Explainable Machine Learning for Scientific Insights and Discoveries

Ribana Roscher*[1,2], Bastian Bohn[3],
Marco F. Duarte[4], and Jochen Garcke*[3,5]

[1]Institute of Geodesy and Geoinformation, University of Bonn, Germany
[2]Institute of Computer Science, University of Osnabrueck, Germany
[3]Institute for Numerical Simulation, University of Bonn, Germany
[4]Dept. of Electrical and Computer Engineering, University of Massachusetts Amherst, USA
[5]Fraunhofer Center for Machine Learning and Fraunhofer SCAI, Sankt Augustin, Germany

Abstract

Machine learning methods have been remarkably successful for a wide range of application areas in the extraction of essential information from data. An exciting and relatively recent development is the uptake of machine learning in the natural sciences, where the major goal is to obtain novel scientific insights and discoveries from observational or simulated data. A prerequisite for obtaining a scientific outcome is domain knowledge, which is needed to gain explainability, but also to enhance scientific consistency. In this article we review explainable machine learning in view of applications in the natural sciences and discuss three core elements which we identified as relevant in this context: *transparency*, *interpretability*, and *explainability*. With respect to these core elements, we provide a survey of recent scientific works incorporating machine learning, and in particular to the way that explainable machine learning is used in their respective application areas.

1 Introduction

Machine learning methods, especially with the rise of deep neural networks (DNNs), are nowadays used widely in commercial applications. This success has also led to a considerable uptake of machine learning (ML) in many scientific areas. Usually these models are trained with regard to high accuracy, but recently there is also a high demand for understanding the way a specific model operates and the underlying reasons for the produced decisions. One motivation behind this is that scientists increasingly adopt ML for optimizing and producing scientific outcomes, where explainability is a prerequisite to ensure the scientific value of the outcome. In this context, research directions such

*R. Roscher and J. Garcke contributed equally to this work

as explainable artificial intelligence (AI) [Samek et al., 2018], informed ML [von Rueden et al., 2019] or intelligible intelligence [Weld and Bansal, 2018] have emerged. Though related, the concepts, goals, and motivations vary, and core technical terms are defined in different ways.

In the natural sciences, the main goals are scientific understanding, inferring causal relationships from observational data, or even achieving new scientific insights with the help of ML algorithms, which automatically process and analyze large amounts of scientific data from experiments, observations, or other sources.

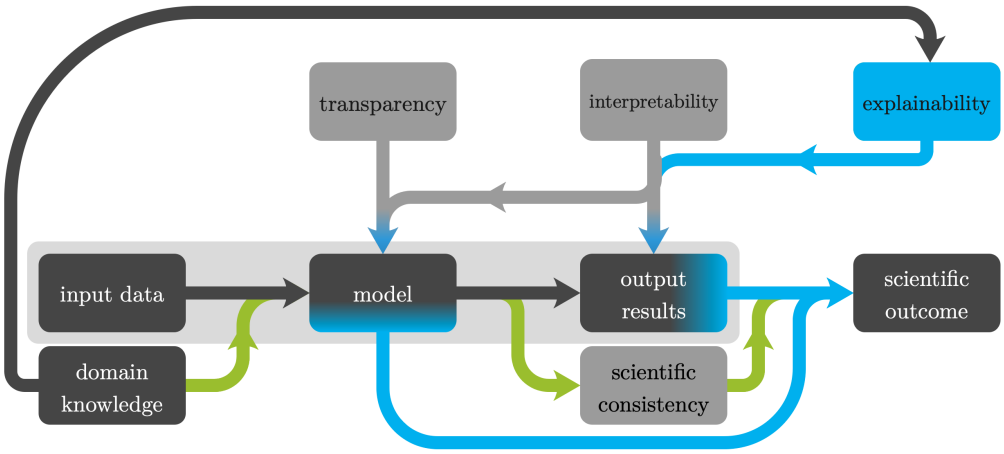

Figure 1: Major machine learning-based chains from which scientific outcomes can be derived: The commonly used, basic machine learning chain (light gray box) learns a black box model from given input data and provides an output. Given the black box model and input-output relations, a scientific outcome can be derived by explaining the output results utilizing domain knowledge. Alternatively, a transparent and interpretable model can be explained using domain knowledge leading to scientific outcomes. Additionally, the incorporation of domain knowledge can promote scientifically consistent solutions (green arrows).

This article provides a survey of ML approaches which are meant to derive scientific outcomes, where we specifically focus on the natural sciences. Given the scientific outcomes, novel insights can be derived helping for a deeper understanding, or scientific discoveries can be revealed which were not known before. *Gaining scientific insights and discoveries* from a ML algorithm means gathering information from its output and/or its parameters regarding the scientific process or experiments underlying the data.

One should note that a data-driven effort of scientific discovery is nothing new, but mimics the revolutionary work of Johannes Kepler and Sir Isaac Newton, which was based on a combination of data-driven and analytical work. As stated by Brunton and Kutz [2019],

> Data science is not replacing mathematical physics and engineering, but is instead augmenting it for the twenty-first century, resulting in more of a

renaissance than a revolution.

What is new is the abundance of high-quality data in the combination with scalable computational and data processing infrastructure.

The main contribution of this survey is the discussion of commonly used ML-based chains leading to scientific outcomes which have been used in the natural sciences (see Fig. 1). A central role play the three elements *transparency*, *interpretability*, and *explainability*, which will be defined and discussed in detail in this survey. The core is the basic ML chain, in which a model is learned from given input data and with a specific learning paradigm, yielding output results utilizing the learned model. In order to derive a scientific outcome, either the output results or the model is explained, where interpretability is the prerequisite for explainability. Moreover, transparency is required to explain a model. A further essential part is *domain knowledge*, which is necessary to achieve explainability, but can also be used to foster *scientific consistency* of the model and the result. Generally, providing domain knowledge to an algorithm means to enhance the input data, model, optimizer, output results, or any other part of the ML algorithm by information gained from domain insights such as laws of nature and chemical, biological, or physical models [von Rueden et al., 2019]. Besides the purpose of explainability, integrating domain knowledge can help with model tractability in scenarios where not enough data is available. It might also increase the performance of a model or reduce computational time.

We will give diverse examples from the natural sciences for approaches which can be related to these topics. Our goal is to foster a better understanding and a clearer overview of ML algorithms applied to data from the natural sciences.

In the broader context, other properties that can be relevant when considering explainability of ML algorithms are safety/trust, accountability, reproducability, transferability, robustness and multi-objective trade-off or mismatched objectives, see e.g. [Doshi-Velez and Kim, 2017, Lipton, 2018]. For example, in societal contexts reasons for a decision often matter. Typical examples are (semi-)automatic loan applications, hiring decisions, or risk assessment for insurance applicants, where one wants to know why a model gives a certain prediction and how one might be affected by those decisions. In this context, and also due to regulatory reasons, one goal is that decisions based on ML models involve a fair and ethical decision making. The importance to give reasons for decisions of a ML algorithm is also high for medical application, where a motivation is the provision of trust in decisions such that patient are comfortable with the decision made. All this is supported by the General Data Protection Regulation, which contains new rules regarding the use of personal information. One component of these rules can be summed up by the phrase "right to an explanation" [Goodman and Flaxman, 2017]. Finally, for ML models deployed for decision-support and automation, in particular in potentially changing environments, an underlying assumption is that robustness and reliability can be better understood, or easier realized, if the model is interpretable Lipton [2018].

The paper is structured as follows. In Sec. 2 we discuss transparency, interpretability, and explainability in the context of this article. While these terms are more methodology-driven and refer to properties of the model and the algorithm, we also describe the role of

additional information and domain knowledge, as well as scientific consistency. In Sec. 3, we highlight several applications from the natural sciences which use these concepts to gain new scientific insights.

2 Terminology

It can be observed that in the literature about explainable ML several descriptive terms are used with diverse meanings, see e.g. Doshi-Velez and Kim [2017], Gilpin et al. [2018], Guidotti et al. [2018], Lipton [2018], Montavon et al. [2018], Murdoch et al. [2019]. Nonetheless, distinct ideas can be identified. For the purpose of this work, we differentiate between *transparency*, *interpretability*, and *explainability*. Roughly speaking, transparency considers the ML approach, interpretability considers the ML model together with data, and explainability considers the model, the data, and human involvement.

Transparency A ML approach is transparent if the processes that extract model parameters from training data and generate labels from testing data can be described and motivated by the approach designer. We say that the transparency of a ML approach concerns its different ingredients: this includes the overall model structure, the individual model components, the learning algorithm, and how the specific solution is obtained by the algorithm. We propose to differentiate between *model transparency*, *design transparency*, and *algorithmic transparency*. Generally, a fully transparent ML method in all aspects is rather doubtful, usually there will be different degrees of transparency.

As an example, consider kernel-based ML approaches [Hofmann et al., 2008, Rasmussen and Williams, 2006]. The obtained model is accessible and transparent, and it is given as a sum of kernel functions. The individual design component is the chosen kernel. Choosing between a linear or non-linear kernel is typically a transparent design decision. However, the commonly used Gaussian kernel based on Euclidean distances can be a non-transparent design decision. In other words, it may not be clear why a given non-linear kernel is taken. Here, domain specific design choices can be made, in particular using suitable distance measures to replace the Euclidean distance, making the design of this model component (more) transparent. In case of Gaussian process regression, the specific choice of the kernel can be built into the optimization of the hyper-parameters using the maximum likelihood framework [Rasmussen and Williams, 2006]. Thereby, design transparency goes over to algorithmic transparency. Furthermore, the obtained specific solution is from a mathematical point of view transparent. Namely, it is the unique solution of a convex optimization problem which can be reproducibly obtained, resulting in algorithmic transparency [Hofmann et al., 2008, Rasmussen and Williams, 2006]. Although, approximations in the specific solution method such as early stopping, matrix approximations, stochastic gradient descent, and others, can result in (some) non-transparency of the algorithm.

Our view is closely related with Lipton [2018], who writes:

> Informally, transparency is the opposite of opacity or "black-boxness." It connotes some sense of understanding the mechanism by which the model

> works. Transparency is considered here at the level of the entire model (simulatability), at the level of individual components such as parameters (decomposability), and at the level of the training algorithm (algorithmic transparency).

As another example, consider DNNs [Goodfellow et al., 2016]. The model is transparent since its input-output relation and structure can be written down in mathematical terms. Individual model components, such as a layer of a DNN, that are chosen based on domain knowledge can be considered as design transparent. Nonetheless, the layers — be it their numbers, size, or involved nonlinearities — are often chosen in an ad-hoc or heuristic fashion and not motivated by knowledge, these decisions are therefore not design transparent. The learning algorithm is typically transparent, e.g., stochastic gradient descent can be easily written down. However, the choice of hyper-parameters such as learning rate, batch size, and others, has more a heuristic, non-transparent algorithmic nature. Due to the presence of several local minima, the solution is usually not easily reproducible; therefore, the obtained specific solution is not (fully) algorithmically transparent.

An important contribution to the understanding of ML algorithms is their mathematical interpretation and derivation, which help to understand when and how to use these approaches. Classical examples are the Kalman filter or principal component analysis, where several mathematical derivations exist for each and enhance their understanding. Note that although there are many mathematical attempts to a better understanding of deep learning, at this stage "the [mathematical] interpretation of DNNs appears to mimic a type of Rorschach test" according to Charles [2018].

Overall, we argue that transparency in its three forms does to a large degree not depend on the specific data, but solely on the ML method. But clearly, the obtained specific solution, in particular the "solution path" to it by the (iterative) algorithm, depends on the training data. The analysis task and the type of attributes usually play a role in achieving design transparency. Moreover, the choice of hyper-parameters might involve model structure, components, or the algorithm, while in an algorithmic determination of hyper-parameters the specific training data comes into play again.

Interpretability We consider interpretability as about making sense of the obtained ML model. Generally, to interpret means "to explain the meaning of" or "present in understandable terms"[1], see also Doshi-Velez and Kim [2017], Gilpin et al. [2018], Guidotti et al. [2018]. We consider explaining as a separate aspect, on top of an interpretation, and focus here on the second aspect. Therefore, the aim of interpretability is to present some of the properties of a ML model in understandable terms to a human. Ideally, one could answer the question from Casert et al. [2019]: "Can we understand on what the ML algorithm bases its decision?" Somewhat formally, Montavon et al. [2018] state:

> An interpretation is the mapping of an abstract concept (e.g., a predicted class) into a domain that the human can make sense of.

[1] https://www.merriam-webster.com/dictionary/interpret

Interpretations can be obtained by way of understandable proxy models, which approximate the predictions of a more complex approach [Gilpin et al., 2018, Guidotti et al., 2018]. Longstanding approaches involve decision trees or rule extraction [Andrews et al., 1995] and linear models. For feature importance, the weights in a linear model are employed to identify attributes which are relevant for a prediction, either global or local. For example, Ribeiro et al. [2016] introduced the model-agnostic approach LIME (Local Interpretable Model-Agnostic Explanations), which gives interpretation by creating locally a linear proxy model in the neighborhood of a datum. Sensitivity analysis can be used to inspect how a model output (locally) depends upon the different input parameters [Saltelli et al., 2004]. Such an extraction of information from the input and the output of a learned model is also called *post hoc interpretability* [Lipton, 2018] or *reverse engineering* [Guidotti et al., 2018].

Visual approaches such as saliency masks or heatmaps show relevant patterns in the input based on feature importance or sensitivity analysis to explain model decisions, in particular for images [Hohman et al., 2018, Montavon et al., 2018, Olah et al., 2018]. In prototype selection, one or several examples similar to the inspected datum are selected, from which criteria for the outcome can be obtained. In the recent surveys Adadi and Berrada [2018], Gilpin et al. [2018], Guidotti et al. [2018] details, further types of interpretation, and specific realization can be found.

In unsupervised learning, the analysis goal can be a better understanding of the data. For an example, by an interpretation of the obtained representation by linear or nonlinear dimensionality reduction [Lee and Verleysen, 2007, Cichocki et al., 2009], or by inspecting the components of a low-rank tensor decomposition [Mørup, 2011].

Note that, in contrast to transparency, to achieve interpretability the data is always involved. Although there are model-agnostic approaches for interpretability, transparency or retaining the model can assist in the interpretation. Furthermore, method specific approaches depend on transparency, for example layer-wise relevance propagation for DNNs exploits the known model layout [Montavon et al., 2018].

While the methods for interpretation allow the inspection of a single datum, Lapuschkin et al. [2019] observe that it becomes quickly very time consuming to investigate large number of individual interpretations. As a step to automate the processing of the individual interpretations for a single datum, they employ spectral clustering of heatmaps of many data to obtain an overall impression of the interpretations for the predictions of the ML algorithm.

Finally, note that the interpretable and human level understanding of the performance of a ML approach can result in a different choice of the ML model, algorithm, or data pre-processing later on.

Explainability While research into explainable ML is widely recognized as important, a joint understanding of the concept of explainability still needs to evolve. It has also been argued, that concerning explanations there is a gap of expectations between ML and so-called explanation sciences such as law, cognitive science, philosophy, and the social sciences [Mittelstadt et al., 2019].

While in philosophy and psychology explanations are in the focus for a long time, a concise definition is not available. For example, explanations can differ in completeness or the degree of causality. We follow a model from a recent review relating insights from the social sciences to explanations in AI [Miller, 2019], which places explanatory questions into three classes: (1) what–questions, such as "What event happened?"; (2) how–questions, such as "How did that event happen?"; and (3) why–questions, such as "Why did that event happen?". From the field of explainable AI we consider a definition from Montavon et al. [2018]:

> An explanation is the collection of features of the interpretable domain, that have contributed for a given example to produce a decision (e.g. classification or regression).

As written in Guidotti et al. [2018], "[in explainable ML] these definitions assume implicitly that the concepts expressed in the understandable terms composing an explanation are self-contained and do not need further explanations."

We believe on the other hand, that a collection of interpretations can be an explanation only with further contextual information, stemming from domain knowledge and related to the analysis goal. In other words, explainability usually cannot be achieved purely algorithmically. On its own, the interpretation of a model — in understandable terms to a human — for an individual datum might not provide an explanation to understand the decision. For example, the most relevant variables might be the same for several data, but the important observation for an understanding could be that different variables are present later in the interpretation. This will depend on the underlying analysis goal. "Why is the decision made?" will need a different explanation than "Why is the decision for datum A different to (the nearby) datum B?".

One should also observe, that explanations can be used to manipulate. For illustration, Baumeister and Newman [1994] distinguish between the intuitive scientist, who seeks to make the most accurate or otherwise optimal decision, and the intuitive lawyer, who desires to justify a preselected conclusion. With that in mind, one often aims for human-centric explanations of black-box models. There are simple or purely algorithmic explanations, for example based on emphasising relevant pixels in an image. In so-called slow judgements tasks, an explanation might more easily enforce confirmation biases. For example, using human-centric explanations as evaluation baselines can be biased towards certain individuals. Further, a review of studies of experimental manipulations that require people to generate explanations or imagine scenarios, indicates that people express greater confidence in a possibility, although false, when asked to generate explanations for it or imagine the possibility [Koehler, 1991].

In this work, we suggest to differentiate between *algorithmic explanations* and *scientific explanations*. With an algorithmic explanation, one aims to reveal underlying causes to the decision of a ML method, this is what explainable ML aims to address. For scientific explanations, Overton [2013] identifies five broad categories to classify the large majority of objects that are explained in science: data, entities, kinds, models, and theories. Furthermore, it is observed, that whether there is a unifying general account of scientific explanation remains an open question.

Finally, for explainability, the goal of the ML 'user' is very relevant. According to Adadi and Berrada [2018], there are essentially four reasons to seek explanations: to justify decisions, to (enhance) control, to improve models, and to discover new knowledge. For regulatory purposes it might be fine to have an explanation by examples or (local) feature analysis, so that certain "formal" aspects can be checked. But, to attain scientific outcomes with ML one wants an understanding. Here, the scientist is using the data, the transparency of the method, and its interpretation to explain the output results (or the data) using domain knowledge and thereby to obtain a scientific outcome.

Domain knowledge As outlined, domain knowledge is an essential part of explainability, but also for treating small data scenarios or for performance reasons. A taxonomy for the explicit integration of knowledge into the ML pipeline, so called *informed ML*, is proposed in von Rueden et al. [2019]. Three aspects are involved:

- type of knowledge,
- representation and transformation of knowledge, and
- integration of knowledge into the ML approach.

See also the related works of Karpatne et al. [2017], who use the term *theory-guided data science*, or physics-informed learning by [Raissi et al., 2017a]. For the purpose of this article, we follow von Rueden et al. [2019] and aim to arrange different the types of knowledge along their degree of formality, from the sciences, over (engineering or production) process flow to world knowledge and finally individual (expert's) intuition. Knowledge can be assigned to several of the types in this incomplete list.

In the sciences, knowledge is often given in terms of mathematical equations, such as analytic expression or differential equations, as relations between instances and/or classes in form of rules or constraints. It can be represented in the form of ontologies, by symmetries, or using similarity measures. Knowledge can be transformed by numerical simulations of models or through human interaction.

As ingredients of a ML approach one considers training data, the hypothesis space, the training algorithm, and the final model. In each of these, one can incorporate additional knowledge. Feature engineering is a common and longstanding way to incorporate knowledge into the training data, while using numerical simulations to generate (additional) training data is a modern phenomena.

Integrating knowledge into the hypothesis space can be achieved by choosing the structure of the model. For example, by defining a specific architecture of a neural network or by choosing a structure of probability distributions which observes existing or non-existing links between variables. An example for the training phase is modifying the loss function according to additional knowledge, e.g., by adding a consistency term. Finally, the obtained model can be put in relation to existing knowledge, e.g., by checking known constraints for the predictions. This aspect we call scientific consistency and deem it especially important to obtain scientific outcomes.

Scientific consistency A fundamental prerequisite for generating reliable outcomes for scientific applications is scientific consistency. This means that the result obtained is plausible and consistent with existing scientific principles. The selection and formulation of the scientific principles to be met is based on domain knowledge, where the way of integration is the core research question in areas such as informed ML. In the chain of Fig. 1, scientific consistency can be considered a priori at the model design stage or a posteriori by analysing the output results. As pointed out by von Rueden et al. [2019], scientific consistency at the design stage can be understood as the result of a regularization effect, where various ways exist to restrict the solution space to scientifically consistent solutions. Reichstein et al. [2019] identify scientific consistency besides interpretability as one of the five major challenges we need to tackle to successfully adopt deep learning approaches in the geosciences. Karpatne et al. [2017] underlines the importance of consistency by defining it as an essential component to measure performance:

> One of the overarching visions of [theory-guided data science] is to include [..] consistency as a critical component of model performance along with training accuracy and model complexity. This can be summarized in a simple way by the following revised objective of model performance [...]: Performance $\propto$ Accuracy + Simplicity + Consistency.

They discuss several ways to restrict the solution space to physically consistent solutions, e.g., by (1) design of the model family such as specific network architectures, (2) guidance of a learning algorithm using, e.g., specific initializations, constraints, or (loss) regularizations, (3) refinement of the model output, e.g., using closed-form equations or model simulations, (4) hybrid models of theory and ML, and (5) augmenting theory-based models using real data such as data assimilation or calibration.

Overall, the explicit restriction of the solution space to scientifically consistent solutions is not a requirement to achieve valuable scientific outcomes. Neglecting this restriction, however, means that a consistent solution cannot be guaranteed, even if an optimal result has been achieved from a mathematical point of view.

3 Scientific Outcomes From Machine Learning

In the next subsections, we will review several examples that use ML and strive for different levels of transparency, interpretability, and explainability to produce scientific outcomes. We will focus on examples which utilize an extensive amount of scientific domain knowledge from the natural sciences. We define two general categories: The first one is the derivation of scientific outcomes by explaining output results. Many works address the derivation of scientific outcomes by learning a ML model and generalizing from known input-output relations to new input-output pairs. Most of these approaches, so far, solely explain what the outcome is from a scientific point of view (scientific explanation), but cannot answer the question why this specific outcome was arrived from an algorithmic point of view (algorithmic explanation). Other approaches attempt to scientifically explain the output in terms of the specific corresponding input. Here,

interpretation tools are utilized, where the model is used only as a means to an end to explain the result and it is not explicitly analyzed itself. This states the lowest degree of explainability with no necessity of a transparent or interpretable model.

The other approach is to derive scientific outcomes by explaining models. Here, interpretation tools are used to project processes in the model into a space which is interpretable, which can then be explained utilizing domain knowledge. Both scientific and algorithmic explanations are used to derive a scientific outcome. That means, even if the scientific outcome is more specifically defined by domain experts, transparency and interpretability of the models are not a prerequisite for these approaches. We recognize that the collection of work included in this section is not exhaustive and hope to include additional relevant references in subsequent versions of this survey.

3.1 Scientific outcomes by explaining output results

3.1.1 Prediction of Intuitive Scientific Outcomes

The works described in this subsection have been developed in the physical domain, where generally two kind of outcomes are derived. The first is the derivation of intuitive physics, that is everyday-observed rules of nature which help us to predict the outcome of events even with a relatively untrained human perception, e.g., whether a tower will collapse [McCloskey, 1983]. The other one is concerned with the estimation of specific physical parameters from which static properties or object behavior can be derived. Chang et al. [2017] denote these respective approaches as bottom-up, where observations are directly mapped to an estimate of some object behavior or the physical outcome of a scene, and as top-down, where parameters are inferred to explain a scene. In both cases, only the scientific explanation is aspired.

A task often considered is the prediction of whether a certain construction collapses in an image or a video. Lerer et al. [2016] and Li et al. [2016] use video simulations to learn intuitive physics, for example about the stability of wooden block towers. Lerer et al. [2016] use ResNet-34 [He et al., 2016] and Googlenet [Szegedy et al., 2015] to predict the fall of towers of wooden blocks, as well as DeepMask [Pinheiro et al., 2015] and a custom network called PhysNet to predict the trajectory of the wooden blocks in case the tower is collapsing. The first task is formulated as a binary classification tasks and the second task is formulated as a semantic segmentation, where each wooden block is defined as one class. In both tasks, PhysNet outperforms human subjects on synthetic data and achieves comparable results on real data. Similar experiments with more complex scenes were conducted by Li et al. [2016] using various popular convolutional neural networks (CNNs). Tompson et al. [2016] and Jeong et al. [2015] use similar approaches for applications such as fluid simulations, where physics based losses are introduced to achieve plausible results.

3.1.2 Prediction of Scientific Parameters and Properties

Although the approaches just described set up scientific outcome prediction as supervised learning problems, there is still a gap between common supervised tasks, e.g.,

classification, object detection, and prediction, and actual understanding of a scene and its reasoning. The methods presented so far do not learn a model that is able to capture and derive the physical properties and dynamics of objects and their environment, as well as their interactions. Therefore, the model cannot inherently explain why a specific outcome was obtained from a scientific viewpoint. Several classification and regression frameworks have been formulated to tackle this challenge.

Stewart and Ermon [2017], for example, detect and track objects in videos in an unsupervised way. For this, they use a regression CNN and introduce terms which measure the consistency of the output when compared to physical laws which specifically and thoroughly describe the dynamics in the video. In this case, the input of the regression network is a video sequence and the output is a time-series of physical parameters such as the height of a thrown object. Wu et al. [2016] introduces Physics101, a dataset which contains over 17000 video clips containing 101 objects of different characteristics, which was build for the task to derive physical parameters such as velocity and mass. In their work, they use the LeNet CNN architecture [LeCun et al., 1998] to capture visual as well as physical characteristics while explicitly integrating physical laws based on material and volume to aim for scientific consistency. Their experiments show that predictions can be made about the behavior of an object after a fall or a collision using estimated physical characteristics, which serve as input to an independent physical simulation model. Monszpart et al. [2016] introduce SMASH, which extracts physical collision parameters from videos of colliding objects, such as pre- and post collision velocities, to use them as input for existing physics engines for modifications. For this, they estimate the position and orientation of objects in videos using constrained least-squares estimation in compliance with physical laws such as momentum conservation. Based on the determined trajectories, parameters such as velocities can be derived.

Also other disciplines use ML to help guide new scientific insights and discoveries. Regression, in particular, has been leveraged often to explain phenomena. Mauro et al. [2016] present an approach for the design of new functional glasses which comprises the prediction of characteristics relevant for manufacturing as well as end-use properties of glass. Among others, they utilize neural networks to estimate the liquidus temperatures for various silicate compositions comprising up to 8 different components. For this, they learn from several hundred composites with known output properties and apply the model to novel, unknown composites. Generally, the identification of an optimized composition of the silicates yielding a suitable liquidus temperature is a costly task and is oftentimes based on trial-and-error.

For organic photovoltaics material, a related approach utilizing quantum chemistry calculations and ML techniques to calibrate theoretical results to experimental data was presented in [Pyzer-Knapp et al., 2016, Lopez et al., 2017]. The authors consider already performed existing experiments as current knowledge, which is embedded within a probabilistic non-parametric mapping. In particular, Gaussian processes were used to learn the deviation of properties calculated by computational models from the experimental analogues. Furthermore, since the prediction results involve a confidence in each calibration point being returned, the user can be informed when the scheme is being used for systems for which it is not suited [Pyzer-Knapp et al., 2016]. In Lopez et al. [2017], 838

high-performing candidate molecules have been identified within the explored molecular space, due to the now possible efficient screening of over 51,000 molecules.

In Ling et al. [2016b], a deep learning approach for Reynolds-averaged Navier–Stokes (RANS) turbulence modelling was presented. Here, a network architecture that embedded invariance using a higher-order multiplicative layer was shown to have significantly more accurate predictions compared to a generic neural network architecture. Further, the improved prediction on a test case that had a different geometry than any of the training cases indicates that improved RANS predictions for more than just interpolation situations seem achievable. A related approach for RANS-modeled Reynolds stresses for high-speed flat-plate turbulent boundary layers was presented in Wang et al. [2019], which uses a systematic approach with basis tensor invariants proposed by Ling et al. [2016a]. Additionally, a metric of prediction confidence and a nonlinear dimensionality reduction technique are employed to provide a priori assessment of the prediction confidence.

In Raissi et al. [2017b], a data-driven algorithm for learning the coefficients of general parametric linear differential equations from noisy data was introduced, solving a so-called inverse problem. The approach employs Gaussian process priors that are tailored to the corresponding and known type of differential operators. Besides classical benchmark problems with different attributes, the approach was used on an example application in functional genomics, determining the structure and dynamics of genetic networks based on real expression data. A related information-based machine learning approach to solve an inverse problem in biomechanical applications was presented in Hoerig et al. [2017]. Here, in mechanical property imaging of soft biological media under quasi-static loads, elasticity imaging parameters are computed from estimated stresses and strains.

Raissi [2018] proposes a nonlinear regression approach employing DNNs to learn closed form representations of partial differential equations from scattered data collected in space and time, thereby uncovering the dynamic dependencies and obtaining a model that can be subsequently used to forecast future states. In benchmark studies, including Burgers' equation, nonlinear Schrödinger equation, or Navier-Stokes equation, the underlying dynamics are learned from numerical simulation data up to a specific time. The obtained model is used to forecast future states, where relative L_2-errors of up to the order of 10^{-3} are observed.

Mottaghi et al. [2016] introduce Newtonian neural networks in order to predict the long-term motion of objects from a single color image. Instead of predicting physical parameters from the image, they introduce 12 Newtonian scenarios serving as physical abstraction, where each scenario is defined by physical parameters defining the dynamics. The image, which contains the object of interest, is mapped to a state in one of these scenarios which best describes the current dynamics in the image. Newtonian neural networks are two parallel CNNs, where one encodes the images, and the other one derives convolutional filters from videos acquired with a game engine simulating each of the 12 Newtonian scenarios. Zhu et al. [2015] introduces a framework which calculates physical concepts from color-depth videos that explains tool and tool-use such as cracking a nut. In their work, they learn task-oriented representations for each tool and task defined

over a graph with spatial, temporal, and causal relations. They distinguish between 13 physical concepts such as painting a wall, and show that the framework is able generalize from known to unseen concepts by selecting appropriate tools and tool-uses.

3.1.3 Interpretation Tools for Scientific Outcomes

Other approaches use interpretation tools to extract information from learned models and to help to scientifically explain the individual output or several outputs jointly. Often, direct approaches are undertaken to present this information via visualizations of learned representations, natural language representations, or the discussion of examples. Nonetheless, human interaction is still required to interpret this additional information, which has to be derived from the learned model during the post-hoc analysis.

For example, ML has been applied to functional magnetic resonance imaging data to design biomarkers that are predictive of psychiatric disorders. However, only "surrogate" labels are available, e.g., behavioral scores, and so the biomarkers themselves are also "surrogates" of the optimal descriptors [Pinho et al., 2018, Varoquaux et al., 2018]. The biomarker design promotes spatially compact pixel selections, producing biomarkers for disease prediction that are focused on regions of the brain; these are then considered by expert physicians [Pinho et al., 2018, Varoquaux et al., 2018].

Kailkhura et al. [2019] discusses explainable ML for scientific discoveries in material sciences. They identify challenges when using ML for material science applications such as the reliability-explainability trade-off. They point out that many works see explainability as the inverse of complexity, leading to an increase in accuracy and reliability when reducing the complexity. In the worst case, this may lead to misleading or incorrect explanations. In their work, they propose an ensemble of simple models to predict material properties along with a novel evaluation metric focusing on trust by quantifying generalization performance. Moreover, their pipeline contains a rationale generator which provides decision-level explanations for individual predictions and model-level explanations for the whole regression model. In detail, they produce explanations in terms of prototypes which are analyzed and explained by an expert, as well as global explanations by estimating feature importance for material sub-classes.

Generally, there has been an increased interest in using automatic approaches for estimating feature importances. Although handcrafted and manually selected features are easier to understand, automatically determined features can reveal previously unknown scientific attributes and structures. Ginsburg et al. [2016], for example, proposes FINE (feature importance in nonlinear embeddings) for the analysis of cancer patterns in ER+ breast cancer tissue slides. This approach relates original and automatically derived features to each other by estimating the relative contributions of the original features to the reduced-dimensionality manifold. This approach can be combined with various non-linear dimensionality reduction techniques.

Ghosal et al. [2018] use interpretation tools for image-based plant stress phenotyping. They train a CNN model and identify the most important feature maps in various layers that isolate the visual cues for stress and disease symptoms. They produce so-called explanation maps as sum of most important features maps indicated by their

activation level. A comparison of manually marked visual cues by an expert and the automatically derived explanation maps reveal a high level of agreement between the automatic approach and human ratings. The goal of their approach is the analysis of the performance of their model, the provision of visual cues which are human-interpretable to support the prediction of the system, and a provision of important cues for the identification of plant stress.

Abbasi-Asl et al. [2018] introduces DeepTune, a stability-driven visualization framework for CNNs, for applications in neuroscience. DeepTune consists of a battery of CNNs that learn multiple complementary representations of natural images. The features from these CNNs are fed into regression models to predict the firing rates of neurons in V4. The combination of these feature extraction and regression modules allow for accurate prediction of V4 neuron responses to additional visual stimuli. Representative visual stimuli for each neuron can then be generated from the trained modules via gradient optimization.

Various interpretability methods have also been used for diverse applications which utilize time-series data. For example, Deming et al. [2016] applied attention modules to models trained on genomic sequences for the identification of important sequence motifs by visualizing the attention mask weights. They propose the genetic architect that finds a suitable network architecture by iteratively searching over various neural network building blocks. They state that the choice of the neural network architecture highly depends on the application domain, which is a challenge if no prior knowledge is available about the network design. Depending on the optimized architecture, attention modules and expert knowledge lead to different scientific insights. Additionally, Singh et al. [2017] use attention modules for genomics in their AttentiveChrome network. The network contains a hierarchy of attention modules to gain insights about where and what the network has focused. Also Choi et al. [2016] developed a hierarchical attention-based interpretation tool called RETAIN (REverse Time AttentIoN) in healthcare. The tool identifies influential past visits of a patient as well as important clinical variables during these visits from the patient's medical history to support medical explanations.

3.2 Scientific Outcomes by Explaining Models

So far, the presented approaches either treat the model as a black box or use it only indirectly by applying interpretation tools to better explain the output. Liao and Poggio [2017] propose a concept called 'object-oriented deep learning' with the goal to convert a DNN to a symbolic description to gain interpretability and explainability. They state that generally in neural networks there is inherently no explicit representation of symbolic concepts like objects or events, but rather a feature-oriented representation, which is difficult to explain. In their representation, objects could be formulated to have disentangled and interpretable properties. Although not commonly used so far, their work state a promising direction towards a higher explainabilty of models. The reviewed approaches in this subsection use the common feature-oriented representation with focus on the disentanglement of the underlying factor of variation in a system, which can be explained by an expert afterwards.

3.2.1 Assigning Scientific Parameters to Model Components

Neural networks, for example, can be customized to a specific scientific application so that the used architecture restricts or promotes properties that are desirable in the data modeled by the network. For example, in plasma physics modeling for inversion, properties such as positivity and smoothness can be promoted by a modified deep learning network [Matos et al., 2018]. Similarly, the properties of contaminant dispersion in soil can be successfully modeled by a long-short-term memory network [Breen et al., 2018].

In contrast to most of the works in Sec. 3.1, which rely on prior knowledge about relevant parameters, some other works derive characteristics of settings without any assumptions about the underlying scientific process. For example, Ehrhardt et al. [2017] derive physical parameters without assuming prior knowledge about the physical processes and without modelling the underlying physical models in order to make predictions in simple physical scenarios over time. Here, the parameters are not only derived as outcome, but also integrated in a recurrent end-to-end long-term prediction network. Therefore, a simulation software and the explicit modelling of the underlying physical laws is not necessary.

Another broad framework [Yair et al., 2017, Dsilva et al., 2018, Holidaya et al., 2019] leverages unsupervised learning approaches to learn low-complexity representations of physical process observations. In many cases where the underlying process features a small number of degrees of freedom, it is shown that nonlinear manifold learning algorithms are able to discern these degrees of freedoms as the component dimensions of low-dimensional nonlinear manifold embeddings, which preserve the underlying geometry of the original data space.

Iten et al. [2018] introduces SciNet, a modified variational autoencoder which learns a representation from experimental data and use the learned representation to derive physical concepts from it rather than the experimental input data. The learned representation is forced to be much simpler as the experimental data and contains the explanatory factors of the system such as the physical parameters. This is proven by the fact that physical parameters and the activations of the neurons in the hidden layers have a linear relationship. Additionally, Ye et al. [2018] construct the bottleneck layer in their neural network to represent physical parameters to predict the outcome of a collision of objects from videos. However, the architecture of the bottleneck layer is not learned, but designed with prior knowledge about the underlying physical process. Daniels et al. [2019] use their ML algorithm 'Sir Isaac' [Daniels and Nemenman, 2015] to infer a dynamical model of biological time series data to understand and predict dynamics of worm behavior. They model a system of differential equations, where the number of hidden variables is determined automatically from the system, and the meaning of them can be explained by an expert.

Feature selection schemes using embedded methods have been recently explored to establish or refine models in physical processes [Rudy et al., 2017] and material sciences [Ghiringhelli et al., 2017, Ouyang et al., 2018]. Using a sparsity-promoting penalty, they propose groups of variables that may explain a property of interest and promoting the simplest model, that is, the model involving the fewest variables possible while

achieving a target accuracy. Their application has also proved fruitful in the broader class of problems leveraging partial differential equation and dynamical system models [Tran and Ward, 2017, Mangan et al., 2016, Schaeffer et al., 2013]. For example, the similarities between the multilayer perceptron architecture and the physical model for transmission electron microscopy makes the application of the former architecture to the latter scientific domain transparent [Pennington et al., 2018, Sun et al., 2018]. Similarly, an application of ML for epidemiology leverages a networked dynamical system model for contagion dynamics, where nodes correspond to subjects with assigned states; thus, most properties of the ML model match the properties of the scientific domain considered [Adiga et al., 2018].

Ma et al. [2018] encode in a DNN the hierarchical structure of a gene ontology tree, either from literature or inferred from large-scale molecular data sets. This enables transparent biological interpretation, while successfully predicting effects of gene mutations on cell proliferation. Furthermore, it is argued that the employed deep hierarchical structure captures many different clusters of features at multiple scales and pushes interpretation from the model input to internal features representing biological subsystems. In their work, while no information about subsystem states was provided during model training, previously undocumented learned subsystem states could be confirmed by molecular measurements.

3.2.2 Understanding Structures and Dynamic Processes

A more sophisticated step is implemented in the neural physics engine framework proposed by Chang et al. [2017], in which a scene is factorized into composable parts with each its own dynamic and common pairwise interactions. A neural network is employed, where the compositional structure of the network is designed in this way that object dynamics and their pairwise interactions can be represented. Based on the current and past observations of a physical scene, the network forecasts future states and physical properties of the system.

In single-cell genomics, computational data-driven analysis methods are employed to reveal the diverse simultaneous facets of a cell's identity. To goal is to obtain a data representation of cell development which allows to determine different aspects of cellular organization and function. So far, there is an emphasis on unsupervised learning approaches [Wagner et al., 2016].

In phylogeny, correlations between genomes from a variety of animal species can be modeled using tree graph priors to infer evolutionary relationships [Molloy and Warnow, 2018].

Lusch et al. [2018] construct a DNN for computing Koopman eigenfunctions from data. Motivated by domain knowledge, they employ an auxiliary network to parametrize the continuous frequency. Thereby, a compact model is obtained, which additionally is interpretable. For example, for the nonlinear pendulum the first two obtained eigenfunctions map into magnitude and phase coordinates, where the magnitude essentially traces level sets of the Hamiltonian energy. This turned out to be consistent with recent theoretical derivations beforehand unknown to the authors.

Listgarten and collaborators have proposed a data-centric approach for scientific design based on the combination of a generative model for the data of interest, e.g., genomes or proteins, and a predictive model for a quantity or property of interest, e.g., disease indicators or protein fluorescence. For example, in genome-wide association studies, the generative model learns to predict on-target and off-target activities across the genome [Listgarten et al., 2018]. For DNA sequence design, these two components are also integrated into a generative adversarial network in order to generate new synthetic data samples that optimize the value of the quantity or property by leveraging an adaptive sampling technique over the generative model [Brookes and Listgarten, 2018].

3.3 Related Surveys about Machine Learning in the Natural Sciences

Butler et al. [2018] give on overview on recent research using ML for molecular and materials science. Given that standard ML models are numerical, the algorithms need suitable numerical representations that capture relevant chemical properties, such as the Coulomb matrix and graphs for molecules, and radial distribution functions that represent crystal structures. Supervised learning systems are in common use to predict numerical properties of chemical compounds and materials. Unsupervised learning and generative models are being used to guide chemical synthesis and compound discovery processes, where deep learning algorithms and generative adversarial networks have been successful. Alternative models exploiting the similarities between organic chemistry and linguistics are based on textual representations of chemical compounds.

Several ML approaches have been used in biology and medicine to derive new insights, as described in Ching et al. [2018] for the broad class of deep learning methods. Supervised learning mostly focuses on the classification of diseases and disease types, patient categorization, and drug interaction prediction. Unsupervised learning has been applied to drug discovery. The authors point out that in addition to the derivation of new findings, an explanation of these is of great importance. Furthermore, the need in deep learning for large training datasets poses a limit to its current applicability beyond imaging (through data augmentation) and so-called 'omics' studies.

Hohman et al. [2018] give a survey of visual analytics in deep learning research, where such systems have been developed to support model explanation, interpretation, debugging, and improvement, and the mainconsumers of these analytics are the model developers and users as well as non-experts.

An overview of approaches in systems biology to design DNNs that encode the hierarchical interactions in the biological networks in the architecture is given in Gazestani and Lewis [2019]. They describe how one can develop flexible deep models that propagate information through the molecular networks to successfully classify cell states.

Reichstein et al. [2019] give an overview of ML research in Earth system science. They conclude, that while the general cycle of exploration, hypotheses generation and testing remains the same, modern data-driven science and ML can extract patterns in observational data to challenge complex theories and Earth system models, and thereby strongly complement and enrich geoscientific research.

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