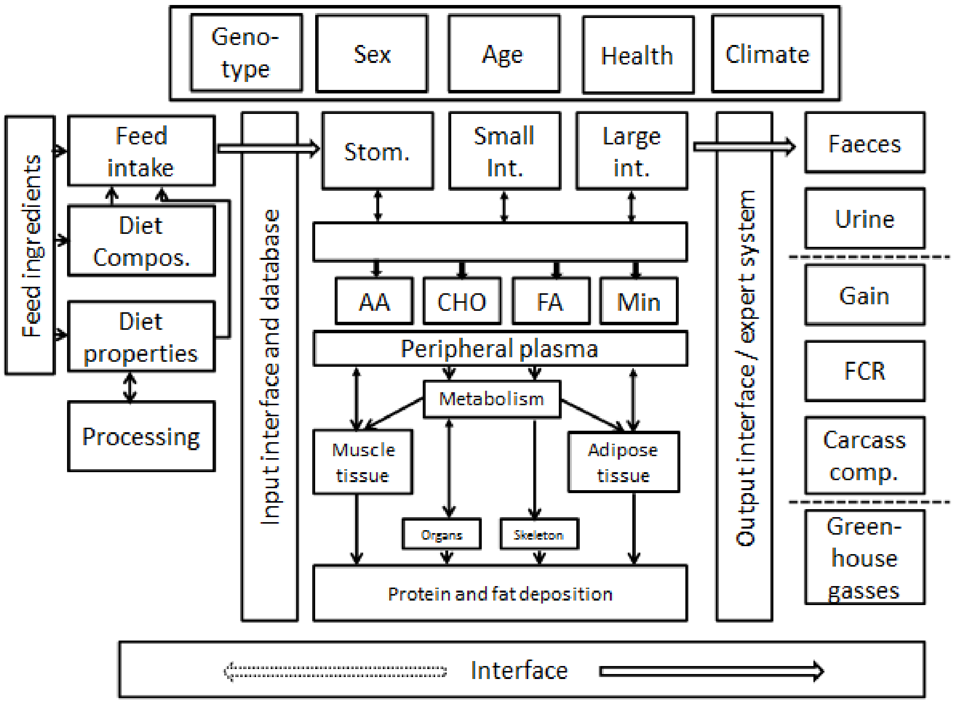


Figure 1 Conceptual framework for a nutrient based response model for growing pigs.

The conceptual framework for a nutrient based response model for growing pigs is given in Figure 1. The animal is defined by its genotype, sex, age, its environment (climate) and its health status as determining factors for its growth performance and capacity to deposit protein, fat and ash in the body.

The diet is the external source of nutrients and characterised by its ingredient and nutrient composition. Physical characteristics of the diet potentially affect both feed intake and physical chemical behaviour influencing digesta passage rate and the enzymatic degradation of nutrients prior to absorption in the various compartments of the GI tract. Processing of feed ingredients and (complete) diets or addition of feed additives such as exogenous enzymes can influence physical chemical characteristics of the diet.

Besides dietary characteristics, feed intake is determined by animal characteristics, physiological status and environmental conditions and actual level of performance.

During the process of enzymatic digestion in the GI tract dietary protein is degraded into peptides and amino acids, starch is degraded into glucose and triglycerides (fats) into monoglycerides, glycerol and fatty acids prior to intestinal absorption. Dietary minerals are partly solubilized prior to absorption from the lumen of the digestive tract. After absorption, nutrients are either utilized or transformed by the intestinal tissue or transported straight into the blood circulation. From there, nutrients are transported into organ and tissues where they are used as building blocks for synthesis of structural cell constituents, as precursors in metabolic processes or as an energy source. With regard to nutrient conversion, the liver plays an important role, but all other organs and tissues also utilize and convert nutrients. In the process of protein turnover, protein in structural tissues and organs is degraded and resulting peptides and amino acids are released in the blood plasma pool. This process contributes to the nutrient homeostasis in blood plasma. Growth is determined by the sum of net deposition of protein, fat and minerals in all organs and tissues in the body. In growing animals such as growing pigs and broilers protein deposition in muscle tissues is a key process determining growth performance.

Dynamic mechanistic models not only predict performance (body weight gain and feed conversion ratio and carcass composition), but also the excretion of non-retained nutrients can be estimated. The former relates to excretion of nutrients via the faeces and urine (e.g. energy, N and P) but also to the excretion/emission of e.g. greenhouse gases (methane, carbon dioxide).

2 Dynamic mechanistic response models

2.1 **Introduction**

During the last decades, modelling of farm animal digestion, metabolism and performance has received considerable interest. Various models have been built for various purposes, varying from evaluation of the nutritional value of diets, simulation of nutrient supply, simulation of metabolism and growth, to the economic evaluation of feeding schemes sometimes at the level of the whole farm. In order to develop a masterplan for future modelling of farm animals it is imperative to understand the history and current state of the art on this topic.

2.2 State of the art (static vs. mechanistic)

Model classification
For our current needs, the different definitions for "model" in the Oxford dictionary are restricted to: a simplified description, especially a mathematical one, of a system or process, to assist calculations and predictions (http://oxforddictionaries.com/definition/english/model). Within this description there are still several different possibilities on "how to model". To describe the digestive process and zootechnical performance of animals, various models have been developed over the last decade, each with different objectives and methods. Models can be classified into a number of categories with specific characteristics. These are: Type of output: Deterministic versus Stochastic, Model approach: Empirical vs. Mechanistic and model time dynamics: Static vs. Dynamic (France et al., 1984). Any model can be described by a combination of these three classifications. Some combinations are more applicable (e.g. Mechanistic Dynamic) than others (e.g. Empirical Dynamic). In reality these classifications are not as black and white as they may seem which will be discussed below for the Empirical versus Mechanistic models.

Type of output: Deterministic versus Stochastic
Deterministic models are models that give one model outcome based on input, whereas stochastic models give a range of outcomes, based on stochastic (change) based equations. The latter models give a better insight in the reliability of and variation around a predicted model outcome. This helps determining the appropriate course of action.
Most currently used feed evaluation models are deterministic giving one value for the feeding value of a raw material. Therefore, in practical feed formulation it is not common to evaluate the chance of deviations between the actual and the calculated nutritional value of the formulation. Only in science some work has been done in this area (Knap, 2000; Vautier et al., 2013).
Some animal models that predict performance (Ferguson, 2006 & pers. comm.) are starting to incorporate stochastic principles, giving greater insight in the variation around their predictions.

Model approach: Empirical versus Mechanistic
Empirical models describe the system of interest by direct relation of model outputs with inputs, disregarding mechanisms that are responsible for this relationship. In growing animals often equations such as the Gompertz curve or similar are used to describe growth depending on age or nutrient intake. In dairy cows, classical Wood curves are used to predict milk production based on lactation stage. This is an example of an empirical relationship. These equations are calibrated by fitting them to actual (empirical) data. Empirical models are focused on describing the end results and focus on prediction.
Mechanistic models predict the end results by describing the separate underlying biological processes. Mechanistic models therefore focus less on prediction and more on understanding of the physiology of the animal. Although the difference between empiric and mechanistic models seem fairly straightforward, in reality most models have mechanistic as well empiric aspects. Although it is possible to develop overall empirical input output models, models will often need some basis of a mechanistic description in order to accommodate the main physiological concepts. Alternatively, the detailed description of physiological processes in mechanistic models will ultimately result an empirical description of such a process.

Time related: Static versus Dynamic
In essence static models predict “a state” of the animal such as body weight, whereas dynamic models predict the time dependent change in the state of a system. Both static and dynamic types of models can be built on linear equations. In dynamic models, time dependency can be included in various ways. For example the word dynamic in relation to a dynamic feed matrix, indicates that the linear non-time depended feed evaluation matrix can be recalculated by changing feed ingredient composition. In more advanced models on nutrient digestion in animals and animal performance the word dynamic indicates that biological processes are simulated over time. The rate of change of these processes over time is typically solved by the use of differential equations that express the change (d) in a parameter called x, relative to a change (d) in time (t) (e.g. dx/dt = equation). The use of differential equations is common place in current modelling systems, and advanced simulation tools are available to simultaneously solve differential equations over time. Mechanistic and dynamic models commonly fit well as the mechanistic physiological processes are better suited to description with differential equations than high level empiric relationships. An advantage of models based on differential equations is that it is easier to integrate interdependencies, thus interactions between various model “state” and “flux” parameters, thus being more able to provide insight into the effect of these interactions on the whole animal.

2.3 Current models

As indicated, in the past decades several models describing feed and nutrient digestion in and performance of farm animals have been developed for different purposes. Early models were mainly directed at the evaluation of energy and protein supply from raw materials and generally are deterministic empirical static models. Examples of such models are the Dutch, French or North American feeding values for ruminants, poultry and swine as given by the respective CVB (CVB, 2011), INRA 2002 or NRC (1994, 2012) publications. More recent models have focused on various parts of the digestive process and nutrient metabolism in farm animals. Some have focused on a description of the nutrient flow through the digestive tract (Bastianelli et al., 1996, Strathe et al., 2008) whereas others have focused on describing the metabolic and growth processes (Birkett & de Lange 2001, Halas et al., 2004). Logically, combinations of these have also been developed.

2.3.1 Feed ingredient evaluation models

Most basic models used to describe the digestive process and nutrient requirements of animals are in use in many least cost formulation systems in the feed industry. Most of these systems predict energy and protein and amino acid availability and nutrient requirements by defined animal categories and have been largely developed in the 60’s and 70’s based on several decades of research. Examples of these systems, still currently in use for different species, are given in Table 2. These systems are classical examples of deterministic empirical static models. These systems were developed to predict energy and protein supply to the animal and with an appropriate set of requirement values work well in linear programming systems. These systems focus on the prediction of the nutritional value of a single feed ingredient, and are typically unable to predict digestive interactions between feed ingredients, that in the complex biological system of the digestive tract are abundantly present. Typical outputs of these models then are the nutritional value of the diet in terms of the energy value (ME or NE), the contents of digestible protein and amino acids and (digestible) macro minerals. For protein and amino acids the model generally does not constitute of more than a linear multiplication of the amount of a nutrient or component (e.g. protein) and the input value for its digestibility for each raw material. In these models digestibility of nutrients within raw materials are often variable based on differences in chemical composition of a raw material (CVB, 2011) often estimated in a linear fashion. These models generally lack a representation of the different digestive processes in the intestinal tract, as nutrient digestibility is an input value. In the animal, nutrient digestibility is the result of diet and digesta passage and digestion kinetics of the nutrients throughout the intestinal tract. Effect of feed components on e.g. stomach emptying rate and digestion rate in the intestinal tract are not (and cannot) be represented. Feed evaluation models have greatly improved accuracy of farm animal feeding and increased our understanding of the digestive processes.

Further increases in understanding of the digestive processes and accuracy of feeding, however, are hampered by the lack of interactivity between feed ingredients as well as between the animal and the diet in the models and the simplistic representation of nutrient digestibility as an input value rather than as a result of interactive digestive processes in the gastrointestinal tract.

Table 2 Various organisations and nationalities that have developed linear feed evaluation models.

Organisation	Origin
NRC	USA
INRA	France
AFRC	United Kingdom
CVB	Netherlands
DLG	Germany

2.3.2 Advanced models of nutrient digestion

As the issues mentioned for feed evaluation models have been recognized for a long time, a number of more advanced nutrient based models have been developed that describe the passage and digestion kinetics of nutrients through the gastrointestinal tract of animals. Table 3 gives an overview of some of the models describing relevant processes in the gastrointestinal tract of pigs. In the early models the focus was mainly on describing the passage kinetics through the small and large intestines (e.g. Bastianelli et al., 1996). Main drivers of these types of models were the choice of the (number of) compartments and the way the flow of digesta from one compartment to the next was modelled, more recently persued by the work of Wilfart et al., (2007) and Belward et al. (2013). More recent models such as the very detailed model of Strathe et al. (2008) combine passage through the digestive tract and digestion kinetics. Figure 2 depicts the pools and flows of nutrients between pools in this model. For this model, the gastrointestinal tract was divided into one compartment for stomach, two for the small intestine and one for the caecum-colon compartment. In this type of model the digestion of the different chemical components is predicted from the modelled digesta passage and digestion kinetics rather than as a fixed input as is the case in most static feed evaluation models. Therefore, to describe digestion of nutrients, the rate of digestion needs to be parameterized and a choice for the type of reaction kinetics is required (e.g. first order versus second order (or higher)). When assuming first order kinetics the fractional rate of degradation of substrate is considered constant, which is often assumed in models describing the ruminal degradation of substrates. Alternatively (e.g. in Strathe et al., 2008), digestion is modelled using an enzyme-kinetic approach, allowing the incorporation of various affinity constants as well as substrate concentrations, or inhibition by end products. As an example of such an approach, the model of Strathe et al. (2008) represents the interaction between fibre and digestion of protein by changing the affinity constants of proteases in the presence of fibre.

Recently some interesting models regarding the absorption of phosphorous (Letourneau et al., 2011) have been developed. Based on the research on-going in the MMM4 project on phosphorus as part of the Feed4Foodure research programme, it will be investigated whether additional modelling of phosphorus processing in the digestive tract and its post absorptive utilization is required. Ahmadi and Rodehutscord (2012) used a meta-analytical approach using a full quadratic model to quantify relationships between dietary non-phytate P (NPP) and phytase levels and performance of laying hens. Egg production, egg mass and feed conversion ratio were considered as model outputs.

To date, static models have focused on the prediction of the feeding value of individual ingredients. In contrast, dynamic models have simulated the interaction between nutrients in the digestive tract. These dynamic models have not dealt with the impact of the source of these nutrients, i.e. the feed ingredients. Prediction of the availability of nutrients from (various mixes of) feed ingredients requires understanding of the complex interactions between feed ingredients, mediated through variation in physical properties of digesta, digesta passage kinetics, and true digestion rates of nutrients from individual feed ingredients. These types of interactive effects have currently been insufficiently modelled.

In summary, innovation is required both in identifying the relevant physical-chemical raw material properties (e.g. fibre content, viscosity, bulking characteristics (see below)) and finding ways to describe raw materials in terms of these properties, combined with modelling the effects of these properties on the digestive process and release of nutrients. This will allow more accurate modelling but will also enable a more detailed description and characterisation of raw materials based on their functional properties in the gastrointestinal tract.

Table 3 Models describing nutrient digestion in pigs.

Authors	Digestion	Type of model
Usry et al., 1991	Digesta flow model	Stochastic
Bastianelli et al., 1996	Detailed nutrient digestion and absorption	Mechanistic interactive
Birket and de Lange, 2001	Mix between Nutrient and response	Linear
Rivest et al., 2000	Protein digestion in dynamic model	Interactive
Strathe et al., 2008	All nutrients in a dynamic model	Interactive
Létourneau-M. et al., 2011	Phosphorus	Interactive
Ahmadi and Rodehutscord, 2012	Phosphorus	Linear
Taghipoor et al., 2012	Nutrient flow and degradation in GI tract	Interactive
Moughan et al., 1984	Dietary protein quality	Linear

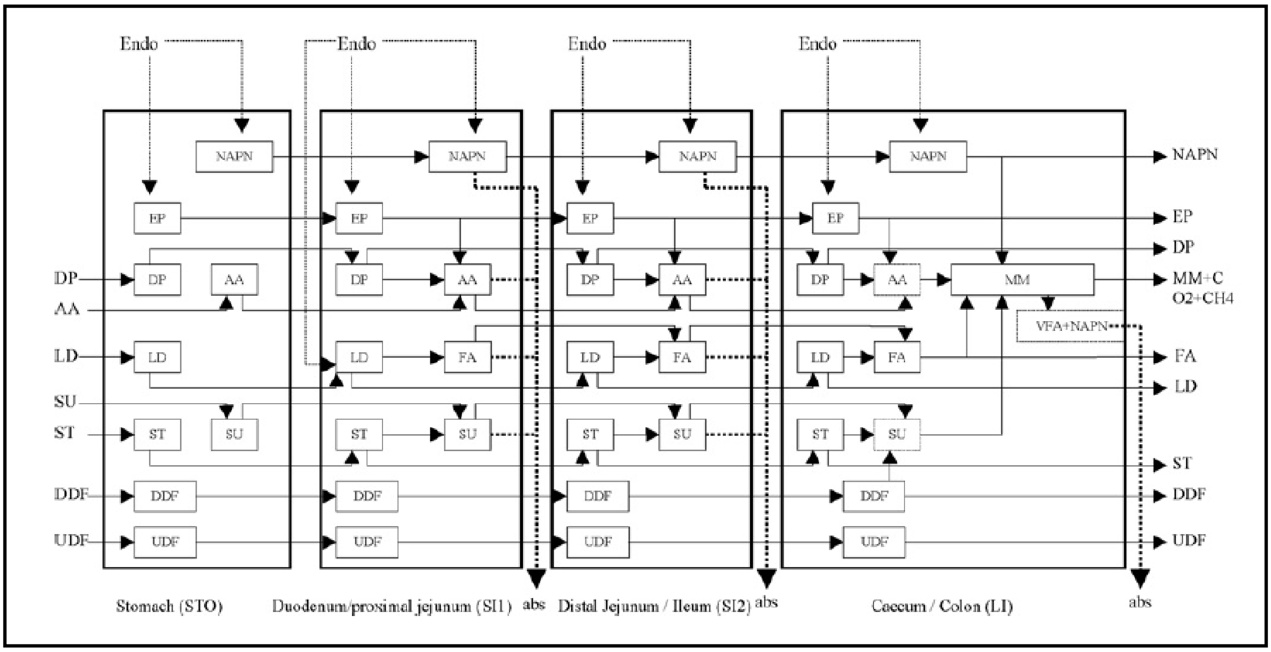


Figure 2 Schematic representation of the pools and fluxes of nutrients in the mechanistic dynamic nutrient model of Strathe et al. (2008).

2.3.3 Models of post absorptive nutrient utilization

Table 4 gives an overview of models that have been developed to predict animal performance in pigs and poultry. As with the models for simulation digestion, described before, various approaches have been used for modelling post-absorptive utilization of nutrients. Generally, in models focusing on the prediction of post-absorptive utilization of nutrients, the biology of digestion is poorly represented. For the modelling of post absorptive nutrient partitioning, various approaches have been used. Some models (e.g. Ferguson, 2006) use Gompertz equations to represent the desired amount of protein in lean tissues and organs as a function of age, sometimes relative to maturity. The animal can attain this protein deposition depending on the availability of all nutrients required. In other models (e.g. Halas et al., 2004) partitioning was based on an enzyme kinetic approach, assuming maximal rates of protein synthesis in particular tissues to represent the potential of a genotype.

For broiler chickens, Talpaz et al. (1986) developed a dynamic linear programming model to obtain a sequence of optimal least-cost rations over time. At a user's choice of time interval, the model calculates daily requirements of total protein, amino acids and energy, and computes the appropriate diets. Emmans (1987) described the effects of genotype, physiological state of the animal, diet composition, and environment on feed intake, growth and body composition in broilers. King (2001) used a computerized, mechanistic, deterministic and dynamic approach for the evaluation of the effects of diet on broiler carcass composition and growth. Daily body weight gain was simulated with information on the initial age and live weight of the bird, number of days over which the diet is to be fed, protein and amino acid densities of the diet, dietary metabolizable energy content, and whether feed intake is to be simulated or based on input values. Output provides information on a daily basis with respect to daily and accumulated deposition and current bird status for protein, fat, water, and ash in the body. Carcass weight, feather weight, live weight, feed consumption, feed deprivation, heat loss, limiting amino acids, feed conversion ratio, and percentage carcass fat are also provided. Aerts et al. (2003a) modelled metabolic heat production responses of broiler chickens to air temperature and light intensity, the two most important environmental variables in practice, using compact transfer function models. A similar approach was used to model the online growth response of broiler chickens to feed supply during the production process. Eits (2004) developed a model that predicts broiler responses (growth rate, feed conversion ratio, carcass yield and breast meat yield) to balance diets for their protein level. The model allows to construct tailor-made dose-response curves without actual experimentation. Gous and Berhe (2006) stated that it is not only the variation between individuals in their response to a given diet or environment that controls the variation in the response of a population of birds to a feeding programme in a given environment. Variation also exists in the environmental conditions to which the birds are subjected, as well as the composition of the diet used. Details on how each of these sources of variation may be modelled are given in Gous & Berhe (2006). Zuidhof (2005) evaluated eight dynamic nonlinear broiler carcass and carcass part yield models statistically for their suitability for predicting weights of carcass parts. In principle there is no preference for either method and choice of modelling approach depends on the objectives of the model. For models with a more direct application goal, the more logical choice is the empirical approach, for which several models have been developed and relationships are starting to become established.

Chwalibog and Baldwin (1995) reviewed empirical systems for predicting nutrient requirements for egg production and discussed the advantages of incorporating mechanistic and dynamic elements. Stochastic modelling in broiler breeders was performed by Alvarez and Hocking (2007). A stochastic model was developed to simulate the egg production of broiler breeders in response to changes in body weight. The first step involved the construction of a diagram incorporating dependent and independent variables and their relationships to ovulation rate and egg production from eight equations based on experimental results. The model was based on existing experimental data, and stochastic processes were invoked for four input parameters. Egg production curves and total egg production were simulated using inputs from a management manual, commercial trial data, and experimental results and were compared with actual rates of lay. The correlations between observed and predicted egg production were high (R^2 = 0.93 to 0.98). The assumptions made in developing the model were described and gaps in biological knowledge were identified.
Kebreab et al. (2009) developed a new dynamic and mechanistic model of P and Ca metabolism in layers to simulate diurnal changes in Ca and P metabolism and to determine the hourly requirements for these minerals by the laying hen. The model consists of eight state variables representing Ca and P pools in the crop, stomachs, plasma, and bone.

Strathe et al. (2011) developed a unified framework for analysing dose-response data in farm animals and applied it to a meta-analysis of digestible methionine requirement studies in laying hens. A database containing methionine dose-response data from 23 trials originating from 15 peer-reviewed publications was constructed. A multivariate nonlinear mixed effects model was chosen as the statistical framework to model egg mass and feed utilization responses simultaneously. The framework accounted for responses being correlated in both the random effects and the errors, which provided a superior fit to data compared with modelling them separately. Linear broken line, quadratic plateau, and monomolecular functions were evaluated for fitting dose response relationships.

Kuhi et al. (2012) stated that mathematical models become valuable tools to answer research and development questions. Modelling growth curves allows nutritionists and poultry researchers to predict dynamic or daily nutrient needs more adequately than using fixed requirements. The potential and validity of a specially reparameterized monomolecular model to partition intake of nutrients between requirements for maintenance and for growth, which were previously demonstrated in models for ruminants, pigs, chickens, turkeys, and broiler breeder pullets, were evaluated for its ability to estimate requirements for ME and protein for maintenance and growth in egg-type pullets. On the basis of the results of this study, along with those previously reported for chickens, turkeys, and broiler breeder pullets, this model appeared advantageous because it can predict the magnitude and direction of responses of growing poultry to changes in dietary ME and CP intake without requiring initial assumptions. The model also has the advantage of biological interpretability of the parameter estimates. One of the main consequences of this interpretability is that the results from several experiments can be pooled to obtain the best estimates of the response coefficients. Alternatively, dynamic, mechanistic models generally provide more insight into the underlying metabolic processes of protein and fat synthesis (rates) and nutrient flows in metabolism. This generally results, however, in an increase in the number of processes that are described and need to be calibrated.

Whittemore and Morgan (1990) were among the first to derive factorial and empirical data to provide a quantitative information resource from which nutrient response models may be constructed in both the gestation and lactation phase of reproductive sows. These data can be used for the development and construction of mixed mechanistic and empirical response models. Data were mainly gathered for building models which can be used for deriving energy and protein requirements during gestation and lactation. They concluded that deductive models require a view of growth to maturity, energy and protein metabolism for the processes of growth, maintenance, thermogenesis, pregnancy, and lactation, together with some view of the relationships between nutrition and litter size, and nutrition and weaning to conception interval. Empirical models avoid the need for factorisation and may depend upon regression relationships from field trials. Given the present level of knowledge at that time, they stated that neither type of model was likely to provide adequately an estimate of nutritional requirement and a mixed format is more appropriate. They concluded that components for models to simulate responses of breeding sows to nutrient regime were available and adequate for the construction of a first generation of mixed deductive and empirical models and that nutrient requirements and recommended feeding allowances could be best derived by use of such models.

A dynamic mathematical model of energy and protein metabolism of lactating sows was described and evaluated by Pettigrew et al. (1992ab) (Figure 3). The model was designed to contribute to a systematic and quantitative understanding of the biological connection between diet and reproduction. It traced the flow of energy-containing nutrients from absorption through intermediary metabolism, into and out of body stores, and into milk. State variables (pools) included lysine, other amino acids, glucose, fatty acids, acetate, propionate, acetyl-coenzyme A, ATP, oxygen, carbon dioxide, urea, lean-body protein, visceral protein, storage triacylglycerol, milk protein, milk triacylglycerol, and milk lactose. The rate of each transaction was a function of substrate and inhibitor concentrations, assuming saturation kinetics. Protein and fat turnover, substrate cycles, and the energy cost of membrane transport were explicitly considered as well. Most kinetic parameters were estimated indirectly. Evaluation of the model with independent data showed that there was a good agreement between simulated and measured values for body weight and fat and protein loss during lactation. The model was shown to be useful in the evaluation of feeding programs and in understanding of biological relationships in lactating sows.

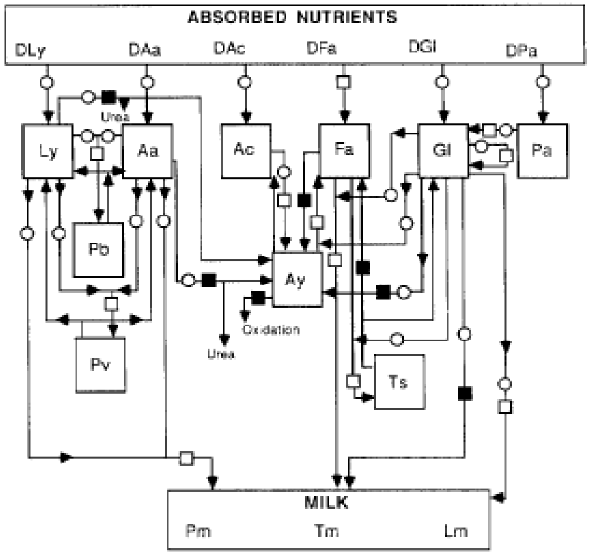


Figure 3 Schematic representation of the model of Pettigrew et al (1992a) for lactating sows. State variables shown are lysine (Lys), other amino acids (Aa), acetic acid (Ac), fatty acids (Fa), glucose (Gl), propionic acid (Pa), acetyl-coenzyme A (Ay), protein in lean body (Pb), protein in viscera (Pv), storage triacylglycerol (Ts), and milk protein (Pm), fat (Tm), and lactose (Lm). Fluxes requiring/yielding adenosine triphosphate (ATP) indicated by o (uses ATP in transport), 0 (uses ATP in reaction), and rn (produces ATP in reaction).

More recently INRA in France developed the so called INRAPorc models for growing pigs and sows. In the InraPorc Sow model (Dourmad et al., 2008) the current state of knowledge in a nutritional model for sows was integrated and made available as a software tool to end-users, mainly nutritionists involved in the pig industry and students in animal nutrition. The sow is represented as different compartments that change over the reproductive cycle. Nutrient flows considered are those of energy and digestible amino acids. Nutrients are used with the highest priority for maintenance and uterine growth or milk production. Subsequently, deposition and/or mobilisation of body proteins and lipids are determined and used for estimating the changes in body weight and backfat thickness of the sow. A decision support tool was built from the set of equations given, with additional modules to describe animal's characteristics and adjust some model parameters to account for variations in genotypes and performance. This tool can be used to determine energy and amino acids requirements of sows according to production objectives, or to predict body composition changes according to a given feeding strategy.

Also NRC (2012) provides models for estimating nutrient requirements and performance of gestating and lactating sows. The model of Dourmad et al. (2008) form the basis for these models with some modifications. The models estimate the requirements for standardized ileal digestible amino acids and nitrogen, standardized total tract digestible phosphorus and for total calcium in lactating and gestating sows. The models are described to be mechanistic, dynamic and deterministic in representing the biology of nutrient and energy utilization at whole-animal level. Cumulative animal performance (growth, gestation and lactation) is represented dynamically over a user defined period of time on iterative calculations with a one-day iteration interval. Dietary energy intake has to be defined by the user and can be varied at different periods during gestation and can be predicted from parity and days into lactation or defined by the model user in the lactation model.

Table 4 Models for the prediction of animal growth and performance.

Author(s)	Species
Pomar et al., 1991a	Young pigs
Pomar et al., 1991b	Sows in lactation
Whittemore and Morgan,1990	Sows in gestation and lactation
Pettigrew et al., 1992ab	Sows in lactation
Van Milgen et al., 2008	Growing pigs and sows
NRC, 2012	Growing pigs, gestating and lactating sows
De Lange et al., 2003	Growing pigs
Halas et al., 2004	Growing pigs
Ferguson et al., 2006	Growing pigs
Strathe et al., 2009	Growing pigs
Chwalibog and Baldwin, 1995	Laying hens
Danfaer, 1991	Animals
Talpaz et al., 1986	Broilers
Emmans, 1987	Broilers
King, 2001	Broilers
Eits et al., 2004	Broilers
Zuidhof, 2005	Broilers
Gous and Berhe, 2006	Broilers
Alvarez and Hocking, 2007	Broiler breeders
Kebreab et al., 2009	Laying hens
Strathe et al., 2011	Laying hens
Kuhi et al. 2012	Laying pullets

2.3.4 Modelling feed intake

In many models simulating animal performance, feed intake is used as an input, driving nutrient partitioning, rather than predicted from mechanisms represented in model equations (see virtually all models describing nutrient digestion (Table 3) and most models prediction growth (Table 4)). For some models, e.g. InraPorc, the user interface enables the user to make choices in the way feed intake is calculated. By default, *ad libitum* feed intake is considered as a genotype trait, and defined for each genotype present in the model. Furthermore, options are available to define feed intake schedules, either user defined, or based on age or body weight. Likely, the absence of feed intake predictions in growth models is caused by the enormous complexity of accurate predictions of feed intake. It is, however, evident that variation in feed intake is one of the main sources of variation in animal performance. The notable exception is the model of Ferguson (2006), who included feed intake predictions in their model, not as a driving force, but it is predicted by the model (Figure 4). The basis for their predictions is the assumption that pigs will eat to grow its potential, unless anything, e.g. a first limiting nutrient, limits the utilization of ingested feed. The basis for the feed intake predictions are therefore equations predicting the desired feed intake. These equations are based on the assumed desire to maintain an inherent body composition, to which the animal will attempt to return whenever possible. Interactions between desired feed intake and environmental or housing characteristics are represented in an empirical way. Constraint factors potentially reducing growth rate from the desired growth rate include gut capacity, physical or social environment and the presence of a first limiting nutrient.

Modelling feed intake patterns within the day in domestic animals has been mainly restricted to the fitting of mathematical equations to measured patterns of feed intake (see e.g. Tolkamp et al., 2011; Da Souza et al., 2013). This allows proper definitions of feeding bouts or meals, and enables the analysis of its duration and frequency under the conditions they are measured. These can be connected to satiating mechanisms (see Da Souza et al., 2013) but model predictions of feed intake patterns throughout the day based on biological mechanisms of satiation (i.e. meal termination) and longer-term satiety are not available.

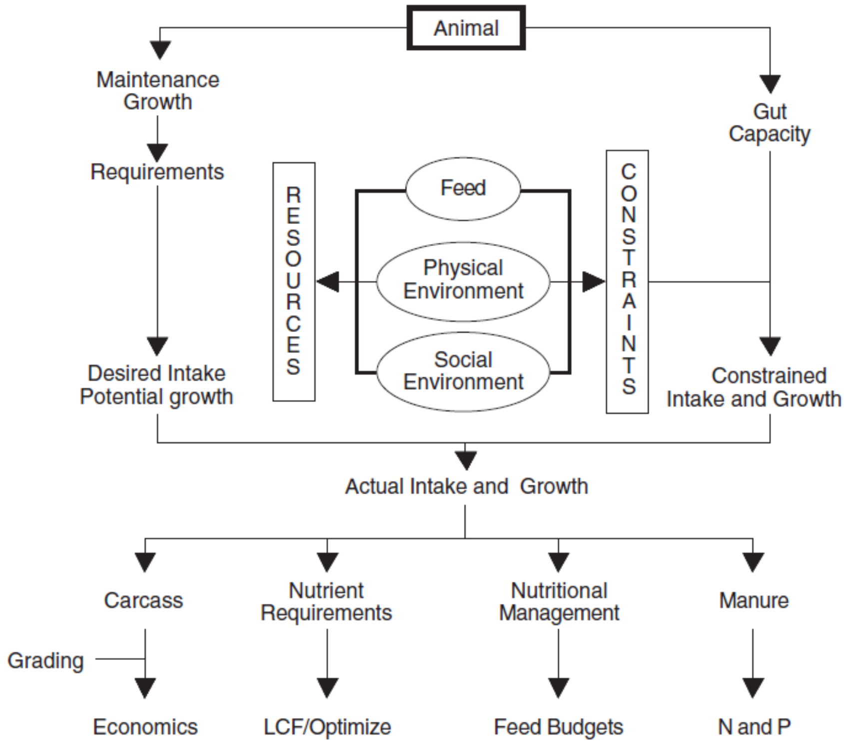


Figure 4 Conceptual framework of processes involved in the modelling of growth and feed intake in pigs (Ferguson, 2006).

2.3.5 Combinations of digestion and post-absorptive models

As both nutrient and response models are obviously modelling different parts of the same animal, ultimately in the current modelling approach they will be combined to form a whole animal model.

2.3.6 Whole farm models

Rather than focusing on animal level also a number of whole farm models for pigs and poultry have been developed (Table 5).

Aerts et al. (2003a) stated that integration of dynamic data-based modelling approaches with new hardware and sensing techniques to measure information from the animals should make it possible to control broiler growth trajectories. Aerts et al. (2003b) proposed dynamic data-based models to describe and control the metabolic response of broiler chickens to the micro-environment. Stacey et al. (2004) developed a prototype real-time system for the control of broiler growth and nutrition intended for commercial use. A semi-mechanistic growth model was developed, based on established models and principles, in which growth is predicted from feed intake and diet composition. The controller first attempts to improve the prediction of the growth model using feedback from past data from the house it is controlling. This is done by optimising a common digestibility parameter. The controller then determines the nutritional strategy for the remainder of the growing period. It optimises diet composition, and optionally the required feed intake, to minimise the root mean square error (RMSE) between the target and predicted growth curves.

A decision support system to evaluate pig production economics (AnaPorkDSS) based on a spreadsheet model to estimate net present value and costs associated with the pig production activity under Spanish conditions was developed by Ezcurra-Ciaurrix & Pla-Aragonès (2009). The model is capable of estimating net present value for a farrowing-to-finish farm producing pigs that are sold to the slaughterhouse. A similar simulation model representing the dynamics of a sow farm was presented by Pla-Aragonès et al. (2008). The model for sow herd dynamics is representing usual management practices implemented in intensive sow farms and an application for planning of piglet production was introduced.

Table 5 Farm models for pigs and poultry.

Author(s)	Species	Description
Pomar et al., 1991c	Dynamic herd simulation	Discrete stochastic
Ezcurra-Ciaurrix & Pla-Aragonès, 2009	AnaPorkDSS	DSS, in spreadsheet, integrated farm
Pla-Aragones et al., 2008	AnaPorkDSS	Sow farm
Aerts et al., 2003a	Broilers	Growth of broilers based on an adaptive compact dynamic process model.
Aerts et al. 2003b	Broilers	Dynamic metabolic response to micro environment
Stacey et al., 2004	Broilers	Semi mechanistic real time

2.4 Objective and Users

The aim of the project is to develop new dynamic mechanistic response models for pigs and poultry predicting the animal's performance and retention of nutrients and output of non-retained nutrients based on the composition and characteristics of feed ingredients and the diet, intake of the diet, digestive processing of nutrients in the gastrointestinal tract and metabolic transformation and retention of nutrients taking into account feed physico-chemical, animal and environmental variables.

Development of a model presenting the dynamic aspects of processes in the gastrointestinal tract and in the metabolism of the target species also provides a basis for predicting variation in animal responses to variation in intake of raw materials with different physico-chemical characteristics.

For the development of a nutrient based dynamic mechanistic response model for pigs and poultry different sub-objectives can be formulated:

a) Prediction of the availability of nutrients from (various mixes of) feed ingredients. To this end, the complex interactions between feed ingredients, mediated through variation in physical properties of digesta, digesta passage kinetics and true digestion rates of nutrients from individual feed ingredients will be explicitly represented and is considered as the main innovative aspect of the model(s).
b) Prediction of the utilization of nutrients, absorbed from the gastrointestinal tract, for accretion of protein, fat, minerals in organs and body tissues, depending on the availability of nutrients from feed ingredients (see a), environmental conditions (e.g. feeding system, climate, stocking density).
c) Models will be mainly based on current knowledge, methods and data to describe dynamic processes in animals. Additional experiments on digestion kinetics and on interaction with diet composition and physical chemical characteristics of feed ingredients, however, may be required for the models to be developed.
d) Knowledge on availability and utilization of nutrients will be used for the dynamic mechanistic response model to predict the digestion of the diet and productivity of the animals based on feed and animal related parameters (e.g. genotype), gastrointestinal and environmental conditions.
e) An improvement of the potential to characterise raw materials in terms of their physico-chemical characteristics that influence digestive processes and ultimately can better explain the interactions between feed ingredients and the process of nutrient digestion and absorption.

The models developed should provide a link between research and practice and are aimed for addressing strategic questions in feed evaluation practice and research and for evaluating the effects of adjustments of feeding strategies. The models have to be useful for research, education and nutritionists in the feed industry. The models will not be developed for on-farm advice. Included in the user group are researchers, nutritionists and students. This implies that the development of a user interface will require careful attention.

2.5 Design of the conceptual model

2.5.1 Principle

The overall modular design has been presented in Figure 1. Although all model compartments are interrelated, it is proposed to distinguish two parts. In the first part, attention will focus on the digestion process (all biological processes until the gut wall), whereas in the second part attention will focus on the modelling of post-absorptive nutrient utilization, including the interactions with the environment. The first part is referred to as the digestion model, the second part as the post-absorptive model. This division is consistent with several of the modelling activities that are reported in literature that often have focussed on one or the other. Prediction of feed intake and its patterns will be dealt with in a more empirical manner (see section 3.1).

2.5.2 Digestion model

The basic principle of the foreseen digestion model is that it will be composed of several anatomical compartments e.g. stomach, small intestine and large intestine each with a degradation (hydrolysis) of feed components and a flow of each component to the next compartment, similar to the model of Strathe et al. (2008) (Figure 2). These compartments may need division into sub-compartments to represent the biological and chemical processes to be modelled. For each component within each compartment, the hydrolysis (into monomers), absorption of the monomers and the transit of the material to the next compartment will be modelled. These two processes are controlled by the physico-chemical properties of the digesta, and by the true degradation characteristics of the component (i.e. protein, starch, fibre, fat) in the feed ingredient considered. The physical properties of the digesta, including its changes when transported throughout the gastrointestinal tract, will be explicitly considered, as a function of the (mix of) feed ingredient(s) inputs. It is expected that new analytical tools for characterising feeds and raw materials will be required in order to accurately predict the intestinal processes. Examples of these physicochemical conditions are: particle size, bulk fill and rheological properties. Ultimately the enzymatic (or microbial) degradation of various feed components in the different sections of the gastrointestinal tract is dependent on these physicochemical characteristics, but also on the intrinsic susceptibility of the substrate (e.g. protein) to enzymatic and microbial degradation. During the construction of the model, insights will be gained for the required level of characterisation of raw materials.

Figure 5 summarizes the processes to be modelled as described above for one chemical component within one compartment. Chemical components are e.g. protein, fat, starch and fibre. The pool of chemical components can be hydrolysed into monomers, e.g. amino acids for protein and glucose for starch or transported to the next compartment. The monomers can be either absorbed or transported into the next compartment. Essentially, digestion within each (sub) compartment is governed by three processes: 1. Hydrolysis/breakdown into monomers, 2. Passage of components and monomers and 3. Absorption of monomers. These three processes are regulated by the physicochemical conditions in the compartment and characteristics of the digesta. These conditions, e.g. particle size, maximum hydrolysis rate, bulk fill and rheological properties are partly a consequence of the feed and partly a consequence of the digestive processes in the compartment or earlier compartments. New prediction models will have to be developed to quantify the relationship between chemical composition of the diet and digesta and the physicochemical conditions. It is expected that a large part of this type of knowledge is already available from food chemistry, making this model a unique combination between animal nutrition and food chemistry knowledge. The physicochemical components of interest will be discussed more in detail in section 3.1.2.

2.5.3 Model for post absorptive utilisation of nutrients

As described in section 2.3.3. several animal response (post absorptive utilisation) models have been developed. The final goal of the models to be built will be to predict digested nutrients from (a mix of) feed ingredients, and subsequently to predict the post-absorptive partitioning of these nutrients. This approach will give most insight into the digestive and metabolic processes in the animal, which are a basis for further research and improvement in predictive performance. In the first phase attention will focus on the development of a complete model, with the major focus on the digestion model, and post-absorptive processes included in a simplified, empirical manner. In the second phase, attention will focus on the post-absorptive modelling of the utilization of nutrients. This model will be connected to the digestion model, and attention will be paid to incorporating the influence of variation in genotype, health and climate.

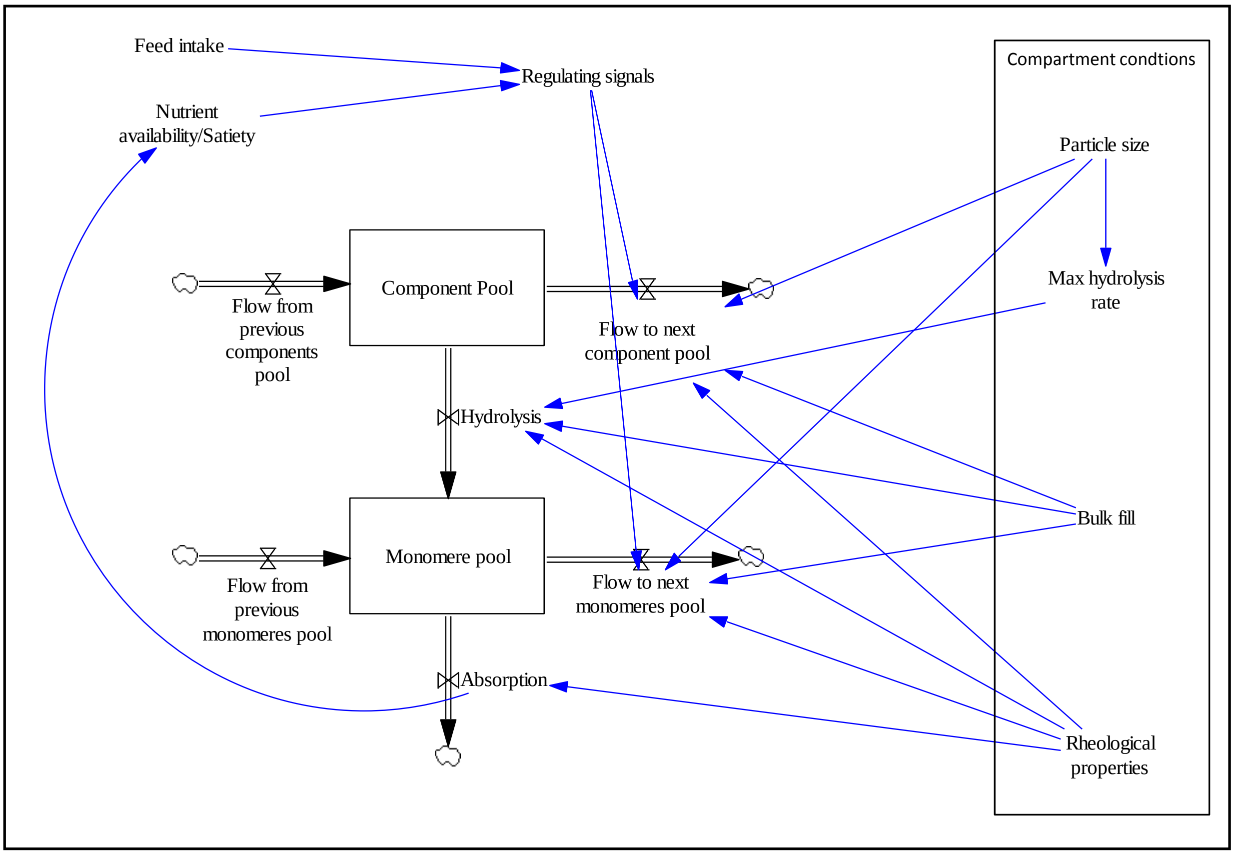


Figure 5 Schematic representation of the hydrolysis, transport and absorption of component X in compartment Y, depending on the physical conditions in compartment Y

2.5.4 Argumentation for the modular design

The module design as proposed will need further definition in the initial stages of model development. In phase 1 the basic module design for the digestion model will be stomach, small intestine (with probably subdivisions) and large intestine (for pigs), where for poultry the crop, gizzard, proventriculus, small intestine (with probably subsections), large intestine and caeca. It can already be estimated that development of a model for poultry will be more complex than for pigs, not just for the higher number of compartments, but also because of reflux of digesta between compartments (Sacranie et al. 2005). As we are striving to increase predictability and understanding of the processes in the gastrointestinal tract it is imperative to also model these processes based on the anatomy of the animal, leading to the modular approach as suggested. Seeing the difference in complexity between pigs and poultry the initial focus will be on modelling the digestive tract in pigs. In the first project phase, post absorptive utilisation of nutrients will be represented in a very simplified, empirical manner. In phase 2, the model for predicting port-absorptive metabolism will be developed using several potential compartments such

as gastrointestinal tract, blood, liver, body tissue stores for fat and protein, bone and potentially others. The exact design will need to be established in phase 2.
Modules/compartments as chosen (will) represent actual anatomic or functional units of the animal to facilitate the calibration of model predictions to actual experimental outcomes. Dividing a model in compartments/modules is a well-established methodology to build dynamic mechanistic models. The subdivision into anatomical or functional compartments helps in determining relevant and less relevant processes to focus the modelling effort. This improves understanding of the animals and helps discover gaps in our knowledge that need further research for improving understanding and predictability.

3 Construction of the models and the required input data

3.1 Input or controlling variables for the digestion model

As described in Chapter 2, the digestion model will predict the availability of nutrients from feed ingredients in time. Inputs for this model are mainly related to diet composition and feed intake, as briefly described below. Effects of changes in input parameters (mostly diet related) can only be predicted by the model if the relevant biological processes are represented. For factors such as mycotoxins, ANF's and environmental impact on digestion, the relevant biological processes are not anticipated to be included in the digestion model and hence, the impact of changes in these factors cannot be predicted.

3.1.1 Feed intake and feed intake patterns

Feed intake is a major determinant of gut volume, gastrointestinal tissue weight and transit of material through the gastrointestinal tract. In addition, feed intake is also regulated by the energy content of the feed and energy requirement of the animal as far as allowed by gastrointestinal capacity for bulky feeds (Kyriazakis and Emmans, 1995). As the regulation of feed intake is multi-factorial and complex, initially, a rather empirical approach to prediction of feed intake will be taken. Following approaches of InraPorc and Ferguson et al. (2006), desired feed intake will be considered as a genotypic trait, and defined as a function of age or body weight. Effects of environmental and housing conditions and social interactions will be explored and may be included using empirical equations. Interactions with the digestion process and nutrient metabolism will be developed along with the development of the digestion and post-absorptive modules. Feed intake patterns will be necessary input for the digestion module (see 3.1.2), and will be estimated from experimental data using procedures as described by Tolkamp et al. (2011) and Da Souza et al (2013). Whenever more information is available between diet composition and feed intake patterns, these can be included.

3.1.2 Parameters related to the diet

Current chemical characterisation of feeds is in general sufficiently advanced for serving as input for future mechanistic feed evaluation models. Current feeding tables (e.g. CVB, 2011) give detailed information on the chemical composition. For various feed components such as protein and fat, more detailed compositional data is available as amino acid and fatty acid composition, respectively. For the carbohydrates, the starches and sugars are fairly well defined although for starch analysis different methods are available that depending on the feedstuff can yield different results. Additionally, sugars although seemingly a homogeneous group can consist of various soluble carbohydrates with a short, yet variable, chain length and physical-chemical characteristics. For the purpose of mechanistic models, however, description of starch and sugars currently seems adequate. Alternatively the group of carbohydrates called fibre is less well characterized into its individual constituents. Currently methods based on separation of fibre related carbohydrates on the basis of solubility in different detergents are a common approach. These generally are NDF, ADF, and ADL, standing for neutral detergent fibre, acid detergent fibre and acid detergent lignin, representing the groups of carbohydrates that are not soluble when cooked in neutral or acid detergent solutions. Of these, NDF is the group encompassing most of the fibre related carbohydrates such as cellulose and various types of insoluble arabinoxylans, however, depending on their solubility pectins (polymers of mainly gluco-uronic acids with side chains), arabinoxylans and ß-glucans are only partly represented in this group. Often the fibre related carbohydrates are termed NSP, non-starch polysaccharides. Although technically a fairly accurate description, quantifying this entity is less straightforward as some propose indirect calculation of this fraction from other analysed chemical components (CVB,2011), whereas others employ wet chemical analytical methods (Englyst and Cummings, 1984). In summary, for protein, fat, starch and sugars, current analytical description of raw materials is likely sufficient for modelling purposes. Regarding the current state of the description of (dietary) fibre it may be needed to expand commonly used parameters to be more accurate. However, the level of characterisation will depend on the functionality needed to accurately represent intestinal processes. Although most minerals are currently out of scope, obviously phosphorus content and form (phytic acid vs phosphate) with related Ca content will be relevant for modelling phosphorus digestive dynamics. Substantial information and a dynamic mechanistic model describing the digestive processes for Ca and phosphorus in the gastrointestinal tract, however, have been developed (Létourneau et al., 2011). Regarding the utilisation of phosphorus and calcium knowledge in poultry (layers) is available from Kebreab et al. (2009) and De Vries et al. (2010).

For building more advanced mechanistic nutrient supply models, chemical as well as physical characterisation of the different components will be required. Additional parameters that characterise feedstuffs in terms of accessibility or susceptibility to enzymatic degradation may be required. Tables 6 and 7 provide an idea as to potential parameters required for feed characterisation.

Table 6 Feed physico-chemical characteristics that can serve as input parameters to nutrient based (ultimately whole animal) models in pigs and poultry.

Feed characteristic	Influence on
Particle size	Passage kinetics / viscosity / accessibility to enzymatic degradation
Soluble components	Effects on viscosity of digesta in the intestinal tract
Viscosity parameters	Effects on viscosity of digesta in the intestinal tract
Water binding capacity	Effects on gut fill and passage rate of digesta

Table 7 Characteristics of feed and feed components that will serve as inputs in the digestion models.

Component	Characteristic
Protein, amino acids and protein structure	Solubility
	Sensitivity to enzymatic degradation
	Sensitivity to microbial breakdown
	Lysine and other AA's (arginine, histidine) availability
Starch	Sensitivity to enzymatic degradation
Fats, fatty acids and fat structure	Fatty acid composition and SN-structure
	Sensitivity to enzymatic digestion
	Sensitivity to micelle formation and absorption (related to fatty acid composition)
	Sensitivity to microbial breakdown
	Bulking properties
	Viscosity properties
	Gelling properties
Phosphorus & Ca	Phytic acid content
	Phytic acid sensitivity to enzymatic breakdown
	Solubility
	Complex forming capacity
ANFs	
Mycotoxins	

Particular feed additives might also affect diet characteristics and nutrient supply, utilization of nutrients in the post-absorptive metabolism and animal performance. Inclusion of their effects into the models will mean that detailed knowledge on the mode of action of the additive needs to be available. This will account for only a limited number of feed additives. For additives such as feed enzymes the affinity of the substrate and the activity for these enzymes will need to be known. For the phase one model, additives that have metabolic effects will not be incorporated. For phase 2, detailed effects of selective additives on parameters governing nutrient distribution in post-absorptive metabolism (e.g. synthesis and breakdown processes in tissues), will need to be available to permit incorporation into the models. The extent to which the effects of selected dietary additives can be realistically included in the models will be evaluated in the further course of the project.

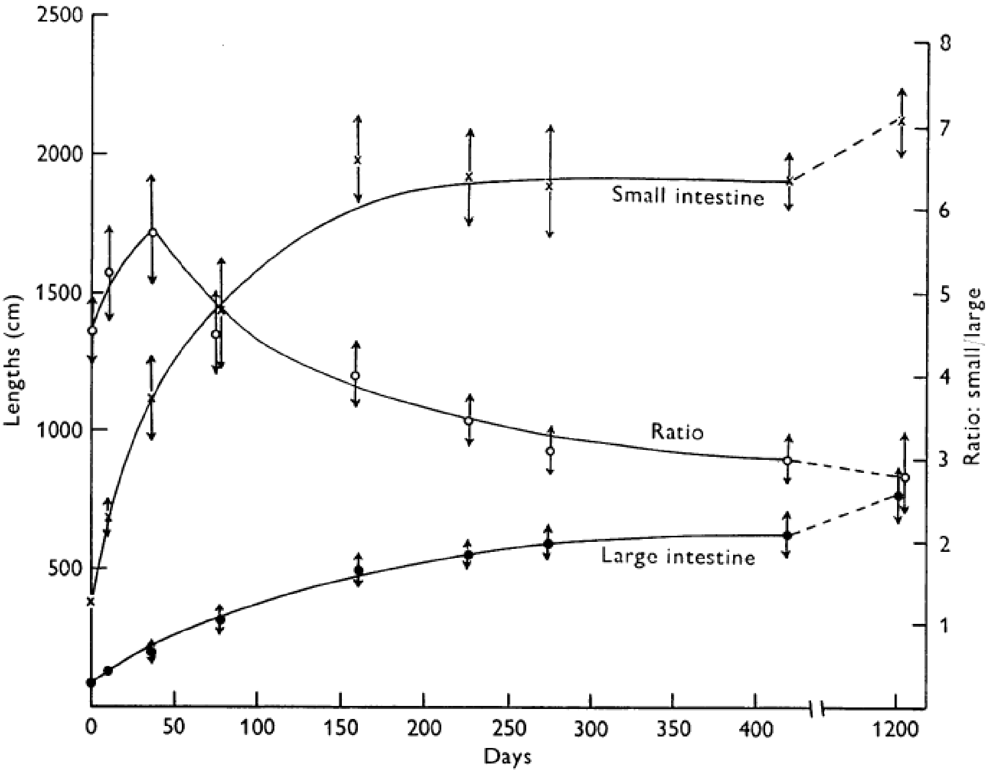
Inclusion of the effects of anti-nutritional factors (ANFs) in feed ingredients in the models will principally only be possible if their detailed mode of action is known. This accounts for only a limited number of ANFs. In the development of the models care will be taken to enable the modelling of the effects of anti-nutritional factors, however, actual incorporation of the effects of anti-nutritional factors is currently out of scope.

The same principles will apply to the effects of mycotoxins, where in theory the effects of mycotoxins could be modelled when the appropriate mechanistic principles are in place. However, modelling the effects of mycotoxins will be out of scope for the current project, as. 1. Mycotoxins are highly unwanted substances that should be controlled in such a way that the animal will not experience a response. 2. Adding the mechanistic principles of action for the different types of mycotoxins would require an enormous effort and is outside the scope of the current project. 3. Many of the mechanisms of action of mycotoxins are not on metabolic partitioning, but on immune, hormone or other physiological systems (Hussein and Brasel, 2001).

Feed processing is often applied to alter nutritional feed characteristics resulting in a changed nutrient supply. The effect of processing as such should therefore be quantifiable in the feed characteristics as described in Tables 6 and 7. This will allow the prediction of the effect of processing through said characteristic on, digestibility, nutrient supply and ultimately animal performance. This kind of analysis shows the benefit of the proposed type of model. In conventional feed evaluation models, digestibility research would be required to arrive at nutrient supply, in the proposed approach the effect on feed characteristics should provide a good estimation for the provision of nutrients from the digestive tract to the post absorptive metabolism.

3.1.3 Parameters related to animals

Animal parameters relevant for describing the digestive processes are thought to be mainly related to feed intake potential and to size and volume of the gastrointestinal tract. Depending on age and body weight, the size and volume of the gastrointestinal tract will differ (McCance, 1974, Figure 6). Size of the gastrointestinal tract and diet, however, may interact such as in the case of fibre, where gastrointestinal tract size grows when being fed fibrous feeds (Pond et al., 1988). Currently, it is envisaged that animal factors such as body weight will be required that parameterize aspects as length and volume of the gastrointestinal tract.
In the development of the post absorptive model it is expected that more parameters related to animals will be required that govern e.g. mature weight and protein deposition parameters. These aspects will be dealt with when the post absorptive model is developed.



The effect of age on the lengths of the small and large intestines and upon the ratio between them. ×—×, small intestine; ○—○, ratio; ●—●, large intestine.

Figure 6 The development of the gastrointestinal tract in pigs with age (McCance et al. 1974).

3.1.4 Parameters related to the environment

As for animal parameters the effect of environmental parameters on the digestive processes will need representation in the model. Environmental conditions are composed of many factors of influence, however, environmental temperature is one of foremost importance (Close, 1987). For the post absorptive model aspects such as environmental temperature or disease pressure, will likely have a role in the model as they can influence the distribution of energy to different tissues (temperature: Lefaucher et al., 1991). For the nutrient digestion models, however, the effects of environmental aspects on the digestive processes will need to be reviewed. There are indications that the effect of environmental temperature on digestive processes is very limited (Jorgensen et al., 1996), however, further literature will need to be studied.

3.2 Controlling variables in the model for post absorptive utilisation of nutrients

As described above, the model for post-absorptive utilization of nutrients will start from the absorbed nutrients from the digestion model. In Figures 7 and 8, a typical example of a schematic representation for the partitioning of post-absorptive modelling of absorbed nutrients over body components (metabolic and anatomical) and environment, taken from Halas et al. (2004), is presented.

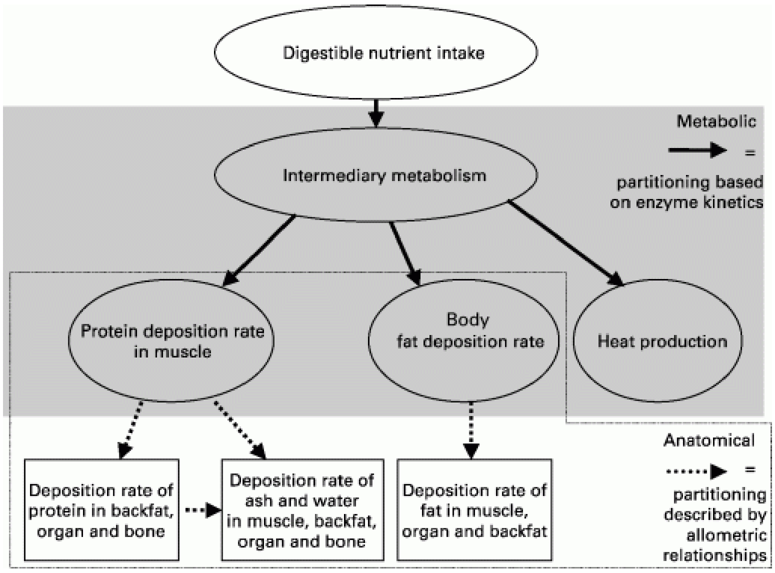


Figure 7 Schematic representation of the approach for modelling protein, fat and energy deposition in pigs from intake of digestible nutrients (Halas et al. 2004).

Although during the construction of such model in phase 2 of the project a different approach may be preferred (e.g. Ferguson et al., 2006; INRAPORC, van Milgen et al., 2008), this figure illustrates the data needed for its construction and use. Firstly, as the post-absorptive model is fed by the absorbed nutrients from the digestion model, the controlling and input variables will largely follow those of the digestion model, described above. Secondly, a detailed characterization of the genotype is needed. This may be done by either calibrating a set of model parameters to data for particular genotypes under well controlled nutritional conditions, or alternatively, by using parameters at slightly higher level of aggregation that can be measured directly in a genotype, e.g. a maximum rate of protein deposition. The extent to which anatomical body composition of broilers and pigs is represented, in addition to the chemical composition, remains to be determined at the onset of phase 2.

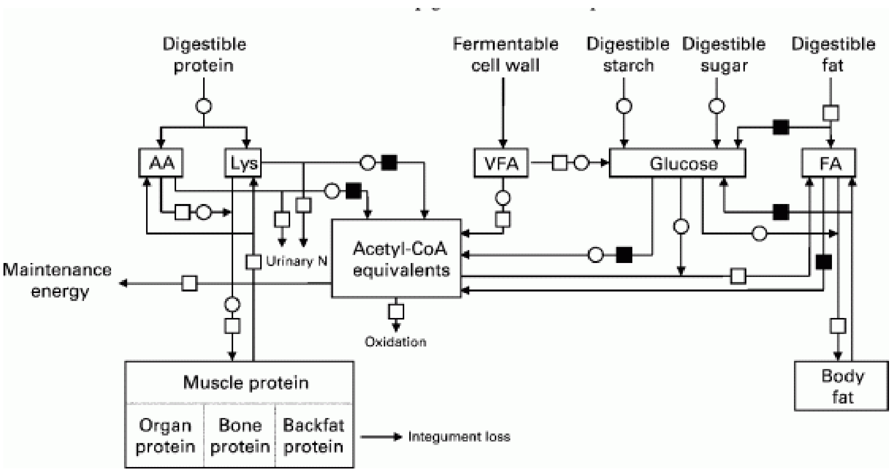


Figure 8 Diagrammatic representation of a growth model for pigs. AA, amino acid; VFA, volatile fatty acid; FA, fatty acid. ○, Energy use in transport; □, energy use in reaction; ■, ATP production in reaction (Halas et al. 2004).

It is anticipated that the models to be developed in the project can predict the influence of variation in health, and environmental factors (e.g. temperature, housing system, stocking density). The extent to which this will be possible depends on the biological processes that are represented in the model. For example, the effect of a decrease in ambient temperature on the increase in maintenance energy expenditure can be easily incorporated in an empirical way. For the influence of changes in health status, it depends on the information available on the processes represented by the model. The final output of the model will be the net protein and energy deposition in the body for growing pigs and broilers kept under different conditions over a given period of time. From the output parameters also practical performance parameters such as body weight gain and feed conversion efficiency can be derived. In addition, the model will also allow to predict the output (loss) of non-retained nutrients (N and P) and end products of oxidation (CO_2). A more detailed outline of the design of the response models will be developed in the further course of the project.

3.3 Phasing of the project

In the development of the complete, final models for each animal category different phases can be distinguished. They are outlined in Table 8.

Table 8 Phases of the project.

Phases	Focus	Aspects
Phase 1	Developing a dynamic digestion model describing digestive processes such as digesta passage, hydrolysis and absorption of nutrients in the different compartments of the gastrointestinal tract.	Apply knowledge on effect of feed characteristics, particle size, bulk fill, rheological properties to digestive processes. Defining new raw material properties as affected by composition and processing.
	Developing a simplified model of post-absorptive nutrient utilization based on existing models and/or empirical relationships	Application oriented development of response models to apply improved prediction of nutrient utilization
	Development of a user interface	Development of a basic functional program.
Phase 2	Developing a dynamic model of post-absorptive nutrient utilization	Apply knowledge on the effects of genotype, age, health and climate on animal response
	Update the user interface	Develop a fully functional program.

The present masterplan focusses on different animal species and categories of animals within species (growing pigs, gestating and lactating sows, broilers and laying hens). Within each animal category emphasis should be given to the modelling of nutrient processing in the digestive system and to the post absorptive metabolism. It is assumed that modelling efforts for one species or category of animals are also of benefit for the development of models for others, both with regard to the modelling of the digestive process and for the post absorptive metabolism of nutrients. The extent of these benefits varies among animal categories. In addition, it should be mentioned that the models to be developed can vary in their degree of complexity and level of modelling of physiological and metabolic processes. In order to deliver models which can be applied by research and industry in a reasonable period of time via a suitable interface, more simple models can be developed for a part of the system first and be linked at a later stage to new parts which consider more details of the actual processing of feeds and nutrients in the gastrointestinal tract or aspects of nutrient metabolism in the post absorptive phase. This strategy favours the application and use of the developed models by the intended stakeholders in an as early as possible stage.

The development nutrient based response models for each of the categories of animals mentioned is a very large effort which require availability of adequate funds, availability of skilled manpower and proper budgeting, planning and timing of execution of the programme and its activities. Within the PPS F4F preliminary budgets have been allocated for this activity over a period of four years (2013-2016) and budgets are finally approved for a period of one year. In addition, alternative options (e.g. funding options within programmes of NWO and EU) will be explored throughout the duration of the programme to find (additional) funds for financing the execution of a part of the activities described in the present masterplan.

Financial constraints within the public private partnership Feed4Foodure (F4F) force to make choices with regard to which models will be developed in a more early phase and which ones will or could be developed later in time. An overview of the time schedule for the development of models is given in Figure 9. It should be emphasised that only a part of the activities in the schedule can be executed within the timeframe of F4F (2013-2016). The time schedule is only indicative for the period after 2016 for reasons of uncertainties about availability of funds for the execution of the scheduled modelling activities. If timely adequate funds are available, the speed of the execution of the modelling programme can be increased by the recruitment of additional skilled scientific staff by WUR.

It is proposed to start to develop a model for nutrient processing and absorption in the digestive tract of growing pigs in 2014. This choice is related to its expected impact of the development and use of model(s) for this animal category compared to the other categories mentioned and to the availability of a larger number of relevant data needed form model development for this animal category. Model development with major involvement of a PhD student is expected to require a period of four years. In order to have a first whole animal model available for growing pigs within four years after the start of the modelling activities of the digestive process, it is foreseen that a more simple model for the post absorptive metabolism is developed in year 3 and 4 after the start of development of the “digestion model”. In an early phase of this 4 year period also attention will be given to the development of an interphase allowing end users (nutritionists in industry and researchers) to use and apply the output of calculations and predictions of the model in a user friendly way. Apart from budgetary and capacity constraints, modelling of the digestive process in broilers could start in 2015 and a first working complete animal model could be available four years later. More in depth modelling of the post absorptive metabolism in growing pigs and broilers will start in a later phase and will be dependent on availability of budget and capacity of staff with appropriate skills and expertise. The former strategy increases the use and application of the models by stakeholders within a reasonable period of time.

It is foreseen that the construction of response based models in sows in gestation and lactation and in laying hens will start in a later phase. The exact timing will be largely dependent on availability of budget and skilled staff. It is foreseen that for the construction of models for both sows and laying hens a significant basis can be obtained from the modelling activities on other animal categories (growing pigs and broilers). This means that construction of models for these animal categories require less capacity on some parts compared to the ones for growing pigs and broilers. It is foreseen that the development of a simple digestion model for sows and laying hens based on the models developed for growing pigs and broilers, respectively, requires a period of one year (data collection and calibration of the models). Thereafter, modelling efforts will be directed to the post absorptive metabolism of nutrients in sows and laying hens. Specific differences between these categories of animals (kept for the production of offspring or eggs) compared to growing animals require specific attention towards the modelling of nutrient processing in specific organs and tissues not considered in growing pigs and laying hens.

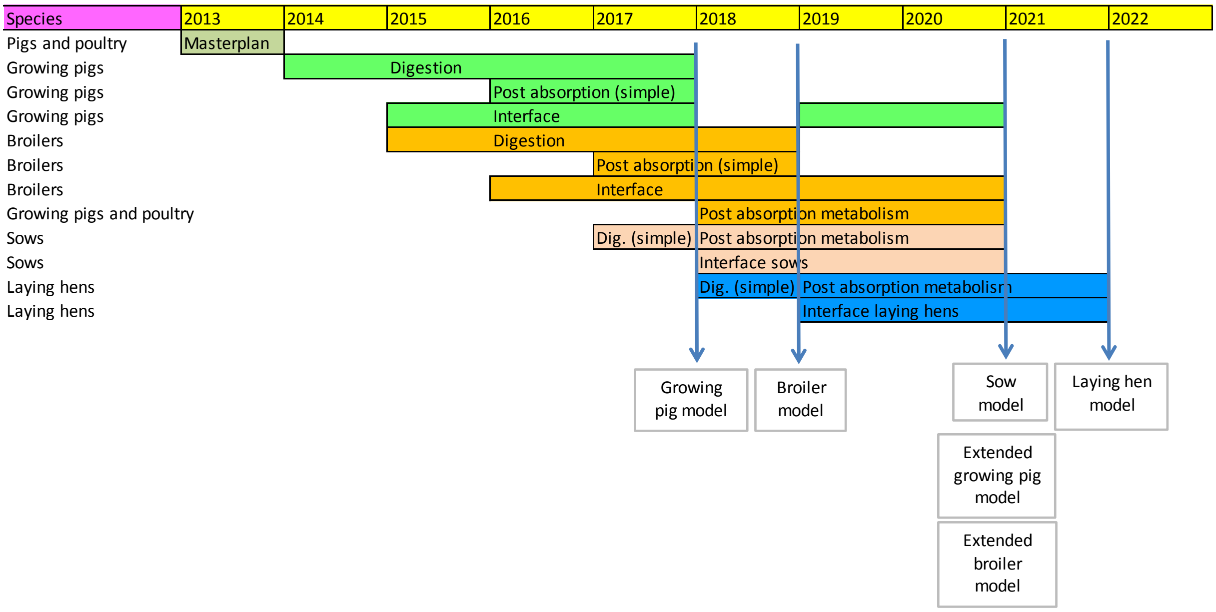


Figure 9 Time frame for the development of nutrient based response models for the different animal species and categories.

4 Available data for model development

Dynamic mechanistic models will be developed for growing pigs and broilers predicting the performance response of the animals based on the supply of hydrolysed and absorbed nutrients in the gastrointestinal tract and their post absorptive metabolism in organs and tissues, taking into account various animal and environmental factors.

Experimental data and concepts will be retrieved from literature to construct the models regarding the nutrient supply and processing in the gut (all activities that occur in the gut up to the absorption by the intestinal mucosa) and response (systemic metabolism of absorbed nutrients) of growing pigs and broilers. Most studies reported in literature focus on only dietary nutrient supply or animal response to a certain nutrient supply. For growing pigs and broilers, however, more knowledge has to be obtained to develop nutrient based response models. Moreover, combining of a (mechanistic) nutrient based approach for pre- as well as for post-absorptive aspects is lacking. Aspects which require more detailed representation by modelling span digestive processes (enzymatic, fermentative) in the gastrointestinal tract, microbial activity in the gastrointestinal tract, absorption of nutrients from digested feed ingredients/feeds in the gastrointestinal tract and post-absorptive utilisation of nutrients (metabolism and retention in “productive” organs and tissues). Many animal related factors (such as genotype , gender, physiological status, health), environmental conditions (such as stocking density, feeding system, climate) and temporal variations (between days and within days) determine the relationship between pre-absorptive nutrient supply and post-absorptive nutrient utilisation and animal response.
Data on the physical chemical characteristics of feed ingredients are required for taking digesta characteristics into consideration in the prediction of the kinetics of nutrient absorption in the gut. Knowledge and data about these characteristics might be available in the area of (human) food chemistry. Contacts will be established with relevant scientific groups in this area inside and outside the Netherlands to identify the availability of knowledge and data on this subject.

In the Topsector Agri & Food programme Feed4Foodure (F4F) various projects were started on three sub-themes: ‘More with Less’, ‘Social Responsible Livestock Farming’ and ‘Diet, Intestinal health and Immunity’ which can contribute data for model development. Also data can be obtained from other F4F projects such as ‘Reducing energy losses’, ‘Reducing nitrogen losses’, ‘Reducing phosphorus losses’ and ‘Reducing copper- and zinc losses’. These projects will be fine-tuned on a regular basis and be adjusted to provide additional data input for the development of the dynamic mechanistic response models in the present project.

WUR has a relatively large network in the area of dynamic mechanistic modelling of pre- and post-absorptive aspects of the animal response to changes in nutrition and nutrient supply in both the monogastric and the ruminant domain. Table 9 gives an overview on the most relevant extant collaborations in this field. The contacts and networks in the international scientific community in the area of modelling of animal responses and digestion and metabolism of nutrients in the target species will be used for both further development of the conceptual framework of the models as well as for provision of experimental data. It is emphasized that although most currently used models predicting animal performance or responses to changes in nutrient supply have been published in the scientific literature with an explanation of the main principles, these models are generally not published in their full detail (with the dynamic mechanistic models developed by WUR so far actually being among those published most precisely and in most detail). To a varying extent, the models have some degree protection for use by third parties. Given the large efforts to develop models and related intellectual properties issues, it cannot be expected that the source code of published models will be obtained from (collaborative) scientists owning these models and this code be included in full or in part, in models to be developed within the framework of the present master plan. Furthermore, concepts specifically addressed in the current master plan essentially lack in these published models.

The existence of relevant data bases at the side of the F4F partners as input for the model development or for model validation will be explored.

Table 9 Current collaborations of WUR with other scientific groups throughout the world in the area of modelling of animal responses towards changes in the supply of diets and nutrients.

Group	Animal species	Topic(s)
University of Reading, Reading, UK	Dairy cows	Rumen fermentation Methanogenesis Milk fat as proxy for methane Microbial interactions Lactic acidosis Digestive functions Intestinal digestive and absorptive functions Amino acid metabolism.
University of California, Davis, US	Dairy cows	Rumen fermentation Methanogenesis P metabolism dairy cows
	Poultry	Ca-P metabolism in laying hens
University of Guelph, Canada	Dairy cows/cattle	Rumen fermentation Methanogenesis Microbial interactions, Development of intestinal (rumen) tissues Amino acid metabolism Excreta composition Growth models cattle
	Pigs	Growth models pigs P metabolism
	Veal calves	Post-absorptive nutrient metabolism
University of Léon, Spain	Ruminants	In vitro fermentation
University of Queensland, Australia	Pigs	Fibre and passage rate
INRA, France	Various animal species	MoU - Feed evaluation

5 Model evaluation

5.1 Introduction

For application of the developed models it is imperative to know the accuracy and precision with which the model predicts the digestive and growth processes being modelled. Apart from accuracy and precision of model predictions of independent data, model responses to variation in model inputs (behavioural analysis) and model assumptions (sensitivity analysis) are required.

5.2 Methods of model evaluation

5.2.1 Sensitivity and behaviour analysis

Behaviour analysis of the model evaluates how biological model components, such as the amount of digesta within a compartment of the gastrointestinal tract, develop in time as influenced by variation in model inputs. Model predicted values for the amount of material in different sections, as well as material and nutrient flow, should remain within physiologically acceptable boundaries when varying input factors. Model behaviour analysis is performed throughout model development as well as before finalizing the model.
Sensitivity analysis shows the change in response of the model when changing in put variables or model parameters. For the digestion model, various model input parameters, e.g. feed intake and maximum digestion rates of nutrients or model parameters e.g. for stomach emptying rate, will be evaluated for their effect on nutrient supply and digestion of feed components. For the animal response models, effects carried over from the sensitivity analysis of the digestion models, as well as new changes in metabolism related parameters, will be evaluated. Changes in response parameters can be expressed in absolute levels. In order to improve the evaluation of the sensitivity of models, however, the dimension less parameter S as described by France and Thornley (1984). The parameter S describes the ratio of change in response relative to the ratio of change in input or model parameters. A value of S of 1 denotes the same relative change in response as the relative change in input or model parameter. Using S, a large number of input and model parameters can be evaluated and compared for their impact on the model.

5.2.2 Validation of models

In addition to the behavioural and sensitivity analysis, comparison of model predictions against independent data is important. During the construction of the models, it will have to be decided whether to use available information for model development (calibration) or for independent model evaluation. For evaluation of certain predictions of the digestion model, the CVB (2011) database, or underlying data, will be useful. For evaluation of the more dynamic aspects of the digestion model and for the post-absorptive model, independent data will be collected throughout phases 1 and 2.
For the comparison with independent data, basic mathematical techniques will be applied for calculating the root mean square prediction errors (RMSPE) and the concordance correlation coefficients (CCC), with analysis of the origin of the error, either from bias, slope or general error.

6 Implementation of the feed evaluation system and development of user interfaces

As mentioned before, the nutrient based dynamic mechanistic response models will be developed for strategic use rather than for use as a tool to optimize diet composition as a daily activity in the feed industry in which cost price of the diet is the optimization target. For the latter linear programming tools (least cost formulation), as currently in use by the feed industry, will remain to be used. The former uses data on the composition, nutritional value and costs of raw materials on the one hand and information on nutrient and ingredient requirements of the diets for a given target animal category, age and physiological status on the other hand. The CVB data base on the chemical composition and nutritional value of feed ingredients for the various farm animal species and categories is an important basis for the daily optimization of diets in The Netherlands.

The new response models will be used for strategic questions in research and for evaluating the effects of adjustments of feeding strategies. As outlined the final models will consist of a digestion model, focused on prediction of the supply of nutrients from (a mixture of) feed ingredients, and of a model on the subsequent partitioning of absorbed nutrients over body components or the environment. The digestion models will use data from the current Dutch CVB table as important input. In this way it is also guaranteed that the basis for input in the new nutrient supply models is linked to input of data on the nutritional value of feed ingredients in programmes used for practical day to day diet formulation in The Netherlands.

The final use of the models by stakeholders requires the construction of interfaces linking the in- and output of the response models to parameters relevant for practice. In addition, the interface should allow to use the models or parts of the models for interactive sessions to generate new knowledge and information on animal responses in relation to a variable dietary input. The construction of the digestion and post-absorptive models for pigs and poultry will take a period of 6 - 8 years. To enable users to benefit from model development as soon as possible, the construction of the user interface will be started in the first year of the project. Model intermediate products will be connected to the user interface to facilitate their immediate use. It is foreseen that the first versions of the models will be available upon completion of the digestion model. These versions will include a simplified representation of the post absorptive metabolism of nutrients.

For the development of user interfaces a core group will be established in which the persons involved in the development of the response models will be involved, as well as representatives from the feed industry as important final users of the interfaces, and experts in interface building. Adequate budget will be allocated to cover the expenses related to this activity.

7 Conclusions

The present masterplan describes the development of new dynamic mechanistic response models for pigs and poultry predicting the animal's performance and retention of nutrients and output of non-retained nutrients. In the execution of the plan, first attention will be given to the development of nutrient response models for growing pigs and broilers. The response will be predicted from the composition and physical chemical characteristics of feed ingredients and the diet, quantitative intake of the diet, digestive processing of nutrients in the gastrointestinal tract and metabolic transformation and retention of nutrients in the body taking into account both animal and environmental variables. The models will be developed for answering strategic questions in feed evaluation practice, for research, for identification of gaps of knowledge in processes related to nutrient processing (hydrolysis and absorption) in the gut and in the post-absorptive metabolism. In addition, they can be used for evaluating the effects of adjustments of feeding strategies or changes in physical chemical characteristics of feed ingredients. Application of the models will allow the pig and poultry production sectors to more precisely adjust diet composition and feeding strategy to the (desired) response of growing animals in terms of producing high quality human food and minimizing environmental nutrient losses under a variety of conditions as found on farms in the Netherlands.

The new models will extend on knowledge included in existing models of pig and poultry production and will include new aspects such as the physical chemical characteristics of feed ingredients, thus connecting directly to feed ingredient databases. The former has not been considered before and is therefore innovative. The post absorptive metabolism of nutrients in organs and tissues will be modelled to predict the response of animals in terms of animal performance, retention of nutrients in the body and loss of nutrients and metabolites of nutrients in the environment, contributing to the environmental footprint of animal production. The animal response will be modelled in dependence of various animal (e.g. genotype, sex, and health status) and environmental factors (e.g. stocking density, and climate). Current prediction models of animal performance generally do not include these factors.

To allow the timely use and exploitation of the results of the modelling efforts by the stakeholders throughout the duration of the project attention will be given to the construction of user interfaces for stakeholders from the beginning of the execution of the project onwards. These interfaces will allow to use the models or parts of the models to generate new knowledge and information on the animal's responses towards a variable dietary input in a user-friendly way.

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