Assessing Model Fitness using Sheaves

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Abstract

The purpose of science is to generate methods to predict outcomes of events. When considering large systems with many parameters, predictions are often subject to high variation and are subsequently hard to verify. This study attempts to address this problem, in particular focusing on metabolism. The analysis showed the accepted model of metabolism has a natural representation as a *sheaf* of sensor data. We find this representation grants us three useful analytic tools. First, it is possible to quantify how well the model corresponds to measured data. Second, using an iterative process called a *consistency radius filtration*, we show it is possible to determine which components of the model are responsible for the highest variation. We note these components may not be an accurate representation of the process being modeled. Third, we build a method (finding the nearest global section) that constructs a new model that minimizes local error for the input data. We propose this new model is better for the given data than the previous model.

1 Introduction

Sheaves are powerful tools for the integration of data of heterogeneous sources or models [7]. As such, they are useful in the interpretation of biological data, which is often harvested from differing populations, individuals, tissues, and cells. Our research aims to apply sheaves in the study of metabolomics data whose inherent variability comes from differing sources, whether the samples are obtained from different cells from the same individual, different individuals, or both. We aim to use sheaves to identify a consensus metabolic response to stimulus, and we aim to use that consensus response to identify the parts of a model that do not conform to the data.

We begin by describing the category in the domain of the sheaf, the category of reactions, $\mathcal{X}$. Then, we describe a mapping from the objects and morphisms of $\mathcal{X}$ into the category in the image of the sheaf functor, which we denote by S, a category of real Euclidean spaces. Finally, we define a consistency structure on $\mathscr{S}$ and describe how the structure can be used in applications.

2 Background

We begin with some necessary background and definitions from category theory. We note that category theory was developed in the study of algebraic topology and is typically presented in this context [2, 3]. However, due to its wide applicability, introductions have been developed strictly for scientific, engineering, and programming contexts [1, 5, 8]. The essentials follow below.

Definition 2.1 (Category)**.** A *category* consists of three parts: (1) objects, (2) morphisms between objects, and (3) a composition function that is associative and merges two morphisms into one. A morphism is a directed relationship between two objects in the category and is commonly represented as an arrow from a source object to a destination object. Often, the objects in the category give these arrows meaning. For example, in a category where the objects are sets, there might be arrows from all subsets to their supersets, so the arrows mean "is a subset of". Multiple arrows may exist between the same pair of objects, and the identity morphism, from an object to itself, must be included for all objects in the category. Finally, for any pair of composable morphisms $f : U \to V$ and $g : V \to W$, their composition $g \circ f : U \to W$ must also be included as a morphism in the category.

Definition 2.2 (Functor)**.** A *functor* is a mapping between categories, such that an object from the domain category has the image of some object in the co-domain category, and morphisms also have an image morphism under the functor. In other words, if $F : \mathcal{X} \to \mathcal{Y}$ is a functor mapping the category

$\mathcal{X}$ into the category $\mathcal{Y}$, for any object $x \in \mathcal{X}$, $F(x)$ is an object of $\mathcal{Y}$. Also, for any morphism between objects of $\mathcal{X}$, $f : x \to x'$, we define the image of f in $\mathcal{Y}$ as $F(f) : F(x) \to F(x')$. Note that this morphism must already exist in $\mathcal{Y}$ for F to be defined. In some cases, it is relevant to consider a mapping that reverses all morphisms, i.e. $F(f)$ would be defined as $F(f) : F(x) \leftarrow F(x')$. These are still considered functors, but are referred to as *contravariant* functors. Conceptually, contravariant functors are not distinct from ordinary functors. The reason is that if the morphisms of any category $\mathcal{X}$ are reversed, the result is still a category. This "opposite" category is denoted $\mathcal{X}^{op}$. All contravariant functors $F : \mathcal{X} \to \mathcal{Y}$ may be considered ordinary functors $F : \mathcal{X}^{op} \to Y$. Functors are qualified as contravariant for the sake of discussing them in the context of $\mathcal{X}$, where $\mathcal{X}$ is more germane than $\mathcal{X}^{op}$.

Definition 2.3 (Sheaf)**.** A sheaf is a special kind of contravariant functor. We discuss this terminology in more detail in the final pages of this report. In addition to being a contravariant functor, sheaves satisfy the *sheaf axioms*, which are defined in terms of objects in the domain category and their covering families. The domain of a sheaf must therefore be a small category equipped with a coverage. We refer the reader to [4] for a discussion of coverage and smallness from a purely categorical perspective. In this work, we only consider sheaves whose domain categories have the following conditions: (1) the objects are the open sets of a topological space, (2) there exists a morphism $f : U \to V$ if $U \subseteq V$, and (3) the composition function is captured by the transitivity of the subset relation. A covering family of an open set U in this domain category is a collection of proper subsets of U whose union equals U. This type of domain category category is also small; for conciseness, we will not include justification here beyond noting that the collections of objects and morphisms of this category type are both sets themselves.

The sheaf axioms also impose conditions on the codomain, namely that the objects of the codomain category are expressible as sets. The morphisms between these sets are referred to as *restrictions*. The image of an element $a \in A$ restricted to B is denoted $a|_B$. In this work, the objects of the codomain category are real-valued vector spaces and the morphisms are linear maps between them. Real-valued vector spaces are sets and thus the sheaf axioms can be applied. The motivation and exact definition of the sheaf in this study can be found in §5.

Let $\mathscr{S} : \mathcal{X} \to \mathcal{Y}$ be a sheaf. The sheaf axioms are given below.

1. (Locality) Let V be an object in $\mathcal{X}$ and $\{U_i\}$ be a covering family of V. For any $v, v' \in \mathscr{S}(V)$, if $f_i(v) = f_j(v')$ for all morphisms $f_i : \mathscr{S}(V) \to \mathscr{S}(U_i)$, then $v = v'$, and
2. (Gluing) for any open set V and its covering family $\{U_i\}$, if there exists a union of sections $s := \bigcup_i (s_i \in \mathscr{S}(U_i))$ such that, for all pairs U_i, U_j, $s_i|_{\mathscr{S}(U_i \cap U_j)} = s_j|_{\mathscr{S}(U_i \cap U_j)}$, then there must exist a section $v \in \mathscr{S}(V)$ corresponding to s, i.e. $v|_{\mathscr{S}(U_i)} = s_i$ for all i.

3 Sheaves on Systems of Linear Equations

One of the most widespread techniques in modeling is to represent a system with linear equations. Classical approaches to solving linear equations focus on minimizing the squared sum of residuals. This is global approach minimizes a weighted sum where each element is weighted by its own magnitude. Our approach will find maximal partitions of equations that are self-consistent (within partition). We describe how sheaves can provide unprecedented information on assessing fitness of models described by systems of linear equations.

3.1 Defining a domain category $\mathscr{C}$

We begin with a set, E, whose elements are linear equations, and a set V of the variables constrained by the equations. We use V and E to define the objects of the domain category $\mathscr{C}$. The objects of $\mathscr{C}$ will be open sets in a topologized partial order on V and E. To define the partial order, we let $V_i \leq E_j$ if V_i is a term in E_j. To topologize, we let the star of each element in the partial order be an open set. These initial open sets will generate our topology. As required, we include in the open sets any set that can be generated by the union or finite intersection of the generators to complete the topology τ. We that note every open set $U \in \tau$ has a subset $E(U)$ of equations and a subset $V(U)$ of variables. Note, if $V_i \in V$ is a term in equations $E_p \subseteq E$, any open set U that contains V_i also contains E_p. However, the converse is not necessarily true: if $E_p \subseteq U$, U may not contain V_i.

Finally, we use τ to define the domain category $\mathscr{C}$. We let the objects of $\mathscr{C}$, $Obj(\mathscr{C})$, be the open sets of τ. We let the morphisms be the subset relation. Explicitly, we include a morphism between open sets U_i and U_j iff $U_i \subseteq U_j$. These morphisms are commonly referred to as *inclusions* and denoted $U_i \hookrightarrow U_j$. Finally, the transitivity of the subset relation ensures morphism compositionality.

3.2 Assessment Sheaf $\mathscr{S}$

We define sheaf $\mathscr{S}$, a contravariant functor mapping the domain category, $\mathscr{C}$, into the codomain category, S. The objects of S are solution spaces to the equations in their preimage. Recall each open set U can be partitioned into variables and equations. We will refer to the variables and equation partitions in U as V_U and E_U, respectively. We define $\mathscr{S}$ formally as follows:

$$\mathscr{S}(U) := \{x | \bigwedge_{E_i \in E_U} x \text{ satisfies } E_i\}. \tag{1}$$

The image of U, $\mathscr{S}(U)$, is the solution space of the system of equations described by E_U. We introduce the following notation when discussing the image $\mathscr{S}(U)$, $E(U)$ refers to the equations of the preimage (this is identical to E_U), and $V(U)$ refers to the set of all variables constrained by the equations $E(U)$. Thus, V_U differs from $V(U)$ in that V_U is the set of variables in the open set U and $V(U)$ are the dimensions the solutions to $E(U)$.

To complete the definition of $\mathscr{S}$, we define the image of the morphisms in $\mathscr{C}$. Recall that morphisms in $\mathscr{C}$ are inclusions $U_i \hookrightarrow U_j$. These image of these inclusions are projections from $\mathscr{S}(U_j)$ into $\mathscr{S}(U_i)$. We formally define the projection morphism $\mathscr{S}(f)$ as follows. Let F be a $n \times m$ matrix, where $m = |V(U_i)|$ and $n = |V(U_j)|$. Furthermore, let $v_1, ..., v_m$ be elements of $V(U_j)$. Finally, let $F_{ij} = 1$ iff $v_i \in V(U_i)$ and 0 otherwise. For all $u_i \in \mathscr{S}(U_j)$, the projection of u_i into $\mathscr{S}(U_1)$ is defined as

$$\mathscr{S}(f)(u_i) := Fu_i. \tag{2}$$

This projection maps solutions to $E(U_j)$ in $V(U_j)$ coordinates to solutions to $E(U_i)$ in the smaller set of coordinates $V(U_i)$. For example, let $V(U_i) = \{v_1, v_2, v_3\}$, $V(U_i) = \{v_1, v_2\}$, and $u_i = \{3, 6, 7\}$. Then,

$$F = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix}, \tag{3}$$

and the morphism

$$\mathscr{S}(f)(u_i) = Fu_i = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix} \{3, 6, 7\}^T = \{3, 6\}^T. \tag{4}$$

Morphisms between images are well defined. Let $U_i \subseteq U_j$ be two open sets in $\mathscr{C}$. Since $U_i \subseteq U_j$, there exits an inclusion morphism $f : U_i \hookrightarrow U_j$ between them. As a contravariant functor, $\mathscr{S}$ defines a morphism $\mathscr{S}(f) : \mathscr{S}(U_j) \to \mathscr{S}(U_i)$. As mentioned, the elements in $\mathscr{S}(U_i)$ are solutions to E_{U_i}. Thus, $\mathscr{S}(f)$ maps solutions to $E(U_j)$ to solutions to $E(U_i)$. Since $U_i \subseteq U_j$, $E(U_i) \subseteq E(U_j)$ Therefore, elements of $\mathscr{S}(U_j)$, by satisfying $E(U_j)$, satisfy all $E(U_i)$. The morphism is thus well defined.

Theorem 3.1. *$\mathscr{S}$ is a sheaf.*

Proof. We prove the theorem by establishing that $\mathscr{S}$ is a functor whose image is a category satisfying the sheaf axioms, locality and gluing, explained in Def. 2.3.

Lemma 3.2. *S is a category.*

Proof. For S to be a category, as elaborated in Def. 2.1, the objects and morphisms must be well-defined, and morphisms must be composable. Having defined the objects and morphisms of S, we verify the compositionality of morphisms. Morphisms of S are linear transformations. Composition in S, $\circ$, is therefore inherited from the compositionality of linear transformations.

□

Lemma 3.3. *$\mathscr{S}$ satisfies locality.*

Proof. To prove locality, we must show that, for any open set U and covering family $F := \{U_1, ..., U_j\}$, there cannot be two elements $s, t \in \mathscr{S}(U)$ such that $s|_{\mathscr{S}(U_i)} = t|_{\mathscr{S}(U_i)}$ for all U_i, unless $s = t$. To begin, recall that, by definition of covering family, $\bigcup_{U_i \in F} U_i = U$, and hence $\bigcup_{U_i \in F} V(U_i) = V(U)$. The set $V(U_i)$ must be a subset of $V(U)$, since, if U_i is a member of the covering family, the morphism $U_i \hookrightarrow U$, denoting inclusion, must exist. Hence, all U_i in the family are subsets of U and $V(U_i) \subseteq V(U)$. Elements $s, t \in \mathscr{S}(U)$ are also elements of $\mathbb{R}^n$, with a dimension corresponding to each element in $V(U)$. For any $U_i \in F$, $V(U_i) \subseteq V(U)$, and therefore $s|_{\mathscr{S}(U_i)}$ has a subset of the coordinates of s, and likewise for t and $t|_{\mathscr{S}(U_i)}$. Recall, the morphism $f : \mathscr{S}(U) \to \mathscr{S}(U_i)$ is nothing more than an identity projection from $\mathbb{R}^n$ to $\mathbb{R}^m$, forgetting the variables from $V(U)$ not included in $V(U_i)$. Then when $s|_{\mathscr{S}(U_i)} = t|_{\mathscr{S}(U_i)}$ both s and t must have the same values in the coordinates corresponding to $V(U_i)$. If $s|_{\mathscr{S}(U_i)} = t|_{\mathscr{S}(U_i)}$ is true for all U_i, then s and t must have the same value for all coordinates and $s = t$.

□

Lemma 3.4. *$\mathscr{S}$ satisfies gluing.*

Proof. Given an open set U and a covering family $F := \{U_1, ..., U_k\}$, gluing requires that, for any collection $\hat{s} := \bigcup_{U_i \in F}(s_i \in \mathscr{S}(U_i))$ such that $\forall U_i, U_j \in F$, $s_i|_{\mathscr{S}(U_i \cap U_j)} = s_j|_{\mathscr{S}(U_i \cap U_j)}$, there must exist a $s \in \mathscr{S}(U)$ such that for each $U_i \in F$, $s|U_i = s_i$. Consider an arbitrary variable $v \in V(U)$. Since F is a covering family of U, we know $V(U) = \bigcup_{U_i \in F} V(U_i)$. Then v must be contained in at least one U_i, and there must exist at least one s_i associating a value to v. We denote the value that s_i sets for v as q_i.

By hypothesis, $s_i \in \mathscr{S}(U_i), s_j \in \mathscr{S}(U_j)$, and $s_i|_{\mathscr{S}(U_i \cap U_j)} = s_j|_{\mathscr{S}(U_i \cap U_j)}$ for each $U_i, U_j \in F$. But recall, the morphism $f : \mathscr{S}(U) \to \mathscr{S}(U_i)$ is nothing more than an identity projection from some $\mathbb{R}^n$ to $\mathbb{R}^m$ for $m \leq n$, forgetting the variables from $V(U)$ not included in $V(U_i)$. Then, each s_i containing a value for v must have the same value q_i, otherwise $s_i|_{\mathscr{S}(U_i \cap U_j)} \neq s_j|_{\mathscr{S}(U_i \cap U_j)}$ for each $U_i, U_j \in F$. Since $v \in V(U)$, s must also contain a value for v, and to satisfy the identity morphisms of $\mathscr{S}$, this value must also be q_i.

Since s requires exactly one value for each $v \in V(U)$, by arbitrariness of $v \in V(U)$, we can conform all of s from the q_i values of all v. If, for all v, s has value q_i, then $s|\mathscr{S}(U_i) = q_i$ for each $U_i \in F$ that contains v, and indeed $s|\mathscr{S}(U_i) = s_i$, as desired.

□

By the Lemmas above, $\mathscr{S}$ must therefore be a sheaf. □

Example 3.5. Suppose we have a an S_0 with three objects. Let $A = \{x, y, z|3x + 2y - z = 0\}, B = \{w, x|2w - 5x = 0\}, C = \{x\}$, and $Obj(E_0) = \{A, B, C\}$. As morphisms, we identify the relationship preserving maps as $hom(E_0) = f : A \to C, g : B \to C$. If $a \in A, b \in B$, then we can write $a = [a_x, a_y, a_z], b = [b_w, b_x]$. We define $f(a)$, in essence, as setting specific values for its governing equation. $f(a) = \{x|3x + 2a_y - a_z = 0\}$ and $g(b) = \{x|2b_w - 5x = 0\}$. We hope x restricts to the same value in each, as that indicates that the data is consistent within our objects, and furthermore when we apply our sheaf, by sheaf gluing, implies that x is part of a self-consistent higher order set, containing w, x, y, z.

3.3 Model Assessment

We propose $\mathscr{S}$ as an improved mechanism to measure consistency on linear systems. Traditionally, linear systems are qualified as consistent based on least squares analysis. Least squares works by finding an approximate solution to a linear system that minimizes some norm (typically $L2$) between itself and the solution space. To illustrate, consider the following system of linear equations and data expressed in matrix form. $\begin{bmatrix} 1 & 2 & 3 \\ 2 & 2 & 3 \end{bmatrix} \times \begin{bmatrix} v_1 \\ v_2 \\ v_3 \end{bmatrix} = \begin{bmatrix} 1 \\ 3 \end{bmatrix}$

Definition 3.6 (Sheaf assignment)**.** An assignment, ϕ, is intended to integrate data and measurements into the abstract framework provided by sheaves. Formally, an assignment can be obtained by selecting an element from the Cartesian product of all open set images,

$$\phi \in \prod_{U \in Obj(\mathscr{C})} \mathscr{S}(U). \tag{5}$$

As such, an assignment contains one element from the image of each open set U in the domain category.

Definition 3.7 (Consistency Structure)**.** An assignment that contains values that are compatible under restriction is deemed *consistent*. We define consistency formally as follows. Given a topology τ, an assignment ϕ, and a sheaf $\mathscr{S}$ with domain τ as described in §3.1-3.2, a *consistency structure* is a set of consistency functions that output a Boolean value,

$$\mathcal{X}_U(\phi) \to \{0, 1\}, \tag{6}$$

one for each open set $U \in \tau$.[1] The function $\mathcal{X}_U$ operates on the the elements of ϕ corresponding to $\mathscr{S}(U_i)$, where $\{U_i\}$ conform the *star* of an open set U as defined in §3.1. Specifically, it is a combination

$$\mathcal{X}_U(\phi) : \bigoplus_i \mathscr{S}(U \subseteq U_i)(\phi_i) \to \{0, 1\}, \tag{7}$$

[1]This consistency structure is analogous to the one defined in [6], though they differ in domain.

where $\mathscr{S}(U \subseteq U_i)(\phi_i)$ is the restriction of ϕ_i to $\mathscr{S}(U)$, and $\oplus$ is model-specific. A canonical example[2] is to let $\oplus$ be $\wedge$ (logical *and*) and

$$\mathcal{X}_U(\phi)(\mathscr{S}(U \subseteq U_i)(\phi_i)) = \begin{cases} 1 & \text{if } \mathscr{S}(U \subseteq U_i)(\phi_i) = \phi_U, \text{and} \\ 0 & \text{otherwise.} \end{cases} \tag{8}$$

For this consistency structure, an assignment ϕ is consistent iff the restrictions of all ϕ_i to ϕ_U equal the value of ϕ_U. Variations of this consistency structure might include some tolerance value δ, where

$$\mathcal{X}_U(\phi)(\mathscr{S}(U \subseteq U_i)(\phi_i)) = 1 \text{ if } |\mathscr{S}(U \subseteq U_i)(\phi_i) - \phi_U| \leq \delta. \tag{9}$$

If $\mathcal{X}_U(\phi) = 1$ for all open sets U in the topology τ, then ϕ is consistent.

3.4 Maximal Consistent Subsections

For each $\mathscr{S}(U_i)$ we look at all the incoming restriction morphisms $\{\mathscr{S}(U_j \leq U_i) | U_j \leq U_i\}$. If our consistency function $\mathscr{C}_i$ evaluates to true, we know the stalk $\mathscr{S}(U_i)$ is self consistent within its immediate locale - the preimage of the restriction morphisms we just dealt with will be in the same maximal consistent subsection as the stalk. If $\mathscr{C}_i$ evaluates to false, we know the restriction morphisms are not consistent, and therefore the stalk $\mathscr{S}(U_i)$ is NOT self consistent within its immediate locale - the preimage of the restriction morphisms will not be included in the same maximal consistent subsection as the stalk.

3.4.1 Algorithm

We start at the bottom level of $\mathscr{S}(\mathscr{X})$, the part of the sheaf with no outgoing restriction morphisms. This corresponds to our individual metabolites. We add each individual metabolite to its own consistent subsection , and note at worst, each metabolite is consistent with itself only. Each level, we test to see if restriction morphisms are deemed consistent via our consistency functions, and proceed based on their return value. If true, we add the node to the current consistent subsection, $\mathscr{S}(\Gamma_i)$. If two subsections argue over a node, we merge the subsections. Finally, if false, we stop the algorithm on that branch. A false value means we have determined the largest consistent subsection the measured metabolic data can exist on.

3.5 Residual Analysis

We bring attention to the standard approach for assessing consistency in systems of linear equations - examining the size of residual error compared to an associated expected solution. For a set of equations E, a set of initial variable measurements V, and final measured values for the variables M, residual analysis typically takes the form of a linear algebra problem. From E construct a matrix of equations A, from V define a vector of variables x representing an expected solution, and from M construct a constant vector of measured values b. If an exact solution were to exist, the equation $Ax = b$ would be true. However, to find residual error, the technique is to find an approximate solution by solving a perturbed problem: $A\tilde{X} = b + \Delta b$. The residual vector is defined as $r = b - A\tilde{x}$ and geometrically is the distance from the measured values to the perturbed measured values in the approximate solution.

3.5.1 Assignment

The first step in defining consistency is to generate our original assignment, $(\mathscr{S}, A)$, . Let m be a set of measured values, one measured value attributed to each metabolic variable, and $V(U)$ be the set of metabolic variables in an open set U. Then we designate our assignment as follows: Take $m_v \subset m$, the subset of m such that it associates exactly one value to each $V(U)$. Then we assign $(\mathscr{S}(U), m_v)$. Extending the same process to each open set conforms A.

3.5.2 Error

Since $\mathscr{S}$ maps to some $\mathbb{R}^n$, there is a natural pseudometric on the space of assignments. For some stalk $\mathscr{S}(U)$, and two values assigned to that stalk, a and b, we define the error between stalk assignments as $E((\mathscr{S}(U), a), (\mathscr{S}(U), b)) := d(a, b)$, the euclidean distance between the assignment values. We call this the *error* of $\mathscr{S}(U)$. Recall *definition 2.8*, and notice minimizing error is the foundation for optimizing Consistency Radius.

[2]This is referred to as the standard consistency structure in [6].

3.5.3 Consistency Radius Filtration

We can compute the error on each pair of stalk assignments joined by restriction morphism. This admits a natural filtration on the error of each pair of assignments, where we slowly add objects that are within ϵ error of a given stalk. We say a restriction morphism $f : \mathscr{S}(U_2) \to \mathscr{S}(U_1)$, with corresponding assignments $(\mathscr{S}(U_2), a_2)$ and $(\mathscr{S}(U_1), a_1)$ enters our space at time t if $d(a_1, a_2) = t$.
Remark: An object entering the filtration signifies how well the restriction respects the assignment. In our scenario, an object that enters the filtration early on means the two stalks have compatible data.

Theorem 3.8. *If a global section exists, our measured data is perfectly consistent with all reaction equations.*

Proof. a little bit tougher than the last one □

4 Numerical Example

We provide a simple numerical example to demonstrate the utility of sheaf consistency. We consider the following reactions and rates for our numerical example:

$$A + 2B \to 5C \text{ at rate } r_1 \tag{10}$$
$$A \to 3B \text{ at rate } r_2. \tag{11}$$

4.1 Category of Reactions

The equations governing the metabolite rates of change are

$$E_1 : \Delta A = -r_1 - r_2, \tag{12}$$
$$E_2 : \Delta B = -2r_1 + 3r_2, \tag{13}$$
$$E_3 : \Delta C = 5r_1. \tag{14}$$

The corresponding partial order is defined by letting a variable $V_i \leq E_j$ if V_i is a term in E_j. Our example has the following partial order:

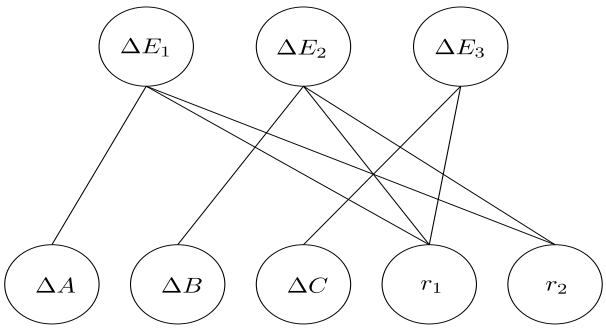

Figure 1: Picture depicting partial order of equations and variables.

We endow this partial order with the upper topology, where the open sets of the topology are the upper sets of each element in the partial order. We note here that all open sets U in the upper topology have the following property: if x is in U, then the upper set of x, $\bigstar(x)$, is also contained in U. Thus, we label our open sets using the smallest number of members whose upper sets conform the set. For example, the open set $\{\Delta A, E_1\}$ is labeled $U_{\bigstar(A)}$, and the open set $\{r_1, \Delta A, E_1, E_2, E_3\}$ is labeled $U_{\bigstar(r_1, \Delta A)}$. Finally, we that note any open set U can be partitioned into a set of variables, denoted V_U, and constraining equations, denoted E_U. The generating open sets for the upper topology are given below:

$$U_{\bigstar(\Delta A)} := E_{U_{\bigstar(\Delta A)}} \cup V_{U_{\bigstar(\Delta A)}} = \{E_1\} \cup \{\Delta A\} = \{E_1, \Delta A\}, \tag{15}$$

$$U_{\bigstar(\Delta B)} := E_{U_{\bigstar(\Delta B)}} \cup V_{U_{\bigstar(\Delta B)}} = \{E_2\} \cup \{\Delta B\} = \{E_2 \cup \Delta B\}, \tag{16}$$

$$U_{\bigstar(\Delta C)} := E_{U_{\bigstar(\Delta C)}} \cup V_{U_{\bigstar(\Delta C)}} = \{E_3\} \cup \{\Delta C\} = \{E_3, \Delta C\}, \tag{17}$$

$$U_{\bigstar(r_1)} := E_{U_{\bigstar(r_1)}} \cup V_{U_{\bigstar(r_1)}} = \{E_1, E_2, E_3\} \cup \{r_1\} = \{E_1, E_2, E_3, r_1\}, \tag{18}$$

$$U_{\bigstar(r_2)} := E_{U_{\bigstar(r_2)}} \cup V_{U_{\bigstar(r_2)}} = \{E_1, E_2\} \cup \{r_2\} = \{E_1, E_2, r_2\}, \tag{19}$$

$$U_{\bigstar(E_1)} := E_{U_{\bigstar(E_1)}} \cup V_{U_{\bigstar(E_1)}} = \{E_1\} \cup \emptyset = \{E_1\}, \tag{20}$$

$$U_{\bigstar(E_2)} := E_{U_{\bigstar(E_2)}} \cup V_{U_{\bigstar(E_2)}} = \{E_1\} \cup \emptyset = \{E_2\}, \tag{21}$$

$$U_{\bigstar(E_3)} := E_{U_{\bigstar(E_3)}} \cup V_{U_{\bigstar(E_3)}} = \{E_3\} \cup \emptyset = \{E_3\}. \tag{22}$$

$$\tag{23}$$

The collection of open sets of a topology is, by definition, closed under union and finite intersection. Thus, we include any set that can be produced by the union or intersection of these generators in the open sets.

Finally, we are ready to define the domain category, $\mathscr{C}$. The objects of $\mathscr{C}$ are the open sets. The morphisms are inclusions, denoted with $\hookrightarrow$. Thus, if $U_1 \subseteq U_2$, then the morphism $U_1 \hookrightarrow U_2$ exists in the category. Transitivity of inclusion ensures morphism compositionality.

4.2 Category of Solutions

We begin our definition of the category of solutions, $S := \mathscr{S}(\mathscr{C})$, by defining objects of S. These are the stalks $\mathscr{S}(U)$ of each open set U. The stalk of U is the set of solutions to the equations in E_U, projected onto the variables in V_U.

For example, the stalk of generator $U_{\bigstar(\Delta A)}$ is the set of solutions to the equations in $E_{U_{\bigstar(\Delta A)}}$ projected onto the variables in $V_{U_{\bigstar(\Delta A)}}$. The set of solutions to $E_{U_{\bigstar(\Delta A)}}$ is the set of solutions to E_1,

$$\{\Delta A, r_1, r_2 \mid \Delta A - r_1 - r_2 = 0\}. \tag{24}$$

The set of variables in $V_{U_{\bigstar(\Delta A)}}$ consists only of ΔA. Therefore, the stalk $\mathscr{S}(U_{\bigstar(\Delta A)})$ of $U_{\bigstar(\Delta A)}$ is

$$\{\Delta A \mid \Delta A - r_1 - r_2 = 0\}. \tag{25}$$

The stalk for $U_{\bigstar(\Delta A)}$ is therefore $\mathbb{R}^1$, since ΔA is unbounded.

In general, stalks projected onto n variables are not n-dimensional. To explain this, we first consider a general stalk $\mathscr{S}(U)$. The elements of this stalk are the solutions the equations $E_i \in E_U$. All equations will have the form

$$E_i := \sum_k r_k + \Delta X = 0, \tag{26}$$

wherein they are expressed as the sum of several rates and a single change in metabolite X. The equations in of E_U define a system of linear equations, typically expressed in matrix form. For example, if we let $E_U := \{E_1, E_2\}$ in our continuing example, the matrix form would be

$$\begin{array}{c} \\ E_1 \\ E_2 \end{array} \begin{array}{c} \begin{array}{cccc} r_1 & r_2 & \Delta A & \Delta B \end{array} \\ \begin{pmatrix} 1 & 2 & 1 & 0 \\ 2 & -3 & 0 & 1 \end{pmatrix} \end{array} \begin{pmatrix} r_1 \\ r_2 \\ \Delta A \\ \Delta B \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}. \tag{27}$$

matrix that has the stoichiometric coefficients. This quantity is at least the number of columns of the matrix minus the number of rows. If all the rows are linearly independent, these two quantities are equal by the fundamental theorem of linear algebra. The rows of any E_U will always be linearly independent, since each E_i corresponds to a single metabolite, which implies its row will have a unique term. Thus, the dimension of any stalk is at most the number of columns minus the number of rows. If V_U is larger than this quantity, then the stalk will be a subspace of its ambient space.

For example, consider the stalk $\mathscr{S}(U_{\bigstar(r_1,r_2,\Delta C)})$, conformed of the points

$$\left\{ r_1, r_2, \Delta C \;\middle|\; \begin{array}{r} \Delta A + r_1 + r_2 = 0 \\ \Delta B + 2r_1 - 3r_2 = 0 \\ \Delta C - 5r_1 = 0 \end{array} \right\}. \tag{28}$$

The corresponding matrix is

$$\begin{array}{c} \\ E_1 \\ E_2 \\ E_3 \end{array} \begin{array}{c} \begin{array}{ccccc} r_1 & r_2 & \Delta A & \Delta B & \Delta C \end{array} \\ \begin{pmatrix} 1 & 2 & 1 & 0 & 0 \\ 2 & -3 & 0 & 1 & 0 \\ -5 & 0 & 0 & 0 & 1 \end{pmatrix} \end{array} \tag{29}$$

Thus, the solutions to the linear system in Eq. 28 lie on a two-dimensional plane. Because we consider three variables, variables r_1, r_2 and ΔC, the resulting space is not $\mathbb{R}^3$.

Open sets with n participating reaction variables are sent to $\mathbb{R}^n$ and inclusion morphisms are sent to restrictions, where restrictions in essence set values of variables. The following is an example path of restrictions. We denote an open set that contains equations E_1, E_2 and V_1, V_2 as $U_{\{E_1,E_2,V_1,V_2\}}$.

$$\mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,\Delta B,\Delta C,r_1,r_2\}}) \to \mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,\Delta B,r_1,r_2\}}) \to \mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,r_1,r_2\}}) \tag{30}$$

$$\to \mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,r_1\}}) \to \mathscr{S}(U_{\{E_1,\Delta A\}}) \tag{31}$$

Assignment
Suppose we are given some measured data.

$$\begin{aligned} \Delta A &= -10 \\ \Delta B &= 15 \\ \Delta C &= 8 \\ r_1 &= 2 \\ r_2 &= 7. \end{aligned}$$

We want to see if this data is consistent with our model. From, the data is consistent if and only if the assignment yields a global section. To do verify if this global section exists, we propagate the initial assignment through the entirety of S by applying restriction morphisms. Following (20), applying the measured values to restricted stalks, we get

$$\begin{aligned} &\mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,\Delta B,\Delta C,r_1,r_2\}}) = \\ &\{(\Delta A, \Delta B, \Delta C, r_1, r_2) \in \mathbb{R}^5 : \Delta A + r_1 + r_2 = 0, \Delta B + 2r_1 - 3r_2 = 0, \Delta C - 5r_1 = 0\} \\ &\mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,\Delta B,r_1,r_2\}}) = \\ &\{(\Delta A, \Delta B, r_1, r_2) \in \mathbb{R}^4 : \Delta A + r_1 + r_2 = 0, \Delta B + 2r_1 - 3r_2 = 0, 8 - 5r_1 = 0\} \\ &\mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,r_1,r_2\}}) = \{(\Delta A, r_1, r_2) \in \mathbb{R}^3 : \Delta A + r_1 + r_2 = 0, 15 + 2r_1 - 3r_2 = 0, 8 - 5r_1 = 0\} \\ &\mathscr{S}(U_{\{E_1,E_2,E_3,\Delta A,r_1\}}) = \{(\Delta A, r_1) \in \mathbb{R}^2 : \Delta A + r_1 + 7 = 0, 15 + 2r_1 - 21 = 0, 8 - 5r_1 = 0\} \\ &\mathscr{S}(U_{\{E_1,\Delta A\}}) = \{(\Delta A) \in \mathbb{R} : \Delta A + 2 + 7 = 0\} \end{aligned}$$

4.3 Consistency

Each stalk $\mathscr{S}(U)$ has a corresponding assignment, a, representing measured data. We can gauge the consistency of a given assignment by comparing values obtained by restricting to $\mathscr{S}(U)$ with a. There are two cases that arise - comparing defined systems, and comparing underdefined systems.

Defined Systems Let $U = U_{E_1,\Delta A}$ be the open set of ΔA. Then its assignment is the solution of its governing reaction equations, in this case just E_1. Then $\mathscr{S}(U) \to -9$ is the assignment. However, there are other stalks that restrict down to $\mathscr{S}(U)$. Consider the open set $V = U_{E_1,E_2,E_3,r_1}$. Then again we attempt to solve the equations to find the assignment for the $[\Delta A, r_1]$ solution vector. In this case, we have an overdefined system, so we average associated to E_1 by summing the errors from each metabolite and rate. First, we consider treating ΔA as a variable, and use the sheaf morphisms to find its assignment, i.e., $\Delta A = -2 - 7 = -9$. Thus, our first error is $|\Delta A - \mathscr{S}(A)| = 1$. We can repeat the process, and we find $-10 = -r_1 - 7 \Rightarrow -r_1 = 3$ so that the error from r_1 is also 1. Finally, $-10 = -2 - r_2 \Rightarrow r_2 = -8$, so the error from r_2 is 1. Summing these errors together gives us the total error for E_1, which is 3.

We can repeat the process for E_2. Succinctly put,

$$\begin{aligned} &\Delta B = -2(2) + 3(7) \Rightarrow \Delta B = 17 \text{ so that error from } \Delta B \text{ is} |15 - 17| = 2 \\ &15 = -2r_1 + 3(7) \Rightarrow r_1 = 3 \text{ so that error from } r_1 \text{ is } |2 - 3| = 1 \\ &15 = -2(2) + 3(r_2) \Rightarrow r_2 = 6.\overline{33} \text{ so that error from } r_1 \text{ is} |6.\overline{33} - 7| = 0.\overline{66} \end{aligned}$$

Summing these errors, we find the total error from E_2 to be $2 + 1 + 0.\overline{66} = 3.\overline{66}$.

Finally, we consider the error for E_3. We have

$$\Delta C = 5(2) \Rightarrow \Delta C = 10 \text{ so that error from } \Delta B \text{ is } —8 - 10— = 2$$
$$8 = 5r_1 \Rightarrow r_1 = 1.6 \text{ so that error from } r_1 \text{ is } —2\text{-}1.6— = 0.4$$

Summing these errors, we find the total error from E_3 is $2 + 0.4 = 2.4$.

4.4 Pieces

Finally, in set notation, the solutions to the equations are:

Definition 4.1 (Poset)**.** A *poset* (partially ordered set) is a pair $(X, \leq)$, where X is a set and $\leq$ is a binary relation on X such that for all $a, b, c \in X$,

1. $a \leq a$ (reflexive)
2. if $a \leq b$ and $b \leq a$, $a = b$ (anti-symmetric)
3. if $a \leq b$ and $b \leq c$, $a \leq c$ (transitive)

Definition 4.2 (Star/Upper Set)**.** Let $(X, \leq)$ be a poset, and $x \in X$. Then define $x_\star = \{y \in X | x \leq y\}$. We call $\star(x)$ the star of x. Note, $\star(x)$ is the smallest upper set containing x.

Definition 4.3 (Consistency Radius)**.** There is a natural pseudometric on the space of assignments. If $a, b \in S$, the distance $C(a, b) = \sup_{U \in \tau} d(a(U), b(U))$. This places a tight upper bound on the difference in values between two corresponding stalks in $\mathscr{S}$. We call this distance the consistency radius.

Definition 4.4 (Metabolic Network)**.** A metabolic network describes the interconversion of biologically relevant molecules necessary for a cell to function. These molecules are commonly referred to as metabolites. Metabolites are either be broken down (for energy or raw materials) or synthesized (to build new cell components) as part of meteabolism. The collection of metabolites and the chemical reactions, often catalyzed by enzymes, that connect them conform a metabolic network.

Definition 4.5 (Stoichiometric Matrix)**.** The chemical reactions of a metabolic network have a stoichiometric description which details the quantities of metabolites produced and consumed by a single iteration of the reaction. For example, a reaction R_1 which breaks down a single molecule of metabolite A into 2 molecules of B and three molecules of C has the following stoichiometric description:

$$A \to 2B + 3C. \tag{32}$$

A collection of reactions can be organized into a stoichiometric matrix. The matrix has one column for each reaction and one row for each metabolite that participates in at least one of the reactions. Assuming a second reaction R_2 with the following stoichiometric description,

$$C \to D, \tag{33}$$

we may define a stoichiometric matrix as follows:

$$\begin{array}{c} \\ A \\ B \\ C \\ D \end{array} \begin{array}{c} \begin{array}{cc} R_1 & R_2 \end{array} \\ \begin{pmatrix} -1 & 0 \\ 2 & 0 \\ 3 & -1 \\ 0 & 1 \end{pmatrix} \end{array}. \tag{34}$$

Note that the metabolites that are consumed in the reaction are given negative coefficients, and those that do not participate in the reaction are given a zero coefficient.

5 Application

The stoichiometric relationships of a metabolic network can be encoded in a sheaf. Using a sheaf allows us to leverage the structure of the metabolic network to identify the measurements that agree locally and evaluate how well the measurements agree globally. To define our metabolic sheaf, we will first define a domain category $\mathscr{C}$. We will then define the functor $\mathscr{S}$ from $\mathscr{C}$ into the codomain category S.

5.1 Domain Category, $\mathscr{C}$

We will begin by defining two sets: E and V. To define E, we must first provide the equation for computing the net change in metabolite m as a function of the rate at which reactions produce or consume it. We can calculate the rate of change per unit time Δ_m as follows:

$$\Delta_m = \sum_k r_k s_{mk}, \tag{35}$$

where r_k is the frequency per unit time of reaction k producing s_{mk} units of metabolite Δ_m. Rewriting Eq. 35 so all the terms are on the left hand side we obtain

$$\left(\sum_k r_k s_{mk}\right) - \Delta_m = 0. \tag{36}$$

The set E is the collection of equations for all metabolites m; hence, the number of elements in E is equal to the number of metabolites in our network. We are now ready to define V. Since both r_k and Δ_m are variables in Eq. 36, we will use the generic term "variable" to refer to either a reaction rate or a metabolite rate of change. V is the set of all variables, so the number of terms in V is equal to the sum of the number of metabolites and the number of reactions of our network.

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