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**COMMENTARY**

# Specific dynamic action: the energy cost of digestion or growth?

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**ABSTRACT**

The physiological processes underlying the post-prandial rise in metabolic rate, most commonly known as the 'specific dynamic action' (SDA), remain debated and controversial. This Commentary examines the SDA response from two opposing hypotheses: (i) the classic interpretation, where the SDA represents the energy cost of digestion, versus (ii) the alternative view that much of the SDA represents the energy cost of growth. The traditional viewpoint implies that individuals with a reduced SDA should grow faster given the same caloric intake, but experimental evidence for this effect remains scarce and inconclusive. Alternatively, we suggest that the SDA reflects an organism's efficacy in allocating the ingested food to growth, emphasising the role of post-absorptive processes, particularly protein synthesis. Although both viewpoints recognise the trade-offs in energy allocation and the dynamic nature of energy distribution among physiological processes, we argue that equating the SDA with 'the energy cost of digestion' oversimplifies the complexities of energy use in relation to the SDA and growth. In many instances, a reduced SDA may reflect diminished nutrient absorption (e.g. due to lower digestive efficiency) rather than increased 'free' energy available for somatic growth. Considering these perspectives, we summarise evidence both for and against the opposing hypotheses with a focus on ectothermic vertebrates. We conclude by presenting a number of future directions for experiments that may clarify what the SDA is, and what it is not.

KEY WORDS: Postprandial metabolism, Energy allocation, Protein synthesis, Metabolism

## Introduction

During the processes of feeding, digestion and nutrient assimilation, animals experience a postprandial rise in metabolic rate, commonly known as the 'specific dynamic action' (SDA; see Glossary; Fig. 1). Over the past two centuries, the SDA has been characterised in most animal taxa, and the influence of a multitude of environmental variables and meal constituents has been studied in detail (McCue, 2006; Secor, 2009, 2017). These studies reveal that the SDA contributes significantly to the energy budget of all animals, and that the energetic allocation to digestion has important implications for ecological communities (Clark et al., 2010; McCue and Lillywhite, 2002; Monnet et al., 2022), trophic interactions (Steell et al., 2019), commercial animal production systems (Goodrich et al., 2022b; Warren and Davis, 1967), animal performance

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(Stieglitz et al., 2018), climate change studies (Jutfelt et al., 2021; Khan et al., 2015), and comparative and environmental physiology (Wang et al., 1995; Wood et al., 2023, 2007). Given the widespread significance of the SDA and a growing understanding of the processes involved, there is a need for a clear and concise interpretation of what the SDA represents, and how it is interpreted.

The term SDA finds its roots in the German phrase 'spezifisch-dynamische Wirkung', coined by the German physiologist Max Rubner in 1885 to describe the distinct metabolic responses to the ingestion of food (Kraut et al., 1981; McCue, 2006). However, this definition does little to describe the relationships that exist between metabolism, feeding and digestion (McCue, 2006). Consequently, the SDA has been linked to a variety of definitions. Some of these terms include 'heat increment' or 'heat increment of feeding' (HiE; see Glossary; Blaxter, 1989), 'diet-induced thermogenesis' (Newsholme and Leech, 1983), 'calorigenic effect' (Pike and Brown, 1975), 'metabolism of plethora' (Lusk, 1922; Mason et al., 1927), 'thermic effect of food' (TEF; Whitney and Rolfes, 1996), 'metabolic scope for growth' (Wieser and Medgyesy, 1990), 'energy cost of digestion' (Secor, 2009), 'energy cost of growth' (Jobling, 1981) and others (McCue, 2006). Today, it is widely accepted that the SDA represents an energy 'tax' on food processing (McDonald, 2002), yielding the most accepted term for the SDA as the 'energy cost of digestion' (Secor, 2009, 2017). This definition implies that the SDA represents the sum of energy spent on the mechanical, physiological and biochemical processes required for feeding, digestion and assimilation. These costs include the energy expended on pre- and post-absorptive processes, such as prey capture, chewing, gastric handling, secretion, peristalsis, absorption, increased ventilation, blood flow redistribution, protein synthesis, excretion and acid–base/ion regulation (e.g. Andrade et al., 2005; Borsook, 1936; Eliason et al., 2007; Eom and Wood, 2023; McCue, 2006; Secor, 2009; Seth et al., 2009; Wood et al., 2007).

If the SDA represents the costs of all postprandial processes, it follows that a smaller SDA for the same caloric intake should result in faster growth, by providing more 'free' energy for allocation to somatic tissues (Secor, 2009). However, attempts to reduce the SDA so as to increase somatic growth have yielded inconclusive results (Goodrich et al., 2022a,b). If the actual costs of the digestive phase of the SDA process are relatively small, such that post-absorptive processes, particularly protein synthesis, account for most of the SDA, we would expect the opposite relationships between SDA and growth, i.e. higher protein synthesis rates would go hand in hand with both more tissue growth and higher SDA 'costs' (Ashworth, 1969; Jobling, 1983, 1981). In a short review, Jobling (1981) argued that postprandial increases in metabolic rate represent the 'energy costs of growth'. This is attributed to the rapid synthesis and turnover of tissue proteins following the influx of amino acids during meal processing. This view suggests that the SDA represents a short-term increase in rates of protein synthesis and turnover following feeding (Jobling, 1983). Indeed, a positive correlation between growth and SDA has been reported for many mammals (Ashworth, 1969; Brody, 1942; Brooke and Ashworth, 1972;

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## Glossary

**Aerobic scope**
The difference between an animal's standard metabolic rate and its maximum metabolic rate, representing the capacity for aerobic activities.

**Alkaline tide**
A temporary rise in bicarbonate ($HCO_3^-$) concentration in the bodily fluids as a result of gastric acid secretion following a meal.

**Chyme**
The semi-fluid mass of partly digested food that moves from the stomach to the small intestine.

**Daily growth coefficient**
A measure of an animal's growth rate over a day.

**Dietary buffering**
The ability of a diet to resist changes in acidity or alkalinity, often related to the inclusion of buffering agents.

**Heat increment of feeding**
The increase in metabolic heat production associated with the digestion and absorption of food.

**Maximum metabolic rate**
The highest rate of oxygen consumption that an organism can achieve under maximal physiological effort or during intense physical activity.

**Oxyntopeptic cells**
Cells in the stomach lining of non-mammalian vertebrates that secrete hydrochloric acid (HCl) and pepsin.

**Routine metabolic rate**
The metabolic rate of an organism during some minor or limited activity (e.g. small fin movements to maintain station in the case of fishes).

**Specific dynamic action**
The elevation of metabolism after a meal.

**Specific growth rate**
Percentage body mass increase per day.

**Standard metabolic rate**
The minimum amount of energy required to maintain essential physiological functions, measured in a fasting, undisturbed and physically inactive organism at a given temperature.

Krieger, 1978) and some invertebrates (Gaffney and Diehl, 1986; Vahl, 1984). Additional insights on the cost of growth have been provided by Jørgensen, (1988), Ricklefs, (2003) and Wieser, (1994). Throughout this Commentary, we explore these current and often contrasting viewpoints regarding the SDA, and synthesise available evidence both for and against existing perspectives. We propose a series of experiments to test existing hypotheses that will help to determine whether the SDA is best defined as the 'energy cost of digestion' or the 'energy cost of growth'.

### The SDA as 'the energy cost of digestion'

The traditional interpretation that the SDA response represents the 'energy cost of digestion' allocates high energy expenditures to the various processes involved in mechanical and chemical breakdown of food macromolecules (digestion), and absorption of the resulting nutrients from the gut into the blood. Although each of these processes undoubtedly will cost energy, this view implies that a smaller SDA for a given caloric intake should provide more available 'free' energy for somatic growth (Jobling, 1994; Monnet et al., 2022; Secor, 2009). Indeed, Warren and Davis (1967) defined the rate of energy consumption ($C$) as the sum of energy spent on metabolism ($M_{resting}+M_{active}+$SDA), excretion [faeces ($F$) and urine ($U$)] and somatic and reproductive tissue growth ($G_s+G_r$):

$$C = (M_{resting} + M_{active} + SDA + (F + U) + (G_s + G_r). \quad (1)$$

In this view, the SDA is separate from growth; in fact, the SDA may 'steal' energy from growth. In commercial animal production

systems, such as aquaculture, attempts have been made to maximise growth by minimising the energy lost to processes such as routine metabolism, excretion and digestion (i.e. SDA; Fu and Xie, 2004; LeGrow and Beamish, 1986; Myrick, 2011; Peres and Oliva-Teles, 2001; Secor, 2009). For fish, the SDA is estimated to contribute 25–50% of total metabolic expenditure or 7–40% of ingested energy (Clark, 2015; McCue, 2006; Miura et al., 1976; Owen, 2001; Secor, 2009; Xie et al., 1997). When considered alongside the traditional interpretation of the SDA as an energy 'tax', these estimates of metabolic expenditure would suggest that there is significant potential to improve fish growth performance by reducing the magnitude of the SDA response. In some cases, such growth benefits have been observed. In comparison to slow-growing insectivores, fast-growing piscivorous ecotypes of rainbow trout (*Oncorhynchus mykiss*) maintain higher digestive efficiency through a reduction in the cost of postprandial metabolism [standard metabolic rate (see Glossary) (SMR)+SDA], and achieve higher growth rates at a comparable ration (Monnet et al., 2022). Yet, this comparison involved different strains of trout, with different trophic habits, both forced to eat a similar pellet diet, so there may be some confounding factors with respect to interpreting the SDA versus growth relationship.

In a commercial setting, a reduction in the SDA may be achieved by altering the type and composition of the diet, or the frequency at which animals are fed (Fu and Xie, 2004; LeGrow and Beamish, 1986; Myrick, 2011; Peres and Oliva-Teles, 2001; Secor, 2009). For example, the acidification of the stomach through hydrochloric acid (HCl) secretion by $H^+/K^+$-ATPases incurs an energetic cost (Kopic et al., 2009; Reenstra and Forte, 1981; Shin et al., 2009), as does recovery from the associated blood alkaline tide (see Glossary; Goodrich et al., 2022b). Specifically, for every $H^+$ pumped into the stomach lumen for gastric acidification, one ATP is consumed by the $H^+/K^+$-ATPases in the oxyntopeptic cells (see Glossary) that line the stomach (Bannister, 1965; Reenstra and Forte, 1981; Shin et al., 2009). This equates to a maximum of 5 $H^+$ into the lumen for every $O_2$ consumed (Bannister, 1965). Simultaneously, energy is used to recover postprandial acid–base balance through the removal of excess blood $HCO_3^-$ from the alkaline tide by vacuolar $H^+$-ATPases at the gills (Wood, 2019). Therefore, providing fish with a pre-acidified meal should theoretically lessen the costs of gastric acid secretion and postprandial acid–base regulation to cause a reduction in the SDA and – based on the traditional view of the SDA – lead to improved fish growth. In juvenile barramundi (*Lates calcarifer*), dietary acidification with HCl causes a ∼45% reduction in the SDA response, but has no significant effect on the specific growth rate (SGR; see Glossary; Goodrich et al., 2022b). Further work determined that an acidified diet alters the expression of key acid–base transporters in the anterior intestine (Goodrich, 2022), potentially affecting the capacity to neutralise acidic chyme (see Glossary) entering from the stomach and possibly reducing intestinal absorptive efficiency. Taken together, these results suggest that the reduced SDA in this study is indicative of an eroded capacity for digestion and assimilation of a meal.

Nonetheless, the extent to which gastric HCl secretion contributes to the SDA remains contentious (Nørgaard et al., 2016; Secor, 2003; Wang and Rindom, 2021). One of the approaches used to determine the contribution of HCl secretion to the SDA is through the use of the commercial antacid omeprazole (Moffatt et al., 2022; Wang and Rindom, 2021). Omeprazole inhibits the function of $H^+/K^+$-ATPase and, hence, gastric acidification and the alkaline tide, as demonstrated in toads (Andersen et al., 2003), snakes (Andrade et al., 2004) and sharks
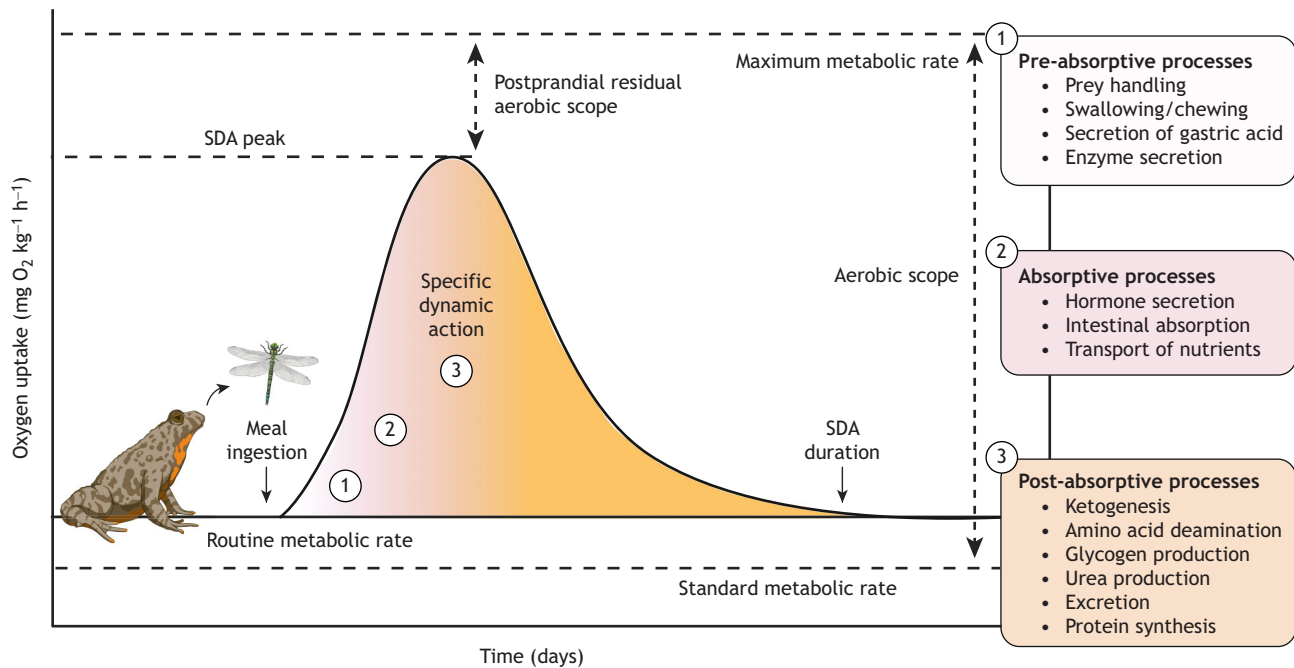
**Fig. 1. Conceptional diagram showing the postprandial metabolic response to feeding known as the specific dynamic action (SDA).** Upon meal ingestion, metabolic rate (≈aerobic metabolic rate) rises above the routine metabolic rate (RMR; solid horizontal line; see Glossary) to reach the SDA peak. Recognising the historical definition of SDA as a rise in metabolic rate above the standard metabolic rate (SMR), we argue that RMR serves as a more ecologically relevant baseline for SDA in most wild organisms. This is because individuals often feed opportunistically, are not consistently in a post-absorptive state, and engage in regular activities such as swimming before, during and after prey consumption. Over a period of hours, days or weeks (depending on species, environment, meal size and/or composition), postprandial metabolism returns to RMR; this period is termed the SDA duration. The total SDA for a meal is represented by the area under the curve, and can be subdivided into the pre-absorptive (1), absorptive (2) and post-absorptive (3) processes associated with digestion. The SDA response falls within the animal's aerobic scope (AS; see Glossary), calculated as the difference between maximum metabolic rate (MMR; see Glossary) and SMR (dashed horizontal line). During digestion, the scope for aerobic activities outside digestion, such as exercise or reproduction, is defined by the postprandial residual aerobic scope (PRAS; (MMR–SDA peak). Figure produced with biorender.com.

(Wood et al., 2009). Notably, recent work in Nile tilapia (*Oreochromis niloticus*) showed that omeprazole treatment reduces the duration and magnitude of the SDA, yet causes a reduction in SGR (Moffatt et al., 2022). The authors suggested that the observed reduction in growth of omeprazole-treated fish could be explained by decreased protein digestion and absorption from the feed, as omeprazole would have prevented both acid-mediated denaturing of ingested proteins at the stomach and pepsin activation for protein digestion (Moffatt et al., 2022). However, earlier findings in *Boa constrictor* contradicted these observations, as omeprazole treatment had no effect on SDA (Andrade et al., 2005), challenging the idea that gastric HCl secretion contributes up to 55% of the SDA in the Burmese python (*Python molurus*; Secor, 2003). Similar investigations using dietary buffering (see Glossary) revealed diverse outcomes with no discernible impact on SDA in snakes (Henriksen et al., 2015; Nørgaard et al., 2016), but notable effects in rainbow trout (Goodrich et al., 2022a). These varying responses suggest that there are species-specific differences in the contribution of the gastric proton pump to the SDA.

Many have assumed that a reduction in the SDA will provide a positive energy benefit to a digesting animal (Boback et al., 2007; Goodrich et al., 2022b; Grayson et al., 2005; Secor, 2009), and that factors that affect the SDA will determine the rate at which energy from food is converted to tissues (Jobling, 1994). However, there is very little empirical evidence to suggest this (Goodrich et al., 2022a, b), and these statements are rarely accompanied by measures of digestibility or growth rates (Boback et al., 2007). Based on available literature, it seems more likely that a reduction in the SDA may be

indicative of a reduction in digestive capacity or efficiency as opposed to any 'energy benefit' or available 'free' energy for allocation.

## The SDA as 'the energy cost of growth'

Work in pythons proposed the 'pay before pumping' model, which suggests that the majority of the 'costs' associated with digestion are 'paid' on intestinal upregulation (and/or gastric acid secretion), so that subsequent 'pumping' or meal absorption can be facilitated (Bury, 2022; Secor et al., 1994; Secor and Diamond, 1995). However, a recent cross-species meta-analysis on snakes concluded that the cost of intestinal upregulation is small and that most of the SDA 'costs' seem to be paid after the SDA peak once intestinal processes are activated (Bury, 2022). Indeed, using pyloric ligation to block the movement of chyme into the intestine removes the SDA response altogether in pythons (*Python regius*; Enok et al., 2013; Wang et al., 2006). Alternating fasting duration in pythons also shows that the costs of the reversible remodelling of the gastrointestinal organs must be small and are unlikely to be a major determinant of the SDA response (Overgaard et al., 2002). This suggests that post-absorptive processes, most likely protein synthesis, are the primary contributors to the SDA. Many studies on a range of fish species have suggested that a larger SDA is associated with a higher rate of protein synthesis (Carter and Brafield, 1992; Hidalgo and Alliot, 1988; McCarthy et al., 1999; McCarthy et al., 1994), and earlier work suggested that protein synthesis, tissue turnover and growth offered the best explanation of the postprandial SDA (Ashworth, 1969; Jobling, 1985, 1983, 1981).

Growth rates are associated with protein cycling or the rates of protein synthesis, degradation and retention (Carter et al., 1993a,b; Houlihan et al., 1989, 1988; McCarthy et al., 1994).

Specifically, tissue growth occurs when the rate of protein synthesis is higher than that of protein degradation (Carter and Houlihan, 2001). Protein synthesis incurs an energetic cost, and is thought to be the primary contributor to the SDA in many ectothermic vertebrates (Borsook, 1936; Brown and Cameron, 1991a,b; McCue et al., 2005; Secor, 2009). Indeed, synthesising 1 g of protein is estimated to cost ∼50 mmol of ATP equivalents or 3.5 kJ (Brown and Cameron, 1991b; Carter et al., 1993a; Houlihan et al., 1988; Jobling, 1985; Lusk, 1922; Reeds et al., 1985). This cost is estimated from the 5 ATP molecules that are used to incorporate 1 amino acid into a protein (Reeds et al., 1985). Assuming 5.24 mg of oxygen are required to synthesise 1 mmol of ATP (Houlihan et al., 1988), the synthesis of 1 g of protein would require ∼262 mg of oxygen. Therefore, it is likely that the oxygen consumption associated with the SDA is directly related to the provision of ATP needed to fuel the rate of protein synthesis that ultimately drives tissue growth (Andrade et al., 2005; Ashworth, 1969; Carter and Brafield, 1992; Goodrich and Clark, 2023; Hidalgo and Alliot, 1988; Jobling, 1983; 1981; McCarthy et al., 1999, 1994; McCue et al., 2005; Millidine et al., 2009; Wang and Rindom, 2021; Wieser and Medgyesy, 1990). Studies on pythons (McCue et al., 2015) and zebrafish (Ferreira et al., 2019) indicate that the primary source of energy for SDA, and therefore protein synthesis, stems from oxidising dietary proteins rather than reliance on endogenous reserves. Indeed, in their study, McCue et al. (2015) demonstrated that the oxidation of dietary proteins peaks at 24 h after meal ingestion to meet almost 90% of the metabolic requirement for the digesting snakes.

Use of the protein synthesis inhibitor cycloheximide has provided insights into the contribution of protein synthesis to the SDA. Cycloheximide reduces the SDA response by 70% in Burmese pythons (McCue et al., 2005), and studies on aquatic ectotherms yield similar results. In fasted channel catfish (*Ictalurus punctatus*), an infusion of an amino acid mix directly into the blood stream induces an SDA response in the absence of feeding (Brown and Cameron, 1991b), and the magnitude of the SDA increases with rates of protein synthesis (Brown and Cameron, 1991a). However, cycloheximide administration prior to amino acid infusion inhibits the SDA response (Brown and Cameron, 1991a,b). Indeed, we are not aware of studies reporting an SDA response in the absence of elevated protein synthesis. In future, measurement of SDA during experimental stimulation of protein synthesis (e.g. by administration of anabolic steroids) would be informative.

Postprandial metabolic rate has also been reported to vary with the quantity or type of protein consumed and its amino acid balance for alligators (*Alligator mississippiensis*; Coulson and Hernandez, 1979), Speke's hinge-back tortoise (*Kinixys spekii*; Hailey, 1998), marine toads (*Bufo marinus*; Secor and Faulkner, 2002), Nile tilapia (*Oreochromis niloticus*; Ross et al., 1992) and rock monitors (*Varanus albigularis*; Secor and Phillips, 1997), but not for southern catfish (*Silurus meridionalis*; Fu et al., 2005a,b), Chacoan horned frogs (*Ceratophrys cranwelli*; Grayson et al., 2005) or rainbow trout (Eliason et al., 2007). In Burmese pythons, the digestion of simple proteins, such as gelatin and collagen, or incomplete mixtures of amino acids, does not cause an SDA comparable to that attained following the consumption of a complete protein meal (McCue et al., 2005). Harper (1971) reported that the SDA coefficients [% of meal energy used in the SDA, i.e. SDA (in kJ)/meal energy (in kJ)×100] for protein, lipid

and carbohydrate were 30%, 13% and 5%, respectively. These results suggest that the SDA should rise with increases in protein to energy ratios. However, altering the digestible protein to digestible energy ratio of a meal causes no measurable effect on the SDA or growth for rainbow trout, and lower dietary protein content is actually associated with a greater protein deposition percentage (Eliason et al., 2007). Similarly, work in southern catfish showed that dietary protein:carbohydrate ratios have no significant effect on the overall SDA coefficient, suggesting that dietary carbohydrate exerts an SDA response similar to that of dietary protein (Fu et al., 2005a,b). Although many studies on the effects of dietary protein and cycloheximide on the SDA indicate that the SDA primarily represents the cost of protein synthesis and growth (Carter and Brafield, 1992; Hidalgo and Alliot, 1988; McCarthy et al., 1999, 1994), there are also a number of exceptions where no or inconsistent relationships between the SDA, protein content and/or growth are seen (Eliason et al., 2007; Fu et al., 2005a,b; Grayson et al., 2005).

### Future directions and experimental design
Given the perspectives presented above, we propose a number of future research avenues aimed at answering two key questions concerning the SDA. These questions and approaches are discussed in more detail below.

### How does the SDA response relate to growth?
Although the metabolic phenotype has already been identified as a key indicator for growth potential in some ectothermic vertebrates (Monnet et al., 2022; Norin et al., 2016; Norin and Clark, 2017; Norin and Malte, 2012), the relationships between the SDA phenotype and growth remain underexplored. For example, we are aware of only a handful of studies that have reported on relationships between the SDA and somatic growth for fish (Carter and Brafield, 1992; Jobling, 1983, 1981; Kiørboe et al., 1987; Wieser and Medgyesy, 1990). However, these studies assessed the SDA–growth relationship in fish fed varying meal rations. Given that meal size is a primary contributor to the magnitude of the SDA (Jobling, 1981; Secor and Faulkner, 2002), the results from these studies (and any future studies employing similar approaches) provide limited capacity to report on the relationships between SDA and growth. To fill this knowledge gap, we propose that future research should assess the relationship between the SDA coefficient and individual SGRs or daily growth coefficients (see Glossary) in animals fed the same meal ration and composition. Similar experiments aimed at exploring the SDA–growth relationship were suggested by Jobling (1981). As discussed previously, we expect that individuals with a relatively high SDA coefficient for the same caloric intake will grow faster than individuals fed the same meal with a comparably smaller SDA coefficient. This view of the SDA is in contrast to current interpretations of the SDA, which suggest that a smaller SDA for the same caloric intake will provide more 'free' energy for allocation to growth (i.e. individuals with a smaller SDA phenotype will grow faster than others; Fig. 2). These studies should be repeated at multiple ration sizes and across different species to determine whether these relationships are consistent across varying meal sizes and animal groups (e.g. fish, reptiles and mammals).

Considering the SDA as the 'energy cost of growth', we also propose that a smaller SDA for the same caloric intake might signify reduced digestive efficiency or digestibility. To explore these ideas, we suggest that future SDA and growth studies incorporate measures of feed digestibility. Measures of apparent digestibility
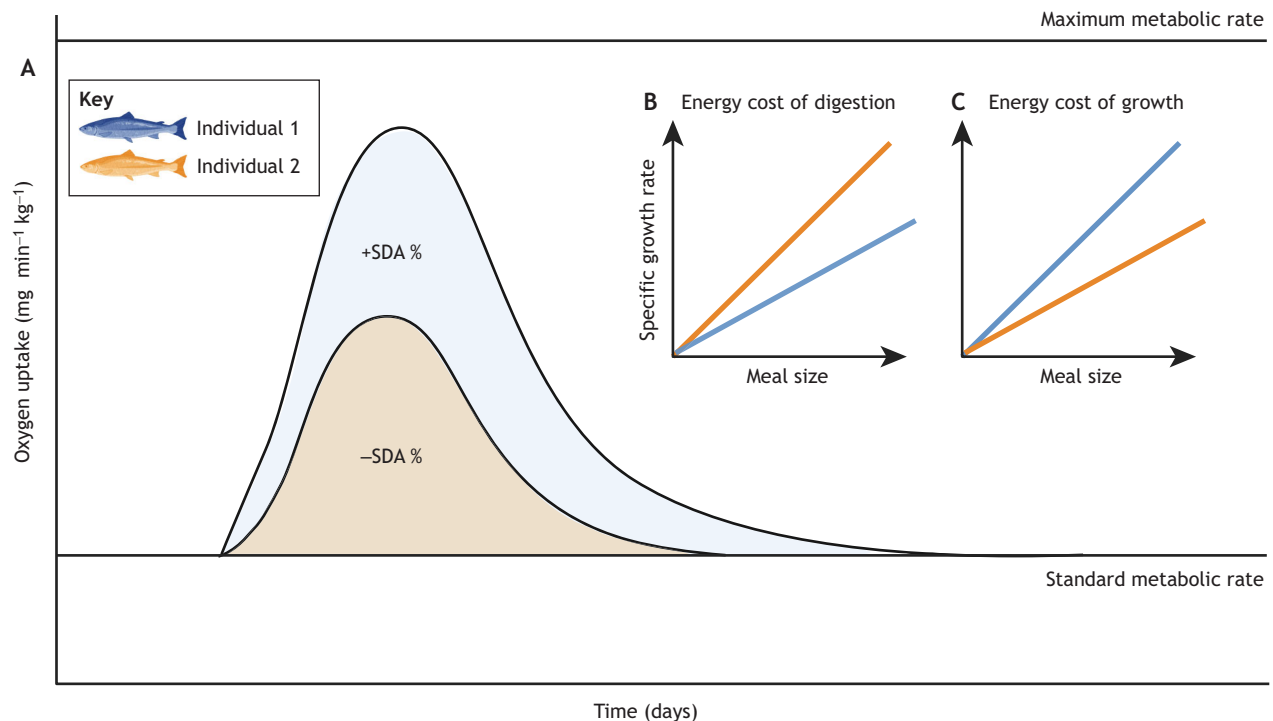
**Fig. 2. Predictions derived from the 'energy cost of digestion' and 'energy cost of growth' hypotheses.** (A) Postprandial SDA of two similarly sized individuals fed the same diet and meal ration. Individual 1 has a longer SDA duration and larger SDA coefficient (+SDA %) compared with individual 2 (−SDA %). Based on current interpretation of the SDA as 'the energy cost of digestion', individuals with a smaller SDA for the same caloric intake and meal size should display a high-growth phenotype through allocation of available 'free' energy to somatic mass production (B). Alternatively, the 'energy cost of growth' hypothesis suggests the opposite, that individuals with a larger SDA for the same caloric intake and meal size should display a high-growth phenotype due to greater rates of net protein synthesis (C). Figure produced with biorender.com.

are common for studies in aquaculture nutrition and usually involve quantifying the content of a nutrient in a feed (%) and comparing this with the content of that same nutrient in an animal's faeces (Forster, 1999). Importantly, future studies must consider that appropriate faecal collection methods for digestibility will vary between species (Glencross, 2011). An understanding of the relationships between digestibility and the SDA is needed if we are to identify the relevance of the latter to animal growth. If a reduced SDA is associated with an eroded capacity for nutrient acquisition, this will provide further evidence of the SDA as an indicator of an animal's growth potential.

### What is the SDA made up of?

Within the literature, there is increasing controversy around the relative contribution of each process to the SDA (Jobling, 1983; Wang and Rindom, 2021). For example, whereas some propose that pre-absorptive mechanisms primarily drive the SDA (Secor, 2003), others contend that post-absorptive processes hold sway (Borsook, 1936; Brown and Cameron, 1991a,b; Jobling, 1983; McCue et al., 2005; Nørgaard et al., 2016). As discussed throughout, gastric acid secretion and protein synthesis are two processes that have consistently emerged as points of contention in the literature with regard to their contribution to the SDA. Consequently, while acknowledging the involvement of numerous processes in the SDA (Fig. 1), this section focuses on methods and experiments designed to determine the relative contribution of gastric acid secretion and protein synthesis to postprandial metabolism. Determining what the SDA is made up of will prove important to understanding how and whether the SDA relates to animal growth and/or digestive performance and efficiency.

The most logical approach to determine what contributes to the SDA would be to directly measure the rates of each process *in vivo*. Historically, rates of protein synthesis and protein metabolism in fish have been assessed *in vivo* using radiolabelled amino acids as a tracer (Garlick et al., 1980). However, the application of radiolabelled tracers is a terminal procedure, hazardous and confined to controlled laboratory conditions. These limitations have led to the development of similar methods that utilise a stable isotope-labelled tracer (Lamarre et al., 2015; Owen et al., 1999). Similarly, measurements of *in vivo* gastric acid secretion among ectothermic vertebrates have involved varying techniques. For example, this process has been measured using stomach catheters with and without pyloric ligation, stomach sponges and ingested pH loggers in combination with auto-titration for species such as brown bullhead (*Ictalurus nebulosus*) (Smit, 1967), cod (*Gadus morhua*) (Holstein, 1979, 1975), leopard sharks (*Triakis semifasciata*) (Papastamatiou, 2007) and toads (Taylor et al., 1985). Although obtaining accurate *in vivo* measures of these processes can be complex, such techniques will prove useful for quantifying the relative contribution of some digestive and/or absorptive processes to the SDA. For example, if the costs of acid secretion are relatively small compared with processes such as protein synthesis, it suggests that the SDA is primarily representative of the costs associated with growth.

As discussed above, the use of the commercial antacid omeprazole can inhibit the $H^+/K^+$-ATPases that line the stomach (Andrade et al., 2004; Moffatt et al., 2022; Tari et al., 1991; Wood et al., 2009). Similarly, cycloheximide can be used to inhibit protein synthesis during digestion (Brown and Cameron, 1991a,b). Omeprazole and cycloheximide function to effectively 'knock
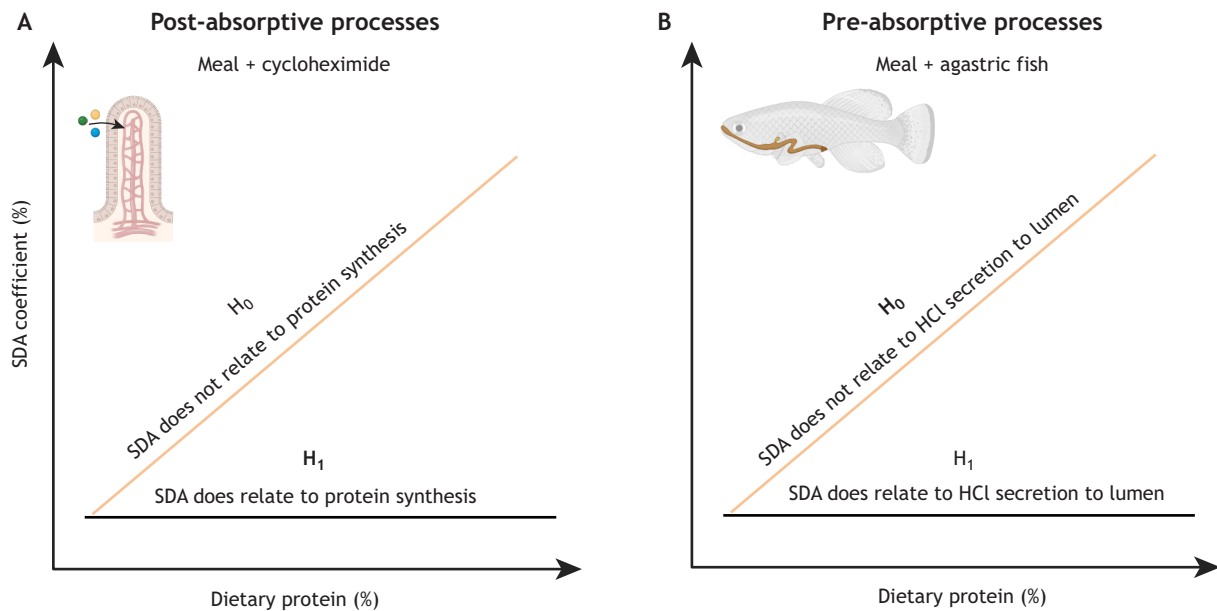
**Fig. 3. Expected outcomes from proposed experiments aimed at identifying the primary contributor to the SDA.** (A) When an animal treated with the protein synthesis inhibitor cycloheximide consumes a meal, an increase in the SDA coefficient (percentage of meal energy used in the SDA) with rising dietary protein content would suggest that the SDA is not related to protein synthesis. Alternatively, no relationship would imply the opposite. (B) In the case of feeding in an agastric (stomachless) fish [e.g. killifish (*Fundulus heteroclitus*), goldfish (*Carassius auratus*), zebrafish (*Danio rerio*)], a positive correlation between SDA coefficient and dietary protein content would indicate that HCl secretion does not contribute to the SDA, whereas no relationship would suggest otherwise. These hypotheses are indicated in the figure ($H_0$ and $H_1$). Figure produced with biorender.com.

out' processes associated with digestion and assimilation, respectively, but we are aware of no studies that have attempted to use dietary protein content in combination with omeprazole and/or cycloheximide to determine the net contribution of HCl secretion and protein synthesis to the SDA. Future studies should therefore assess the SDA response in animals treated with omeprazole, cycloheximide or a combination of the two across diets with varying protein content (%). If the SDA is a function of protein synthesis, there would be no relationship between the SDA and dietary protein content in an animal treated with cycloheximide (Fig. 3A). Similar experiments aimed at exploring the SDA–protein synthesis relationship were suggested by Brown and Cameron (1991b). Likewise, HCl secretion to the stomach in gastric species is necessary for the breakdown of proteins from ingested food. If HCl secretion is a primary contributor to the SDA, there would be no relationship between the SDA and dietary protein content in an animal treated with omeprazole. However, omeprazole may inadvertently limit protein synthesis, as ingested proteins from food will not be properly processed in the stomach (Moffatt et al., 2022), thereby removing both the process of HCl secretion and the rise in protein synthesis from the SDA. Therefore, as an alternative to the use of cycloheximide and omeprazole, we recommend a comparative experiment with agastric and gastric fishes. Agastric species, such as the killifish (*Fundulus heteroclitus*) (Wood et al., 2010), goldfish (*Carassius auratus*) and zebrafish (*Danio rerio*), lack an acid-secreting stomach yet still experience an SDA (Ferreira et al., 2019; Pang et al., 2011). If gastric HCl secretion contributes importantly to the SDA response, there would be no relationship between the SDA and dietary protein content in an agastric species (Fig. 3B). The results should be compared with those from closely related gastric species fed on the same protein-only diet to determine the net contribution of either process to the SDA.

Lastly and importantly, numerous factors can complicate SDA research. It has been well documented that external variables, such

as ration size (Beamish, 1974; Fu et al., 2005a,b), respirometry type (Chabot et al., 2016), feeding method (voluntary versus involuntary; Cooper and Wilson, 2008), temperature (Jutfelt et al., 2021; Tirsgaard et al., 2015), hypoxia (Eliason and Farrell, 2014; Jordan and Steffensen, 2007; Wang et al., 2009), stress (Chabot et al., 2016), meal composition and meal type (Jordan and Steffensen, 2007; Khan et al., 2015), can all cause measurable changes in metabolism during digestion, thereby affecting the SDA response. Similarly, obtaining accurate measures of the SDA response is challenging owing to factors that independently elevate metabolic rate. Elevated metabolism associated with handling stress, spontaneous activity and/or daily activity patterns will affect the quantification of the exact magnitude, peak and duration of the SDA. It is critical that future research on the relationships between the SDA and growth standardises meal rations, environmental parameters, feed type and energy content both between and within individual measures of the SDA.

**Conclusions**

Expanding our comprehension of the SDA provides insight into the diverse evolutionary strategies and associated physiological mechanisms that animals employ to meet their energetic and nutritional requirements, but also carries important implications for the sustainability of global food production. The efficiency of growth in farmed animals, a critical aspect of food production, stands to benefit from a deeper understanding of the relationships between the SDA and growth. Given the growing coverage of SDA studies in the literature, there is a need to define what this response truly represents. Throughout this Commentary, we have contrasted two opposing perspectives: the classical interpretation of the SDA as the 'energy cost of digestion' and the alternative viewpoint presenting the SDA as the 'energy cost of growth'. Despite the conventional interpretation of the SDA as an energy 'tax' on food processing, evidence supporting a link between a reduced SDA and

enhanced animal growth is limited. In contrast, there is considerable evidence that protein synthesis is a major contributor to the SDA. It is therefore more probable that the SDA represents an increase in rates of protein synthesis and turnover, which will relate to somatic tissue production. If this alternative interpretation of the SDA holds true, a larger SDA for the same caloric intake should coincide with greater animal growth rates. Further research is necessary to bridge these perspectives, and we hope that the ideas and experiments proposed in this Commentary will help to clarify what the SDA is and what it is not.

## ECR Spotlight
This article has an associated ECR Spotlight interview with Harriet Goodrich.

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