Information topology identifies emergent model classes

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We introduce the concept of information topology by considering the information geometry of models of the same physical system under different experimental conditions. By varying the experimental conditions, statistical inference imposes different metrics on the system’s parameter space, leading to different geometric properties, such as distance and curvature. Experimental conditions that preserve the structural identifiability of the parameters are related by diffeomorphisms and form an information topology. Experimental conditions that lead to a manifold collapse correspond to a different topology and require a modification of the underlying theory in order to construct a model whose parameters are identifiable (either structurally or practically). For many models the relevant topological feature is a hierarchical structure of boundaries (faces, edges, corners, etc.) which we represent as a hierarchical graph. The tips of this hierarchical graph correspond to dominant modes that govern the macroscopic, collective behavior of the system. We refer to these modes as emergent model classes. When new parameters are added to the model, we consider how the simple, original topology is embedded in the new, larger parameter space. When the emergent model classes are unstable to the introduction of new parameters, we classify the new parameters as relevant. In contrast, model classes are stable to the introduction of irrelevant parameters. In this way, information topology provides a unified mathematical language for understanding the relationship between experimental data, mathematical models, and the underlying theories from which they are derived and can provide a concrete framework for identifying an appropriate representation of a physical system.

I. INTRODUCTION

Mathematical modeling is a central component of nearly all scientific inquiry. From an information theoretic perspective, the utility of mathematical modeling is the formal process by which information from experiments is encoded into a physical theory that allows precise, quantitative predictions for potential, new experiments. The appropriate representation of a physical system depends not just on the intrinsic nature of the system, but also the questions one wishes to ask about it. Since different experimental probes of the same system have different information content, it is unreasonable to expect the same model to be equally useful for describing all experimental conditions. Recently it has been suggested that the general success of effective models and emergent theories can be attributed to an information theoretic “parameter space compression” [1]. When the experimental probes of a system are coarsened, microscopic details arrange themselves in a hierarchy of decreasing importance. It has also been shown that this compression can be used to explicitly construct simplified models of complex systems to reveal the emergent physics governing its behavior [2].

From this perspective, the questions of the nature and origin of emergence depends as much on the choice of experiments as it does on the intrinsic nature of the system itself. Since different experimental conditions lead to different information, it is natural that the encoding of that information, i.e. which mathematical model or system representation, should be customized to the choice of experiments. As an extreme example, although we expect that the properties of any macroscopic system to ultimately derive from properties of the fundamental particles that make it up, encoding that behavior in terms of those fundamental particles is neither efficient nor illuminating. In general, a complete microscopic formulation of a system requires an unreasonable amount of information and poses numerous computational and analytical challenges. A fundamental question in many fields of scientific inquiry, including materials research, systems biology, climate, and economics, is what is the appropriate representation of the system. It is often accepted that the simplest model is the best (provided it is sufficiently accurate) as it communicates the relevant information in the most efficient way while avoiding any unnecessary complications. In this paper we develop a general mathematical formalism, which we call Information Topology for describing the informational relationships among experiments, mathematical models, and the underlying theories from which they are derived.

We define a model to be a probability distribution for the outcome of an experiment or collection of experiments, \( P(\xi) \). Here \( P \) represents the probability of observing some outcome \( \xi \). This is a very restrictive definition that interprets even slightly different experimental conditions as different models. Functionally, this definition can be understood as a computational algorithm for making predictions at specific experimental conditions. More generally, we are interested in families of models, represented as parameterized probability distributions \( P(\xi, \theta) \), where \( \theta \) is an \( N \)-dimensional vector of parameters. Infor-
mation from experiments then become encoded as trust regions for statistically-inferred parameter values.

The formulation of a specific model family $P(\xi, \theta)$ occurs when more abstract physical principles are applied to the specific experimental conditions of interest. For example, a systems biology model formulated as a set of coupled differential equations is constructed from a knowledge of the participating biochemical reactions. The information about the chemical reactions constitute the physical principles from which specific models may be derived. Different experimental conditions, e.g., which reactants are actually present, lead to different mathematical models derived from the same underlying theory. Unlike the abstract principles, the models give precise, mathematical predictions for real experiments, e.g., at what time points to measure which concentrations with what accuracy. The underlying theory, in contrast, provides the rules for constructing mathematical models of specific conditions.

Although the underlying principles may be colloquially referred to as a model, in this work we refer to them as the underlying theory as they are functionally distinct from our definition of model given above. Note that the underlying theory gives rise to a whole class of models, depending on the experimental conditions. This class of models is not necessarily the same as the family of models related through the parameters $\theta$. In general, we can partition the parameters into two sets, those parameters specific to experimental conditions and those connected to the underlying theory. In this work, we assume that the parameters $\theta$ reflect the specifics of the underlying theory and that any parameters related to experimental conditions have been subsumed into the definition of $P(\xi, \theta)$.

With these definitions, we can formalize the process by which information from experiments is related to the information content of models and in turn the underlying theory. This process is statistics, which unites theory and experiment into the problem of parameter inference. Most of the relevant questions are therefore equivalent to a parameter inference problem. That is, what constraints do experimental results place on parameter values and vice versa. A powerful language for studying these relationships is information geometry, i.e., the application of differential geometry to statistics\cite{3,12}. Through the parameters $\theta$, the mathematical model $P(\xi, \theta)$ is equivalent to a mapping between parameters (i.e., physical principles) and data, so interpreting a model as a manifold embedded in data space is a natural construction. In this paper we show that as the experimental conditions are altered, so are many of the specific geometric properties (such as distance, curvature, etc.). However, models originating from the same underlying theory, share a unifying topological structure. Thus, if information geometry is the equivalent to a particular statistical model, information topology is equivalent to the corresponding underlying theory. This relationship is graphically illustrated in figure 1.

To make this concept more concrete, we here consider the concept of identifiability of a statistical model. In general, there are two classes of identifiability issues, structural and practical. Structural identifiability refers to the potential to accurately infer unique parameter values from a model given an infinite number of repeated experiments with perfect data, i.e., data accurately described by the model. Structural identifiability is further categorized as either global or local. Global identifiability means that the inferred parameters are unique when considering the entire domain of physically relevant parameters. Local identifiability, on the other hand, means that there exists in parameter space an open neighborhood centered on the inferred parameters in which the inferred parameters are unique\cite{13,14}.

Local identifiability is closely related to the Fisher Information Matrix (FIM):

$$g = \left\langle \left( \frac{\partial \log P}{\partial \theta} \right)^2 \right\rangle = \left\langle \left( \frac{\partial^2 \log P}{\partial \theta^2} \right) \right\rangle,$$

where $\langle \cdot \rangle$ means expectation with respect to the model. It can be shown that a model is locally identifiable at parameter values $\theta$ if and only if the FIM is non-singular at $\theta$\cite{19}. Qualitatively, a locally non-identifiable model has redundant parameters so that the parameter values can be changed in a coordinated way such that the predictions of the model are unchanged. The null space of

![Image](317x569 to 562x740)

**FIG. 1: Information Topology and Underlying Theories** An underlying theory is defined by a parameter space. Applying the physical principles of such a theory to precise experimental conditions leads to a family of statistical models and imposes a metric on the theory’s parameter space. This family of models can be interpreted as a statistical manifold embedded in the space of all possible experimental outcomes and is the domain of information geometry. Changing the details of the experimental conditions leads to different models with the same parameter space but different metrics and by extension different model manifolds. Experimental conditions that do not change the key structural characteristics of the manifold form an information topology description of the underlying physical theory from which they arise.
the FIM is precise linear subspace in which parameter values can be shifted without changing the model.

The other type of identifiability is practical. Although it may be in principle possible to uniquely identify true parameter values, in practice the number of repeated experiments necessary to obtain a reasonable estimate may be unweidy. Practical non-identifiability is also related to the FIM through the Cramer-Rao inequality:

\[ \text{Cov}(\hat{\theta}) \geq g^{-1}/n, \]  

(2)

where \( \text{Cov}(\hat{\theta}) \) is the asymptotic covariance matrix of an unbiased estimator \( \hat{\theta} \) and \( n \) is the number of repeated samples. If the FIM is not singular but approximately so, it may take an unreasonable sample size, i.e., large value of \( n \), to obtain accurate estimates.

It is not uncommon, particularly in models with many parameters, for the FIM to be poorly conditioned leading to practical identifiability problems, a phenomenon known as sloppiness[18, 21]. When this occurs, one possible solution is the repeated application of experimental design techniques[20, 22–29]. The basic strategy is to selectively choose experiments with complementary information content so as to systematically remove the small eigenvalues in the FIM. Alternatively, as mentioned above, it has been suggested that the lack of information in macroscopic or coarsened experimental data may be the underlying cause for the general success of effective models and emergent theories[1]. Previously, using the geometric interpretation of information theory, it has been shown that simple, reduced models can often be systematically constructed by identifying the boundaries of a very thin model manifold[2].

In the next section, we expand on the concept of information topology, in which different models (i.e., different experimental conditions) originating from a common underlying theory have a common structure that is invariant to a restricted class of experimental conditions (diffeomorphisms, i.e., differentiable mappings). Experimental conditions which lead to structural changes in the manifold, what we call manifold collapse, require modified underlying theories in order to formulate identifiable models (section III). In section IV, we show that topological structure of an underlying theory can be graphically represented as a hierarchical graph. This visualization naturally leads to a reinterpretation of the model parameters in terms of refining approximations to more general model classes. Topologically, these model classes correspond to hyper-corners of the model manifold and are the reduced models found in reference[1]. In section V, we consider how topologies are embedded within one another as new parameters are added to a model, allowing us to identify stable and unstable model classes and classify parameters as either relevant or irrelevant.

II. INFORMATION TOPOLOGY AND MATHEMATICAL MODELING

The basic principle behind the geometric interpretation is that the FIM in Eq. (1) can be interpreted as a Riemannian metric tensor. (Although we use the FIM as the measure of distance throughout this paper, our results generalize to any distance measure among models as we discuss in the supplement.) A model, i.e., the realization of an underlying theory applied to specific experimental conditions, is therefore equivalent to a Riemannian manifold. We present here four simple illustrative examples that will then serve to highlight the principles we explore throughout this paper.

First, we consider a model as the sum and difference of exponentials:

\[ \xi_i(\theta_1, \theta_2) = \left\{ \begin{array}{ll}
    e^{-\theta_1 t_i} + e^{-\theta_2 t_i} + z_i & 1 \leq i \leq M_s \\
    e^{-\theta_1 t_i} - e^{-\theta_2 t_i} + z_i & M_s < i \leq M_s + M_d
\end{array} \right. \]  

(3)

where \( z_i \) is normally distributed random variable with zero mean and standard deviation \( \sigma_i \) and \( M_s \) and \( M_d \) are the number of observations of the sum and differences respectively. This model could describe, for example, the radioactivity of a sample with two radioactive components in the case it is possible to distinguish between the two types of radiation, i.e., it is possible to measure both the total radiation and the difference in radiation types as in Eq. (3).

Here the time points \( t_i \) and experimental accuracy \( \sigma_i \) are the specific experimental conditions that lead to different manifolds. For a fixed choice of \( t_i \) and \( \sigma_i \), varying the two parameters \( \theta_1 \) and \( \theta_2 \) define a statistical manifold. Distance on this manifold is defined by how much data it would take to distinguish two sets of parameter values. Manifolds of this sort can be visualized in a way to approximate the geometry of the actual manifold. We discuss the process for generating visualizations in the supplemental material.

For the model in Eq. (3), two different realizations (i.e., different choices of \( t_i \) and \( \sigma_i \)) are given in Figures 2 and 3. Specifically, both manifolds correspond to a sampling of time points logarithmically spaced between 0.1 and 10. Figure 2 corresponds to \( \sigma_i = 1 \) for all values of \( i \) while Figure 3 has \( \sigma_i = 1 \) for \( i < M_s \) and \( \sigma_i = 1/2 \) for \( i > M_s \). Notice that since the precise experimental conditions that led to Figures 2 and 3 are different, many important geometrical features of the manifolds are also different (distances, curvatures, etc.). However, because these manifolds are ultimately derived from the same underlying theory, they share important structural characteristics. Specifically in this case, they are both topologically equivalent to a square.

Next, we consider two different generalizations of the Ising model, a canonical model from statistical mechanics. The typical Ising model is formulated with two parameters corresponding to the two relevant parameters under a renormalization group coarsening and which de-
FIG. 2: Exponential Model Visualization. A visualization of the model manifold described by Eq. (3) for one possible realization of the experimental conditions. An alternative realization is given in Figure 3.

FIG. 3: Alternate Exponential Model Visualization. An alternative realization of the model described by Eq. (3) with different experimental conditions that those that led to Figure 2. Notice that by changing the experimental conditions, the extrinsic properties of the model manifold may change. The manifold may stretch and bend, but the manifold remains topologically equivalent to a square.

fine the associated universality class. Microscopically, however, models within this universality class are very different. We give two different microscopic formulations that serve to illustrate how these differences are systematically compressed into the same macroscopic universality class. The two models we consider here are defined by the Hamiltonians

\[ H = - \sum_i J_i s_i s_{i+1}, \]  

(4)

and

\[ H = - \sum_{i, \alpha} J_\alpha s_i s_{i+\alpha}. \]  

(5)

In Eqs. (4) and (5), \( s_i \) are spin random variables arranged in a one-dimensional chain that can take values \( \pm 1 \). The probability of a particular configuration is then given by a Boltzmann distribution

\[ P \propto e^{-H}, \]  

(6)

where we have taken \( k_B T = 1 \) and the normalization is determined by summing all the states.

The parameters \( J_i \) in Eq. (4) are the site-specific nearest neighbor coupling of the magnetic moments \( s_i \). This corresponds to a microscopic model of an inhomogeneous magnet with short range interactions. On the other hand, the parameters \( J_\alpha \) in Eq. (5) are the nearest and second nearest neighbor coupling of the magnetic moments. This corresponds to a homogeneous magnet with long range interactions. A visualization of the model manifold for Eq. (4) is given in Figure 4 for the case of three spins and two parameters. The model manifold for Eq. (5) is given in Figure 5 for the case of two parameters and four spins with periodic boundary conditions. Because these models are derived from different underlying principles, the topological features are different (a square vs. a triangle).

A final example is drawn from biochemistry, an enzyme-substrate reaction: \( E + S \leftrightarrow ES \rightarrow E + P \). Modeled as three mass-action reactions, the time-dependence of the concentration of each chemical species is determined by the set of differential equations

\[
\frac{d}{dt}[E] = -k_f[E][S] + k_r[ES] + k_{\text{cat}}[ES] \\
\frac{d}{dt}[S] = -k_f[E][S] + k_r[ES] \\
\frac{d}{dt}[ES] = k_f[E][S] - k_r[ES] - k_{\text{cat}}[ES] \\
\frac{d}{dt}[P] = k_{\text{cat}}[ES].
\]  

(7-10)

We take the data to be the values of each of the chemical species at various times with added random Gaussian noise of variable size. This model has three parameters, the three reaction rates \( k_f, k_r, k_{\text{cat}} \), so that the model manifold represents a volume rather than a surface as in
conditions are chosen to be a known mixture of colors that enclose this volume. Initial conditions this structural identifiability of the parameters in the underlying theory will be preserved (at least locally). To answer this question, we use the fact that a model is locally structurally identifiable, if and only if the FIM is non-singular. Therefore, structural preserving experimental conditions can distort the distances measured on the model manifold provided there are no new singularities introduced into the metric tensor. Topologically, these types of transformations are known as diffeomorphisms, i.e., differentiable transformations of the model manifold.

Notice that each of the manifolds in Figures 2-6 are bounded by edges which are in turn bounded by corners. Thus, we restrict our attention to experimental conditions that are diffeomorphic to those in these figures, then this hierarchical structure of boundaries and edges will be preserved. This suggests that the hierarchical boundary structure is a feature of the underlying theory and not of the specific experimental conditions. Indeed, we now give explicit formulas and interpretations for each of these limits and find that these boundaries always represent an extreme limit of the principles in the underlying theory.

The simplest example is in Figures 2-4 in which the model manifold is diffeomorphic to a square. The limits of the four edges correspond to either of the parameters reaching their physically limiting values individually: $\theta_\mu \to \infty$ or $\theta_\mu \to 0$. Because these limits act on the underlying physical principles, it is not difficult to ascribe a physical interpretation to these edges. They are the cases in which one of the radioactive species either decays instantly or not at all relative to the experimental time scales.

The generalized Ising model in Eq. (4) (depicted graphically in Figure 4) is likewise diffeomorphic to a square. The four limiting cases are likewise each of the two parameters reaching the limits of their physically relevant values: $J_\mu \to \pm \infty$. These limits physically correspond to perfect, local ferromagnetism or anti-ferromagnetism between two particular spins.

Now consider the generalized Ising model in Eq. (5) and visualized in Figure 5. This model manifold is diffeomorphic to a triangle. Because this model is constructed to be translationally invariant, it is natural to consider a Fourier transform of the spins as in [reference, supplement]. One limiting case corresponds to the limit of $J_1 \to \infty$, $J_2 \to -\infty$ such that $J_1 + 2J_2 \to \text{finite}$. This limit corresponds to the case in which only states with no high-frequency component occur and is a ferromagnetic limit (high-frequency oscillations in the spins correspond to anti-ferromagnetic order). Another limit occurs when $J_1 \to \infty$, $J_2 \to -\infty$ such that $J_1 - 2J_2 \to \text{finite}$ and corresponds to the case of no low-frequency oscillations in the spins, i.e., an anti-ferromagnetic limit. Finally, the limit $J_2 \to \infty$ with $J_1$ remaining finite and corresponds to the limit of no mid-frequency oscillations, i.e., a mixture of ferro and anti-ferromagnetic domains.

Finally, the five surface boundaries of the enzyme-substrate reaction correspond to the limits $k_r \to 0$, i.e., the first reaction is no longer reversible (green surface in Figure 4). The red surface in Figure 4 corresponds to...
k_r, k_c \to \infty \text{ such that } K = k_c/k_r \text{ remains finite, interpreted as the case in which the first reaction is always in equilibrium. Evaluating this limit is one way in which the form of the famous Michaelis-Menten reaction can be obtained as we discuss below. The blue surface in Figure 6 corresponds to } k_{cat} \to 0, \text{ i.e., the second reaction does not occur. The yellow surface corresponds to } k_f \to 0, \text{ i.e., the first reaction proceeds only in the backwards direction. The purple surface correspond to the limit } k_r, k_{cat} \to \infty \text{ such that the ratio } k_r/k_{cat} \text{ remains finite, corresponding to the case that the intermediate complex [ES] never accumulates. We will find in section [IV] that, by interpreting these limits and their topological relationship, the model can be reparameterized in a way to reflect the emergent hierarchical structure of the model.}

III. MANIFOLD COLLAPSE LEADS TO CHANGES IN MODEL STRUCTURE

We now consider how the analysis described in section II changes when the choice of experiments alters the topological structures of the manifolds. Since the models in section II were constructed to be identifiable, a structural change here corresponds to a coarsening of the information content. In most cases, this corresponds to simply not observing some of the potential model predictions. In the language of mathematical probability, this means the distribution is marginalized over a subset of the random variables resulting is a coarse-grained set of observations. Geometrically, the corresponding manifolds are compressed along specific directions that depend on which predictions are marginalized. In this way, manifolds may be compressed, folded, or edges may be glued together. On the other hand, reversing this process can result in manifolds that are stretched or torn.

Consider the exponential model introduced above in Eq. (3) in the limit in which the difference in the exponential terms are not observed. This occurs if the specific radioactive products of the two decay channels are indistinguishable, of if the experimental cost of observing the difference is prohibitive so that the experiment is not performed. In this case, Eq. (3) is modified to be

$$\xi_i(\theta_1, \theta_2) = e^{-\theta_1 t_i} + e^{-\theta_2 t_i} + z_i. \quad (11)$$

The manifold of this model is given in Figure 7. Notice that the topological structure of the manifold is fundamentally different from that in Figures 2 and 3 corresponding to a change in the underlying physical theory. The relationship between the coarsened manifold and the original manifold is illustrated by the colored lines in Figures 7 and 8. In effect, the manifold has been folded in half such that the two white lines in Figure 8 are identified with each other and correspond to the white line in Figure 7. Similarly for the blue, green and red lines. The black line is the “fold line.”

FIG. 7: Coarse-grained Exponential Model. If only the sume of the exponential terms is observed, then the model manifold is structurally different from that in Figures 2 and 3; it is now a square. The topological change reflects a change in the information content of the underlying theory and manifests itself as a structural non-identifiability in the resulting model.

FIG. 8: Full Exponential Model showing which points will be identified under coarse-graining. In transitioning from the manifolds in Figures 2 and 3, the (square) manifold is effectively folded in half to produce the triangle structure in Figure 7. Here, lines of the same color on the original topology become identified with each other after coarsening. The black line corresponds to the fold line.

The black “fold line” in Figures 7 and 8 corresponds to the curve for which $\theta_1 = \theta_2$ in the model. This line is significant because for the coarsened model in Eq. (11), the Fisher Information is singular along this line. This singularity is the mathematical indication of the corresponding structural change. For all other points on the model, the Fisher Information remains nonsingular, so that the model is still structurally identifiable in the local sense almost everywhere. However, the model is no longer globally identifiable since each point on the manifold corresponds to two points in parameter space.

The structural change illustrated in Figures 7 and 8 corresponds to a change in the principles governing the underlying theory. This change is a loss of information regarding the distinguishability of the radioactive products.
In order to construct an identifiable model, the underlying theory must be modified. In this case, the physical domain of the parameters can be restricted to $\theta_1 > \theta_2$, i.e., we arbitrarily order the parameters so that they cannot be identified with a specific radioactive agent.

Now consider the generalized Ising model in Eq. (4). For the specific case of three spins visualized in Figure 4, we now consider the effect of observing only spins one and three and marginalizing the distribution over spin two. This corresponds to a typical Renormalization Group (RG) coarsening operation. In this case, the two dimensional manifold in Figure 4 collapses to a one-dimensional curve. The nature of this collapse is illustrated by the colored lines in Figure 9. After marginalizing the distribution, the colored lines each collapse to a single point. Additionally, the manifold is “folded up” so that the disconnected lines of the same color in Figure 4 each map to the same point. That is, the blue line near the top and near the bottom each collapse to a single point and the manifold is folded in half to identify these points similar to the folding in the exponential model.

It is interesting to consider the effect on the standard Ising model corresponding to $J_1 = J_2$ in Eq. (4). This one-dimensional curve is illustrated by the black line in Figure 9. Notice that it is folded in half by the coarse-graining.

Since the previously two-dimensional manifold is collapsed to a one-dimensional curve, the FIM matrix is singular for all parameter values upon coarsening. Thus the new model is structurally non-identifiable. The underlying theory must be modified in order to construct an identifiable model. In this case, the information lost is the nature of the short-range interactions. Are they ferro-magnetic or anti-ferromagnetic? After coarsening, the answer to this question is forever lost. As shown in reference [], the new model can be exactly represented by an effective interaction between spins one and three:

$$H = -\tilde{J}s_1s_3.$$  \hspace{1cm} (12)

We quantify this effective interaction with renormalized parameter $\tilde{J}$. The origin of this interaction is understood to be mediated by the microscopic interactions described by $J_1$ and $J_2$ which now cannot be identified.

The generalized Ising model in Eq. (5), however, coarsens in a different way. We begin by marginalizing the distribution in nearly the same way. We observe only spins one and three, ignoring spins two and four. The two dimensional surface in Figure 9 then collapses to a one dimensional curve. The details of this collapse are illustrated in Figure 10 in which lines of a single color collapse to a single point. Notice that the manifold is not “folded” in same way as that in Figure 9. Indeed, two edges of the triangle are simply brought together and the third edge is collapsed to a point. Considering the curve $J_2 = 0$ (given by the black line in Figure 10), which corresponds to the standard Ising model, we see that this curve is in fact folded in half, just as it was in Figure 9.

As noted before, although they belong to the same universality class, these two generalized Ising models are microscopically very different. Specifically, Eq. (4) corresponds to a inhomogeneous magnet with short-range interactions, while Eq. (5) is a homogeneous magnet with long-range interactions. These differences are captured.
in the different topological structures the manifolds exhibit. However, upon coarsening, both models collapse to a one-dimensional curve. In fact, they collapse to the same as a three dimensional volume. However, several of the boundaries of the manifold in Figure 6 has collapsed. The yellow and blue surfaces have collapsed to points and the purple surface has collapsed to a line. The resulting model is structurally identifiable, but not practically identifiable. The practical non-identifiability is closely related to the topological changes of the boundary structure.

Finally, we turn our attention the enzyme-substrate model. To coarsen this model, we consider an alternative initial condition in which only $[E]$ and $[S]$ have nonzero initial condition and observe only the predictions corresponding to the final product $[P]$ (ignoring the time course of the other three variables). The corresponding model manifold is illustrated in Figure 11. Notice that if $k_{\text{cat}} = 0$ in Eqs. (7), that no product can be produced. Consequently, the blue and yellow surfaces in Figure 6 are collapsed to a single point in Figure 11. However, the collapse is not uniform across the manifold. In fact, the manifold illustrated in Figure 11 is still a three-dimensional volume. However, it has been compressed, so that the two remaining surfaces (red and green) are very close to one another and are therefore practically non-identifiable. Thus, in principle it is possible to identify all of the parameters in the model using only product data. However, in practice the near-collapse of the manifold makes it practically non-identifiable.

Although the manifold in Figure 11 remains a three dimensional volume, the structure of the manifold has changed from that in Figure 6. This structural change represents the informational dependence among $k_f$, $k_r$, and $k_{\text{cat}}$. The practical non-identifiability of the resulting coarsening is intimately tied this informational overlap and is manifest as a structural change in the model's topology. Inspecting Figure 6, we see that the blue and yellow surfaces are necessary to “pull apart” the red and green surfaces. If the choice of data collapses the blue and yellow surface to a single point (as in Figure 11), it becomes difficult to statistically distinguish between the red and green models (as well as all the models between them). We discuss this phenomenon in more detail in the next section. We will see that the relevant topology of an underlying theory may be visualized in the form of a hierarchical graph, which in turn leads to a reinterpretation of the model parameters in terms of the emergent physical theories that arise from manifold collapse. In the case of practical non-identifiability, the collapse of the boundary structure leads to a hierarchical reinterpretation of the underlying theory in terms of governing model classes.

### IV. Hypercorners Define Model Classes

#### A. Boundary structure classes

As noted before, the models we have considered here have manifolds with an intrinsic hierarchical structure. They are bounded by (hyper-)surfaces of one less dimension, which are in turn bounded by other (hyper-)surfaces of even lower dimension. This structure is derived from the nature of the underlying theory. These theories all combine several simple physical principles together to describe a composite system. Such constructions are very common and will generally result in a hierarchical boundary structure for model manifolds. In general, however, models that share this basic construction will have many more than two or three parameters making them difficult to visualize in data space as we have done here. However, the relationships among this hierarchy of hyper-surfaces can be represented as a hierarchical graph structure, as in Figure 12.

The representation in Figure 12 is the relationship among the model manifold, its boundaries, corners, etc. The complete model is represented as a single manifold of dimension $N$ (where $N$ is the number of parameters), given by the top node of the graph in the figure. This manifold may be bounded by a collection of hyper-surfaces of dimension $N-1$, i.e., the second row in the figure. Likewise, each of these hyper-surfaces may be bounded by a collection of hyper-surfaces of dimension $N-2$, i.e., the third row in the figure.

The arrows connecting the top node to the nodes in the first row show that each of these surfaces is a boundary to the node above it. The arrows connecting the second and third rows similarly represent which $N-2$ dimensional hypersurfaces are boundaries to which $N-1$ dimensional hypersurfaces. In this way, a hierarchical graph may be constructed summarizing the geometric relationship among all the limiting cases of the model.
FIG. 12: **Hierarchical Graphs.** The relationship among boundaries, corners, hyper-corners, etc. may be summarized in a hierarchical graph diagram. The top node of the graph represents the full \(N\)-dimensional model. The first row of nodes correspond to the surfaces of dimension \(N-1\) that bound this model. The next row represents the \(N-2\)-dimensional surfaces that bound those in the previous row, and so forth. The tips of the graph correspond to models of dimension zero (i.e. a single point) or unbounded submanifolds.

The tips of the graph (surfaces of dimension \(N-n\) in the figure labeled by Greek letters) correspond to either single points (models with no parameters) or unbounded manifolds. All the example manifolds we consider in this paper are absolutely bounded, so the tips of the graphs we consider below are points of dimension zero. We refer to these graph tips as hyper-corners of the model manifold.

The manifolds in Figures 2, 3, and 4 are each topologically equivalent to a square. In Figure 13 (top center) we construct the hierarchical graph corresponding to the square topology. As we saw in the previous section, upon coarsening the experimental conditions these manifolds collapse into either a triangle (lower left) or a line segment (lower right). The manifold in Figure 5 is topologically a triangle and has the same hierarchical graph structure as that in Figure 8, i.e., the lower left graph in Figure 13. Upon coarsening, it also collapses to a line segment (lower right).

We now consider the case of the enzyme-substrate model. The hierarchical graph corresponding to the geometry in Figure 6 is given in Figure 14. As a three dimensional model, this graph has one more row of nodes than those in Figure 13. The three dimensional volume is bounded by five two-dimensional surfaces. These two-dimensional surfaces are mostly triangles, each bounded by 3 line segments. The one exception is the green surface which is topologically a square and is bounded by four line segments. All together, there are eight different line segments represented by the third row in Figure 14. These line segments are each bounded by two points with there being five points altogether.

Notice in Figure 14 that the number of nodes on each line initially increases as one progresses down the graph (increasing from one to five to eight) but then decreases again near the bottom (going from eight to five). We find this property be a general feature of more complex models. Since the number of nodes on each row is the number of ways in which the limiting approximations of the first row can be combined to give unique limiting models, there is an initial combinatorial explosion of possible manifold boundaries. However, when a large number of these limiting approximation are combined, the combinatorial complexity will decrease, analogous to the behavior of binomial coefficients.

Because of this general structure, the number of nodes in the graph will typically grow exponentially with the number of first-order limiting approximations. Individual nodes in the graph describe qualitatively distinct behaviors that a system could exhibit. Broadly speaking, the combinatorial explosion illustrated by the hierarchical graph is indicative of the amazing range of physical phenomena observed through the universe, which are ultimately derived from the interactions of a small number of distinct fundamental particles.

We now consider the topology of the manifold in Figure 11 which is given in Figure 15. Upon coarsening the experimental conditions, both the yellow and blue surfaces collapse to a point while the purple surface col-
FIG. 14: Hierarchical graph of the Enzyme-Substrate Model Topology. The enzyme-substrate topology consists of a solid with five surfaces, eight edges, and five corners. Four of the five corners are topologically triangles. As such, the sub-graph formed by taking the R node (for example) as the top node is equivalent to the triangle structure in Figure 13. The green face, however, is a square, so the sub-graph formed by taking the G node as the top node is equivalent to that of the square in Figure 14. Upon coarsening, the topology changes and is given in Figure 15.

The phenomenon illustrated in Fig. 15 is related to the manifold collapse described in section III. However, in this case, it is the boundaries, rather than the manifold itself, that collapse to lower-dimensional objects. By collapsing the boundaries, the structure of the whole manifold becomes long and thin as illustrated in Fig. 11 and described as a hyper-ribbon in references [11, 12].

The thinness of the manifold is equivalent to practically non-identifiable parameters. Thus, the practical non-identifiability of this model is intimately related to structural non-identifiability of the model in its limiting cases.

There is evidence that this phenomenon occurs generally. Consider, for example, the model in Eq. (5) for the case of two parameters and eight spin sites. The model is topologically a triangle (as for the four spin case in Fig. 5). However, coarse-graining over the odd-numbered spins results in a model that has two structurally identifiable parameters, but a manifold with only two boundaries instead of three. (The resulting manifold is topologically equivalent to either the red or green surfaces in Fig. 11). Because of this boundary collapse, the resulting manifold is long and narrow and the two parameters are practically non-identifiable. As noted in reference [1], this practical non-identifiability occurs only after coarsening, which we here identify as a consequence of a global structural change in the boundary structure. Furthermore, this phenomenon has been observed for other models in the literature. For example, it was noted for a model of waterborne disease transmission that the model because structurally non-identifiable in the limit of fast water transmission [30].

B. Euler Characteristic from Hierarchical Graphs

From the hierarchical graphs given in Figures 13 and 15, it is possible to calculate the Euler-characteristic of the corresponding manifolds. The Euler-characteristic is a topologically invariant number calculated as the alter-
nating sum

\[ \chi = k_0 - k_1 + k_2 - k_3 + \ldots, \quad (13) \]

where \( k_i \) is the number of surfaces of dimension \( i \) bounding the manifold. That is \( k_i \) is the number of nodes in each row of the hierarchical graph counting from the bottom. It is straightforward to check that for each of the models considered here, \( \chi = 1 \). The significance of this number is that all of the manifolds we consider here are orientable and none have holes or handles (such as would a donut or a coffee mug). We anticipate that these are properties that will be common for many models, but it is possible to find other examples.

C. Hierarchical graphs identify important parameter combinations

A useful insight of the hierarchical graph visualization of the model topology lies is a reinterpretation of the model parameters. Quite often, particularly for sloppy or practically non-identifiable models, the \( N \) independent parameter combinations of a model are not equally important for explaining the model behavior. Indeed, for many choices of experimental conditions, there is a clear hierarchy of importance in the model parameters that is revealed by an eigenvalue decomposition of the FIM. The eigenvectors of the FIM can then be interpreted as the parameter combinations that are relatively important or irrelevant for understanding the model behavior. Unfortunately, this interpretation is based on a local, linear analysis. In reality, the truly important parameters combinations are nonlinear combinations of the model’s bare parameters. Identifying and interpreting the appropriate nonlinear combination requires a global, topological analysis. To illustrate, we consider the enzyme-substrate model which, of the four models we consider is the most complicated and exhibits the richest emergent behavior.

To understand the emergent chemistry of the enzyme-substrate model, we reconsider the differences in the experimental conditions that lead to the manifolds in Figures 6 and 11. The first (unrealistic) experimental conditions were chosen in a way to make all of the parameters easily identifiable. They correspond to stimulating an enzyme at \( t = 0 \) with a dose of the ES complex and measuring the subsequent time course for all four chemical species. Since the ES complex is unstable (spontaneously decays into both an enzyme-substrate pair as well as an enzyme-product pair) this stimulus would be difficult to achieve experimentally. Furthermore, it is often more practical to only observe the time course for the resulting product, \( P \). The second (more realistic) experimental conditions therefore correspond to stimulating an enzyme at \( t = 0 \) with a dose of substrate and observing the subsequent time course of only the resulting product.

Notice that the coarsened manifold in Figure 11 remains a three-dimensional volume without any folding or other sort of collapse of the manifold interior. As such, the model is structurally identifiable for this experimental condition. However, the manifold is very thin and as such it is practically non-identifiable. The practical non-identifiability is closely related to the collapse of the boundaries under the new experimental conditions.

By considering the equations of the model when only observing the concentration of the product \( P \), any information about the rates \( k_f \) and \( k_r \) of necessity must be inferred through the third reaction described by \( k_{\text{cat}} \). Furthermore, when only the substrate is stimulated, any information about this stimulation must first pass through the parameter \( k_f \). It is precisely this informational dependence that is described by the boundary collapse. Indeed, the blue surface corresponds to the limit \( k_{\text{cat}} \to 0 \) so it will always collapse to a point if only \( |P| \) is observed. For models near this limit, little information is gained if only the product is observed. Similarly, the yellow surface corresponds to the limit \( k_f \to 0 \) which will always collapse to a point if only the substrate is stimulated. For models near this limit, little information is propagated if only the substrate is stimulated. Although a complete collapse of the manifold only occurs for the boundaries, this structural change necessarily draws many different points on the manifold very near one another leading to a hierarchy of importance in the parameters. Points that under different experimental conditions could be distinguished become practically non-identifiable under these more realistic conditions. In fact, the entire volume could be well-approximated by either the red or green surfaces (or indeed any other surface between them). This observation is the basis for the manifold boundary approximation method of model reduction described previously[citation].

We now consider the functional form of the two relevant surfaces (red and green) under realistic experimental conditions. The green surface corresponds to the limit \( k_r \to 0 \), while the red surface corresponds to the limit \( k_f, k_r \to \infty \) with \( K = k_r / k_f \) remaining finite. The former corresponds to the approximation that the first reaction is not reversible while the latter corresponds to the approximation that the first reaction is always in equilibrium. It is information distinguishing between these limits that is practically unknowable.

The latter approximation \( (k_f, k_r \to \infty) \) is equivalent to the equilibrium derivation of the well-known Michaelis-Menten rate law:

\[ \frac{d[P]}{dt} = \frac{k_{\text{cat}} E_0 [S]}{K + [S]}; \quad (14) \]

where \( E_0 = [E] + [ES] \) is the total amount of enzyme (a constant determined by experimental conditions). This functional form is useful for revealing the emergent behavior of the system: for large substrate concentrations, the reaction rate saturates to \( k_{\text{cat}} E_0 \) with the parameter \( K \) being the characteristic concentration at which the saturation effect becomes important.

The two edges that join the red and green surfaces can then be found as limiting approximations to Eq. (14).
They are $K \to 0$, which corresponds to the approximation that that the reaction is always saturated, i.e., a constant production rate:

$$\frac{d}{dt}[P] = k_{\text{cat}}E_0.$$  \hspace{1cm} (15)

Alternatively, the second limit corresponds to $k_{\text{cat}}, K \to \infty$ with $k_{\text{eff}} = k_{\text{cat}}/K$ remaining finite leading to the form

$$\frac{d}{dt}[P] = k_{\text{eff}}E_0[S],$$  \hspace{1cm} (16)

which corresponds to the limit that the Michaelis-Menten approximation always remains in the linear domain. Notice that Eqs. (15) and (16) correspond to very simple reaction types: constant production rate and linear production rate. These two models further reduce to the same models in the limit $k_{\text{cat}}, k_{\text{eff}} \to 0$ or $k_{\text{cat}}, k_{\text{eff}} \to \infty$. These two limiting cases correspond to the nodes labeled a and b in Figure 15. The two models in Eqs. (15) and (16) correspond to nodes RG and P in Figure 15 while Eq. (14) corresponds to node R. Thus, the sequence of models constructed above correspond to traversing a single path along the graph in a vertical direction. If the path is chosen appropriately, i.e., so that each approximation corresponds to the narrowest width of the manifold, then this sequence of limiting approximations naturally identifies the nonlinear combinations of parameters that are the most important for describing the model's behavior. By then traversing the path backwards, i.e., from bottom to top, the model is reconstructed with model parameters reinterpreted as a sequence of small refinements to more general model classes.

In this picture, the tips of the hierarchical graph (i.e., the hyper-corners of the model manifold) correspond to the simplest, most flexible model form customized to the pertinent experimental conditions. We refer to these simplified models as model classes, in analog to universality classes commonly encountered in statistical physics. Indeed, this process is not unlike the type of modeling done with universal behavior, for example near critical points. A Renormalization Group analysis can be used to identify the relevant model parameters, i.e., the tips of the hierarchical graph. However, data analysis may require non-universal refinements to the model, such as finite size effects corresponding to models moving up the graph, in order to accurately carry out a fit[21].

For models of moderate complexity, constructing the hierarchical graph will reveal important insights regarding the informational relationship among model parameters such as we have done above for the enzyme-substrate model. Such insights are important for experimental design considerations and parameter interpretation.

On the other hand, for more complex models, it may be impractical to explicitly construct the entire graph. In these cases, most of the benefit can still be found by identifying a single path down the graph from the top node to the most important tip (model class). This in fact, is effectively the same analysis proposed by the Manifold Boundary Approximation Method (MBAM) of model reduction.

The MBAM algorithm described in reference[2] constructs a geodesic defined by the geometry of a particular experimental condition. This geodesic originates from some predefined “true” parameter values and proceeds along the least sensitive parameter direction as measured by the eigenvalues of the Fisher Information. However, the result of this algorithm is to identify a topological feature of the manifold (i.e., the boundary). As such, many of the requirements of the manifold boundary approximation method (i.e., initial parameter values and explicit experimental conditions) are incidental to the process for finding the boundary and are not necessary for the validity of the final reduced model. Indeed, the result of this process identifies a single model class governing the system behavior for a particular experiment condition; however, that reduced model class will be likely be valid for a larger group of experimental conditions provided they preserve the topological features of the manifold.

V. TOPOLOGICAL EMBEDDING DEFINES STABILITY OF MODEL CLASSES

In this section, we consider how adding parameters to a model affects its topology. This question is complementary to that considered above in which the underlying theory was held fixed and the observations were coarsened. We now ask, given a set of observations, what is the appropriate representation of the physical system? In other words, given several competing underlying theories, which parameters are relevant for describing the observed behavior? Identifying the relevant parameters, as we show in this section, involves understanding how the competing topologies are embedded within a larger theory. We will illustrate this using statistical mechanics and models of crystalline structures in alloys. Although the discussion of this section uses alloy modeling as a specific example, the general principles of identifying relevant parameters generalize to other model classes.

A. Model classes are ground states of statistical mechanics models

Consider a model of a two-dimensional four by four square lattice with periodic boundary conditions in which sites can be occupied by an atom two types, i.e., a binary system. Our model class consists of five parameters describing interactions up to fifth-nearest neighbors. Specifically, our Hamiltonian takes the form

$$H = -\sum_{k=1}^{5} \sum_{d(i,j)=d_k} J_k s_i s_j,$$  \hspace{1cm} (17)
where the first sum indicates a sum over interactions (up to fifth nearest neighbor) and the second sum indicates a sum over sites such that the distance between sites $i$ and $j$ is equal to the $k^{th}$ nearest neighbor distance. The random variables $s_i$ take on values $\pm 1$, indicating which atom type occupies the site, according to a Boltzmann distribution $P(s) \propto e^{-E}$ where we have absorbed the temperature dependence into the definition of $J_k$. This model has 16 binary random variables and therefore can exhibit $2^{16} = 65536$ distinct configurations. Many of these states are symmetrically equivalent; only 432 configurations are crystallographically distinct.

The topology of this model is summarized by the hierarchical graph in Fig. 16. Although this model corresponds to a five-dimensional manifold (and is thus difficult to visualize), from the graph structure it can be seen that the manifold has six hyper-corners corresponding to zero-dimensional limiting cases (six nodes on the bottom row). These six points form the boundaries for 15 lines (second row from the bottom). Continuing to work up the graph, these lines form the boundaries for 20 triangles, which form the boundaries for 15 tetrahedra, which form the boundaries for 6 first-order boundaries of the manifold. These first order boundaries are each 4 dimensional objects bounded by five tetrahedra.

As argued in previous sections, the tips of the hierarchical graph define the dominant behaviors of the model and a sequence of models beginning from the tips and progressing toward the head node (i.e. moving up the graph) correspond to refining approximations to this dominant behavior. Consider now the nature of these limiting approximations. Moving from the head node to a first order boundary (i.e. any node from 1 to 6) corresponds to a limiting case in which $J_k \rightarrow \pm \infty$, i.e., a zero-temperature limit. In these limits, many of the possible configurations are “frozen out” so that the models corresponding to the nodes 1 through 6 have between 21 and 65 structurally distinct states being modeled. Although this is a zero-temperature limit, the remaining states are not limited to the ground state configurations. Rather, the discarded states are those that are first to become irrelevant at low temperatures.

Similar limits correspond to approximations that move down the hierarchical graph. At each level, more and more states are removed. Each level removes the next group of states least relevant in the low temperature limit. The final result of this process is that only the ground states remain for models at the tips of the graph. Each tip corresponds to a structurally distinct ground state of the model class, as illustrated in Fig. 16.

The process of systematically removing high-energy states from a model is reminiscent of a renormalization group procedure. Indeed, the sequence of approximations corresponding to the path labeled $0 \rightarrow 1 \rightarrow 7 \rightarrow 22 \rightarrow 42 \rightarrow 57$ is equivalent to a typical renormalization group coarsening in which high frequency degrees of freedom are removed. However, for many parameter values, high-frequency configurations do not correspond to high energy. Indeed, for some parameter values, the checkerboard configuration is a ground state (node 62). Information topology naturally identifies the sequence of states least relevant for a member of the model class and leads to approximate effective models in which these states are removed, exactly analogous to a renormalization group procedure although applicable to a much broader class of models.

We now consider a more practical question: what are the ground state structures of a binary alloy on a three-dimensional lattice? This system can be modeled in much the same basic way as before:

$$H(s) = -\sum_i \Pi_i(s) \theta_i,$$

where $s$ is a vector of all possible configurations on the two atom types on the lattice and $\Pi_i(s)$ are the energy contributions of a cluster expansion. The parameters then are interpreted as the contributions to the energy from nearest neighbor, next nearest neighbor interactions, etc., but can include also many body interactions. For a real alloy, one expects that the true energy involves contributions from all of these terms. However, including all order of the cluster expansion is both impractical and not theoretically enlightening.

We anticipate that the cluster expansion in Eq. (18) can be truncated at some finite number of terms. For example, the energy will be dominated by a few large terms in the sum while other terms are less important. However, the question of which are the relevant param-
ters to include is more complicated than simply identifying which parameters are small in actual alloys. In particular, certain alloy configurations may be unstable to small perturbations in other parameters. Identifying an appropriate model involves identifying the appropriate parameter combinations that produce ground states (i.e., emergent model classes) that are stable with respect to the perturbation in the parameters that are left out.

B. Topological embedding identifies relevant and irrelevant parameters

We now consider sequence of models defined in Eq. (18) found by truncating the series at different numbers of parameters. For a binary alloy on an FCC lattice, the manifold for a two parameter model (with both nearest and second nearest neighbor two-body interactions) is illustrated in Figure 17. Topologically, this two parameter model is a pentagon (five sides and five corners). We now consider the effect of truncating this model to a one parameter model. We do this by setting each of the two parameters to zero and varying the other parameter. These one parameter models are illustrated by the red and blue curves in Figure 17.

The corners of the two parameter model are illustrated by white dots in Figure 17. These dots represent the emergent model classes of the two parameter model (in this case the distinct ground states of the alloy). Because the one parameter models are each included as special cases of the two parameter model, their topology is embedded within the topology of the more general class. We summarize the relationship between the topologies of two parameter model and each of the one parameter models by the dashed lines in Figure 18. For example, because each of the red and blue curves are subsets of the full two parameter model, we draw a dashed line from the head node of the two parameter graph to the head nodes of each of the one parameter graphs. Furthermore, because both end points of the blue curve correspond to corners of the full model, we connect the relevant tips of the graphs with dashed lines with two arrows to indicate equivalence (Fig. 18 top). In contrast, only one end point of the red curve is a corner of the two parameter model. The other end point lies on an edge. We indicate that this end point is a subset of an edge by a dashed line connecting the relevant nodes of the graph (Fig. 18 bottom).

We now consider the physical meaning of the relationships summarized by the graphs in Figure 18. The tips of the red and blue curves in Figure 17 represent the emergent model classes (ground states) for the one parameter models. Notice that one of the ground states for the red curve is not a ground state for the two parameter model and using such a simple model would incorrectly predict the existence of a stable structure corresponding to this end point. The reason for this is not that the missing parameter is large in an actual alloy system, but that that configuration is unstable to arbitrarily small perturbations in this parameter.

This instability is manifest in the way the one parameter topology is embedded in that of the two parameter model. Specifically, the end point of one parameter model lies on an edge and not a point of the two parameter model. Qualitatively, we can understand the effect of adding a second parameter to be “splitting” the unstable node into smaller pieces, some of which make up actual ground states further down the graph of the true model.

If a model class is unstable to the addition of a new parameter, we classify this parameter as relevant for modeling the actual physical behavior. Similarly, if a model
class is stable to the introduction of a new parameter, we classify the parameter as irrelevant. Although the discussion here has revolved around finding ground states for alloy models, the language of information topology allows the same notions of stability of model classes and relevant and irrelevant parameters to extend to other diverse systems. In this way, the question of what representation is appropriate for a particular physical system can be answered in a systematic way.

VI. DISCUSSION

In this paper we have presented a mathematical framework for understanding the informational relationships among physical theories, mathematical models, and experimental conditions. A cornerstone of this formalism is the distinction between an underlying theory and a mathematical model. The former refers to a collection of physical principles, the details of which are encoded into a parameterization, such as chemical reaction rates or bond strengths. Application of these physical principles to specific experimental conditions leads to precise, quantifiable predictions that we refer to as the mathematical model. In other words, a mathematical model can be thought of as a realization of the physical principles under specific experimental conditions. The underlying theory will generally correspond to a large family of mathematical models. While mathematical models inherit parameters from the theory from which they were derived, the parameters themselves are a property of that underlying theory, encoding the details of the physical principles involved.

When predictions from mathematical models are compared for specific experimental conditions, statistical distance between predictions provides a natural metric to measure the similarity and distinguishability of competing models. We have interpreted this distance as a metric on the parameter space of the model. Varying the experimental conditions changes the statistical metric, causing the model manifold to be stretched and warped. Therefore, specific geometric properties of the parameter space, such as distance and curvature, are specific to the precise experimental conditions and are not inherently connected to the underlying theory. However, if we consider the set of experimental conditions for which the parameterization remains structurally identifiable (at least in the local sense), then the parameters of the underlying theory define a topological space. We refer to the subsequent topological analysis as Information Topology.

We have seen that for many models, topological properties can be visualized as a hierarchical graph. This graph is useful since it naturally encodes the hierarchical relationship among the model’s parameters (i.e. sloppiness) that has been observed in a diverse class of models. In particular, we identify the tips of the hierarchical graph as simplified model classes that govern the emergent or collective behavior of the system. Systematically moving up the graph then corresponds to a sequence of refining approximations to this primary macroscopic mode. For example, we have seen that for an enzyme-substrate chemical reaction (common in biochemistry) that the tips of the graph correspond to the zero and first order reactions (i.e. the saturated and linear regimes of the enzyme reaction), while moving up the graph one level corresponds to the celebrated Michaelis-Menten reaction which interpolates between these two limits. For statistical mechanics models, we have seen that the graph tips correspond to structurally distinct ground states,
while moving up the graph introduces the states most relevant as the temperature is raised.

Working in reverse, effective, simplified models may be systematically constructed by identifying the approximations moving down the graph. This is precisely the procedure of the Manifold Boundary Approximation Method (MBAM) introduced elsewhere[2]. Using this procedure, well-known approximations, such as Michaelis-Menten in biochemistry and renormalization group in statistical physics may be recovered for specific types of models. The current formalism is much more general however, producing new approximations for well-studied systems (such as we have seen for crystal structures) and identifying approximations in systems that previously defied reduction[2].

We have shown that as parameters are added to a model, we can identify the emergent behavior of the smaller model as being either stable or unstable to the introduction of new parameters. This distinction leads naturally to the classification of parameters as either relevant or irrelevant based on whether or not the emergent behavior is stable or unstable when the parameter is added. This question is answered by considering the way that the two topological spaces are embedded within one another.

The framework described in this paper presents a unified theory for understanding the relationship between microscopic components, the collective behaviors that the system can exhibit, and the informational relationship among these regimes for different experimental conditions. The problem of mathematical modeling in complex systems is an important one that spans many disciplines. We anticipate that the concept of an information topology will be useful for studying systems in statistical mechanics, biology, chemistry, engineering, climate, and economics among others. Application of the concepts in this paper may also be useful for problems related to experimental design, engineering and control, as well as providing a deeper understanding and explanation of the emergent physical principles that govern a system’s behavior.

[1] B. B. Machta, R. Chachra, M. K. Transtrum, J. P. Sethna: Science 342 (2013) 604
[2] M. K. Transtrum, P. Qiu: Physical Review Letters 113 (2014) 098701
[3] C. R. Rao: Sankhya: The Indian Journal of Statistics 9 (1949) 246
[4] E. Beale: Journal of the Royal Statistical Society, Series B (Methodological) (1960) 41
[5] D. M. Bates, D. G. Watts: Journal of the Royal Statistical Society, Series B (Methodological) (1980) 1
[6] S.-i. Amari: Differential-geometrical methods in statistics: Springer (1985)
[7] S.-i. Amari, O. E. Barndorff-Nielsen, R. Kass, S. Lauritzen, C. Rao: Lecture Notes-Monograph Series (1987) 1
[8] R. E. Kass: Statistical Science (1989) 188
[9] M. K. Murray, J. W. Rice: Differential geometry and statistics, vol. 48: CRC Press (1993)
[10] S.-i. Amari, H. Nagaoka: Methods of information geometry, vol. 191: American Mathematical Soc. (2007)
[11] M. K. Transtrum, B. B. Machta, J. P. Sethna: Physical review letters 104 (2010) 060201
[12] M. K. Transtrum, B. B. Machta, J. P. Sethna: Physical Review E 83 (2011) 036701
[13] T. J. Rothenberg: Econometrica: Journal of the Econometric Society (1971) 577
[14] C. Cobelli, J. J. Distefano 3rd: American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 239 (1980) R7
[15] K. S. Brown, J. P. Sethna: Physical Review E 68 (2003) 021904
[16] K. S. Brown, C. C. Hill, G. A. Calero, C. R. Myers, K. H. Lee, J. P. Sethna, R. A. Cerione: Physical biology 1 (2004) 184
[17] S. L. Frederiksen, K. W. Jacobsen, K. S. Brown, J. P. Sethna: Physical review letters 93 (2004) 165501
[18] J. J. Waterfall, F. P. Casey, R. N. Gutenkunst, K. S. Brown, C. R. Myers, P. W. Brouwer, V. Elser, J. P. Sethna: Physical review letters 97 (2006) 150601
[19] R. N. Gutenkunst, J. J. Waterfall, F. P. Casey, K. S. Brown, C. R. Myers, J. P. Sethna: PLoS computational biology 3 (2007) e189
[20] F. P. Casey, D. Baird, Q. Feng, R. N. Gutenkunst, J. J. Waterfall, C. R. Myers, K. S. Brown, R. A. Cerione, J. P. Sethna: IET systems biology 1 (2007) 190
[21] B. C. Daniels, Y.-J. Chen, J. P. Sethna, R. N. Gutenkunst, C. R. Myers: Current opinion in biotechnology 19 (2008) 389
[22] D. Fuller, U. Klingmüller, J. Timmer: Simulation 79 (2003) 717
[23] K.-H. Cho, S.-Y. Shin, W. Kolch, O. Wolkenhauer: Simulation 79 (2003) 726
[24] E. Balsa-Canto, A. A. Alonso, J. R. Banga: IET systems biology 2 (2008) 163
[25] J. F. Apgar, J. E. Toettcher, D. Endy, F. M. White, B. Tidor: PLoS computational biology 4 (2008) e30
[26] J. F. Apgar, D. K. Witmer, F. M. White, B. Tidor: Molecular BioSystems 6 (2010) 1890
[27] K. Erguler, M. P. Stumpf: Molecular BioSystems 7 (2011) 1593
[28] R. Chachra, M. K. Transtrum, J. P. Sethna: Molecular BioSystems 7 (2011) 2522
[29] M. K. Transtrum, P. Qiu: BMC bioinformatics 13 (2012) 181
[30] M. C. Eisenberg, S. L. Robertson, J. H. Tien: Journal of theoretical biology 324 (2013) 84
[31] Y.-J. Chen, S. Papanikolaou, J. P. Sethna, S. Zapperi, G. Durin: Physical Review E 84 (2011) 061103
Supplemental Information

A. Visualization Methods

In this section we describe how the manifold visualizations found in the main text were generated. The examples throughout the text were chosen to consist of either two or three parameters, corresponding to manifolds of two or three dimensions, so that their topological structure could be more easily visualized. However, these manifolds are embedded in a data space of often much higher dimension. It is therefore necessary to project this high-dimensional embedding space into a three dimensional subspace in order to generate the figures found in the main text.

In order to generate low-dimensional projections, we first constructed a grid of the parameter space and evaluated the model prediction at each point. The corresponding grid of model predictions correspond to a grid of vectors in the high-dimensional embedding space. We then performed a principal component analysis of this grid of prediction vectors and projected the grid onto each of the principle components. We then created the visualization by truncating all but the first three principle components. For figures visualization two-dimensional manifolds, we have colored the manifold according to the fourth principal component, effectively visualizing a four-dimensional embedding. For three-dimensional manifolds, i.e., the enzyme-substrate model, we have colored each boundary of the volume a solid color to help illustrate the topological structure.

B. Embedding space for non least-squares models

In this paper we have used the Fisher Information Matrix (FIM) as the Riemannian metric for measuring distances between models. When the model in question is a least-squares model, then there is a natural Euclidean metric in behavior space corresponding to the sum of squares defined by the $\chi^2$ cost function. This Euclidean metric induces a non-euclidean metric on the embedded model that is equivalent to the Fisher Information [3-12].

A similar Euclidean embedding space can be found for an arbitrary probabilistic model $P(\xi, \theta)$. We derive this metric for the case of discrete probability distributions, but the result also holds for probability densities. This embedding space can be found by constructing the variable $z_i(\theta) = 2\sqrt{P_i(\theta)}$ where the index $i$ labels each configuration of the random variable $\xi$. Imposing a Euclidean metric on the variables $z_i$ gives

$$ds^2 = \sum_i dz_i^2 = \sum_i \frac{dP_i^2}{P_i} = \left\langle \frac{dP^2}{P^2} \right\rangle,$$  \hspace{1cm} (19)

where in the last term we have written the sum as an expectation value. Note that

$$\frac{dP}{P} = d\log P = \sum \frac{\partial P}{\partial \theta^\mu} d\theta^\mu,$$  \hspace{1cm} (20)

from which it follows that

$$ds^2 = \sum_{\mu\nu} \left\langle \frac{\partial \log P \partial \log P}{\partial \theta^\mu \partial \theta^\nu} \right\rangle d\theta^\mu d\theta^\nu,$$  \hspace{1cm} (21)

so that the induced metric on the manifold is

$$g_{\mu\nu} = \left\langle \frac{\partial \log P \partial \log P}{\partial \theta^\mu \partial \theta^\nu} \right\rangle,$$  \hspace{1cm} (22)

which is the Fisher Information Metric.

Notice that normalization requires that $\sum_i z_i^2 = 4 \sum_i P_i^2 = 4$, so that the variables $z_i$ correspond to a hyper-sphere embedded in a Euclidean data space. The model manifold is then embedded in this hyper-sphere. We interpret this Euclidean, hyper-sphere embedding in the same way as the Euclidean embedding space for least squares models, i.e., as a data or behavior space.

C. Topology and alternate metrics

In the main text of the paper, we have used the Fisher Information Matrix (FIM) as the metric that defines relative distances between models of the same model class, i.e., same underlying theory. Since a model class is characterized by its parameterization, we found that changing the experimental conditions for the underlying theory lead to different metrics on the same parameter space. Although the FIM has many desirable statistical properties, it is not the unique measure of statistical distance between probability distributions. Other notable examples include the Hellinger distance, total variation distance, the Levy-Prokhorov metric, Bhattacharyya distance, earth mover's distance (also known as the Wasserstein or Kantorovich metric) and the energy distance. Furthermore, there are many other distance measures that are applicable to specific types of models and not probability distributions generally, such as the $H_\infty$ norm in control theory applicable to dynamical systems. (While all of these metrics are valid measures of statistical distance, they are not all Riemannian metrics, i.e., they do not define an inner product. Indeed, one of the advantages of the FIM is that it corresponds to a Riemannian metric, thus allowing the use of differential geometry.)

Alternating metrics among the many possible choices is in many ways analogous to changing experimental conditions. The net effect is to change the meaning of distance among members of the model class. As such, the results of this paper can be applied to alternative metrics.

Furthermore, there are many measures of statistical divergence that, while not properly metrics (they may not satisfy either symmetry or the triangle inequality),
are often interpreted as a type of distance measure. A class of such divergences are the f-divergences, among which the Kullback-Leibler divergence is a well-known example. (Interestingly, the FIM corresponds to the f-divergence for infinitesimally separated distributions.) Other classes of divergences include the M-divergences and S-divergences. Specific examples include Renyi’s divergence and the Jensen-Shannon divergence. Although not proper metrics, statistical divergences do define a topological space. Consequently, the topological properties of model classes introduced in this paper can be applied given only a divergence rather than a proper metric.