1 Nutrigranometry I: using right-angle triangles to quantify nutritional trade-offs in 2 multidimensional performance landscapes

3 Authors: Juliano Morimoto^{1*}, Pedro Conceição², Christen Mirth³, Mathieu Lihoreau⁴

4 Authors' affiliations:

5 ¹ School of Biological Sciences, University of Aberdeen, Zoology Building, Tillydrone Ave,
6 Aberdeen AB24 2TZ

7 ² Institute of Mathematics, University of Aberdeen, King's College, Aberdeen AB24 3FX

8 ³ School of Biological Sciences, Monash, University, Melbourne, Victoria, Australia

9 ⁴ Research Center on Animal Cognition (CRCA), Center for Integrative Biology (CBI);
10 CNRS, University Paul Sabatier – Toulouse III, France.

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12 * Correspondence:

13 Dr Juliano Morimoto

14 juliano.morimoto@abdn.ac.uk

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19 Authors' contributions

20 JM conceptualised the nutrigranometry model, coded the scripts to conduct the analysis, and
21 wrote the first draft of the manuscript. JM and PC implemented the use of persistence
22 homology. All authors contributed to the revising and editing of the manuscript and approved
23 its submission.

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25

26 **Abstract**

27 Animals regulate their diet in order to maximise the expression of fitness traits that often
 28 have different nutritional needs. These nutritional trade-offs have been experimentally
 29 uncovered using the Geometric framework for nutrition (GF). However, current analytical
 30 methods to measure such responses rely on either visual inspection or complex models
 31 applied to multidimensional performance landscapes, making these approaches subjective, or
 32 conceptually difficult, computationally expensive, and in some cases inaccurate. This limits
 33 our ability to understand how animal nutrition evolved to support life-histories within and
 34 between species. Here, we introduce a simple trigonometric model to measure nutritional
 35 trade-offs in multidimensional landscapes ('Nutrignonometry'). Nutrignonometry is both
 36 conceptually and computationally easier than current approaches, as it harnesses the
 37 trigonometric relationships of right-angle triangles instead of vector calculations. Using
 38 landmark GF datasets, we first show how polynomial (Bayesian) regressions can be used for
 39 precise and accurate predictions of peaks and valleys in performance landscapes, irrespective
 40 of the underlying structure of the data (i.e., individual food intakes vs fixed diet ratios). Using
 41 trigonometric relationships, we then identified the known nutritional trade-off between
 42 lifespan and reproductive rate both in terms of nutrient balance and concentration.
 43 Nutrignonometry enables a fast, reliable and reproducible quantification of nutritional trade-
 44 offs in multidimensional performance landscapes, thereby broadening the potential for future
 45 developments in comparative research on the evolution of animal nutrition.

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49 **Introduction**

50 Animals often require different nutrient blends to maximize concurrent life-history traits,
 51 creating the potential for a conflict between nutrient allocation (Simpson and Raubenheimer
 52 2012; Raubenheimer and Simpson 2020). When the optimum nutrition for several traits
 53 cannot be achieved simultaneously, a compromise in feeding decisions must exist in order to
 54 support the expression of one trait over another ('nutritional trade-off') (Lee et al. 2008;
 55 Maklakov et al. 2008). Previous research has identified nutritional trade-offs between
 56 lifespan and reproduction or between immunity and reproduction across many different taxa
 57 including *D. melanogaster* (Lee et al. 2008; Ponton et al. 2015), tephritid fruit flies (Fanson
 58 and Taylor 2012; Fanson et al. 2012), crickets (Maklakov et al. 2008; Rapkin et al. 2018; Guo
 59 et al. 2021; Treidel et al. 2021) and mice (Solon-Biet et al. 2014) [see also reviews by
 60 (Ponton et al. 2011; Schwenke et al. 2016)]. Even traits related to different aspects of the
 61 same life-history can vary in nutritional requirements during the lifetime of an animal, as
 62 seen for pre- and post-mating traits related to reproduction of many insect species such as
 63 sperm number and viability (Bunning et al. 2015), fertilization success across sperm
 64 competitive contexts (Morimoto and Wigby 2016), cuticular hydrocarbons, courtship song
 65 and sperm viability (Ng et al. 2018) as well as size and numbers of eupyrene and apyrene
 66 sperms (Gage and Cook 1994). Thus, nutritional trade-offs are likely ubiquitous and impose
 67 significant constraints on the feeding behaviour of individuals.

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69 Measuring nutritional trade-offs can be challenging because of the interactive effects of
 70 nutrient ratios and concentrations on the expression of life-histories (Stearns 1992; Roff
 71 2002; Hunt et al. 2004; Simpson and Raubenheimer 2012). In the last decades, however, a
 72 method known as Geometric Framework of Nutrition (GF) has emerged as a powerful
 73 unifying framework capable of disentangling the multidimensional effects of nutrients (both

ratios and concentrations) on life-history traits and fitness (Simpson and Raubenheimer 1993a). The GF has been applied to a diverse range of nutritional studies across species such as flies (Lee et al. 2008; Reddiex et al. 2013; Jensen et al. 2015; Ponton et al. 2015; Morimoto and Wigby 2016; Kutz et al. 2019) (Fanson and Taylor 2012; Fanson et al. 2012) (Barragan-Fonseca et al. 2018, 2021), crickets (Ng et al. 2018) (Rapkin et al. 2018) (Maklakov et al. 2008), cockroaches (Bunning et al. 2015), domestic cats and dogs (Hewson-Hughes et al. 2011, 2013), and mice (Solon-Biet et al. 2014; Morimoto et al. 2019), being paramount for advancing our understanding of complex physiological and behavioural processes across ecological environments and even human health (Simpson et al. 2017). As a result, developing a simple, intuitive, and accurate quantitative method for quantifying nutritional trade-offs has become a key issue for comparative nutrition, which will allow new avenues of research for insights into the evolution of physiological and behavioural modulation of nutritional responses (Morimoto and Lihoreau 2020).

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Recent initiatives have been made but these are complex to navigate and therefore studies continue to be published with visual inspection or with inaccurate methods to quantify the strength of nutritional trade-offs in GF landscapes [e.g., (Polak et al. 2017; Ng et al. 2018, 2019; Kutz et al. 2019; Ma et al. 2020; Barragan-Fonseca et al. 2021)]. Why is it so difficult to measure nutritional trade-offs in GF multidimensional fitness landscapes? The fundamental limitation in all models so far is identifying and delimitating the region of interest (i.e., peaks and, to a lesser extent, valleys) for comparisons of distances between peaks of different traits (or same trait between species). For instance, (Rapkin et al. 2018) proposed the use of regression slopes (rather than the coordinates of the optimum) nutrients onto the fitness trait i as coordinates of a vector $\vec{v}_i$. From this, the angle θ' between vectors $\vec{v}_i$ and $\vec{v}_j$ for traits i and j , respectively, can be calculated as the estimate of the strength of the

99 nutritional trade-off. However, in this approach, the domain of each vector coordinate is all
100 real numbers $\mathbb{R}$ even though the domain of the fitness landscape is constrained to all positive
101 real numbers $\mathbb{R}^+$. Consequently, this violates the domain constraints of the nutritional space
102 upon which GF is performed, which in turn result in overestimation of the strength of
103 nutritional trade-offs (Morimoto and Lihoreau 2019). To address this limitation, we proposed
104 to use the coordinates of the peak (or valley) from the nutritional space as vector coordinates
105 for the position vector $\vec{v}_i$, from which the angle θ between position vectors $\vec{v}_i$ and $\vec{v}_j$ for traits
106 i and j , respectively, can be estimated as measure of the strength of the nutritional trade-off.
107 This overcomes the violation of domains between vector coordinates and the nutritional
108 space [in (Rapkin et al. 2018)] and therefore ensures that the estimate of θ is calculated in the
109 same domain of the GF fitness landscapes. However, this Vector of Positions approach relies
110 on the peak estimates from a SVM machine learning model which is computationally
111 expensive particularly in n dimensions, where $n > 3$, and sensitive to the characteristics of the
112 input data (e.g., if the data contains food intakes as in (Lee et al. 2008; House et al. 2015;
113 Jensen et al. 2015; Morimoto and Lihoreau 2019) or a grid of fixed diet ratios as in (Kutz et
114 al. 2019)], identifying local as well as global peaks that introduce noise into the analysis
115 (shown here). Albeit useful, the Vector of Positions approach can be cumbersome to
116 implement across different datasets, computationally expensive to obtain estimates of peaks
117 (or valleys), and as a result can generate inaccurate estimates of the strength of nutritional
118 trade-offs. Thus, to date, there are no proposed solutions that address the above limitations,
119 which creates a significant bottleneck in studies of nutrition that limits the multidimensional
120 power of the GF framework.

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122 Here, we address the limitations of current models by proposing a simpler framework
123 (Nutrignonometry) upon which the strength of nutritional trade-offs can be calculated in 3D

fitness landscapes, irrespective of the structure of the nutritional data to analyze. Using landmark GF datasets, we first investigated the performance of different ‘off-the-shelf’ machine learning models in predicting the peak in the fitness landscapes, in order to find the most accurate and computationally inexpensive model. We achieved this by integrating several measurements of predictive error, variance in predicted peak area, and topological characteristics of the predicted peak region. Next, we used simple trigonometric functions and relationships to estimate the strength of nutritional trade-offs both in terms of nutrient balance as well as nutrient concentration, or both. Our approach opens new avenues of research in multidimensional nutrition, and allows for physiological and comparative studies to be performed in a consistent and reproducible way from which insights onto the evolution of animal nutrition can be gained across the tree of life.

Material and Methods

Nutrigonometry

Studies using GF define the food components (typically macro-nutrients) that will be investigated, which together compose the ‘nutritional space’. For example, in studies where protein and carbohydrate effects are investigated, there is a 2D nutritional space (one dimension for each nutrient) onto which the performance landscape of the trait is mapped. This rationale can be extended to n number of nutrients (Simpson and Raubenheimer 1993*b*), albeit to date, studies with two nutrients are the most common (Morimoto and Lihoreau 2020). If we consider this 2D nutritional space as a rectangular space in which an infinite number of nutritional rails (i.e., imaginary lines that pass through the origin with arbitrary positive slope) exist that divides the space in right-angle triangles, then it is possible to use simple trigonometric functions to estimate the angle α_i and the hypotenuse of the triangle, for all fitness traits mapped onto the nutritional space. The angle α_i is the angle of the

nutritional rail, relative from the x-axis, that passes through the peak in the landscape for the trait i , and the hypotenuse h_i of the triangle shows how far from the origin the peak in the landscape sits for the trait i (Fig 1a). α_i and h_i can be calculated using Pythagorean theorem and the relationship between the angle and the sides of right-angle triangles (i.e., sines and cosines), as shown in Fig 1a.

Once α_i are known, we can estimate the angle θ [as in (Morimoto and Lihoreau 2019)] which is the difference in the angle between nutritional rails that maximize two traits, i and j , and provides a measure of the strength of the nutritional trade-off that exists between traits i and j (Fig 1b). The larger the angle $\theta_{i,j}$, the strongest the nutritional trade-off in terms of nutrient balance (and potentially nutritional compromise) between traits. Likewise, we can compare the difference $h_{i,j}$ in the estimates of the hypotenuse h_j and h_i to quantify nutritional trade-offs in relation to nutrient concentration (Fig 1b). These metrics allowed us to disentangle the following scenarios in which nutritional trade-off can occur:

- (I) When $\theta_{i,j}$ is large but $h_{i,j}$ is small ('Strong nutritional trade-off in terms of nutrient balance')
- (II) When $\theta_{i,j}$ is small but $h_{i,j}$ is large ('Strong nutritional trade-off in terms of nutrient concentration'),
- (III) When $\theta_{i,j}$ and $h_{i,j}$ are large ('Strong nutritional trade-off in terms of both nutrient balance and concentration')
- (IV) When $\theta_{i,j}$ and $h_{i,j}$ are small ('Weak or no nutritional trade-off') (Fig 1c).

Here when applying this model for empirical datasets (see below), inferences on the strength of nutritional trade-offs were made using confidence intervals for $h_{i,j}$ and $\theta_{i,j}$, whereby nutritional trade-offs were stronger when confidence intervals did not overlap zero and the

magnitude of the difference was large. Estimates are presented in the units of the nutrient space in which the data was collected (e.g., mg), while angles are presented in degrees. Confidence intervals for both $h_{i,j}$ and $\theta_{i,j}$ were calculated using the significance threshold of 0.05 and the quartiles of a t -distribution. All analyses and plots were done in R version 3.6.2 (R Core Team 2019).

Predicting peak (or valley) location and size

As with previous approaches, the model presented here depends on accurate estimates of the coordinates for the peak in the multidimensional performance landscape. Without this, estimates of $h_{i,j}$ and θ are inaccurate which in turn affects the ability of the model to estimate the strength of nutritional trade-offs. To overcome this, the basic algorithms underpinning the identification of peak regions in multidimensional fitness landscapes were designed as following:

- 1) Empirical data was split into training (75%) and test (25%) datasets;
- 2) A machine learning model was fitted to the training set using 10-fold cross-validation, with the fitness trait as dependent variable and the nutrient intakes (or fixed ratios) as independent variables. The model included main and interactive effects of protein and carbohydrate, as well as quadratic effects of each nutrient (for non-linear relationships);
- 3) The model's predictive performance was evaluated with root-mean-square-error (RMSE) with respect to the observed values of the test dataset;
- 4) A set of 500 random points corresponding to (protein, carbohydrate) coordinates were generated covering the nutritional space, and the model of step 2 was used to predict the value of the fitness value for each point;

- 5) A quantile threshold was used to crop the data to the specific region of interest. For instance, for peaks in the nutritional landscape, the default value used throughout this study was set to 0.95 (i.e., the highest 5% predicted fitness values are subset, from which coordinates of protein and carbohydrate are used).
- 6) Steps 4-5 were repeated 100 times.

We then made statistical inferences on peak area from 95% confidence intervals using the ‘ci’ function of the ‘Rmisc’ package (Hope et al. 2013) whereby we resampled with replacement the selected random points obtained from steps 5 and 6 above. To test the performance of nutrigonometry in estimating nutritional trade-offs, we used the most commonly used models to test relationships between traits in behavioral ecology (e.g., general linear model), machine learning models used in regression models in ecology and evolution [e.g., Random Forest, (Rabinovich 2021)], as well as models that have been specifically used to analyse multidimensional performance landscapes in GF studies (e.g., SVM, GAMs) (Ponton et al. 2015; Morimoto and Lihoreau 2019). In particular, we tested the performance of Bayesian linear regression (Bayes), general linear regression (LM), k-nearest neighbors (KNN), Gradient boost (GBoost), random forest (RF), support vector machine (SVM) with radial basis function as well as generalized additive models (GAMs) with both smooth term or tensor product term. With the exception of GAMs that were fitted using the ‘mgcv’ package (Wood and Wood 2015), all other models were fitted using the ‘tidymodels’ package of the tidyverse (Wickham et al. 2019). For the Bayesian regression, we used the flexible Cauchy prior from the ‘rstanarm’ package for all analysis (Goodrich et al. 2020). Fitness landscapes were estimated using the ‘Tps’ function of the ‘fields’ package (Nychka et al. 2017). All plots were done using the ‘ggplot2’ package (Wickham 2016). All models were fitted to a training set (75% of the data) and model performance (i.e., RMSE) was calculated from the performance of the models in the remaining test dataset (25%).

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224 *Goodness-of-estimate of the models*

225 In addition to RSME, we estimated the area (in squared units in which the data is collected)
 226 of the polygon delimited by the estimated predicted peak region ('Area') and the horizontal
 227 (protein) and vertical (carbohydrate) spread of the datapoints of the predicted peak region
 228 ('Nutrient spread') as proxies of the goodness-of-estimate of the models (Fig 1d). The smaller
 229 the RMSE, the better is the model in predicting the fitness value of the peak region (the z-
 230 axis). Furthermore, the smaller the area and nutrient spread, the more compact the prediction
 231 of the peak region in the nutritional space. Note that RMSE values do not interfere with
 232 accuracy of estimates of $h_{i,j}$ and θ , and thus the estimates of nutritional trade-offs, because
 233 the z-axis is not used in the calculation of angles and hypotenuses (Fig 1d). A model can
 234 have high RMSE and still be the best predictive model as long as the predicted peak correctly
 235 matches with the observed peak in the landscape.

236

237 *Topological structure of the estimated peak*

238 Even in cases where area and nutrient spread of the predicted peak region are small, it is
 239 important to have evenly-spaced datapoints within the predicted peak region. This is because
 240 predictions of regions which contain holes can lead to mis-estimation of the strength of
 241 nutritional trade-offs by potentially adding noise to the set of protein and carbohydrate
 242 coordinates used to calculate $h_{i,j}$ and θ . We measured the topological structure of the
 243 predicted peak region using the concept of persistence homology (PH), which in simple
 244 terms, allows us to investigate the overall structural organisation of the data [see Text S1 and
 245 (Zomorodian and Carlsson 2005; Weinberger 2011) for details of the concept] (Fig 1d). PH
 246 was estimated using the 'TDAstats' package (Wadhwa et al. 2018). Together, the estimates of

RMSE, area, nutrient spread, and PH provided a comprehensive suite of metrics to assess the quality of model predictions for the peak region in fitness landscapes.

Datasets used for model application

We demonstrate the applications of the Nutrignonometry framework using two datasets, which vary in structure. The first dataset is a landmark dataset which contains *Drosophila melanogaster* individual adult nutrient intake as well as the consequences of nutrient intake to lifespan and reproduction (Lee et al. 2008). This dataset was previously used to test the Vector of Position approach and therefore has important benchmark status in the field (Morimoto and Lihoreau 2019). We also investigate the effect of data structure on Nutrignonometry estimates of peak and valley regions. In GF, data can be divided into two structures: intake data and fixed ratio data. Intake data is ideal in GF studies because it allows for exploration of *realized* nutritional effects, that is, nutritional effects exerted upon traits given by the amount of nutrient eaten (Simpson and Raubenheimer 1993b). However, collecting intake data can be cumbersome or challenging, and recent approaches have adapted GF experiments to draw landscapes of traits based on the fixed ratio of the nutrients in the diets (Kutz et al. 2019). To date, however, we still do not know how this adaptation influence estimates of nutritional trade-offs in multidimensional performance landscapes. Here, to test whether the structure of the data is important for model predictions, we used Lee et al., (2008) dataset with individual intakes (‘intakes’) as well as with fixed ratios (‘fixed’). Using this data and for the purpose of the demonstration of Nutrignonometry, we estimated the nutritional trade-off between lifespan and reproductive rate which are known to trade-off in this species. We also used a second dataset from (Kutz et al. 2019), which studied how temperature modulates nutritional responses of larval development and adult fitness in *D. melanogaster*, as an additional proof-of-application of our model in fixed ratio datasets (see

Fig S1). Lastly, we demonstrated how the best performing models in our peak analysis can be used to predict valley regions (Fig S2 and Fig S3).

Comparison with intake target

Drosophila melanogaster balance their nutrient intake to a P:C ratio of 1:4 when given the possibility to self-select multiple nutritionally complementary foods (Lee et al. 2008). We then used the peak predictions of the Nutrignonometry framework to test whether the observed P:C ratios that maximized lifespan and reproductive rates coincided with the P:C ratio of 1:4 reached by flies in choice situations. To achieve this, we calculated the 95% confidence interval as described for the peak area but in this case, for the P:C ratio of each trait. Whenever the confidence interval overlapped 1:4, we inferred that the estimate of peak ratio did not statistically differ from the intake target of 1:4.

Results

Simple (Bayesian) linear regressions outshine machine learning models when predicting peak region in multidimensional landscapes

All models generated predictions of peak region in nutritional landscapes irrespective of data structure although the accuracy and topology of the predicted regions varied (Fig 2 and Fig 3). In general, GAMs with tensor product and smooth function as well as Bayes and LM linear models generated peak predictions for both lifespan and reproductive rate that were significantly more accurate (narrower in area) than other models when the structure of the data was composed of food intakes (Fig 2, Table S1 and Table S2). When the data structure changed to fixed ratios, LM, GAM with tensor product, Bayes, and KNN predicted peaks with smaller area for lifespan and all but KNN perform within similar scales for the peak prediction of reproductive rate (Fig 2, Table S1 and Table S2). In comparison, GAM smooth

did not perform well in predicting peak region that was homogenous and accurate to the performance landscape, particularly when the data structure was fixed ratio. The performance of the models was independent of patterns in the estimates of RMSE and nutrient spread which showed no clear pattern of performance with the exception of LM and Bayes that displayed consistently lower spread when the structure of the data were intakes (Fig 3 and Fig 4; Table S2). Interestingly, machine learning models consistently underperformed, predicting peak regions that were wider and less accurate and homogenous (Fig 2 and 3, Table S1 and S2). The underlying reason for this is unclear, but similar patterns were observed when predicting the peak region of (Kutz et al. 2019) dataset (see Fig S1 and Table S3). Bayes, GAMs (both smooth and tensor product) and LM also performed well when predicting valley regions (see Fig S2 and S3). These results indicate that simple (Bayesian) linear regression provide consistently the best models to estimate the region of the peak of fitness landscapes irrespective of the structure of the data, and that GAMs with tensor product (and to a smaller extent, smooth function) can be used when the data are individual intakes.

Better models lead to accurate estimates of known nutritional trade-offs in multidimensional landscapes

GAMs (both smooth and tensor product), Bayes, LM, and KNN models were the only models that correctly identified the nutritional trade-off measured by θ between lifespan and reproductive rate for data with individual intakes (Table 1). Given the variability in the area, spread, and topology of the predicted region, estimates of $h_{i,j}$ and θ were more accurate (narrower confidence intervals) for GAMs (smooth and tensor product), Bayes and LM compared with KNN. GAMs, Bayes and LM were the only ones that identified a trade-off on the hypotenuse estimate $h_{i,j}$ for data of individual intakes, while KNN was the only model that identified this trade-off in data with fixed ratio. GAM smooth was the only model that

failed to identify this trade-off when the data was composed of fixed ratios (Table 1). Thus, overall, simpler models are more suitable to generate peak predictions that accurately describe nutritional trade-offs in multidimensional performance landscapes for data of different structures.

Comparing trait optimum with intake target

We then used the estimated peak regions for lifespan and reproductive rate (both individual intake and fixed ratio data structures) to estimate the optimum P:C ratio that maximises each trait as well as whether or not these optima coincided with the P:C ratio obtained when individuals are allowed to balance their diet (i.e., 1:4). All models predicted a significantly lower P:C ratio for the optimum that maximizes reproductive rate relative to lifespan as expected from the original visual comparison of landscapes (around 1:2 for reproductive rate and >1:9 for lifespan) (Table 2). However, none of the estimates overlapped 1:4, suggesting that *D. melanogaster* females likely have to compromise the nutrient intake to maximise either lifespan or reproductive rate, but not both simultaneously.

Discussion

We proposed a new simple analytical framework to analyse nutritional trade-offs in multidimensional fitness landscapes. Nutrigonometry uses trigonometric relationships from right-angle triangles to identify and compare peaks (or valleys) in 3D fitness landscapes between traits. Using landmark GF datasets with different structures, we demonstrated the accuracy and performance of standard (machine learning) models in finding the peak regions in these multidimensional landscapes and subsequently quantifying the strength of nutritional trade-offs between traits. As with the Vector of Positions approach (Morimoto and Lihoreau 2019), the Nutrigonometry strictly considers coordinates in the real positive region of the

nutrient space, whereby the true separation between key regions (peaks and valleys) are quantified within the correct domain in which the fitness landscapes exist. However, contrary to previous methods (Rapkin et al. 2018; Morimoto and Lihoreau 2019), the Nutrignonometry does not rely on vector calculations but instead harnesses the trigonometric relationships of right-angle triangles to estimate nutritional trade-offs. This is a major advance of the model as it considerably simplifies the framework both in conceptual and computational terms. Nutrignonometry thus significantly advances our ability to generate reliable and reproducible estimates of nutritional trade-offs within and between species, facilitating quantitative (comparative studies) of animal nutrition.

Multidimensional studies of nutrition through the GF have been increasingly used to gain insight into animal and human nutrition (Lee et al. 2008; Behmer 2009; Felton et al. 2009; Simpson and Raubenheimer 2012; Hewson-Hughes et al. 2013; Gosby et al. 2014; Solon-Biet et al. 2014). Likewise, the complexity of the applications has also increased, ranging from studies with few nutrients (e.g., protein and carbohydrates, salts) through to high-dimensional studies investigating individual fatty acids and amino acids (Simpson et al. 2006; Grandison et al. 2009; Arien et al. 2015; Arganda et al. 2017; Piper et al. 2017). This means that analytical frameworks that are simple and robust must be developed to support the development of the field. Nutrignonometry provides such foundation, by demonstrating the best approach to investigate nutritional trade-offs in 3D fitness landscapes. Because Nutrignonometry uses trigonometric relationships of right-angle triangle, it is applicable to n dimensions. However, given the often counter-intuitive geometrical effects of high dimensionality [e.g., (Milman 1998; Watanabe 2021)], such expansion to higher dimensions requires further investigation as the topic of future developments. Nevertheless, given the broad use of 3D fitness landscapes in GF studies (Morimoto and Lihoreau 2020),

Nutritionometry readily enables important quantifications of nutritional trade-offs that were otherwise absent or cumbersome to produce. For instance, using a range of models, Nutritionometry uses right-angle triangles to compare the ratio of nutrients that maximise lifespan and reproductive rate along with the strength of nutritional trade-offs between these traits in a landmark paper in the field (Lee et al. 2008). Moreover, Nutritionometry is capable of comparing the nutrient ratio which maximises lifespan and reproductive rate with the nutrient ratio that is balanced by individuals when given a choice, providing important insights into the dietary choices underpinning nutritional compromises. Such quantification can bring new fundamental insights into our understanding of nutritional trade-offs such as strength and the direction of the trade-offs (e.g. nutrient balance vs concentration, see Fig. 1), as well as how much animals actually resolve these trade-offs when they have the opportunity to do so and whether, for instance, they favour one trait of another (distance between optimal trade-off and observed nutrient intake target, see Table 2).

An important trend in the field of multidimensional nutrition is the study of nutritional effects across physiological pathways and across levels of biological organization (Lihoreau et al. 2014; Simpson et al. 2015). These studies generate multiple 3D landscapes that are often compared visually, without rigorous analytical methods to measure nutritional trade-offs. For example, eleven 3D-landscapes of the expression of genes involved in the Insulin/IGF pathway were visually compared to provide insights into how a key endocrine pathway is regulated based on nutrient intake, and how gene expression can underlie expression of life-histories (Post and Tatar 2016; McDonald et al. 2021). Likewise, twelve 3D-landscapes with gut microbial diversity or abundance were visually compared to better understand how nutrient composition can modulate host-microbe interactions (Ng et al. 2019). Similar visual comparisons have been made to understand the effects of nutrition on host-endosymbiont

relationship (Ponton et al. 2015). The analytical framework proposed here will allow researchers to move beyond visual comparisons to quantitatively assess how landscapes differ using a rigorous and reproducible framework. As a result, Nutrigonometry yields considerable advances to the status quo in the field, enabling a deeper understanding of the role of nutrition in host-microbial interactions as well as animal physiology, behaviour and ecology.

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Data accessibility

Kutz et al. data is available here: doi.org/10.26180/5cfe1ddaaafac. Lee et al. dataset is available in Dryad: [doi:10.5061/dryad.tp7519s](https://doi.org/10.5061/dryad.tp7519s). R script with functions for the implementation of the Nutrigonometry framework is available in the Supplementary Materials.

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Table caption

Table 1. Nutrignonometry quantification of nutritional trade-offs between lifespan and reproduction. Estimates of $\theta_{i,j}$ (in degrees) and $h_{i,j}$ (in mg) for the nutritional trade-off between lifespan and reproductive rate. Analysis from the data presented in Lee et al. (2008). Confidence intervals overlapping zero implies no difference in the peaks. Magnitude of the estimates indicate the strength of nutritional trade-offs (i.e., larger magnitudes indicate stronger nutritional trade-offs). Note that $\theta_{i,j}$ is bound between 0 and 90 degrees (i.e., 0 and $\frac{\pi}{2}$).

Table 2. Nutrignonometry estimates of nutritional compromises. Estimates of optimal intake that maximises lifespan and reproductive rate based on the predicted peak region. Comparison made with the visual peak ratio from Lee et al. (2008). Note that all models show that the estimated peak ratio between traits do not overlap and thus, corroborate the inference of a nutritional trade-off between traits, leading to a nutritional compromise. Note also that all but one model (i.e., GAM smooth for fixed ratio reproductive rate data) predicted peak region ~1:4, which is the ratio that individuals balance when given the ability to balance their diet ('choice'). All other models suggest that a P:C ratio of 1:4 is lower than the ratio needed to maximise lifespan but higher than that for reproductive rate, further supporting the concept of a nutritional compromise.

Figure caption

Figure 1. Nutrignonometry framework. (a) Considering an infinite number of nutritional rails that divide the nutritional space into right-angle triangles, the angle and the hypotenuse can be calculated from trigonometric relationships. (b) Nutrignonometry applied to compare two traits is simple as it allows for the estimates of the strength of nutritional trade-offs in terms of nutrient balance (angle) and nutrient concentration (the difference), given in absolute terms. (c) Plausible scenarios for the estimates of and. (d) Metrics used to the peak prediction in the 3D landscape. RMSE was calculated as root-mean-square difference between the predicted and observed values of the trait (z-axis) in the peak region. Nutrient spread (both carbohydrate and protein) was calculated as the standard deviation of the predicted peak region. The area of the polygon that encapsulates the predicted peak region was also estimated as a proxy of prediction performance. Lastly, the topology of the predicted datapoints for the peak region was analysed using the concept of persistence homology (see Methods) to identify homogeneity in predicted point structure.

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635 **Figure 2. Nutrigrigonometry framework to predict peak region in lifespan and**
636 **reproductive rate landscape with different data structure.** (a) Lifespan landscapes with
637 individual intake (top left panel) and fixed ratio (top right panel) from Lee et al. (2008) with
638 the overlaid predicted peak regions. (b) Reproductive rate landscapes with individual intake
639 (bottom left panel) and fixed ratio (bottom right panel) from Lee et al. (2008) with the
640 overlaid predicted peak regions. For the landscapes, red represents peaks while light green
641 represents valleys. For the predicted region, dark blue represents points with lower predicted
642 z-values whereas bright yellow represents points with higher predicted z-values. The shaded
643 polygon was added to facilitate visualisation of the predicted peak region and the
644 homogeneity of points within the predicted peak.

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Figure 3. Persistence Homology (PH) to investigate topological structure of the predicted peak region using Nutrignonometry. (a) PH plots for the topological analysis of the predicted peak region in lifespan of data containing the structure of individual intake (top left) and fixed intake data (top right). (b) PH plots for the topological analysis of the predicted peak region in reproductive rate with data of structure containing individual intake (bottom left) and fixed intake data (bottom right). Homogenous predicted peaks have red (dimension 0) and blue (dimension 1) points that are closer, as opposed to more heterogeneous predicted peaks upon which (some) points can be farther from each other. Note the different scales upon which the data is plotted (needed to aid visualisation of point clouds).

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685 **Figure 4. RMSE and peak area estimates in the Nutrigenometry peak region**
686 **predictions.** (a) RMSE and predicted peak area (i.e., area of the shaded polygon from the
687 predicted region for lifespan and reproductive rate data), with structure containing individual
688 intakes. (b) RMSE and predicted peak area (i.e., area of the shaded polygon from the
689 predicted region for lifespan and reproductive rate data), with structure containing fixed
690 ratios. Note that models with high RMSE can still be the best predictors of peak region.

691

692 Supplementary Material

693 **Text S1. What is Persistence Homology (PH)? A brief introduction.**

694

695 **Table S1. Area of the predicted peak region for all models.** All values are given in unit
696 squared of nutrient intake or diet composition (for fixed ratios).

Table S2. Nutrient spread of the predicted peak region for all models. All values are given in units of nutrient intake or diet composition (for fixed ratios).

Table S3. Nutrignonometry quantification of nutritional trade-offs in developmental time between two developmental temperatures. Estimates of $\theta_{i,j}$ (in degrees) and $h_{i,j}$ (in g/L). Analysis from the data presented in Kutz et al. (2018). Confidence intervals overlapping zero implies no difference in the peaks. Magnitude of the estimates indicate the strength of nutritional trade-offs (i.e., larger magnitudes indicate stronger nutritional trade-offs). Note that $\theta_{i,j}$ is bound between 0 and 90 degrees (i.e., 0 and $\frac{\pi}{2}$).

Figure S1. (a) 3D landscape for developmental time at 25°C (top left) and 28°C (bottom left) (from Kutz et al., 2019) with the overlaid predicted peak regions. For the landscape, red represents peaks while light green represents valleys. For the predicted region, dark blue points represent points with lower predicted z-values whereas bright yellow represents points with higher predicted z-values. The shaded polygon was added to facilitate visualisation of the predicted peak region and the homogeneity of points within the predicted peak. (b) RMSE and predicted peak area (i.e., area of the shaded polygon in panel a) for the models of developmental time at 25°C (top right) and 28°C (bottom right) values of each model. Note that models with high RMSE can still be the best predictors of peak region. (c) Persistence homology (PH) plots for the topological analysis of the predicted peak region of the 3D landscape for developmental time at 25°C (top panel) and 28°C (bottom panel) (from Kutz et al., 2019). x and y- axes represent birth and death, respectively, of topological structures. The diagonal line represents the line in which the birth and death co-occur. Homogenous predicted peaks have red (dimension 0) and blue (dimension 1) points that are closer, as opposed to more heterogeneous predicted peaks upon which points are farther from each other.

Figure S2. Prediction of the valley regions for lifespan using individual intake data from Lee et al. (2008). Note that we used the best performing models for the peak region (see Main text).

Figure S3. Prediction of the valley regions for reproductive rate using individual intake data from Lee et al. (2008). Note that we used the best performing models for the peak region (see Main text).

R Script. R script with functions for the implementation of the Nutrignonometry framework (separate file).

Table 1. Nutrigonometry quantification of nutritional trade-offs between lifespan and reproduction. Estimates of $\theta_{i,j}$ (in degrees) and $h_{i,j}$ (in mg) for the nutritional trade-off between lifespan and reproductive rate. Analysis from the data presented in Lee et al. (2008). Confidence intervals overlapping zero implies no difference in the peaks. Magnitude of the estimates indicate the strength of nutritional trade-offs (i.e., larger magnitudes indicate stronger nutritional trade-offs). Note that $\theta_{i,j}$ is bound between 0 and 90 degrees (i.e., 0 and $\frac{\pi}{2}$).

Parameter	Model	Estimate	Std	LwrCI	UprCI
Trade-off (intakes)	$\theta_{i,j}$	SVM	14.456	10.728	-6.574 35.485
		RF	14.508	8.109	-1.388 30.404
		GAM_tensor	16.128	4.984	6.358 25.897
		GAM_smooth	16.166	4.962	6.438 25.893
		GBoost	17.063	9.575	-1.706 35.831
		LM	17.940	4.826	8.479 27.400
		Bayes	18.205	4.709	8.974 27.436
		KNN	21.203	6.181	9.088 33.318
	$h_{i,j}$	SVM	16.792	65.723	-112.038 145.622
		KNN	50.015	48.137	-44.343 144.373
		GBoost	52.851	75.218	-94.591 200.293
		RF	58.561	66.066	-70.943 188.064
		LM	75.870	35.142	6.984 144.757
		Bayes	76.729	34.444	9.211 144.247
		GAM_smooth	120.245	29.406	62.604 177.886
		GAM_tensor	124.533	27.930	69.784 179.282
Trade-off (fixed)	$\theta_{i,j}$	GAM_smooth	9.645	5.897	-1.916 21.205
		SVM	11.840	5.649	0.767 22.913
		RF	17.368	5.848	5.906 28.831
		GBoost	20.177	5.057	10.264 30.090
		GAM_tensor	21.177	3.872	13.588 28.766
		Bayes	26.454	5.876	14.935 37.973
		LM	26.499	5.903	14.928 38.070
		KNN	31.428	7.186	17.342 45.513
	$h_{i,j}$	SVM	2.381	68.888	-132.653 137.416
		RF	4.819	64.841	-122.283 131.921
		GBoost	9.377	65.605	-119.222 137.975
		Bayes	41.461	34.912	-26.974 109.896
		LM	42.305	34.429	-25.182 109.791
		GAM_smooth	46.635	40.358	-32.475 125.745
		GAM_tensor	49.009	32.855	-15.394 113.412
		KNN	82.516	30.388	22.949 142.083

Table 2. Nutrigenometry estimates of nutritional compromises. Estimates of optimal intake that maximises lifespan and reproductive rate based on the predicted peak region. Comparison made with the visual peak ratio from Lee et al. (2008). Note that all models show that the estimated peak ratio between traits do not overlap and thus, corroborate the inference of a nutritional trade-off between traits, leading to a nutritional compromise. Note also that all but one model (i.e., GAM smooth for fixed ratio reproductive rate data) predicted peak region ~1:4, which is the ratio that individuals balance when given the ability to balance their diet ('choice'). All other models suggest that a P:C ratio of 1:4 is lower than the ratio needed to maximise lifespan but higher than that for reproductive rate, further supporting the concept of a nutritional compromise.

Data	Trait	Model	Mean	Upr CI	Lwr CI	Target (Visual)
Peak Ratio (intakes)	Lifespan	GBoost	5.235	5.205	5.265	16
		RF	5.533	5.508	5.557	
		SVM	5.864	5.836	5.892	
		LM	9.084	9.048	9.120	
		Bayes	9.154	9.118	9.190	
		KNN	12.075	12.015	12.135	
		GAM_smooth	13.055	12.997	13.114	
		GAM_tensor	13.108	13.049	13.168	
	Reproductive rate	GBoost	1.858	1.853	1.864	2
		KNN	2.041	2.037	2.045	
		RF	2.138	2.133	2.144	
		SVM	2.147	2.138	2.156	
		Bayes	2.194	2.191	2.197	
		LM	2.215	2.212	2.219	
		GAM_smooth	2.644	2.639	2.650	
		GAM_tensor	2.661	2.656	2.667	
Peak Ratio (fixed)	Lifespan	GBoost	13.078	12.987	13.170	16
		SVM	14.946	14.873	15.019	
		RF	15.107	15.045	15.169	
		GAM_smooth	16.977	16.859	17.097	
		GAM_tensor	20.623	20.536	20.710	
		KNN	26.050	25.929	26.173	
		Bayes	32.426	32.237	32.617	
		LM	32.933	32.744	33.125	
	Reproductive rate	KNN	1.467	1.463	1.470	2
		LM	1.836	1.832	1.839	
		Bayes	1.841	1.837	1.845	
		GBoost	2.171	2.168	2.174	
		GAM_tensor	2.244	2.241	2.248	
		RF	2.545	2.539	2.552	
		SVM	3.527	3.516	3.538	
		GAM_smooth	4.280	4.265	4.296	