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Review Article

Large intestinal dynamics differ between fowl and swine: Anatomical modifications, microbial collaboration, and digestive advantages from fibrolytic enzymes

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ABSTRACT

The large intestinal systems of fowl and swine recover nutrients from ileal indigesta by a strategically different manner. Indigesta with fowl enter a short colon where retro-peristalsis using urine from the urodeum carries small particulates and solutes into both ceca while coarse materials collect in the cloaca. Fowl repetitively add fine and soluble materials into both ceca to continue fermentation until complexity of the remainder exceeds microbial action, then contents apart from faeces are entirely evacuated. Indigesta with swine initially enter a short cecum followed by a lengthy progression through to the rectal ampulla. Wall out-pocketings of circular muscle or haustrae occur throughout the length of the pig's cecum and helicoidal colon. Each pocket carries contents acquired earlier in the cecum. Motility collects fines and solutes into haustrae during their progression through the colon whereas coarse particulates assemble in the core. Haustrae contents continually ferment during movement to the distal colon with resulting volatile fatty acids (VFA) and electrolytes being absorbed. Mucin loosely covers the lumen surface in caeca as well as helicoidal colon that may capture microbes from active intestinal contents as well as release others to sustain fermentation. The microbial community continually modifies to accommodate fibre complexity as encountered. Resistant starches (RS) and simple oligosaccharides rapidly ferment to yield VFA while encouraging butyric acid in the cecum and anterior colon, whereas non-starch polysaccharides (NSP) complexity requires extended durations through the remaining colon that enhance acetic acid. Residual fibre eventually results in undue complexity for fermentation and consolidates at termination of the colon. These compact pellets are placed on core contents to form faeces having a nodular surface. Acetic, propionic, and butyric acids represent the bulk of VFA and are derived from non-digestible carbohydrates. Fibrolytic enzymes, when supplemented to feed, may increase the proportion of oligosaccharides and simpler NSP to further the rate as well as extent of fermentation. Active absorption of VFA by mucosal enterocytes employs its ionized form together with Na^{+}, whereas direct membrane passage occurs when non-dissociated. Most absorbed VFA favour use by the host with a portion of butyric acid together with by-products from protein digestion being retained to reform mucin and sustain mucosal integrity.

1. Introduction

Although fowl and swine are considered simple stomached animals, many differences exist in the operation of their gastrointestinal tracts (GIT). Birds eat more food relative to their metabolic size, whereas time needed to fulfil passage through the GIT approximates half that of mammals (McWorter et al., 2009). Swine employ approximately 3 to 4 h for ingesta to pass through the small intestine (Rayner and Wenham, 1986; Martens et al., 2019) with the large intestine requiring another 8 to 9 h before the appearance of

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associated excreta (Hecker and Grovum, 1975) and as much as 40 h mean retention time (Wilfart et al., 2007). On the other hand, poultry only require 3 to 5 h for dietary markers incorporated in food to appear in faeces (Kaupp and Ivey, 1923; Golian and Polin, 1984; Hughes, 2008).

Food digested by the small intestine provides the greatest proportion of dietary nutrients for the body, with far lesser amounts being subsequently recovered by the large intestine. The large intestine relies on microbial fermentation of indigesta to recover available nutrients, particularly energy, which amounts to 5%–15% of maintenance requirements for fowl as well as swine (Annison et al., 1968; Imoto and Nakioka, 1978; Kass et al., 1980). The basic strategy employed by the large intestine to recover nutrients is substantially different between fowl and swine. Fowl depend on caecal fermentation of fine and soluble materials separated in the colon, whereas the resulting coarse particulates are rapidly excreted from the cloaca; however, swine employ an extensive microbial exposure through the entire colon with all indigesta after a short residence in the cecum (Moran, 1982).

The size, surface area and aqueous compatibility of feed particles are related to their composition and this influences the potential for digestion by the small intestine. These same characteristics with the indigesta remaining after the small intestine dictate the ease of fermentation by the large intestinal microbial population and hence the recovery of the remaining nutrients. Large particulates are likely to be composed of lignin and cellulose fibrils, creating a physical resilience and resistance to microbial digestion, whereas resistant starches (RS), oligosaccharides, and non-starch polysaccharides (NSP) can provide considerable energy. Corn is a low fibre grain and when milled into particulates of uniform dimension, yield similar live performance improvements with both chicks and piglets (Kim et al., 2002). On the other hand, high fibre grains and milling by-products present a wide array of particulates that vary in RS, NSP, cellulosics, and lignin (Evers et al., 1999; Bach Knudsen, 2014). Feedstuffs expressing such diversification generally provide more DE when fed to swine than poultry, but differ little in CP availability (Rostagno, 2005). This disadvantage in recovery of digestible energy (DE) with fowl has been attributed to a rapid excretion of large particulates, whereas all contributors to indigesta would be subject to an extended fermentation and additional recovery of volatile fatty acids (VFA) during passage through the pig's large intestine (Moran, 2022).

Improved animal performance readily occurs when feed is supplemented with fibrolytic enzymes, particularly the xylanases. Generally, such advantage can be attributed to a reduction in particulate size, while improving their aqueous compatibility (Amerah et al., 2008; Pollet et al., 2010). These improvements are generally more apparent when xylanases are added to wheat-based feeds, yielding considerable amounts of oligosaccharides (Van Den Broek and Vorag., 2008; Bautil et al., 2019a, b). Certain oligosaccharides or prebiotics, when added directly to feed, frequently improve animal performance beyond benefits expected from their associated energy. Such advantage has been attributed to an augmentation of the existing microbial population that extends fermentative capacity, hence the term stimbiotics (González-Ortiz et al., 2019). The following is a broad view of the large intestinal systems of fowl and swine that details their structures and nature of operation. The intention is to rationalize differences in performance that often occurs between animals and feedstuffs. Many of these differences can be attributed to modifications in the terms of operation, altered microbial populations and resulting advantages when fibrolytic enzymes are employed.

2. Anatomy

The large intestinal systems of fowl and swine comprise 3 parts, each of which differs from the other in appearance and extent of functioning. Fowl have two long ceca connected to one short colon that extends to the cloaca (Fig. 1), whereas swine have one short cecum followed by an extended colon that terminates at the rectum (Fig. 2). Having 2 well developed ceca is typical of avian species consuming extensive amounts of grain and high fibre foods (Degoliere et al., 1999). Swine are omnivores and accepting of diverse foods, and this is reflected in their large intestine which as a proportion of the entire GIT is intermediate between non-ruminant herbivores and ruminants. The large intestinal systems of fowl and swine are at their greatest proportion of the total GIT either after hatch or parturition when nutrition is dependent on the maternal parent. Subsequent growth of the small intestine becomes extensive to eventually dominate the GIT with both species. As the proportion of the large intestine diminishes, so does an extensive

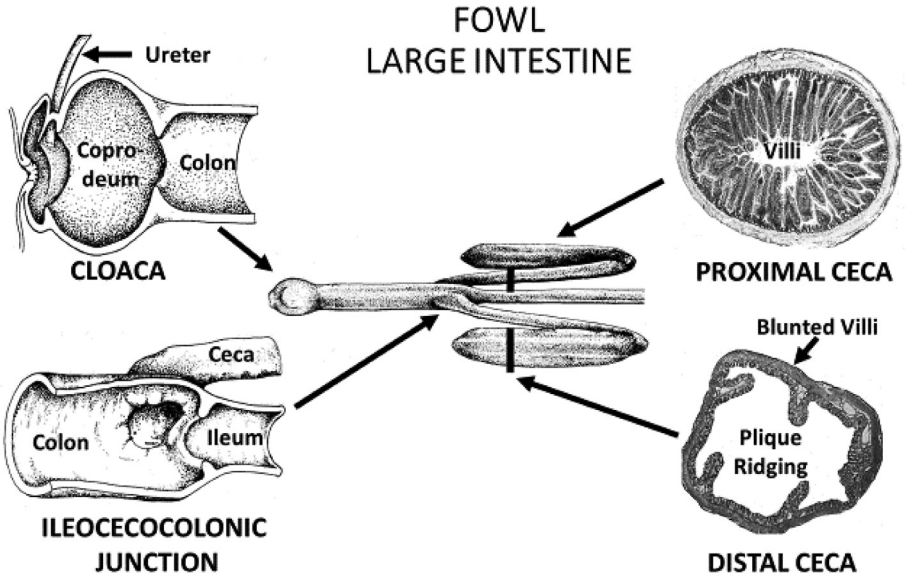

Fig. 1. Graphic description of the fowl's large intestinal system (Moran, 1982).

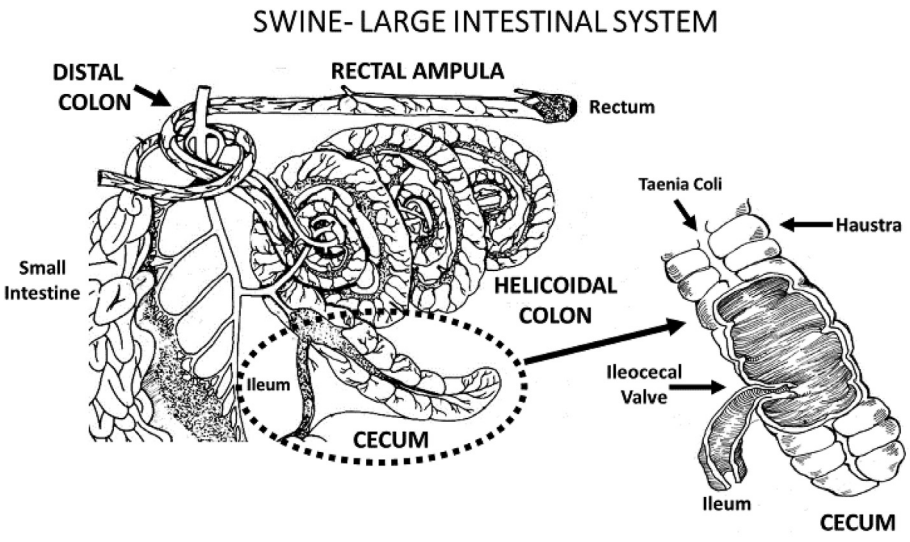

Fig. 2. Graphic description of the pig's large intestinal system (Moran, 1982).

microbial population become well established (McCance, 1974; Crompton and Walters, 1979; Ijaz et al., 2018). These microbes with fowl are most concentrated within their ceca (Mead, 1989; Rinttila and Apajalahti, 2013), whereas the cecum-anterior colon is particularly favourable with swine (Durmic et al., 1998; Inoue et al., 2005). As discussed below, as indigesta moves distally, the ease and extent to which it can be fermented is diminished due to the increasing complexity of the remaining fibre fractions. The large intestine of swine should not be considered as a single fermentation vat but as an increasingly specialised series of sections in which the complexity and capability of the resident microbiota rise in concert with the increasing intransigence of the remaining fibre fractions.

Lumen conditions within the ileum of established animals are completely different than those of the large intestine. Extensive villi in the small intestine greatly expand surface area for rapid absorption of nutrients released in the lumen during digestion. A vast vascular system within the small intestine's lamina propria further acts to rapidly evacuate nutrients from enterocytes once absorbed (Aharinejad et al., 1991). Prominence of villi and vascular system provide ready access to oxygen for active transport of nutrients, while further diffusion into the lumen discourages development of anaerobes. The large intestine is the direct opposite, by presenting a relatively flat mucosa because villi are closely associated to each other. In turn, the mucosal surface presents narrow crevices enabling mucin to be readily released from laterally positioned goblet cells. The vascular system within the lamina propria is poorly developed thereby restricting the mucosa access to oxygen as well as blood borne nutrients (Johansson et al., 2011).

Lumen microbial populations in the small intestine exhibit drastic differences in numbers and membership upon transition to large intestine. Established swine have an aerobe-facultative anaerobe combination near termination of the ileum, which is geometrically replaced by strict anaerobes once within the cecum-proximal colon (Zhao et al., 2015; Wang et al., 2020). Prominent genera in the ileum are focused on rapid metabolism of easily fermentable substrates and these are replaced by those adapted to an increasingly slower transit rate and metabolism (Molist et al., 2014; Hoogeveen et al., 2021) as digesta transits through the large intestine as discussed in section 3. These inhabitants evolve with maturation of the intestine as they need to adapt to the change in substrate supply and conditions prevalent in the aging intestine.

The valve between the small and large intestine has the objective of minimising exchange of contents and microbes. The fowl's ileal valve transiently opens with the approach of a forward peristaltic wave that creates a pressure transfer of indigesta into the colon before closing. Swine have an ileal valve at the cecum-colon juncture which appears to be less exclusive in sharing lumen contents than fowl. Frenula arise from a projection of the ileal valve into the lumen at the cecum-colon juncture. These frenula act to direct indigesta into the cecum when open (Fig. 2), while concurrently minimizing advancement into the colon (Rayner and Wenham, 1986; Prado et al., 2002). The converse occurs when the ileal valve is closed and cecum contents are moved into the colon. Ileal musculature preceding the valve, with both fowl and swine, is well developed to accommodate a thickened content as fibre increases while digestible nutrients and water content decrease.

Once indigesta enters the fowl's colon, retro-peristalsis initiated at the cloaca conveys urine back through the colon to “wash” and segregate lumen particulates. Given closure of the ileal valve, a portion of the indigesta enters both ceca with each cycle (Lai and Duke, 1978; Duke, 1989). The combination of small entrances and villi projecting into the ceca core restricts entry to fluid, colloids and fines. Coarse materials move caudally with reversal of peristalsis. Large particulates progressively enter and collect in the coprodeum at the end of the colon (Fenna and Boag, 1974). The cloaca has 3 chambers, with the coprodeum evacuating contents as often as filling occurs (Waldenstedt and Björnhag, 1995; Brummermann and Braun, 1995; Son and Karasawa, 2004). The primary basis for a short duration of dietary markers passing through the GIT with fowl can be rationalized as dye, associated with coarse particulates, being evacuated “early” with its appearance in faeces.

The fowl's mucosa throughout the cloaca, colon, and ceca is adept at recovering water and electrolytes in urine derived from the kidneys. Urine released into the urodeum has the option of either being directly excreted as a watery collage with cloacal faeces or conveyed back through the colon. The extent of urine participating in retro-peristalsis, rather than direct excretion, varies to accommodate differences between dietary intake of electrolytes and water and their necessity to sustain nutrient requirements (Pácha, 1993). Uric acid is particularly dominant in urine and marginally soluble. A partial precipitation occurs in the coprodeum contents during aboral movement and water absorption, hence the

appearance of a "white cap" on faecal excreta (Dahm et al., 1980; Elbrønd et al., 1997).

Particulate segregation of indigesta also occurs within the large intestine of swine but is accomplished through modifications of the wall's major muscle layers. The cecum, together with the subsequent helicoidal colon, have their longitudinal fibres gather into bundles throughout the length as *taeniae coli* (Fig. 2). Three bundles separately run the length of the cecum, with 2 continuing as opposites through the helicoidal colon. The third bundle proceeds from the end of the cecum to terminate at the ceco-colonic valve. Contractions of the valve initiate movements of the third bundle that may aid in the segregation of indigesta entering from the ileum. Motility involving the circular fibres is suspected of creating "bulging" of the wall in the absence of "overhead stabilization" by longitudinal muscle fibres. These bulgings, or haustrae, collect fluid, colloids and fine materials within its body, whereas coarse and lighter particulates assemble at the core (Huizinga et al., 1983; Thornton et al., 1983; Barbiers et al., 1994). Such particulate segregation into haustrae parallels the fowl's ceca; however, the contents of haustrae are not fixed in place but move the contents "gathered" earlier in the cecum and restricted to each haustrae. Although haustrae contents originate at the cecum, they progressively move caudally and in doing so present "new" surfaces to the contents during this movement (Lentle and Janssen, 2008; Moran, 2022).

Longitudinal muscle fibres eventually resume their equilateral positioning over the circular muscle layer to eliminate the haustrae. After the many hours of haustrae contents being conveyed to the distal colon, microbiological fermentation has decreased the quantity of contents. Essentially, RS and oligosaccharides are the first to disappear, with the residual fibre progressively increasing in structural complexity. This residual material eventually condenses into a "pellet" that is "pasted" onto the adjacent core before entering the rectal ampulla. As a result, mammalian faeces typically present a "nodulation" of the surface that is expected to vary with the amount and type of dietary fibre. Essentially, swine excrete coarse fibre, together with spent "fine" residues as a composite, whereas fowl void ceca contents apart from cloacal excreta.

3. Microbial characteristics

Effectiveness of the large intestine at recovering nutrients from ileal indigesta almost exclusively depends on "digestion" by its microbial population. Initial membership is largely attributed to interactions between neonate, maternal parent and immediate environment, to create an ever-developing population (Binek et al., 2000; Rehman et al., 2007). Defining microbes present at any one time is elusive because the community is continuously being modified (Collinder et al., 2001; Lu et al.,2003; Torok et al., 2008; Tanakawa et al., 2001). This flux in membership represents a continual adaptation to fulfilling fermentation of indigesta as encountered (Barnes and Impey, 1970; Robinson et al., 1981; Wei et al., 2013; Sergeant et al., 2014). Such microbial modification is particularly dramatic during the first few weeks of life with the Bacteroidetes, Firmicutes, and Proteobacteria being especially influential (Vahjen et al., 1998; Lee et al., 2020). Adhikari et al. (2019) observed significant increases in genera such as *Moryella*, *Dialister*, *Clostridium*, *Streptococcus*, *Prevotella*, and *Bacteroides* being established within the piglet by 27-d post-weaning. In his review on factors influencing variation of the pig's gut microbial population, Wang et al. (2020) emphasized that the most influential aspects on membership, beyond age, was the nature of dietary carbohydrates reaching the large intestine together with their diurnal rhythmicity and extent of microbial exposure. Simplistically, the small intestine continually receives food to provide the bulk of nutrition throughout the "day." Subsequent fermentation of resulting indigesta that is collected, eventually assumes maximisation at "night" as contributions from the small intestine dissipate. VFA now provide the body with energy, whereas absorption of electrolytes and water are of potential advantage to sustaining their requirements.

RS and oligosaccharides are quantitatively minor carbohydrate components and NSP dominate while indigestible protein can be prominent. Increasing the structural complexity of dietary carbohydrates, from RS and oligosaccharides to NSP through to the cellulosics, progressively extends the duration necessary for the microbial population to fulfil fermentation. Dietary supplementation with xylanases generally reduces particulate size while improving aqueous compatibility of products to enhance the overall rate of fermentation (Dänicke et al., 1999; Nitrayová et al., 2009; Cowieson et al., 2010). The digestive capability of the microbes addressing carbohydrate complexity is not uniformly shared among members of the population but presented by an array of individual "talents" (Hartemink et al., 1990; Wang et al., 2004; Lan et al., 2007; Apajalahti and Rinttila, 2019). RS and oligosaccharides are most labile and readily fermented, whereas escalating complexity from varying sources of NSP require additional "effort" by "competent" members. Presumably, the change in membership of the population at any one location of the large intestine is a response to the complexity of the substrates at-hand and enzymatic necessities to continue fermentation (Sergeant et al., 2014).

Microbes located at any one location within the large intestine likely relate to the concentrations of carbohydrates amenable to fermentation. Fowl caeca are divided with the distal two-thirds "folding over" the proximal one-third within the body cavity. Elimination of coarse material from indigesta reduces the volume entering caeca. The proximal portion has prominent villi that partially resorb water and electrolytes to further decrease volume before entry of the remainder into the distal portion where fermentation dominates (Danziger, 1989; Strong et al., 1989). Overall size of ceca appears to be a function of ongoing encounters with the amount of indigesta generated from total food intake and transfer resulting of indigesta generated from the colon. Cecal volume, once established, seems to remain unchanged on a "routine basis." Cecal fermentation initially favours utilization of the most labile carbohydrates with the remainder following, as dictated by complexity. In time, carbohydrate contents progressively increase in complexity. Accommodating the intermittent additions of indigesta from the colon into the ceca seems to occur by a corresponding loss of VFA and electrolytes. The extent of wall "distension" arising from these repetitive additions seems to "signal" the necessity for evacuation of contents (Hodgkiss, 1984; Clench and Mathias, 1996; Jansen et al., 2009). Given a "simple" day, caecal evacuation first occurs at the "beginning" of each day after an "overnight" completion of fermentation from the previous day's intake with resumption of feed intake (Takahashi et al., 2004). Such evacuations are expected to vary with the nature and extent of dietary fibre intake, together with duration of either lighting or feed access. Once evacuated, "new" indigesta entering caeca can be accommodated by a "flattening" of wall plique ridging (Fig. 1).

Given that fermentation of caeca contents fosters an increase in contents fibre complexity, more "talented" microbes become a necessity. Such modifications can be expected to alter the rate and proportions of VFA being formed. RS and oligosaccharides initially encourage a rapid generation of VFA with specific ability to enhance butyric acid concentrations (Topping et al., 2003). Caecal motility continuously contributes microbes into the lumen from the population residing in its thick mucus lining of its walls. Membership of this population is modified to sustain fermentation (Fuller and Turvey, 1971; Zhu and Joerget, 2003). "Adjustments" in microbial

membership seems plausible given their rapid regeneration that accommodates digestive capability (Table 1).

Caecal contents, when "spent", are largely evacuated as a peristaltic "rush" that must be preceded by faecal clearance from the coprodeum. Caecal droppings are usually "pasty" in appearance and vary from being "thick", when having an extended proportion of unfermented complex fibre, to presentation of fluids that occurs with dietary milk products having lactose, to create gas and "bloating" (personal experience). The colour of excreta is largely a function of bile pigments arising from degradation of senile red blood cells by the liver. Fowl only form an intense green biliverdin that is directly incorporated into bile. Given short-term microbial exposure during colon-cloacal retention, faeces retain a greenish "tinge," whereas brown stercobilin arises with caecal droppings because of an extended microbial reduction (Moran, 1982). Swine bile is reddish green, due to a partial biliverdin conversion to red bilirubin in the liver; however, extended duration of both in the colon leads to stercobilin and dominance as a brownish stool. Excreta appearance may also reflect undigested feedstuffs, e.g., yellow from corn products, green with alfalfa, etc.

Unlike fowl, swine do not continuously accumulate indigesta at any one place in the large intestine but, generate successive haustrae as indigesta enters the cecum. Increasing the level of dietary fibre consumed as well as an exaggerated food intake act to expand haustrae size and the large intestine in total. The fines and solutes within haustrae move caudally at a slower pace than coarse materials in the core (Brunsgaard, 1998). Wall contractions are expected to continually circulate contents within each haustrae during its progression through the colon. The rate of fermentation within haustrae is expected to decrease with time during the progression along the colon as contents escalate in complexity (Table 2). Accordingly, fine fibre represents the greatest rate of loss in DM once past the anterior colon, whereas, coarse fibre progressively assumes the greatest proportion with progression to the distal colon.

Table 1
Measurements on one cecum and contents of 12-week-old fowl.[1]

Item	Time of day[2], h		
	10:30	12:30	15:30
Lumen contents			
Wet weight, g	4.25	4.38	4.25
pH	7.30	7.12	7.09
Dry matter, g wet weight	0.49	0.42	0.43
Volatile fatty acid, μmol/g wet weight			
Acetic	18.27	19.65	20.07
Propionic	5.88	6.16	6.03
Butyric	3.11	4.01	6.43
Iso-butyric	0.33	0.24	0.23
Valeric	0.53	0.50	0.68
Iso-valeric	0.55	0.44	0.43

[1] Selected data from Savory and Knox (1991).
[2] Time based on a 14-h day length initiated at 06:00 in the morning.

Two layers of mucin are presented at the lumen surface, both with haustrae of swine and caeca with fowl. The top layer of mucin is sufficiently loose to enable lumen microbes to either be enveloped or released in relation to fermentative capability. Microbial concentration adjacent to the mucosa within each haustrae is elevated because of localized fine and soluble fibre, whereas coarse fibre in the core supports fewer microbes and a decreased production of VFA (Table 3). The underlying layer of mucin adjacent to the enterocyte surface has a separate structure and purpose. The depth of this layer can be defined by the protrusion of membrane associated mucin fibres or glycocalyx from enterocyte microvilli that create a comparatively "rigid" internal structure and basis for microbe exclusion. This matrix further acts as a "molecular filter" by restricting entry to solutes and small resultants from lumen digestion that finalizes nutrient recovery by the enterocyte.

As the contents of individual haustrae are "carried" caudally, progressive anaerobic fermentation usually releases gasses from reductive activities. In this respect, hydrogen arises to form CH_4 from CO_2 at hand; however, such generation is not apparent at the cecum-proximal colon of swine until "easily" fermented contents dissipate and complex fibre become prominent at the distal colon (Jensen and Jørgensen, 1994). Saturation of unsaturated fatty acids easily act as an alternate electron "sink" for hydrogen to "delay" appearance of CH_4 (Jørgensen and Just, 1988).

4. Nutrient recovery

4.1. Volatile fatty acids (VFA)

The helicoidal colon follows the cecum that is presented as a length of intestine having 2 different directions of coiling within the body cavity. Centripetal coiling is the first to appear with

Table 3
Microbial count at progressive lengths along the pig's large intestine and from core to wall at each location.[1]

Colon location	Bacteria, $\times 10^{10}$/g dry matter	
	Mean	Range
Lumen		
Proximal	14.9	12.9 to 15.1
Middle	13.8	13.1 to 14.1
Distal	10.9	7.7 to 12.9
Surface		
Proximal	17.6	16.6 to 18.1
Middle	13.9	13.4 to 14.1
Distal	10.6	7.4 to 11.5
Wall		
Proximal	7.2	1.4 to 9.5
Middle	6.4	1.3 to 14.1
Distal	1.6	0.08 to 4.4

[1] Four Large White SPF pigs from 20 to 25 weeks of age given common feed without antimicrobials. Selected data from Russell (1979).

Table 2
Moisture and dry matter contents from progressive sections within the pig's large intestine[1].

Item	Cecum	Colon location			Rectum
		Centripetal	Centrifugal	Distal	
Average diameter, cm	4.00	3.00	1.75	1.00	1.50
Total content, g dry matter	639	660	502	369	184
Total content, g moisture	100	123	109	84	46
Retention, min	376	465	409	346	173
Passage rate, min/cm	1.00	1.75	1.50	1.00	0.50
H_2O absorptivity, g/100 cm^2 per min	1.064	0.037	0.015	0.100	0.200
Na^+, meq/kg contents	103	83	78	56	41

[1] Selected data from Heckler and Grovum (1975) of 3 Landrace pigs approximating 55 kg and 15 months of age.

reversal at the central flexure, followed by centrifugal coiling. Associated haustrae have a progressively diminishing volume. Fermentation is particularly rapid within the cecum and through the initial part of the centripetal colon, when RS and oligosaccharides would be consumed. The presence of RS has been shown to foster *Lachnospiraceae* and *Ruminococcus* phylotypes in the cecum-anterior colon which are readily capable of producing butyric acid (Umu et al., 2015; Haenan et al., 2013; Metzler-Zebeli et al., 2015).

Concentration of VFAs within haustrae, together with convection of contents, dictate mucosal contact and transfer though surface mucins to the enterocyte surface and absorption. The concentrations of VFA vary with the extent of fermentation to influence pH. The VFAs have pKa's approximating 4 to 5 with the pH of lumen contents decreasing from approximately 7.0 to 5.5 as their collective concentrations escalate (Govers et al., 1999). Low pH's in the lumen predominate when substantial RS and oligosaccharides are present to increase the rate of fermentation. An exceptional covering of mucin mitigates direct threat to cell surfaces from high concentrations of VFA and intensive microbial activity. Mucin has polymers of ionizable oligosaccharides projecting from its protein core that involve combinations of N-acetygalactosamine, N-acetylglucosamine, galactose, fucose, and sialic acids. Mucins are divided into neutral sialomucin and acidic sulphated sulfomucin, both of which buffer the area immediate to the unstirred water layer (McFadden et al., 1985; Montague et al., 2004). Mucin released from goblet cells is initially retained by entanglement with the glycocalyx to create the unstirred water layer and a localized pH approximating pH 6.5 to 6.8. Mucin is continually being lost from the unstirred water layer necessitating replacement by surface goblet cells. In turn, mucin released from glycocalyx capture loosely accrues at the lumen surface commensurate with a “gentle” motility compared to small intestine, then lost by erosion.

The importance of pH at the enterocyte membrane relates to optimizing nutrient electronic forms near the enterocyte surface for absorption. Simplistically, VFA when ionized are actively absorbed by Na^+ dependent transporters, whereas non-dissociated forms use electroneutral carboxylate transporters for direct membrane passage (Engelhardt and Rechkemmer, 1983). Having both type transporters operating concurrently permit an increased range of pH's to maximize VFA absorption (Fig. 3), that are operational with swine as well as fowl (Holtug et al., 1992; Calonge et al., 1992; Breves and Krumscheid, 1997; Herrmann et al., 2011). Indigesta at the proximal colon with swine not only provides the greatest concentration of VFA but amount of Na^+ for ionic absorption. Both VFA and Na^+ decrease during the progression of the colon and rate of absorption (Table 2). Presumably, pH of the unstirred water layer can be modified by releasing either neutral or acidic mucins that in turn optimizes terms for absorption of nutrients at-hand.

Given that the amount of fowl caeca contents remain largely unchanged once initial filling occurs, then further entry of indigesta must be accommodated. Presumably, such compensation involves a corresponding loss in content from absorption of FFA, electrolytes, and water. Although lumen contents may largely remain static in amount, its composition is expected to progressively change with accrual of more complex NSP. Increasing complexity of contents decreases the rate of fermentation, while necessitating a more “effective” microflora to do so (Table 1). Similar alterations in complexity and VFA yield seem apparent during the progression of haustrae contents from cecum to distal colon (Umu et al., 2015; Metzler-Zebeli et al., 2019). As haustrae contents alter, the respective surface mucins seem to accommodate pH to optimize VFA absorption. Apparently, mucin released by goblet cells at the distal helicoidal colon can become more acidic to improve recovery of non-dissociated VFA as Na^+ and K^+ availability for active transport diminishes (Brunsgaard, 1997). The absorptive surface with the caeca of fowl may not be confronted with extensive reductions in Na^+ as continual amounts may arise from retro-peristaltically conveyed urine.

4.2. Amino acids and other sources of nitrogen

Nitrogen (N) compounds conveyed into the large intestine from ileum, with both fowl and swine, are largely endogenous loss from the small intestine together with indigestible protein attributable to low quality feedstuffs. Fowl are unique by further contributing urinary waste refluxed from the urodeum. This N is dominated by uric acid with minor amounts of NH_4^+ and free amino acids (Karasawa, 1999). Mucins digested in the large intestine provide

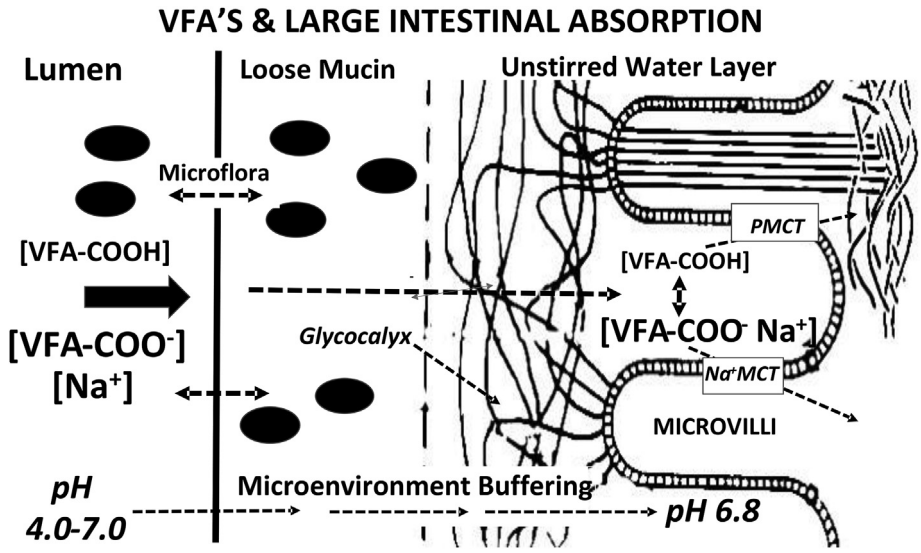

Fig. 3. Volatile fatty acid (VFA) absorption from the large intestinal lumen. Lumen pH decreases with increasing concentration of VFA. Near neutral terms in the lumen facilitate a greater concentration of the ionic form compared to the non-dissociated acid. Na^+ is expected to accompany ionized form during absorption by the sodium coupled monocarboxylate transport proteins (SMCT1) encoded by solute carrier family 5 member 8 (SLC5A8), whereas non-dissociated form is transported by the H^+ coupled low-affinity monocarboxylate transporter protein (MCT1, encoded by *SLC16A1* gene), and potentially other transporters as well. It should be noted that these transporters are also present in the distal small intestine also. Rate of absorption is a combination of both means of transportation.

considerable threonine, cysteine and a full array of non-essential amino acids as well as oligosaccharides (Kamisoyama et al., 2011). Undigested dietary proteins are typically connective tissues from animal and vegetable source feedstuffs that also provide generous amounts of non-essential amino acids (Ringli et al., 2001; Rhodes and Stone, 2002; Ryser et al., 2003).

Although mucins arriving from the small intestine are refractory to the pancreatic proteases, microbes in the large intestine must be more than adept at freeing its associated amino acids, peptides and oligosaccharides. Amino acids and peptides arising during microbial proteolytic action seem to be most accessible to the microbe population at-hand rather than absorbed by a "distant" and limited mucosa. Productive use of amino acids generated by microflora depends on a concurrent access to carbohydrates, which represent a preferable source of energy to avoid their putrefaction (Drochner, W., 1987; Apajalahti and Vienola, 2016). Mucin associated with endogenous loss from small intestine is expected to parallel objectives as those of mucins lining the large intestine's lumen. Mucins at each location act to protect the mucosa from adverse terms while concurrently filtering nutrients for absorption at the enterocyte surface. Mucins from the upper GIT seem to be a meaningful asset for re-use to form those at large intestine's surface. Cecectomized birds defecate more endogenous N from the small intestine than large intestine, which likely relates to reduced mucosa (Parsons, 1984). From another perspective, germ-free birds excrete more endogenous N in their faeces compared to conventional birds to suggest less catabolism in the absence of a viable population (Salter and Fulford, 1974).

Total amino acids in the excreta leaving the large intestine vary more extensively compared to those with indigesta from the ileum. Holmes et al. (1947) noted that swine receiving feed having protein sufficient to meet animal requirements, led to lesser amounts of amino acids leaving the ileum than associated with faeces. Using a protein free feed also led to greater amounts of amino acids with faeces than entering the ileum. Presumably, the microbial population participated in synthesizing a portion of these amino acids from diverse sources of N arising at hand. Such change in amino acids exhibited a pattern resembling mucin, that occurred over the extended duration and distance between ileum and rectum. Sauer et al. (1980) examined amino acid absorption resulting from a wide array of feed formulations for swine, prior to the ileum and then again after faecal excretion (Table 4). Net amounts of actual amino acids retained from ileum to rectum approximated 6% to 7% of the total, with its pattern paralleling mucin. The net amounts of amino acids either being synthesized when dietary protein was inadequate or absorbed when protein was adequate also resembled that of mucin.

Mucosa structure differs between small and large intestine in two major respects. First, the large intestine has a lumen surface having a particularly extensive layering of mucin facing the lumen, whereas the small intestine only exposes the unstirred water layer. Secondly, the vascular system of the small intestine extensively permeates the lamina propria, whereas blood vessels in large intestinal mucosa are sparce, to minimize ready access to oxygen and nutrients from body resources. The lumen surface itself is presented as a mosaic of enterocytes and goblet cells that are collectively referred to as "colonocytes." Enterocytes are devoted to nutrient absorption, with goblet cells continuously replacing surface mucins. Nutrients available from the lumen must first proceed through two layers of mucin layering before being absorbed by enterocytes. Once released from enterocytes, absorbed nutrients first address the needs of goblet cells which are obligated to mucin synthesis in replacement of losses from the lumen surface.

Butyric acid is a significant source of energy for the mucosa and produced in generous amounts by lumen microbes when easily fermentable carbohydrates are accessible (Umu et al., 2015; Metzler-Zebeli et al., 2019). Although all VFAs have been established as being largely transferred through the mucosa and used by the host, butyric acid is different, being meaningfully retained by the mucosa for diverse uses, particularly mucin formation (Finnie et al., 1995; Bach Knudsen, 2018). Mucin formation is also enhanced when swine are fed easily fermentable RS and oligosaccharides (Umu et al., 2015; Bach Knudsen et al., 2019). Oligosaccharide supplementation to pig feed not only accentuates microbial production of butyric acid but also increases goblet cell number, mucosal thickness and mucin production (Breves and Krumscheid, 1997; Breves et al., 2001).

The cecum-anterior colon is first to receive readily fermentable sources of carbohydrate that in turn foster mucin formation for surface replacement. Eventually, depletion of these "labile" carbohydrates reduces such fermentation, before attaining distal aspects of the colon. Reduced access to butyric acid has been implicated in an array of health problems encountered by the large intestine (Govers et al., 1999). In turn, various commercial attempts have been made to increase rapidly fermentable carbohydrates in the diet to extend butyric acid formation and mitigate threats to the mucosa.

Mucin formation requires amino acids for synthesis; however, their ready access from either the lumen or submucosal vascular system is not apparent. Amino acids released from catabolism of endogenous and undigestible proteins by lumen microflora appears most accessible to the population at-hand with minimal recovery by the mucosa. Active absorption of amino acids and monosaccharides from the lumen of the chick's ceca has been shown to be measurable after hatch then "disappear" once a microflora population is established (Holdsworth and Wilson, 1967; Planas et al., 1986; Obst and Diamond, 1989). A parallel situation has also been observed with the piglet (Smith and James, 1976). Microflora in the pig's large intestine not only consume nutrients presented by indigesta but release them, particularly VFA. Vitamin

Table 4
Apparent ileal and faecal amino acid digestibility of common feeds by the pig and their disappearance during large intestinal transit.[1]

Amino acid	Digestibility, %		Large intestine[2]	
	Ileum	Total	Fractional digestibility, %	Digestibility, %
N × 6.25	75.3	82.9	7.6	30.8
Arginine	87.9	94.2	4.5	37.2
Histidine	85.1	91.8	4.5	30.2
Isoleucine	81.1	86.0	4.9	25.9
Leucine	82.9	88.0	5.1	29.8
Lysine	84.7	85.4	0.7	4.6
Methionine	84.8	84.0	0.8	5.3
Phenylalanine	82.6	88.2	5.6	32.2
Threonine	72.7	84.2	14.5	53.1
Tryptophan	78.7	88.6	9.9	46.5
Valine	79.3	85.8	6.5	31.4
Alanine	74.0	81.5	7.5	28.8
Aspartic acid	76.7	86.4	9.7	41.6
Cystine	72.5	85.0	12.5	45.5
Glutamic acid	88.2	93.5	5.3	44.9
Glycine	67.1	84.9	17.8	54.1
Proline	79.3	93.2	13.9	67.1
Serine	78.5	88.6	10.1	47.0
Tyrosine	82.3	87.7	5.4	30.5
Average	79.9	87.5	7.6	37.8

[1] Adapted from Sauer et al. (1980). Values are an average of 36 experiments involving practical complete feeds varying in corn, soybean meal, meat and bone meal, wheat bran, and dried skim milk.
[2] Fractional digestibility refers to the percentage of total dietary nutrient digested in the large intestine whereas digestibility refers to the percentage of nutrient entering the large intestine which is digested in this section.

B_6 is one of note that is microbially produced in significant amounts, released into the lumen then subsequently absorbed by the mucosa (Kircheβner et al., 1989). Synthesis of mucin relies heavily on vitamin B_6 because of its involvement in a multitude of transaminations required to form diverse, non-essential amino acids that are prominent in its protein (Moran, 2016). In a complementary view, NH_4^+can arise in substantial quantity in the lumen from protein catabolism, then appear in multiple non-essential amino acids within the mucosa when butyric acid is concurrently accessible (Blachier et al., 2009). Dengler et al. (2021) observed that a mix of colonocytes given butyrate in culture as an energy source could readily endure reduced access to oxygen while facilitating mucin synthesis.

In vitro measurements of amino acid absorption from the lumen may not be valid because of an interrupted transfer through the mucosa. Darcy-Vrillon et al. (1996) examined in vitro responses of added VFA and glucose to swine colonocytes when receiving extremes in NH_4^+. Increasing cellular access to NH_4^+ enhanced consumption of butyric acid whereas additional glucose was shown to enter glycolysis but not be oxidized but substantially enhance fructose-1-phosphatase activity. Transamination of fructose-1-phosphate using glutamine is central to the synthesis of hexosamines and construction of oligosaccharides for mucin synthesis. Glutamic acid, glutamine together with other non-essential amino acids, are known to be readily formed within the intestinal mucosa when NH_4^+ is accessible (Blachier et al., 2009; Hou and Wu, 2018). A continuous provision of mucin's two major components provides for a maintenance of mucosa integrity in the face of continuous threats.

Although endogenous N from the ileum is not digested by pancreatic proteolytic enzymes, these mucins can be degraded by diverse proteases of microbial origin in the large intestine. Given that ileal endogenous N largely represents indigestible mucin derived from the upper intestine, then its reuse for similar purposes by the large intestine would be “opportune.” The RS and oligosaccharides do not succumb within the small intestine but are readily consumed to provide butyric acid within the large intestine. This “extra” performance may indirectly relate to advantages from butyric acid that “secure” the mucosal surface from threats to health while also acting as a source of energy.

5. Implications for enzyme interventions

Given the above-mentioned idiosyncrasies of poultry and swine large intestinal systems, it is apparent that the efficacy of exogenous enzymes whose function relies on interaction with the large intestinal microbiota, will be subject to these conditions.

5.1. Poultry

Exogenous fibrolytic enzymes that function by providing soluble, fermentable poly- and oligosaccharides for metabolism by the large intestinal microbiota will likely vary in their efficacy during the day. Once the caeca have voided and refilled, its content will initially reflect the solubles and particulates small enough to enter from the ileal indigesta. This array of carbohydrate and proteins are refractory to pancreatic enzymes but subject to microbiota attack. The use of a fibrolytic enzyme will likely increase both the soluble component (through degradation of insoluble fibre) and the particulates through size reduction of larger material as it progresses through the small intestine. Indeed the ileal phase may be even more complicated in that mature birds seem to harbour a microbiota capable of fermenting the shorter oligosaccharides before they exit the ileum (Dale et al., 2020). Presumably, this maturation would be accelerated in the presence of a fibrolytic enzyme or an AXOS (Bautil et al., 2019a, b; Bautil et al., 2020). Consequently, the concentration of soluble material entering the caeca will be greater in enzyme-supplemented birds, but the content will be biased towards larger and marginally less rapidly fermented oligosaccharides. Regardless, the soluble material will be more rapidly fermented than the particulates, thus, the presence of the exogenous enzyme would be expected to increase the quantity of soluble fibre and thus the rate and extent of VFA production. However, as the day progresses and the most fermentable material has been utilized, the relative proportion of insoluble material will likely increase. Maintenance of VFA production will rely on the relative rates of dissolution of insoluble material to that of soluble for fermentation. Recent work has suggested that inclusion of an exogenous xylanolytic enzyme increases caecal xylanase activity, either directly or through a stimbiotic mechanism, or both (Bautil et al., 2019a, b; Gonzalez et al., 2021). Thus, the relevance of an exogenous fibre degrading enzyme may become even more evident later, as the day progresses, if it contributes significantly to conversion of insoluble to soluble fibre in situ in the caeca. This raises the question as to whether the selection of the next generation exogenous fibre degrading enzyme should concentrate on targeting the insoluble material that is “left” after several hours of residence in the caeca. The goal would be to maintain soluble, fermentable fibre production. Regardless, it is important to note that at present, an added exogenous enzyme can contribute to both ileal and caecal release of soluble, fermentable fibre from the insoluble matrix (and of course contribute to depolymerization of the already soluble fibre fractions) but the nature of the substrate will change markedly as it transits from small to large intestine.

Furthermore, if the presented hypothesis is correct then it suggests that the time since last void should be taken into consideration when sampling caecal contents for any metric of interest. Whether it be the identity, activity, or density of the microbiota, these will all change with time throughout the day, which complicates interpretation of experimental data when samples are collected over several hours. The huge variability in caecal microbiota noted between studies (Stanley et al., 2017) now has an additional factor to account for such findings and consider when interpreting these data. Finally, the concentration of the fermentative activity in the distal two thirds of the caeca means that when total caecal contents are collected, they do not necessarily represent the fermentative capacity of the most active part of the caeca.

5.2. Swine

The key difference of note between pigs and chickens as far as fibre degrading enzymes is concerned, is the fact that the chicken separates and voids most insoluble, large particulate material directly from colon to the faeces, effectively making no attempt to ferment it. There is no such “voiding” of the “difficult” material to ferment in swine due to the physiological structure of the intestines so they benefit from extended exogenous enzyme activity on fibre that otherwise would escape exposure to such activity with fowl. This difference is not only due to physiological but also temporal differences, the pig investing significantly more time in large intestinal digestion than the chicken. Regardless, the initial offering to the large intestine is the soluble and insoluble fibre that exits the ileum, and this can be markedly altered by the presence of an NSPase. Replacing 30% of a corn soy diet with corn bran resulted in an increase in ileal viscosity and pH coupled with reduced ileal nutrient and fibre digestibility. All were restored to some degree in the presence of a xylanase, which indicates that the enzyme not only alters ileal digestion but also the flow and identity of nutrients, including fibre, entering the caecum (Petry et al., 2021). The

resultant effect of the enzyme was a 300% increase in neutral detergent fibre (NDF) disappearance in the caeca, coupled with a marginal reduction in the colon content compared with the control, with the overall effect being a 10% increase in NDF digestibility at the faecal level. This clearly suggests that the presence of the xylanase markedly increases total fibre digestibility but more so by acceleration of caecal rather than colonic fermentation. It also suggests that fermentable material was becoming increasingly limited in the enzyme treated pigs with transit of material through the colon, perhaps warranting some adaption whereby the size of the colon may be reduced from this loss.

The identity of the material in the core and in the haustra of the caecum and colon differ markedly from one another and moreover change with passage through the intestine, becoming more intransigent and thus less fermentable. This presents an opportunity for any exogenous enzyme that can target such intransigent material to release soluble "fuel" for both the core and the haustra. Such a benefit may be augmented through a stimbiotic effect, whereby feeding such an exogenous enzyme may encourage increased fibre degrading enzyme output by the resident microbiota. Feeding xylanases has been shown to markedly increase ileal, caecal and colonic contents of xylanases and cellulases (Marinho et al., 2007) and feeding xylo-oligosaccharides to elevate large intestinal fibre degrading enzymes, suggesting a stimbiotic mechanism exists in swine as well (Petry et al., 2021). Thus, fibrolytic enzymes likely impose a combination of direct and indirect effects to accelerate degradation of the more susceptible carbohydrates to complete fermentation in the haustra and perhaps even in the core (Singh. et al., 2012). Unfortunately, at present it has not been possible to separate haustra from core effects due to collection of caecal, colonic, and faecal material being a composite of both so the haustra and core samples are homogenized together. Thus, the proposals noted above remain a hypothesis until data are available to collect these samples separately and thus confirm or reject its relevance. If the core material in the colon is where most of the colonic material is fermented, then the hypothesis presented above will need modification.

Both species appear to be open to ileal and caecal phases of NSPase activity. The former phase enhances the quantity of rapidly fermentable material that is generated in the ileum and enters the caeca for more of a fast burn than a long-sustained fermentation, whereas in the caecal phase (or caecal/colonic in the pig), the benefits would stem from the enzyme continuing to release soluble NSP from the more intransigent insoluble material that may enable a more sustained fermentation throughout the length of the colon.

6. Conclusions

Fowl and swine differ extensively in the recovery of nutrients remaining with ileal indigesta. Fermentable substrates concentrate in the caeca of fowl whereas swine collect them in haustrae outpocketing of the colon. Both locations foster fermentation by exchanging microflora extensively embedded in surface mucin. Dietary supplementation with fibrolytic enzymes partly reduces the complexity of fibre prior to the large intestine; however, benefits other than altered viscosity within the lumen are not readily perceived until access to microbial activity becomes extensive. RS and oligosaccharides in feed and those generated from fibrolytic action are the first to ferment and enhance yield of butyric acid and mucin production, whereas NSP complexity delays fermentation with acetic and propionic acids at favour.

Continued fermentation eliminates labile carbohydrates while collecting all forms of resistant fibre in caeca to dominate contents before evacuation, whereas contents in the haustrae concentrate complex fibre during movement from cecum until finalized at the rectum. Fowl void caecal contents distinctly separate from faeces, whereas swine have remaining residues in haustrae adhere on coarse fibre in the core, creating nodulated faeces. Most VFA are used as a source of energy by the host, whereas the mucosa retains some butyric acid to continue cell operation. N-products arising during fermentation of proteins are variable quantities, with a portion also being held within the mucosa. Presumably, enterocytes absorb by-products from the lumen while goblet cells use and recover some absorbed products to re-synthesize mucins that sustain surface protection. The large intestinal systems of fowl and swine both recover meaningful amounts of energy, microminerals and water largely for the host with a portion of butyric acid and N by-products remaining for mucin formation that maintains mucosal integrity.

Author contributions

Conceptualized by **Edwin T Moran** originally and extended by **Michael R. Bedford**; visualisation by **Edwin T. Moran**; writing original draft and reviewing and editing was undertaken by **Edwin T. Moran** and **Michael R. Bedford**.

Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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