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Center for Protein Diagnostics

Theory is Dead! Long Live Theory!

A short manifesto for hypothesis-centric machine learning

TBI Winterseminar, Bled, Slovenia
February 15, 2023

Axel Mosig
Ruhr-University Bochum, Germany

Theory is dead!

The End of Theory: The Data Deluge Makes the Scientific Method Obsolete

By Chris Anderson 06.23.08

"... The scientific method is built around testable hypotheses. These models, for the most part, are systems visualized in the minds of scientists. The models are then tested, and experiments confirm or falsify theoretical models of how the world works. This is the way science has worked for hundreds of years.

...

... **But faced with massive data, this approach to science — hypothesize, model, test — is becoming obsolete**.

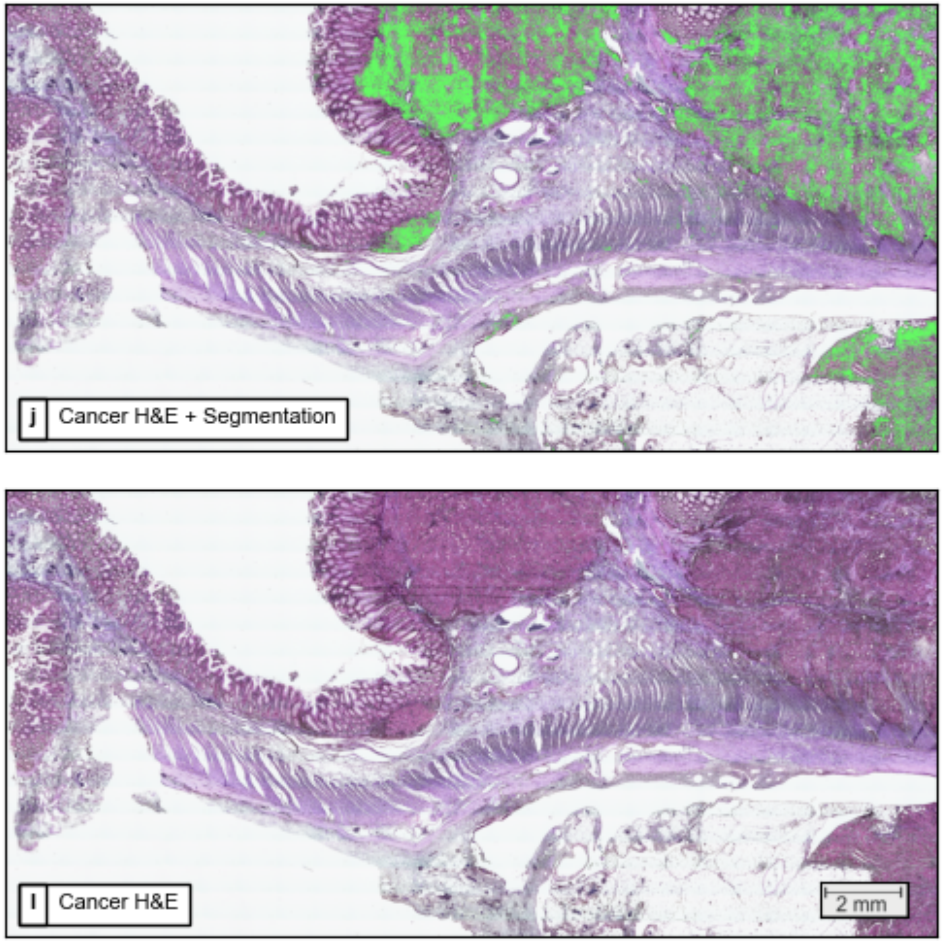
...the science equivalent of Fukuyama's "end of history"...

Data-centric learning: Computational pathology

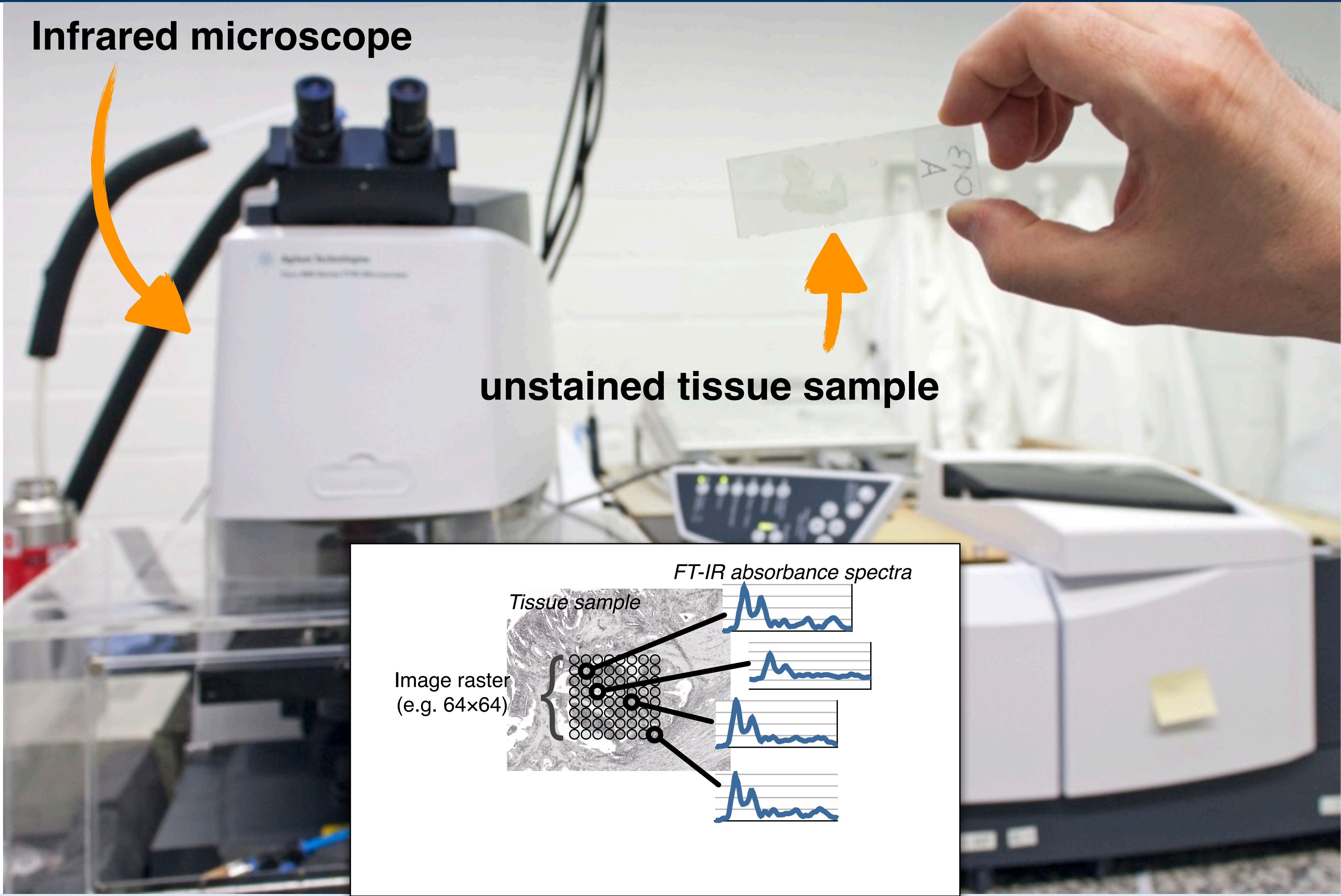
Conventional light microscope

Thin section of tissue sample stained by hematoxylin and eosine (H&E)

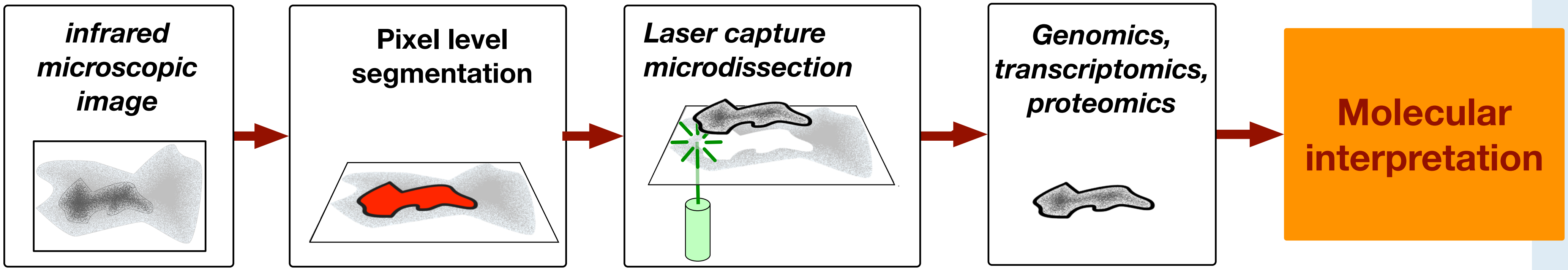
tumor



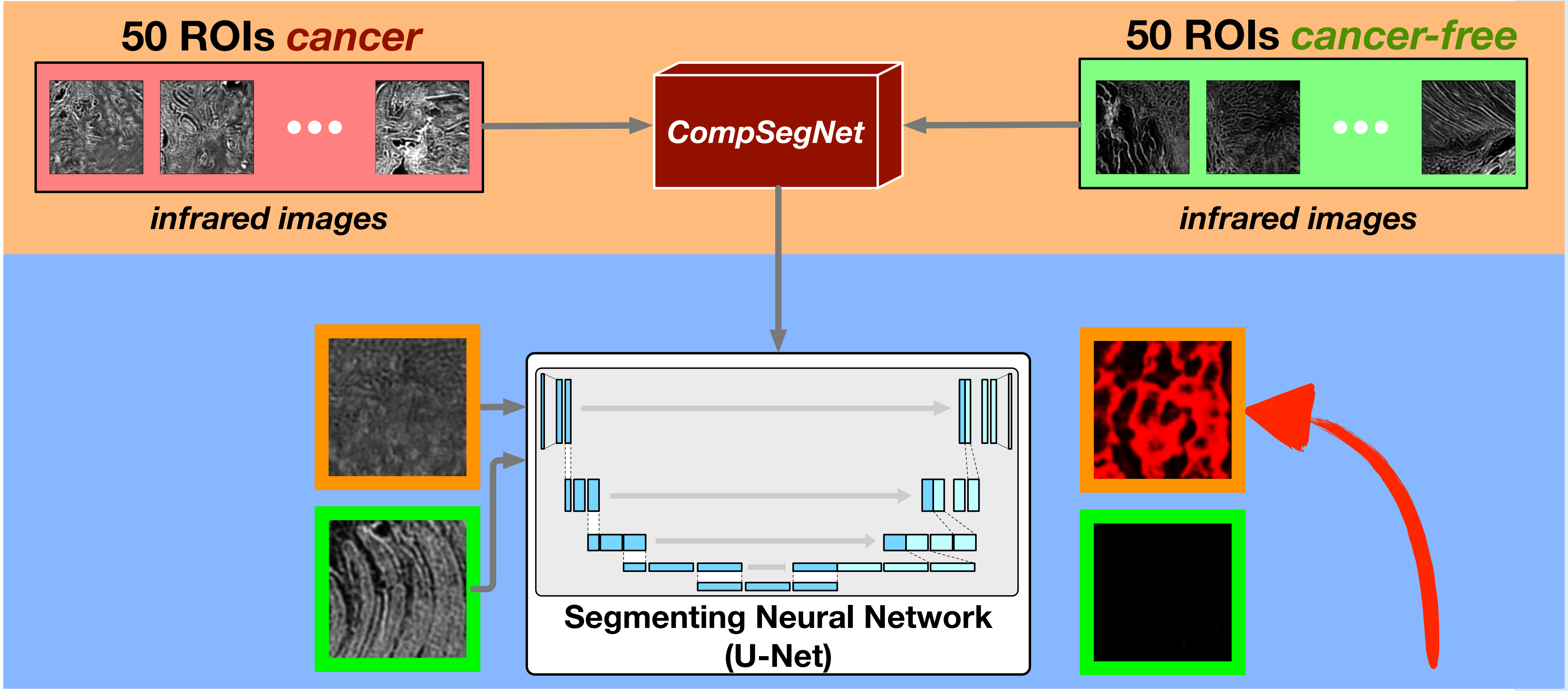
Computational Pathology without labels



Molecularly interpretable microscopy?



Inferring pixel level segmentations: The Comparative Segmentation Network

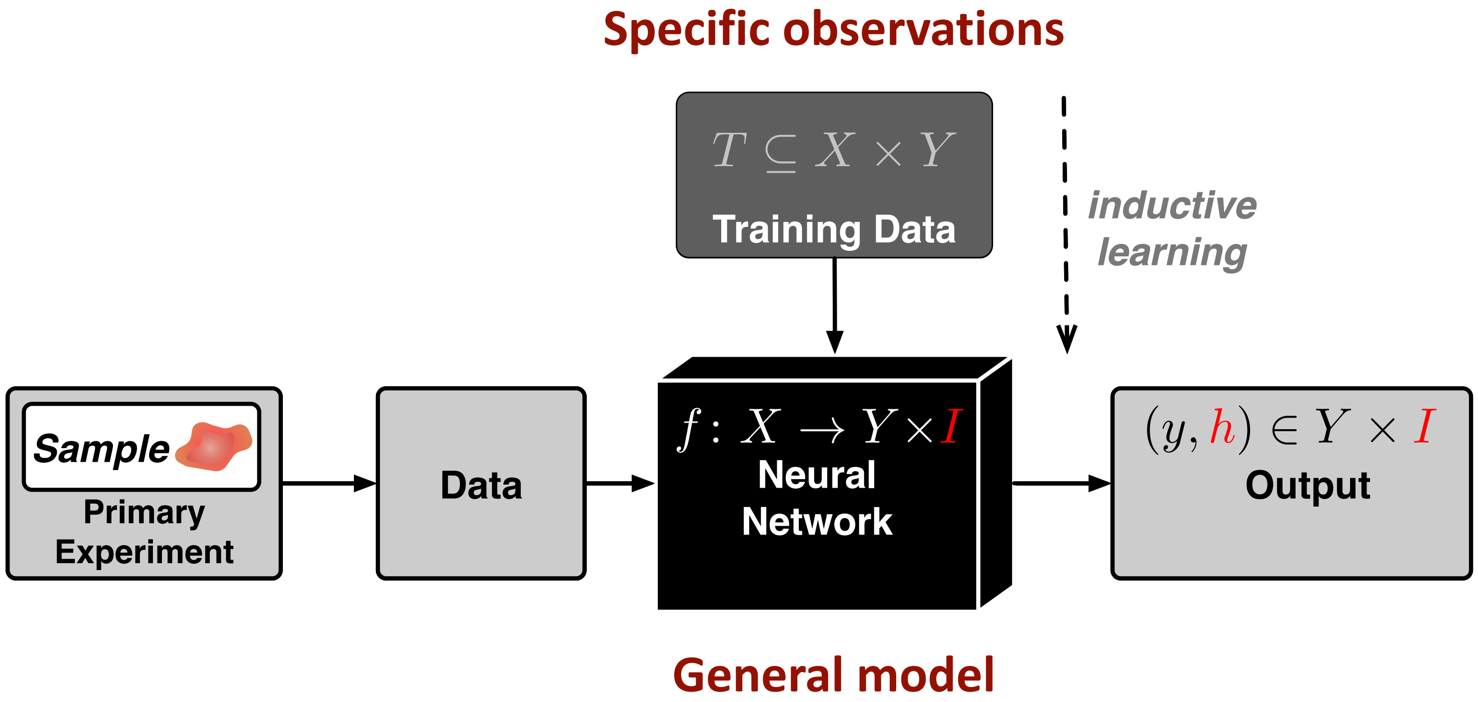


"I-space"

Interpretable
Intermediate
Induced
Internal

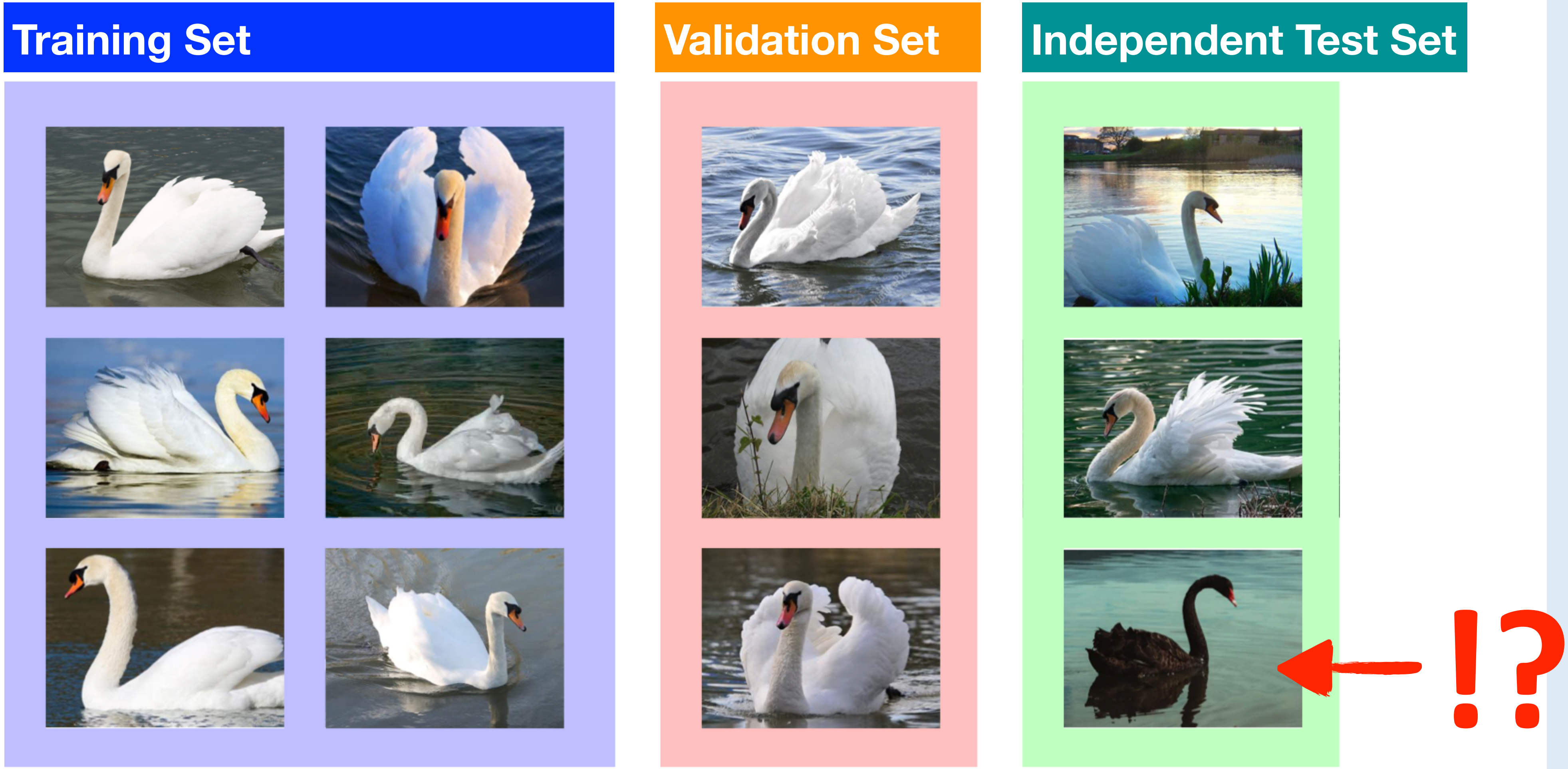
Schuhmacher, Schörner et al., Medical Image Analysis (2022)

Supervised learning and inductive inference



Supervised learning relies on generalization

Why generalization is difficult in philosophy



The Problem of Induction:

"Even after the observation of the frequent conjunction of objects, we have no reason to draw any inference concerning any object beyond those of which we have had experience."

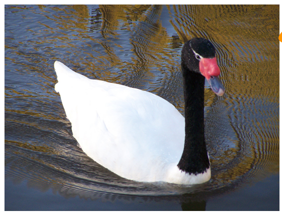
(1739)

Why generalization is difficult in biology

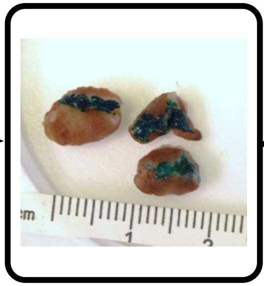
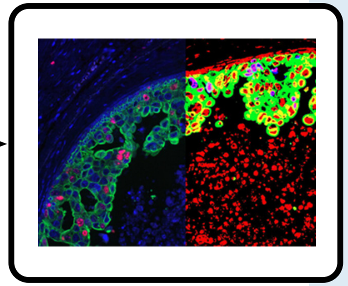
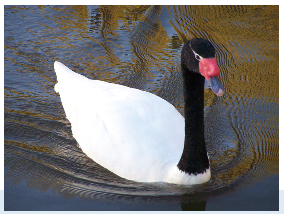
Christopher Phiel, PhD • 3rd+
Associate Professor of Molecular Biology, University of Colora...
5d • Edited •

+ Follow

Students often wonder why experiments don't work despite following the protocol. To show how that could happen I gave everyone in my Molecular Biology Lab class a box of brownie mix and asked them to follow the instructions on the box. Here are the results. None of them are the same. Imagine how much the details matter in molecular biology when trying to replicate data. It was a fun and delicious exercise. And everyone earned brownie points.



Sources of variance

Patient	Sample Extraction	Sample Preparation	Imaging Device	Data Processing
				
Age	Type of Surgery	Type of fixation	Type of microscope	Type of data compression
Genotype	Sample handling	Substrate material	Device age	Preprocessing
Environment. factors			Device settings / calibration	Software versions
...			...	...

Why generalization is difficult in mathematics

The Lack of A Priori Distinctions Between Learning Algorithms

David H. Wolpert
The Santa Fe Institute, 1399 Hyde Park Rd.,
Santa Fe, NM, 87501, USA

(1996)

ARTICLE — Communicated by Steven Nowlan

The Lack of A Priori Distinctions Between Learning Algorithms

David H. Wolpert
The Santa Fe Institute, 1399 Hyde Park Rd.,
Santa Fe, NM, 87501, USA

This is the first of two papers that use off-training set (OTS) error to investigate the assumption-free relationship between learning algorithms. This first paper discusses the senses in which there are no a priori distinctions between learning algorithms. (The second paper discusses the senses in which there are such distinctions.) In this first paper it is shown, loosely speaking, that for any two algorithms A and B, there are "as many" targets (or priors over targets) for which A has lower expected OTS error than B as vice versa, for loss functions like zero-one loss. In particular, this is true if A is cross-validation and B is "anti-cross-validation" (choose the learning algorithm with largest cross-validation error). This paper ends with a discussion of the implications of these results for computational learning theory. It is shown that one *cannot* say: if empirical misclassification rate is low, the Vapnik–Chervonenkis dimension of your generalizer is small, and the training set is large, then with high probability your OTS error is small. Other implications for "membership queries" algorithms and

"Even after the observation of the frequent conjunction of objects, we have no reason to draw any inference concerning any object beyond those of which we have had experience."
David Hume, in *A Treatise of Human Nature*, Book I, part 3, Section 12.

1 Introduction

Much of modern supervised learning theory gives the impression that one can deduce something about the efficacy of a particular learning algorithm (generalizer) without the need for any assumptions about the target input–output relationship one is trying to learn with that algorithm. At most, it would appear, to make such a deduction one has to know something about the training set as well as about the learning algorithm.

Consider for example the following quotes from some well-known papers: "Theoretical studies link the generalization error of a learning

Neural Computation **8, 1341–1390** (1996)

"Even after the observation of the frequent conjunction of objects, we have no reason to draw any inference concerning any object beyond those of which we have had experience."

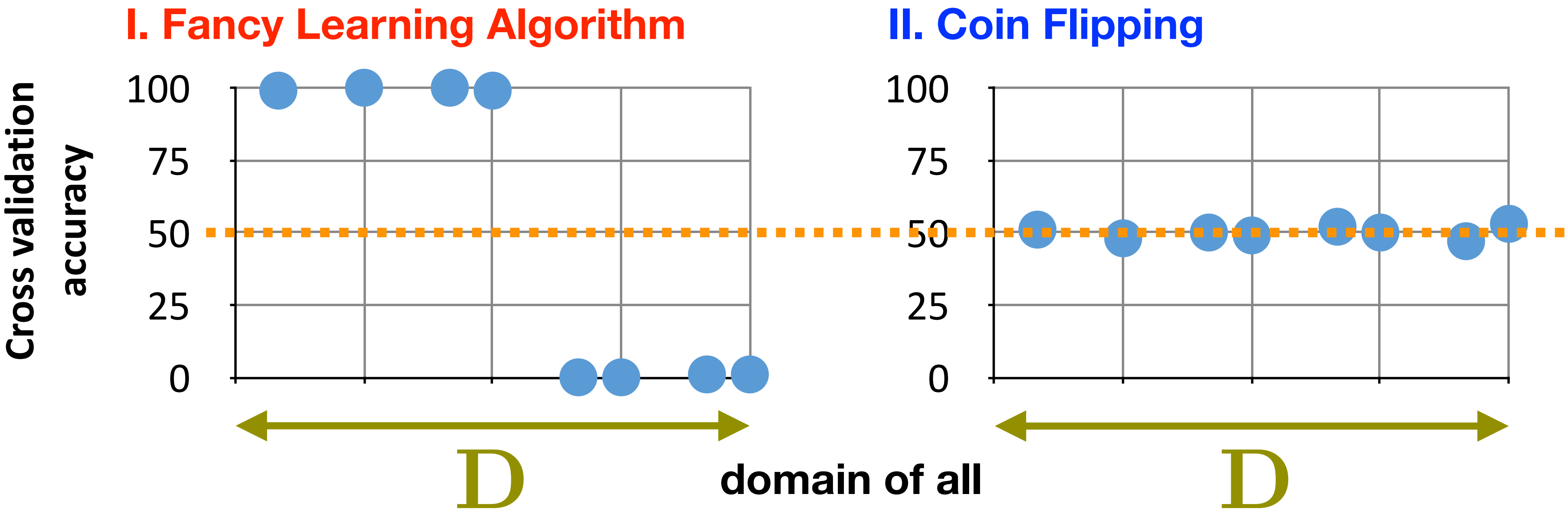
David Hume, in *A Treatise of Human Nature*, Book I, part 3, Section 12.

(1739)

"No-free-lunch theorem"

The no-free-lunch theorem in a nutshell

Compare two learning algorithms:



domain of all mathematically possible data sets

On average across $\mathbb{D}$, all learning algorithms perform equal.

On which instances in $\mathbb{D}$ does a learning algorithm perform well?

$\rightsquigarrow$ **Inductive bias of a learning algorithm!**

What should guide inductive bias?

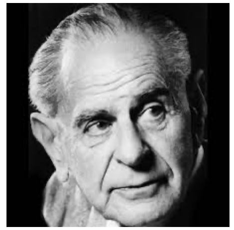
If machine learning is so unreliable, why can we trust scientific reasoning?

Explanation is at the heart of the scientific method

Targeted Observation

falsifiable!

Sample **Experiment** ← **Prediction** ← **Hypothesis** ← **Domain Knowledge**



deductive reasoning

Specific sample ← **General hypothesis**

Explanation!

Refutation ← **Conjecture**

Example:
Can one learn the laws of gravity by watching youtube?

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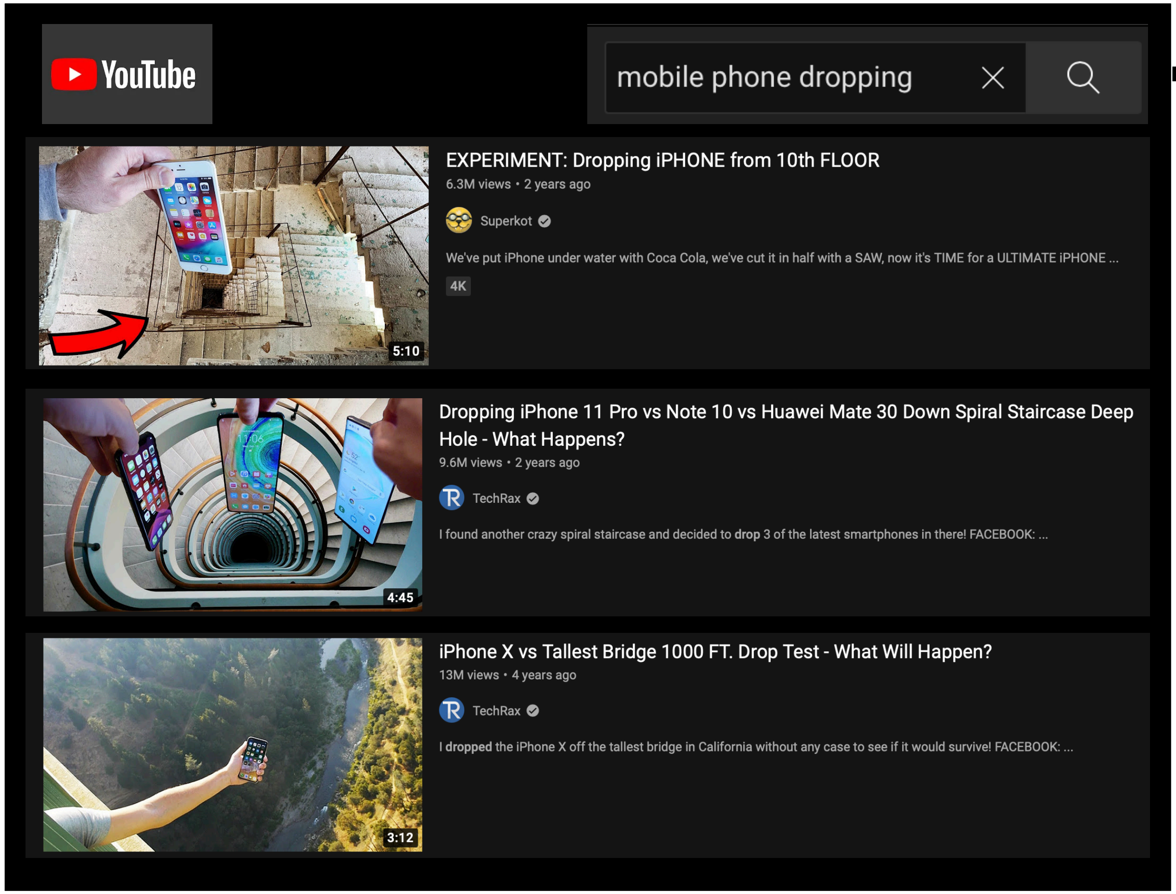
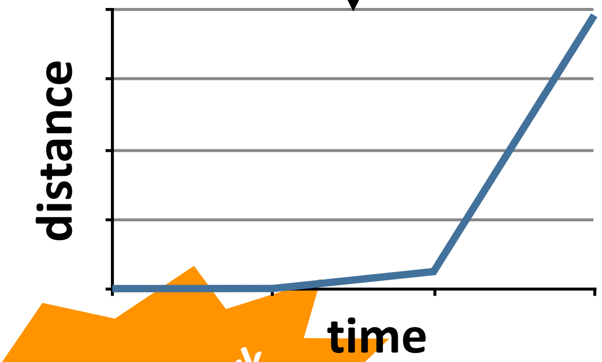
"Watch youtube, and identify some laws of nature"

(The youtube equivalent of a GWAS or GSEA...)



Neural network that identifies and tracks mobile phones and estimates distances



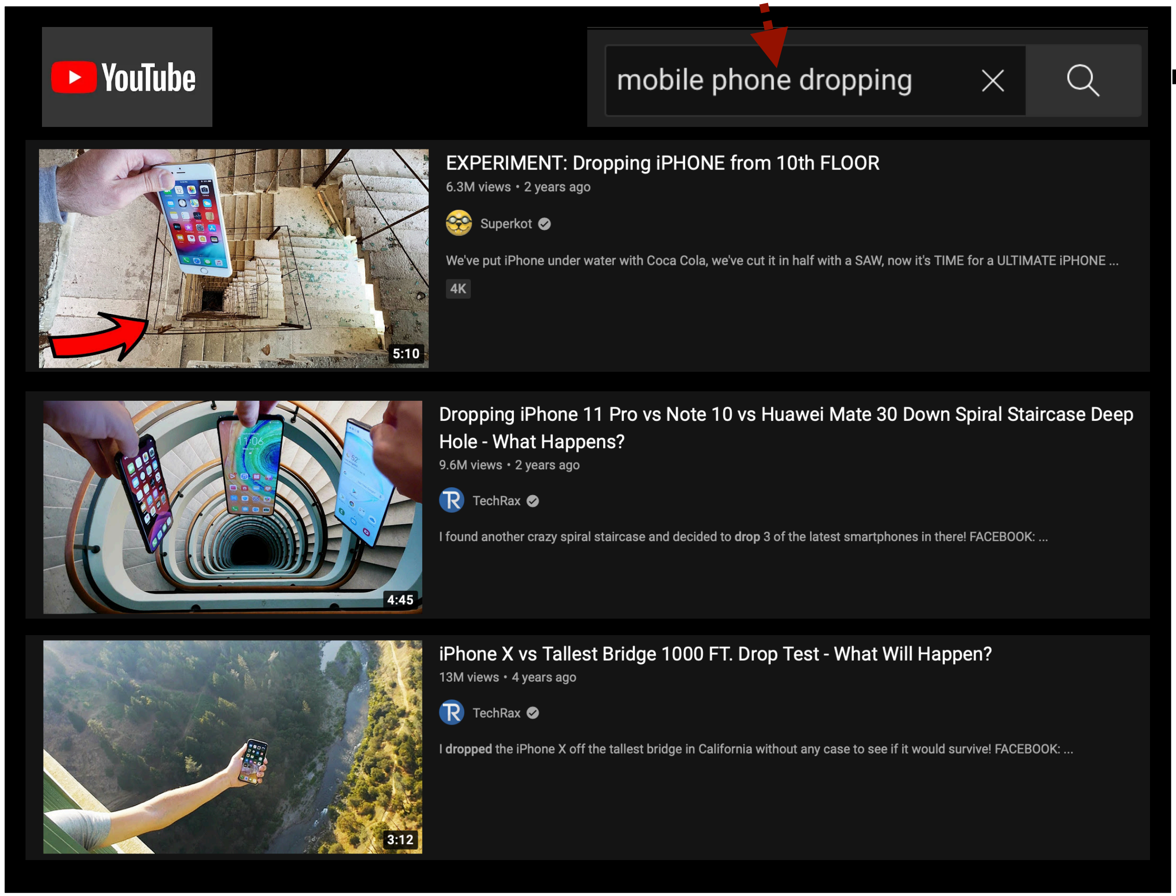
My neural network has learned physics!?

$$F = m \cdot 9.81$$

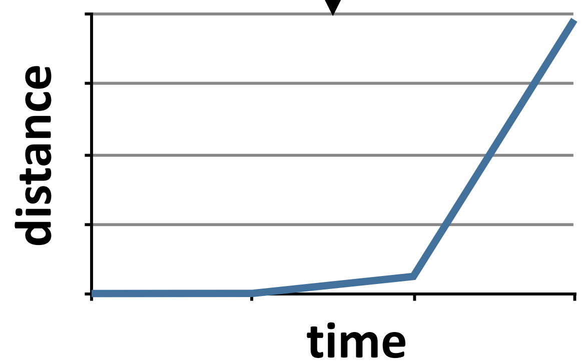
Example:
Can one learn the laws of gravity by watching youtube?

Puts assumption and knowledge into training data

Requires suitable inductive bias and background knowledge



Neural network that identifies and tracks mobile phones and estimates distances

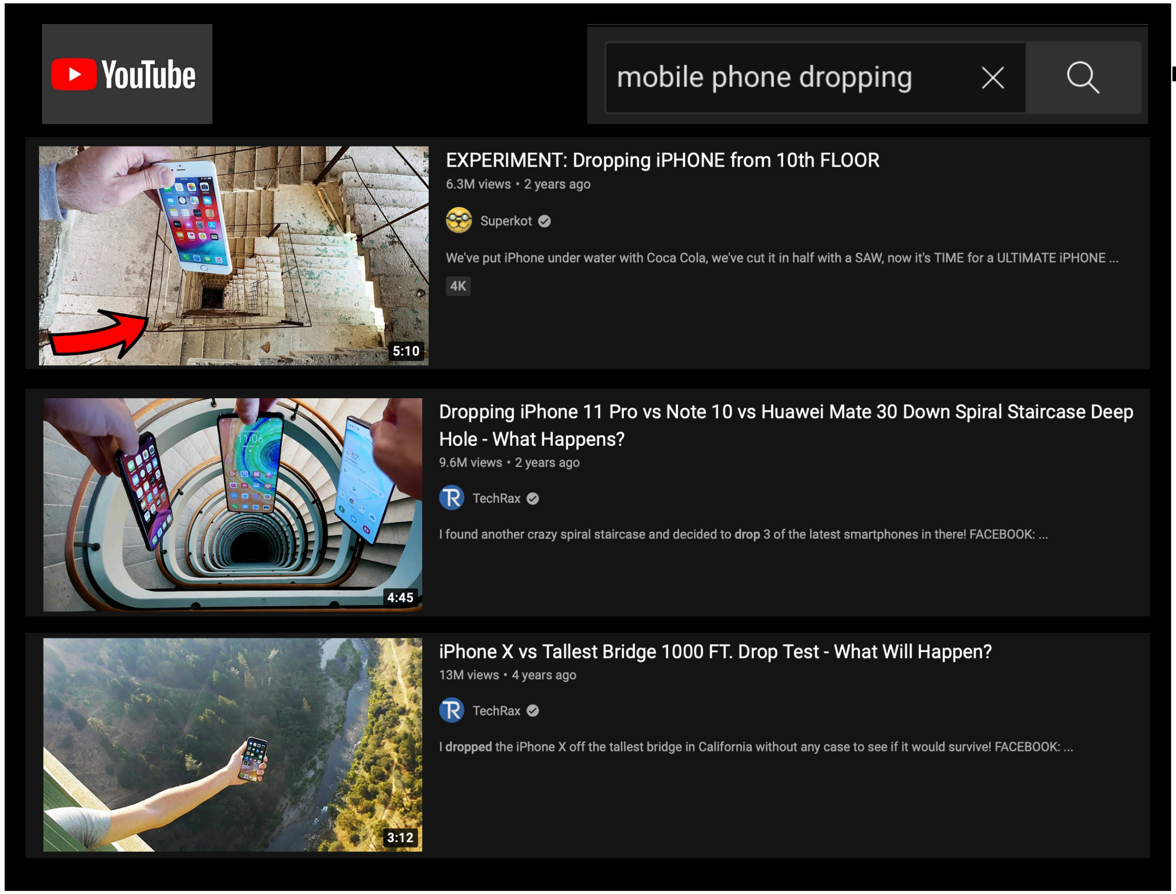


$$F = m \cdot 9.81$$

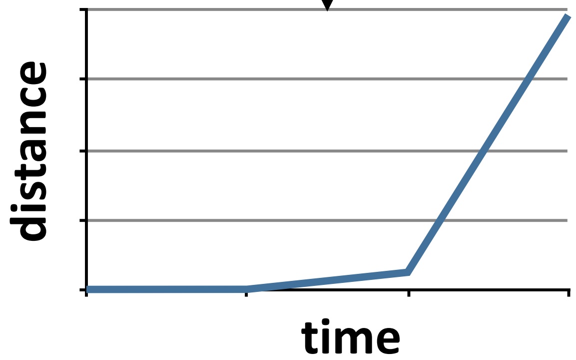
Learning from targeted observation

Hypothesis: $F = m \cdot a$

Targeted observation and guided inductive bias!



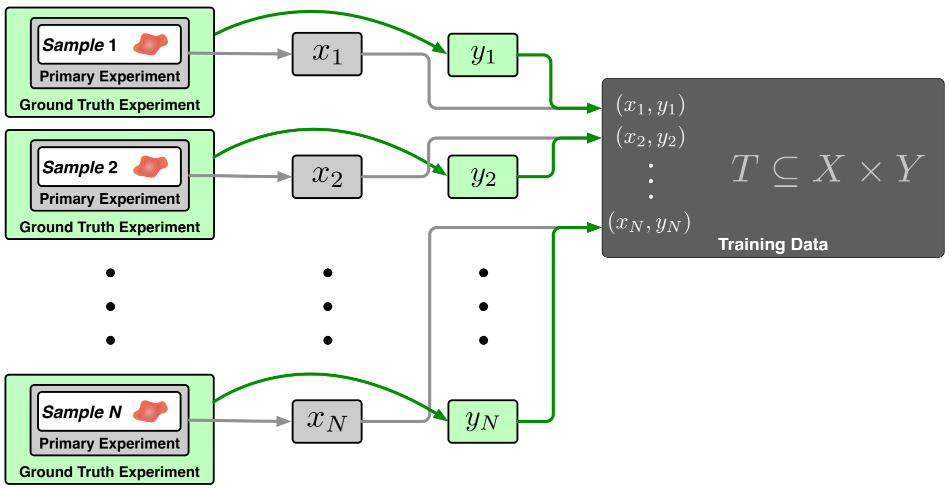
Neural network that identifies and tracks mobile phones and estimates distances



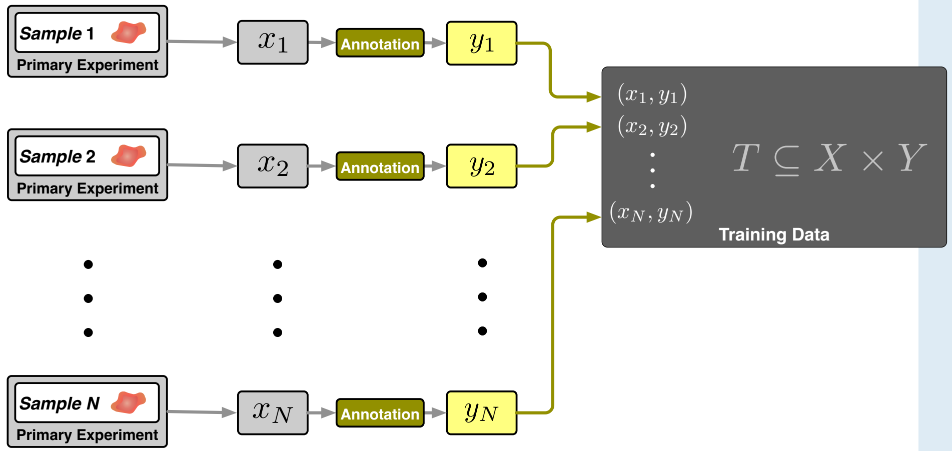
$$F = m \cdot 9.81$$

Machine learning models as hypotheses?

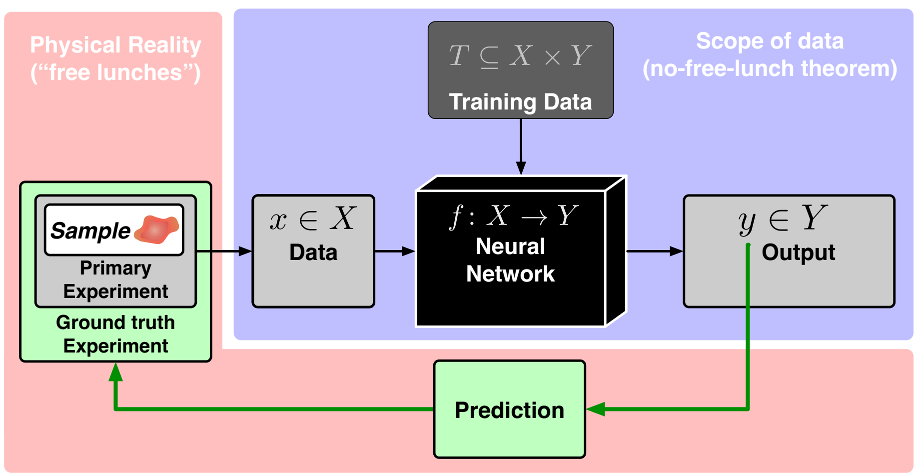
Strong ground truth (e.g. protein folding)



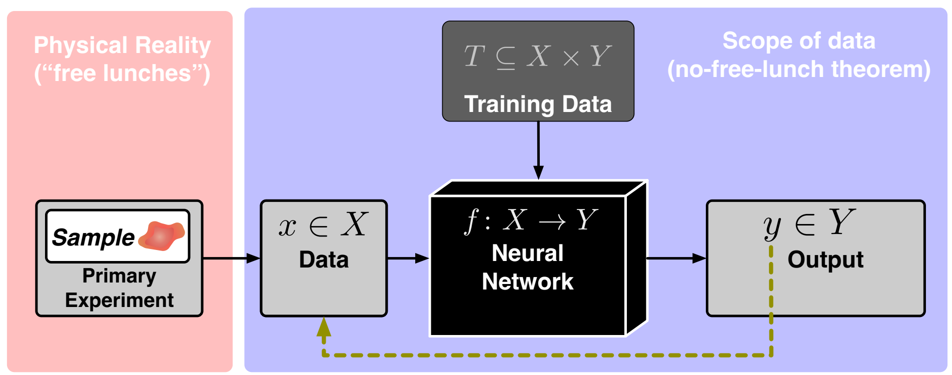
Weak ground truth (e.g. ImageNet)



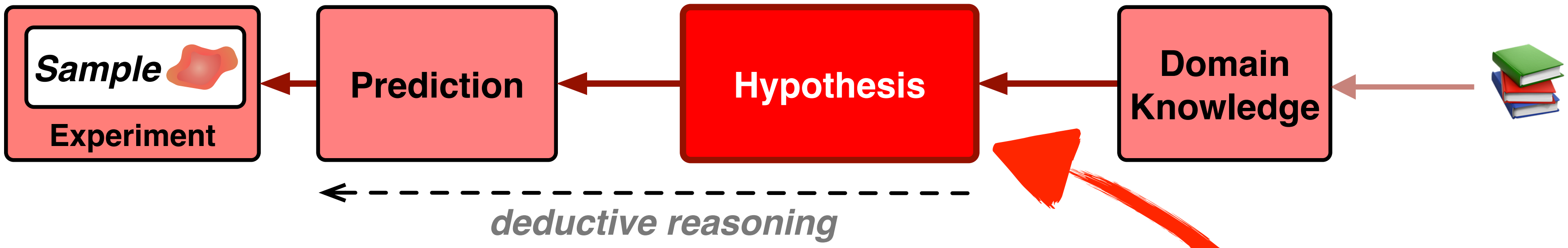
Strong falsifiability



Weak falsifiability

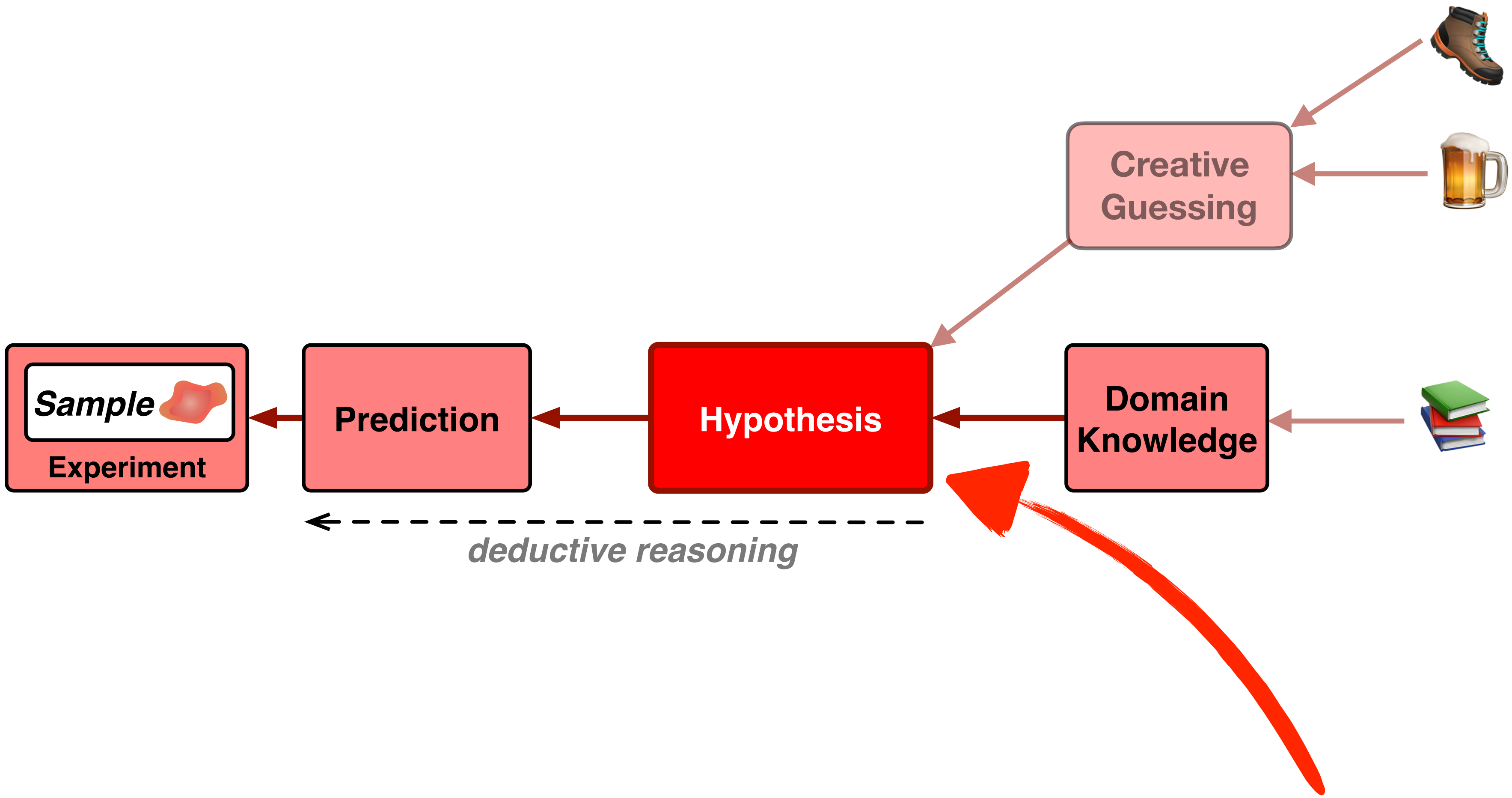


Hypotheses as explanations



How does the explanation (hypothesis) come about?

Hypotheses as explanations



How does the explanation (hypothesis) come about?

Deductive conjecture-and-refutation reasoning

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Deductive conjecture-first reasoning as knowledge generating process

System / Process	*Conjecture*	*Refutation*	*Description / storage of conjecture*
Scientific method	***Hypothesis***	***Falsification***	***Scientific Literature***
Evolution	***Mutation***	***Death, inhibted reproduction***	***Genome***
Human/animal cognition (concept learning)	***Concepts***	***Pain, fear, dissatisfaction, ...***	***Brain***

Supervised learning is not conjecture-first learning!

Can explainable artificial intelligence (XAI) rescue supervised learning from the problem of induction?

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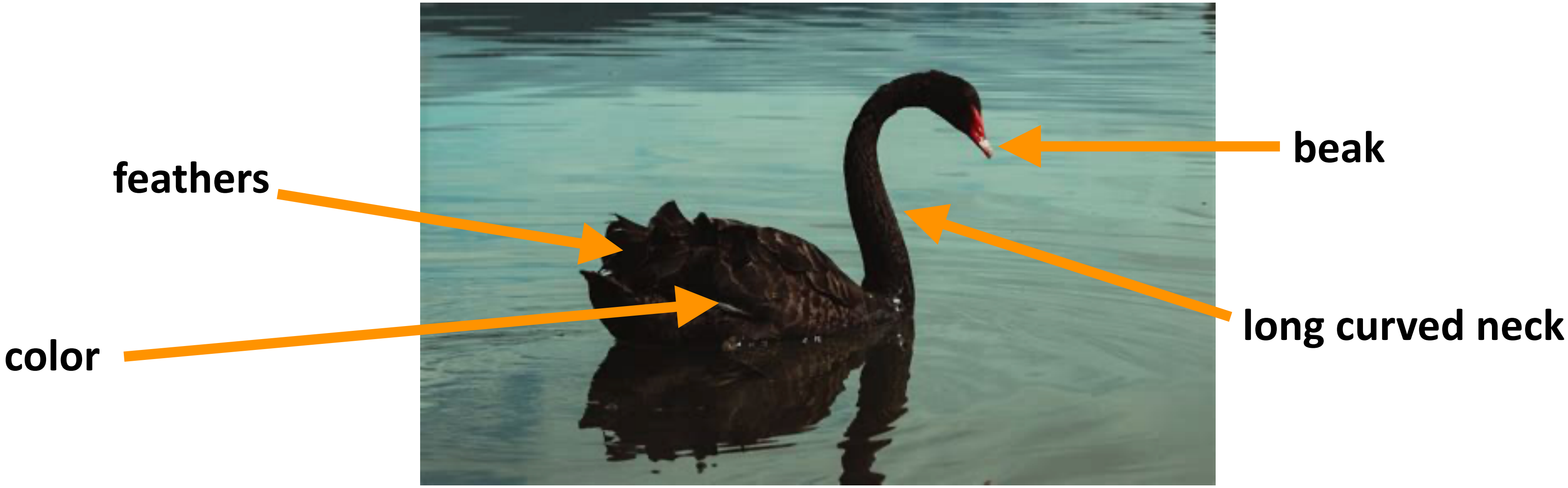


Definition 1. An interpretation is the mapping of an abstract concept (e.g. a predicted class) into a domain that the human can make sense of.

Definition 2. 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).

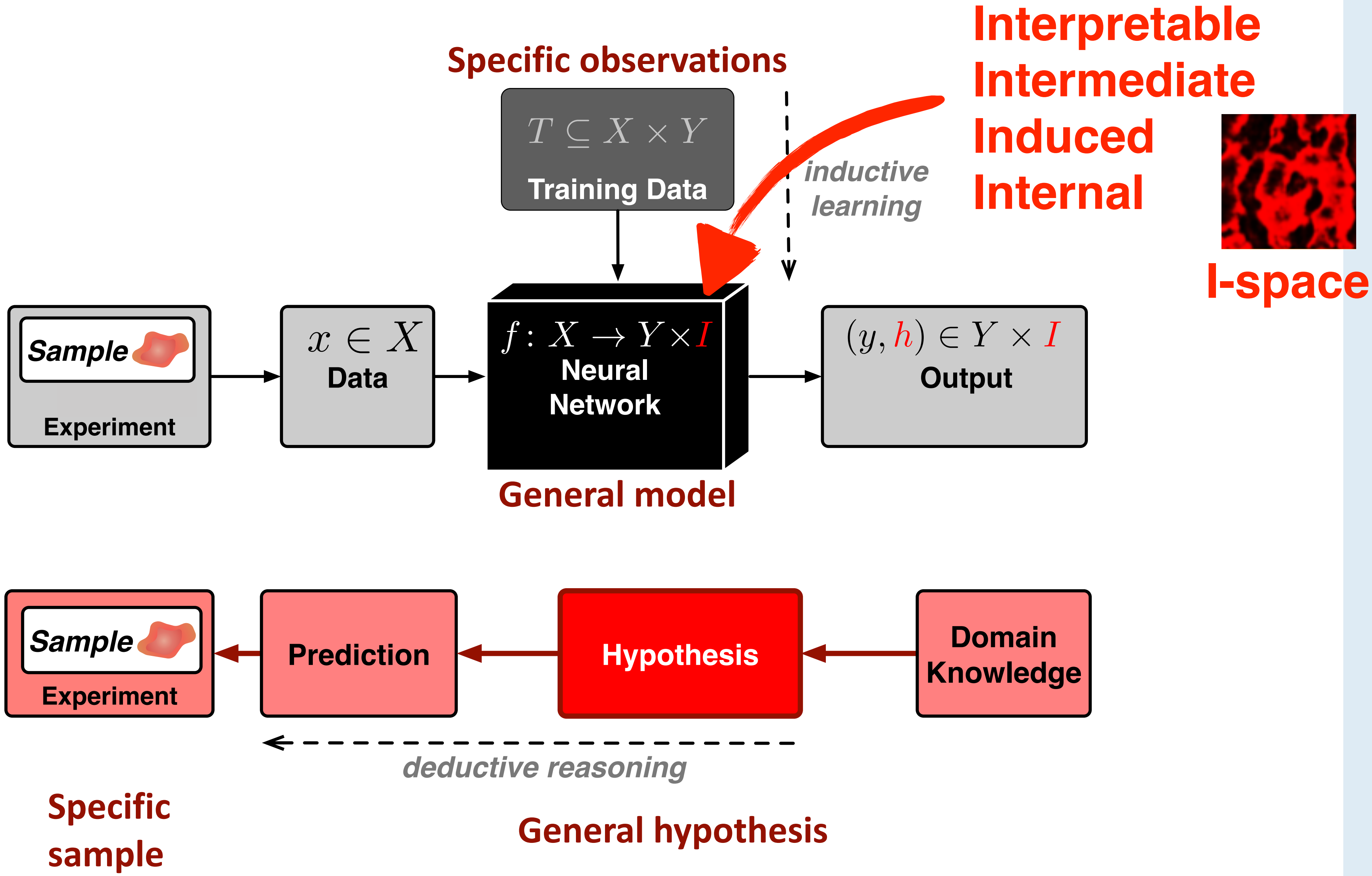
Explainable AI science or pseudo-science?

Methods for interpreting and understanding deep neural networks

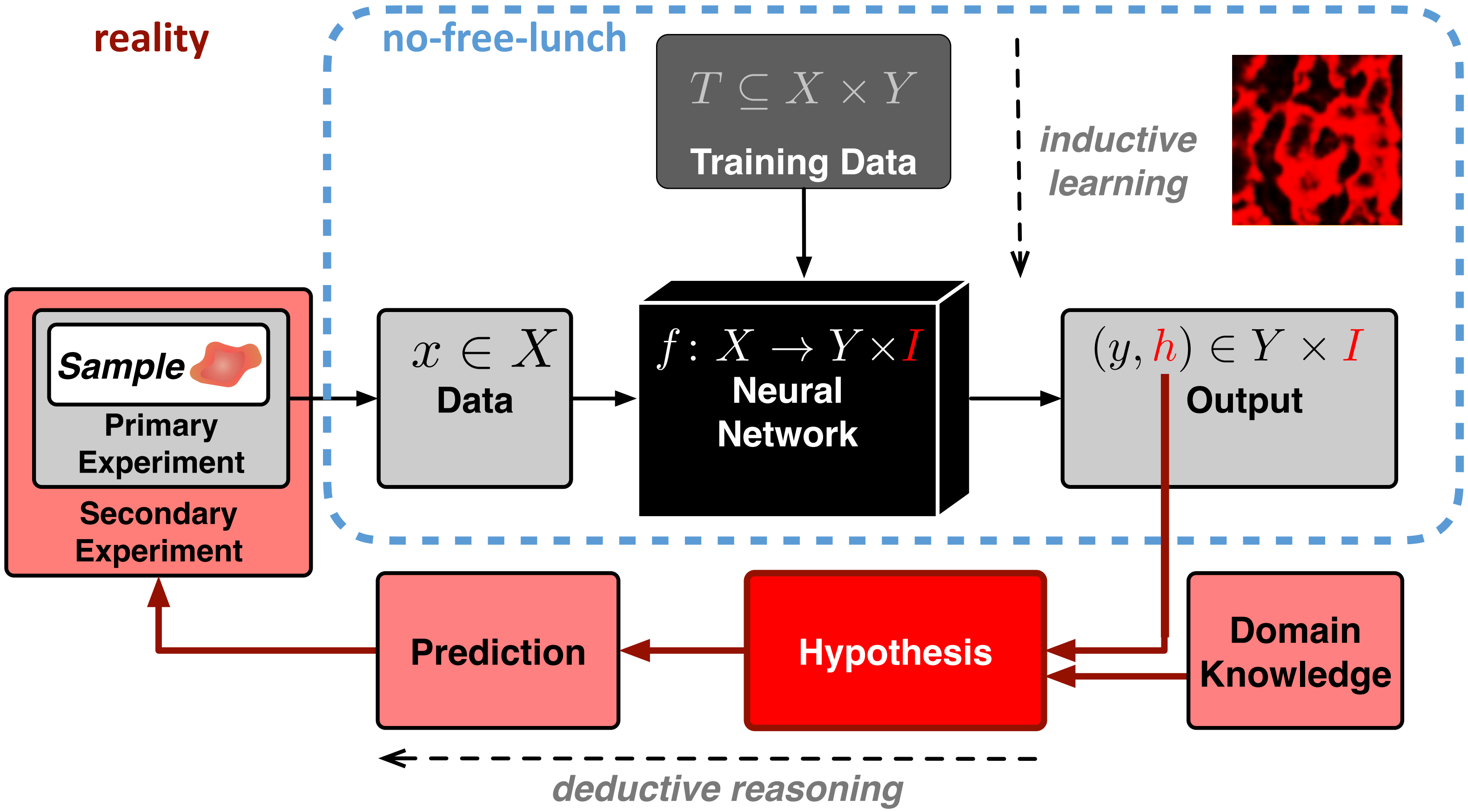
Grégoire Montavon [a,*], Wojciech Samek [b,*], Klaus-Robert Müller [a,c,d,**]

Digital Signal Processing 73 (2018) 1–15

Machine Learning vs. Scientific Method



Long live theory!



An explanation of a machine learning model is a (falsifiable) hypothesis that connects the inferred output of a the model with the sample that the input data originate from.

Schuhmacher, Schörner et al., Medical Image Analysis (2022)

Machine learning models as hypotheses: A taxonomy and an analogy

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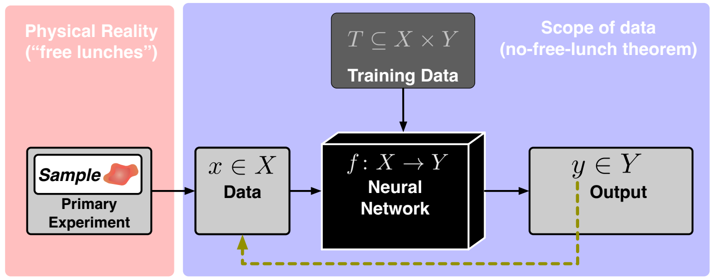
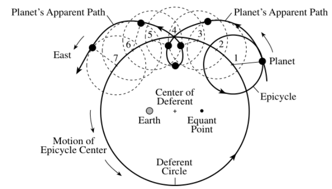
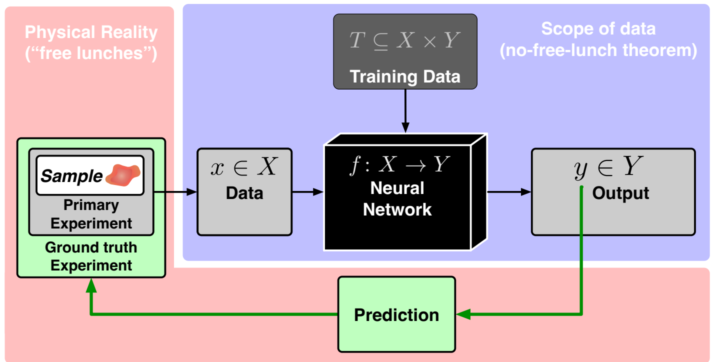
Weak falsifiability

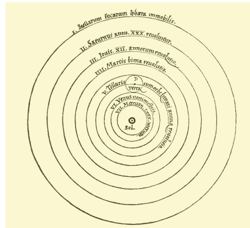


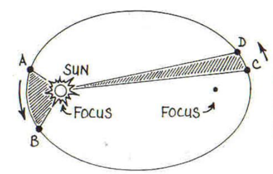


"Ptolomaean"

Strong falsifiability

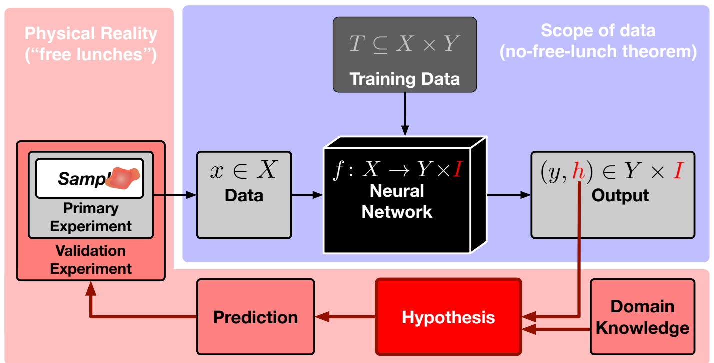




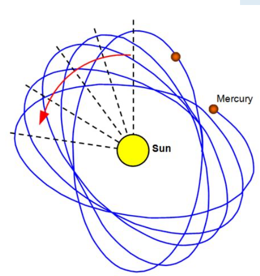


"Copernican / Keplerean"

Explanation-based strong falsifiability



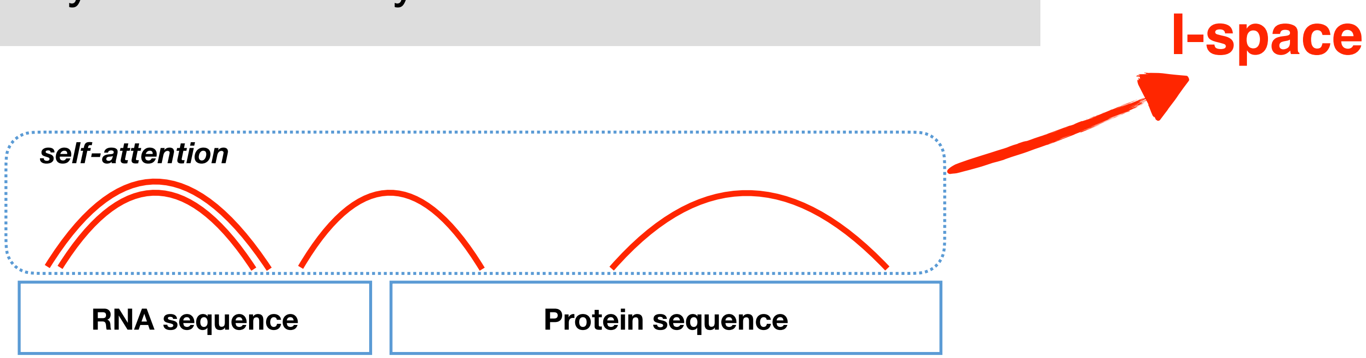
$F = GMm/r^2$



"Newtonean / Einsteinean"

Outlook: Deductive validation in structural biology

Train attention-based neural network to identify evolutionarily informative features



Hypothesis
Self-attention indicates co-evolution, and whatever co-evolves interacts with each other

Deductive validation
Test co-evolving interactions experimentally

Conclusions and Outlook

- Falsifiable hypotheses as explanations identify XAI as missing link between machine learning and the scientific method
- Using inductive bias as a modeling tool leads to interpretable machine learning
- Deductive validation escapes the no-free-lunch theorem

Acknowledgments

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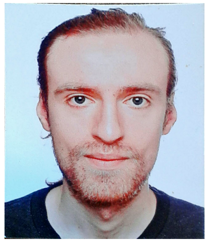



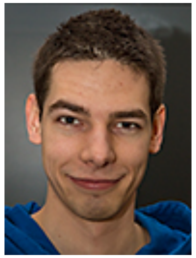

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Thank You!