An instance of inference: treatment effect estimation

Some general goals

- Predict the health state of an individual after treatment.
- Develop a strategy for steering the treatment over time.
- Understand the mechanisms underlying illness and recovery.

Variables

- Holistic: health state, treatment, individual, environment.
- x: quantifiers of the health state.
- z: factors characterizing the patient and the current conditions, including current or past values of x. Some may be known or measurable, some latent.
- a: features of the treatment under consideration.

Observations o from past and the current patient: values of x, z and a, or of quantities related to them.

General tasks

- Build a model for the effect of action a on the outcome x, qualified by factors z:

  $a, z \to x$: regression, classification

  $\rho(x|a, z)$: conditional probability estimation

  $x^i \sim \rho(:|a, z)$: simulation
- Uncover hidden parameters: factor discovery, clustering, dimensional reduction: $x, a \to z$
- Figure out the current state and model parameters: filtering, data assimilation, diagnosis: $o^{1,\dots,n} \to z^n, \alpha^{(n)}, x$
- Steer the treatment: optimal control, reinforcement learning: $z, x \to a$

Tensions and challenges 1

Interpretability

Do we care more about predicting or understanding? Model simplicity versus accuracy and detail.

Model versus data-driven inference: a full palette between field knowledge-based models and black boxes.

Tensions and challenges 2

Identifiability

A model detailed enough to be deemed realistic by a practitioner may include parameters that the data cannot robustly pin down.

Big data.

Lacking the right tools for analysis, excessive information may, somewhat paradoxically, deteriorate the quality of a prediction.

Some partial solutions

Regularizers: for robustness, to enforce regularity, to promote interpretability and to mitigate overfitting. Examples: penalizers –such as ridge regression– and priors on the parameters.

Cross-validation: training and testing populations.

Tensions and challenges 3

Observational studies vs. randomized experiments

Individualization of prediction vs. aggregation of data

Variability of data type

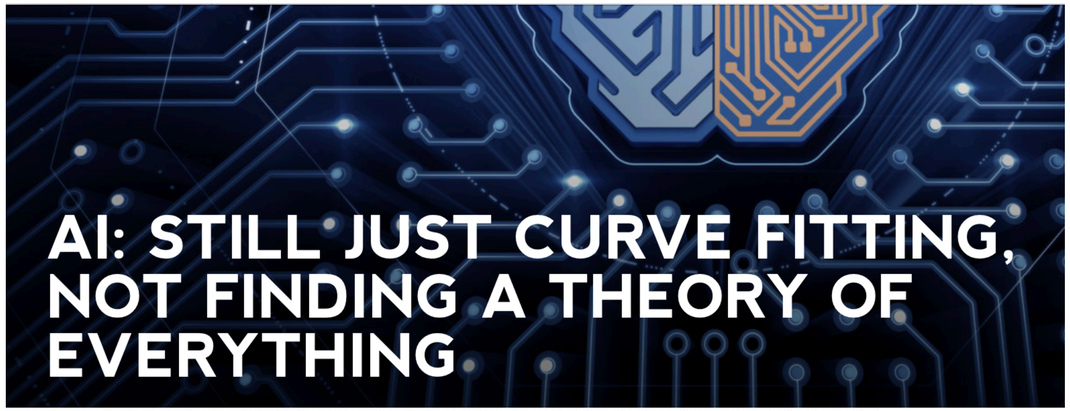
Reliability of data, robustness to outliers

Fairness

Demystifying Machine Learning

It's just…

- *Interpolation*
- *Curve fitting*
- *Regression*
- *etc.*



Inferring a predictive function

machine learning

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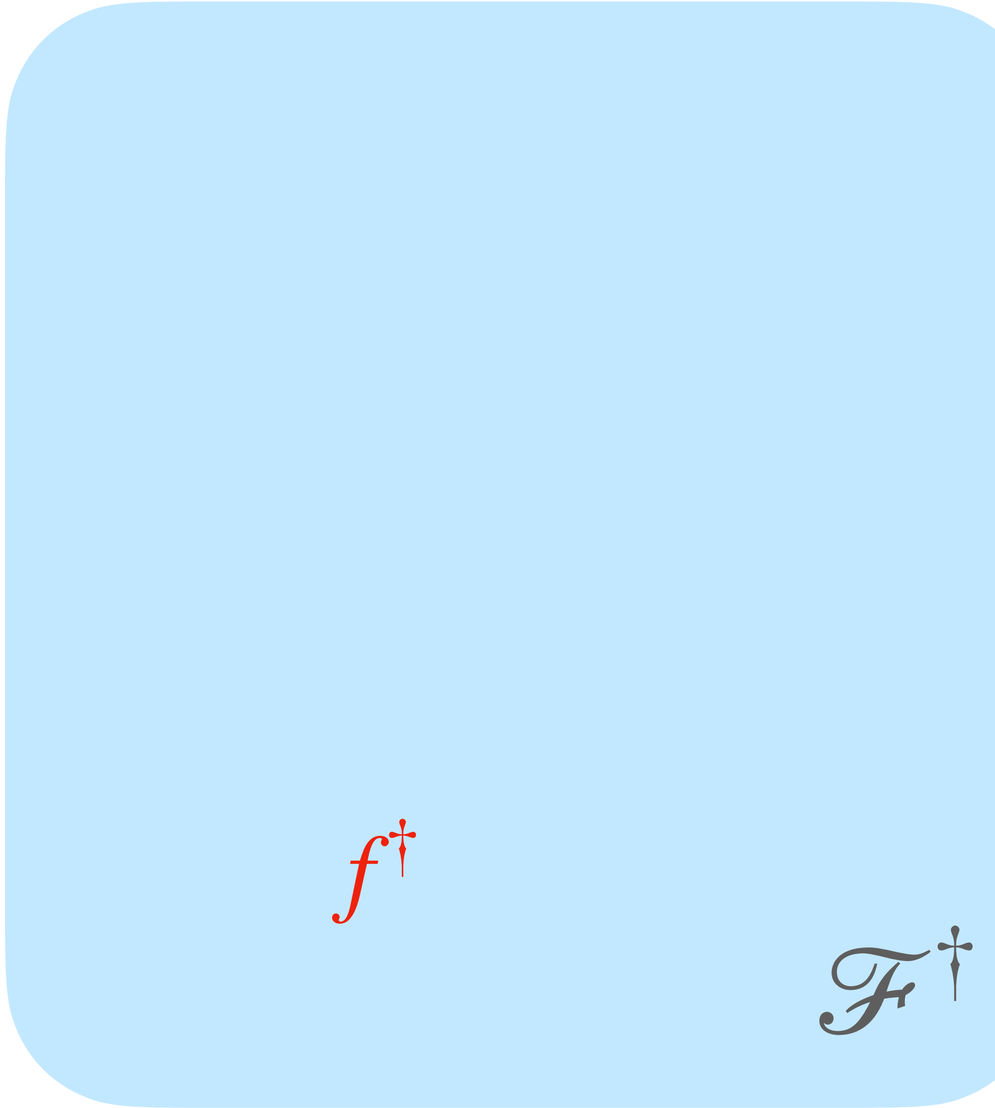

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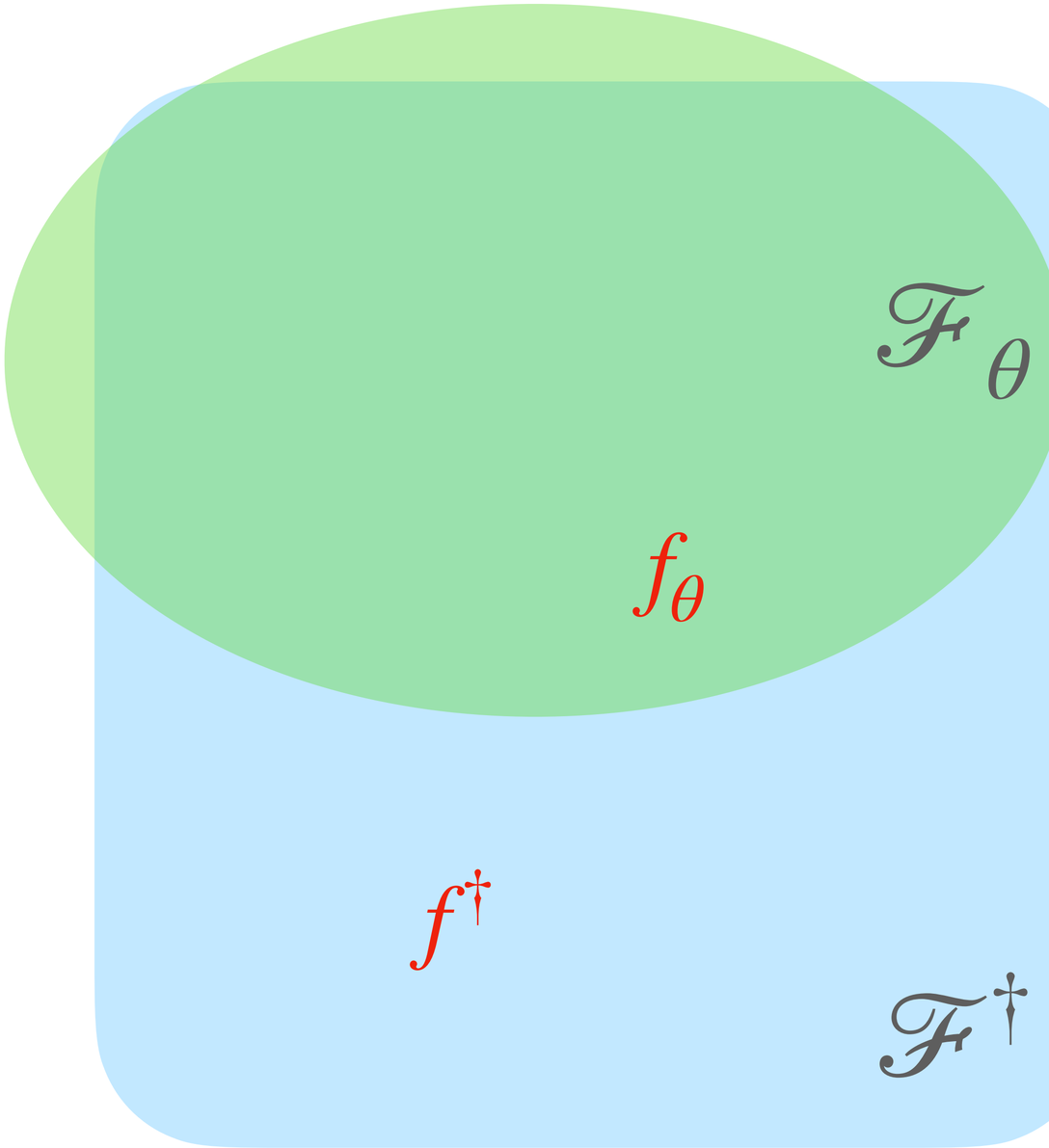

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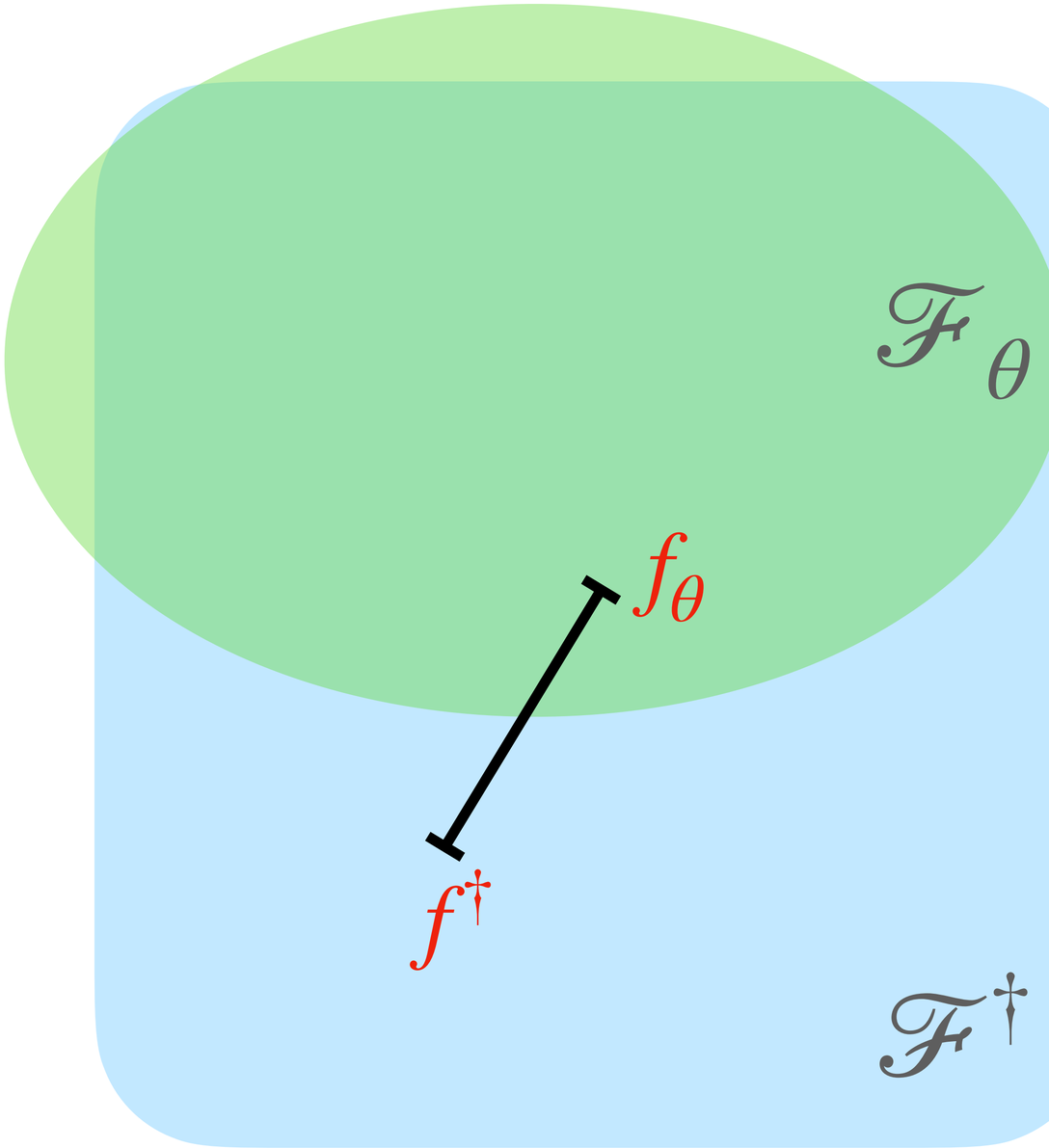

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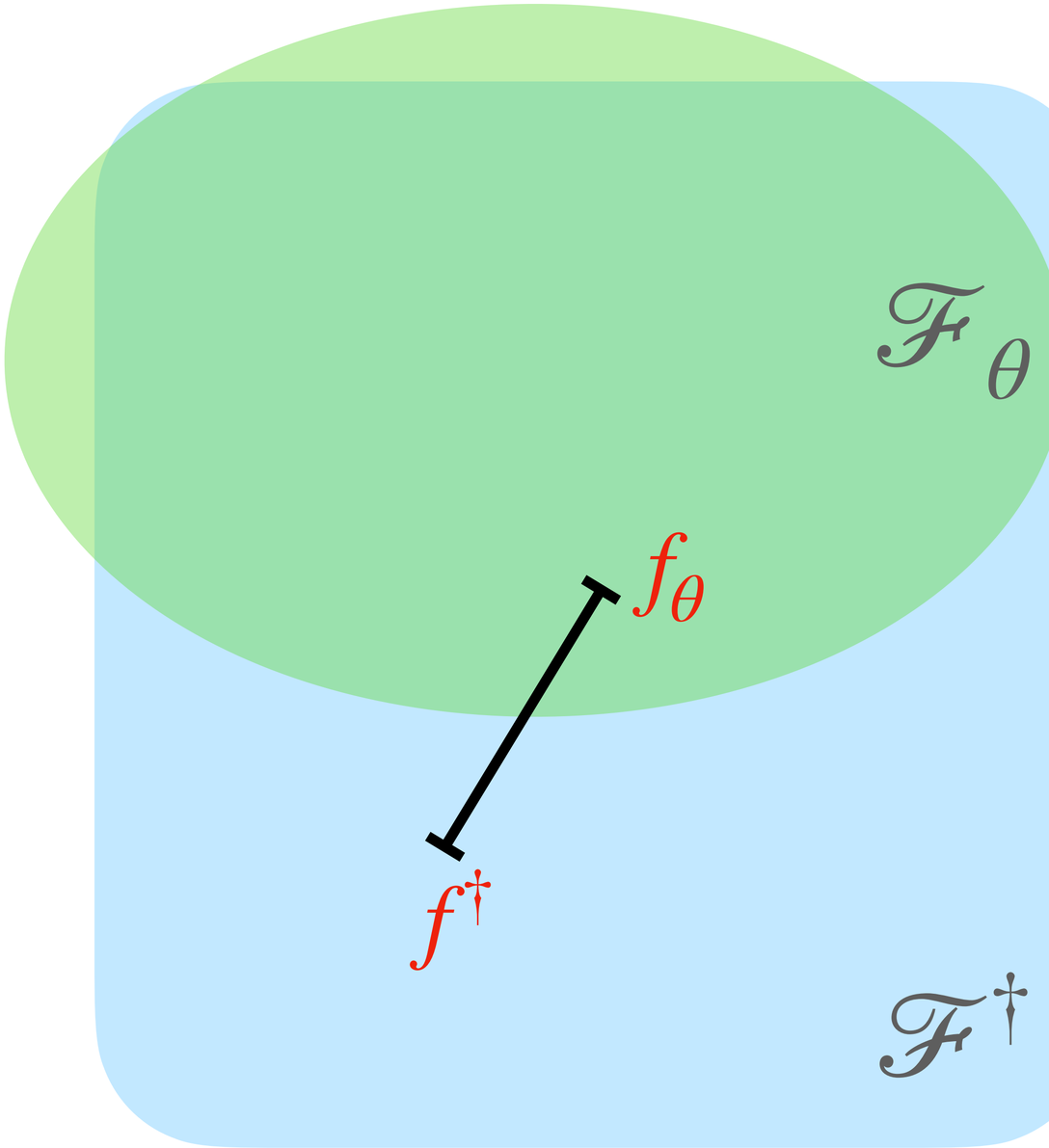

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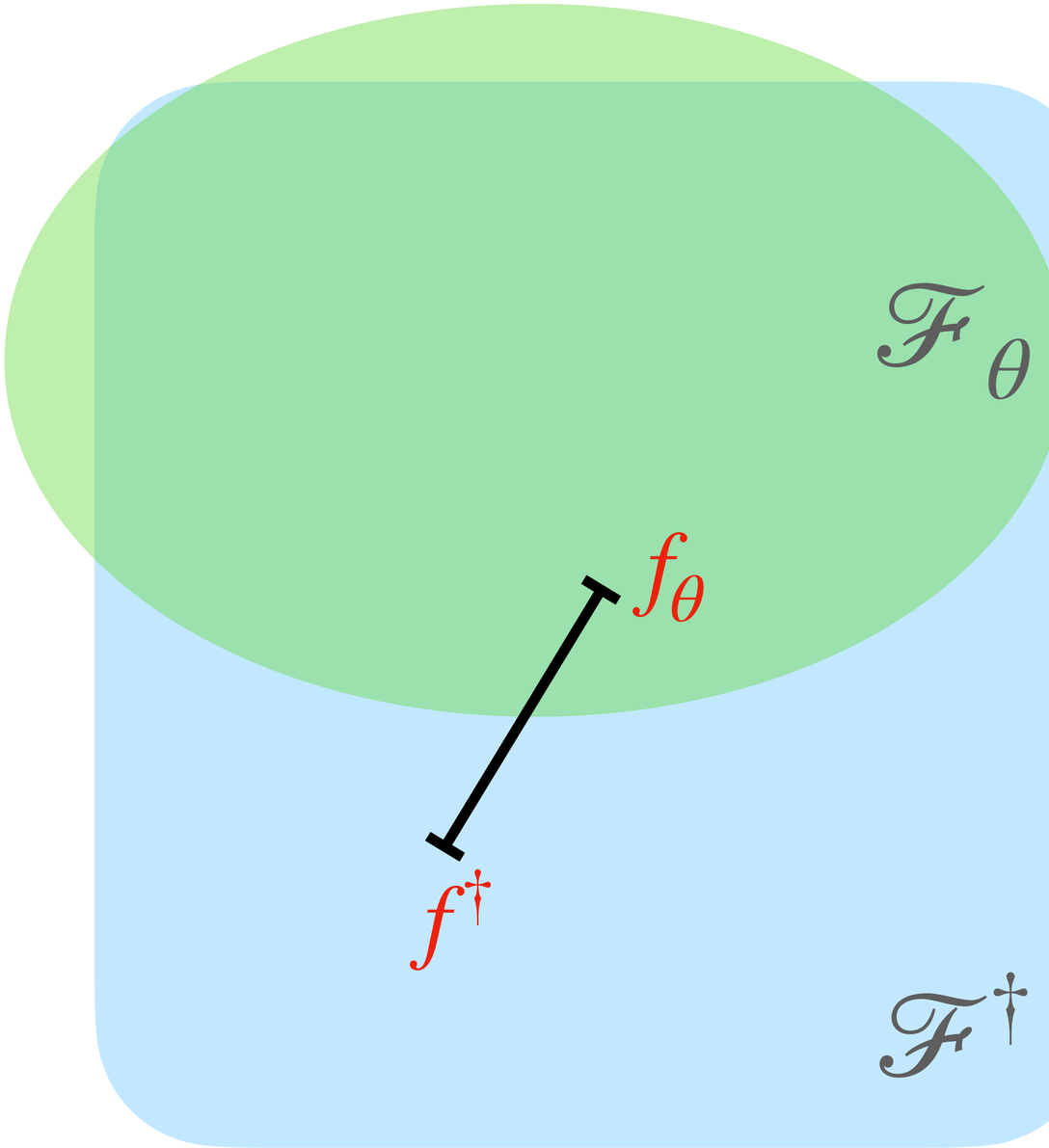

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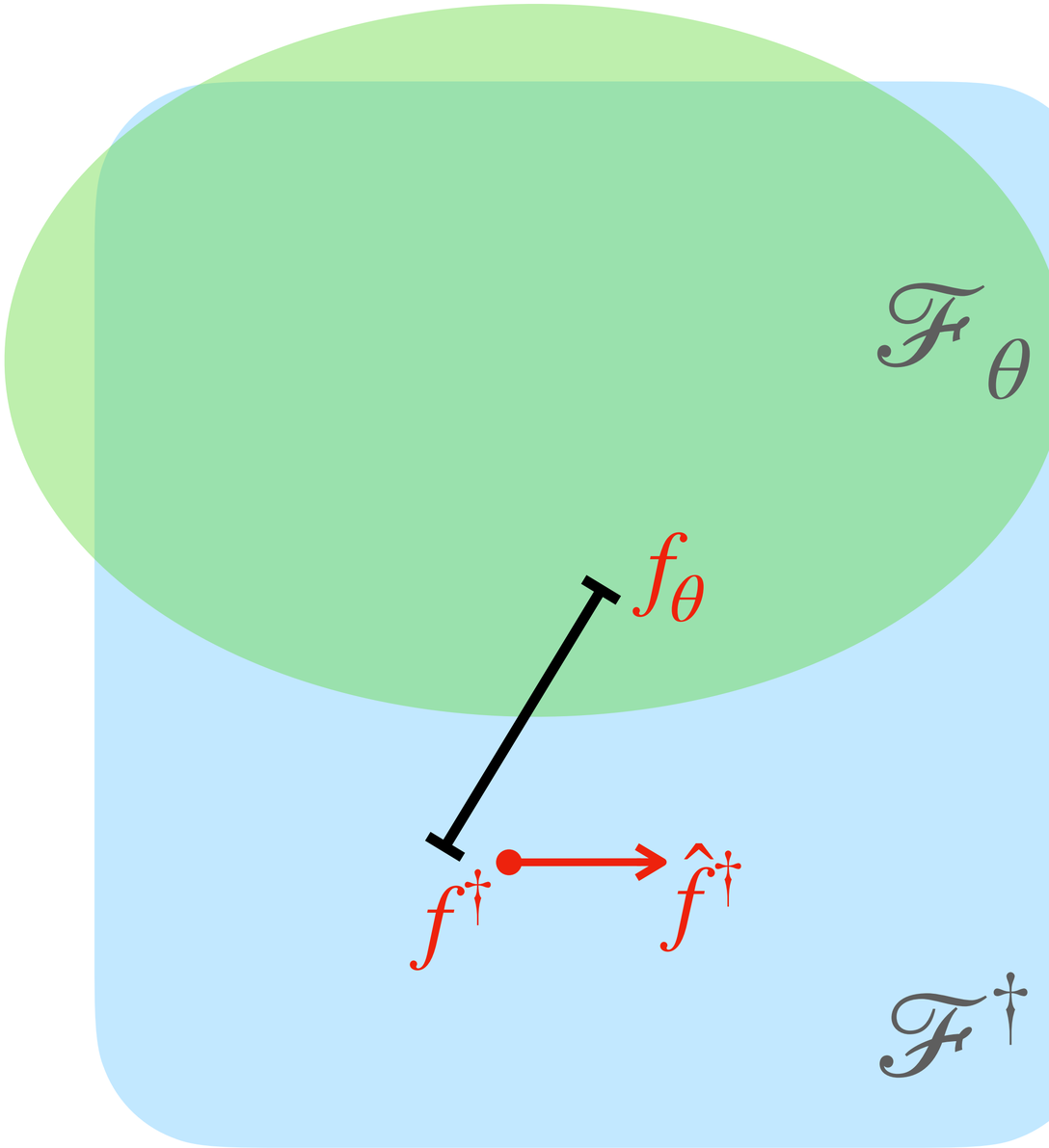

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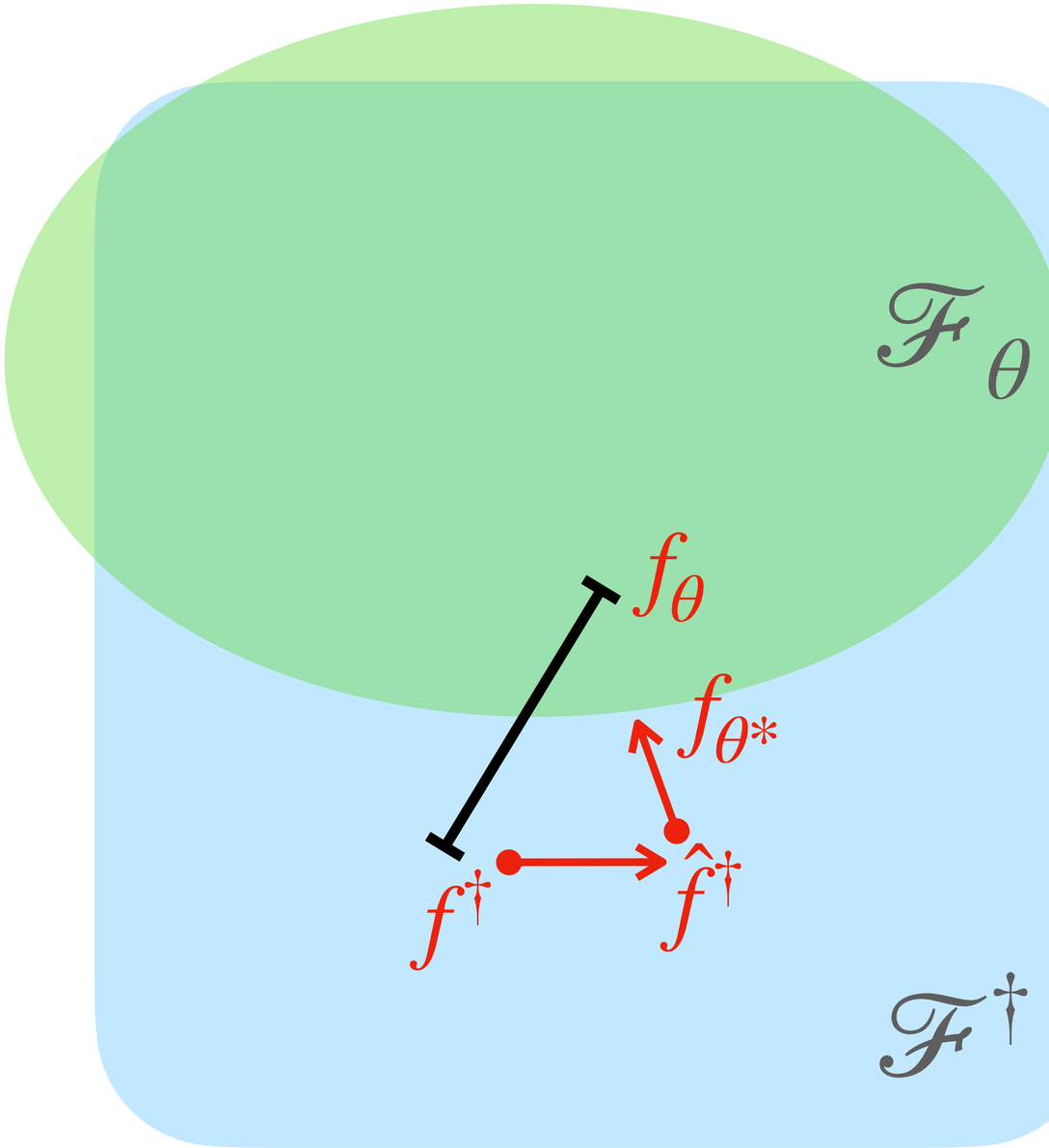

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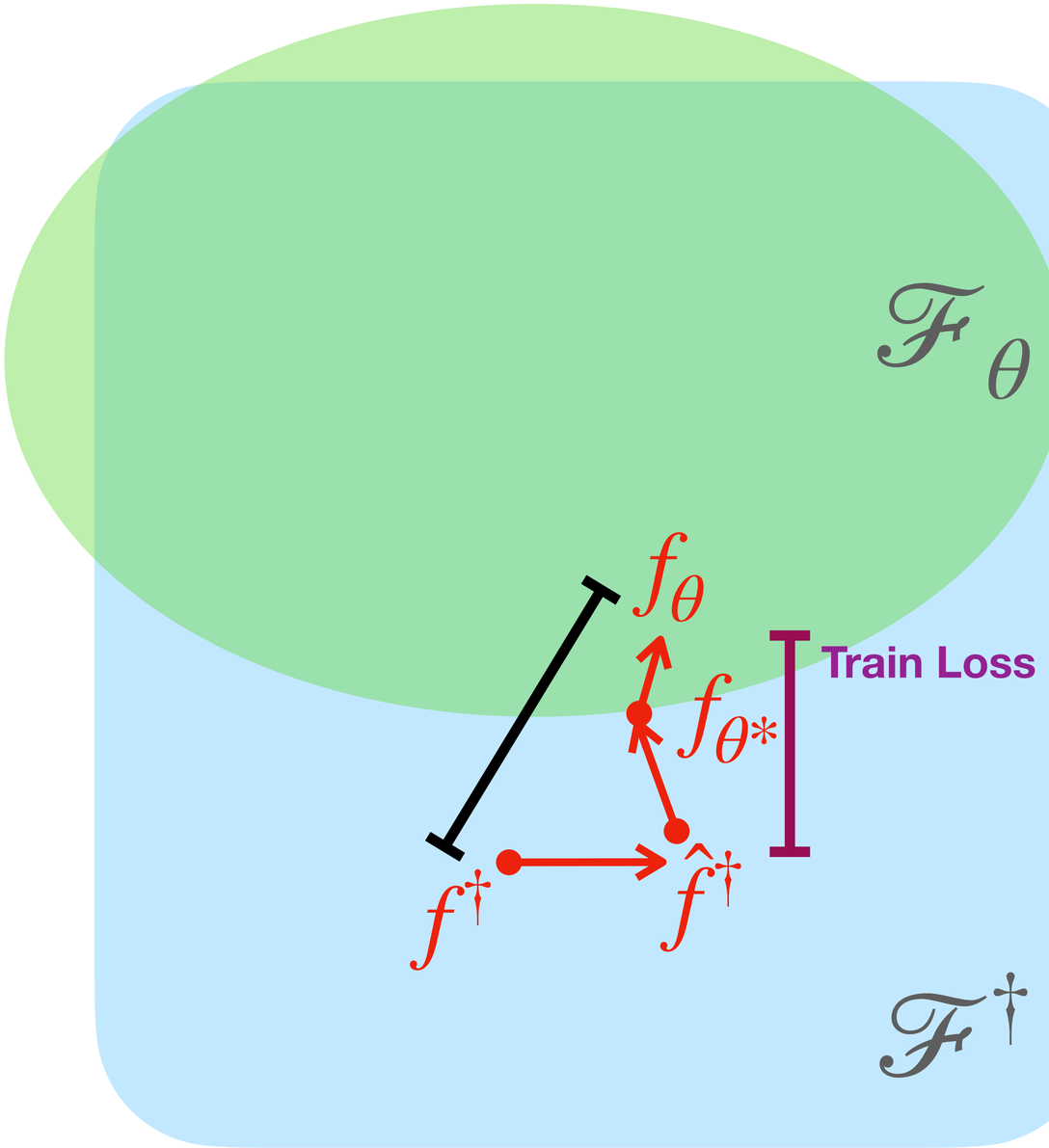

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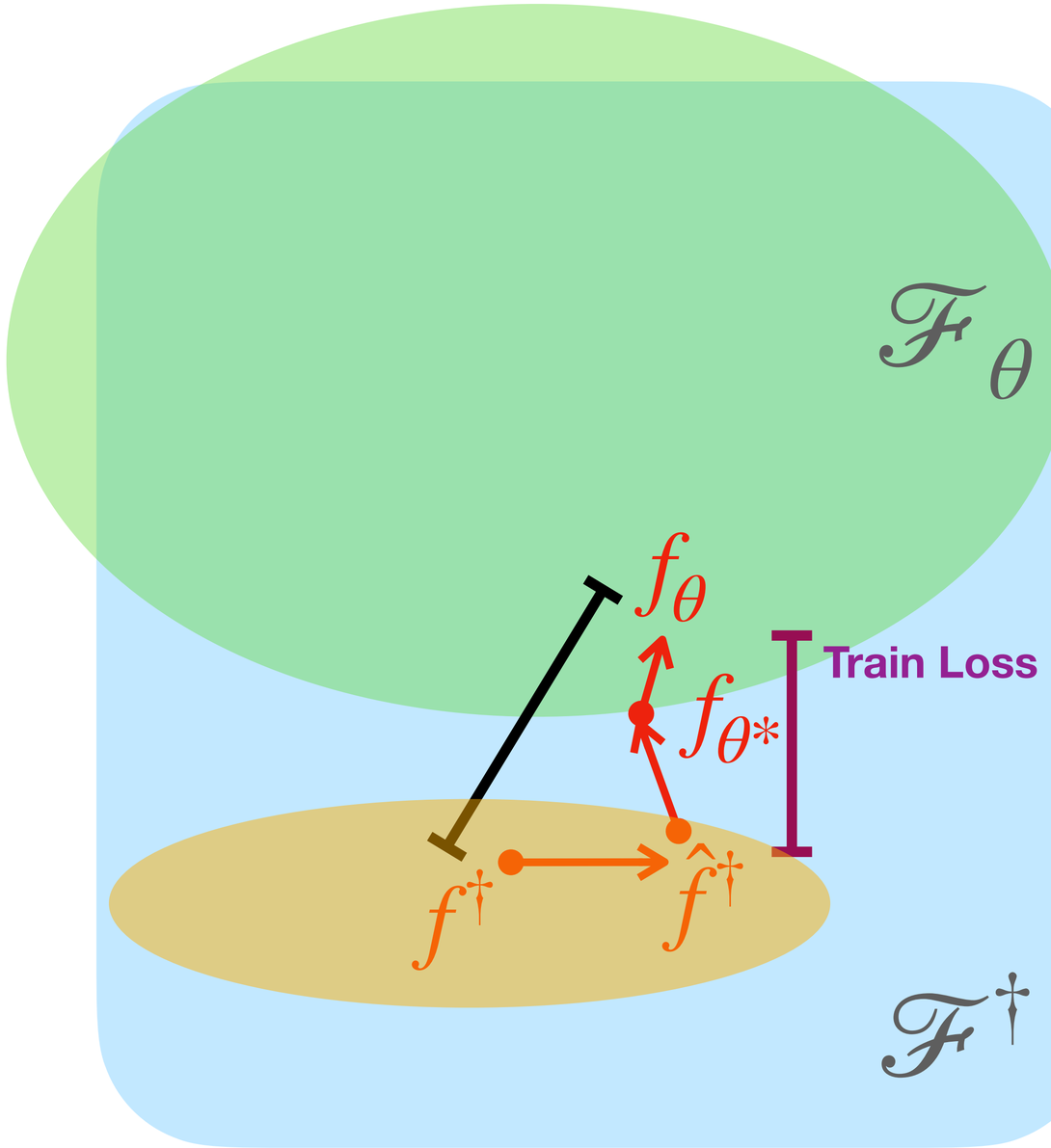

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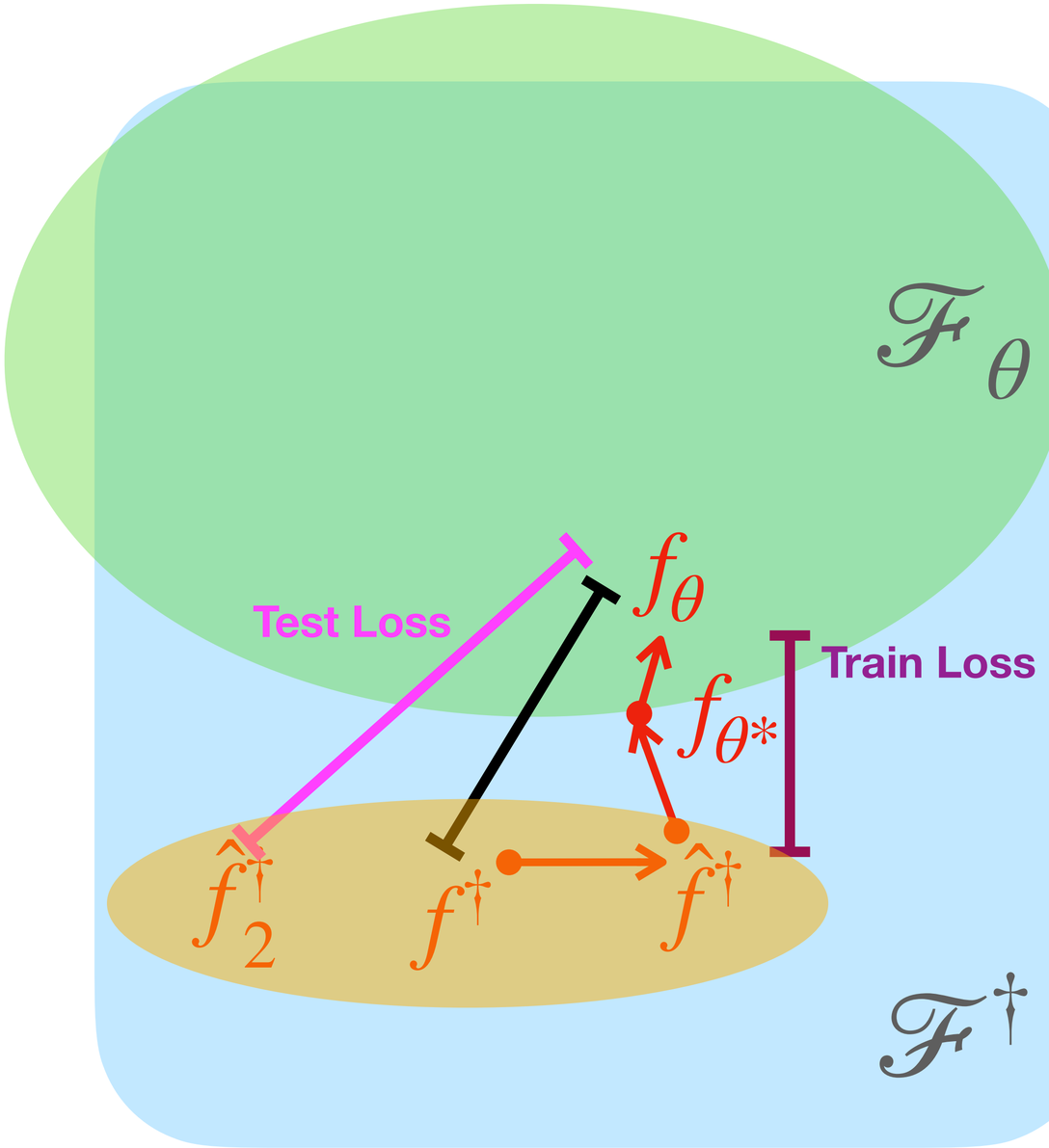
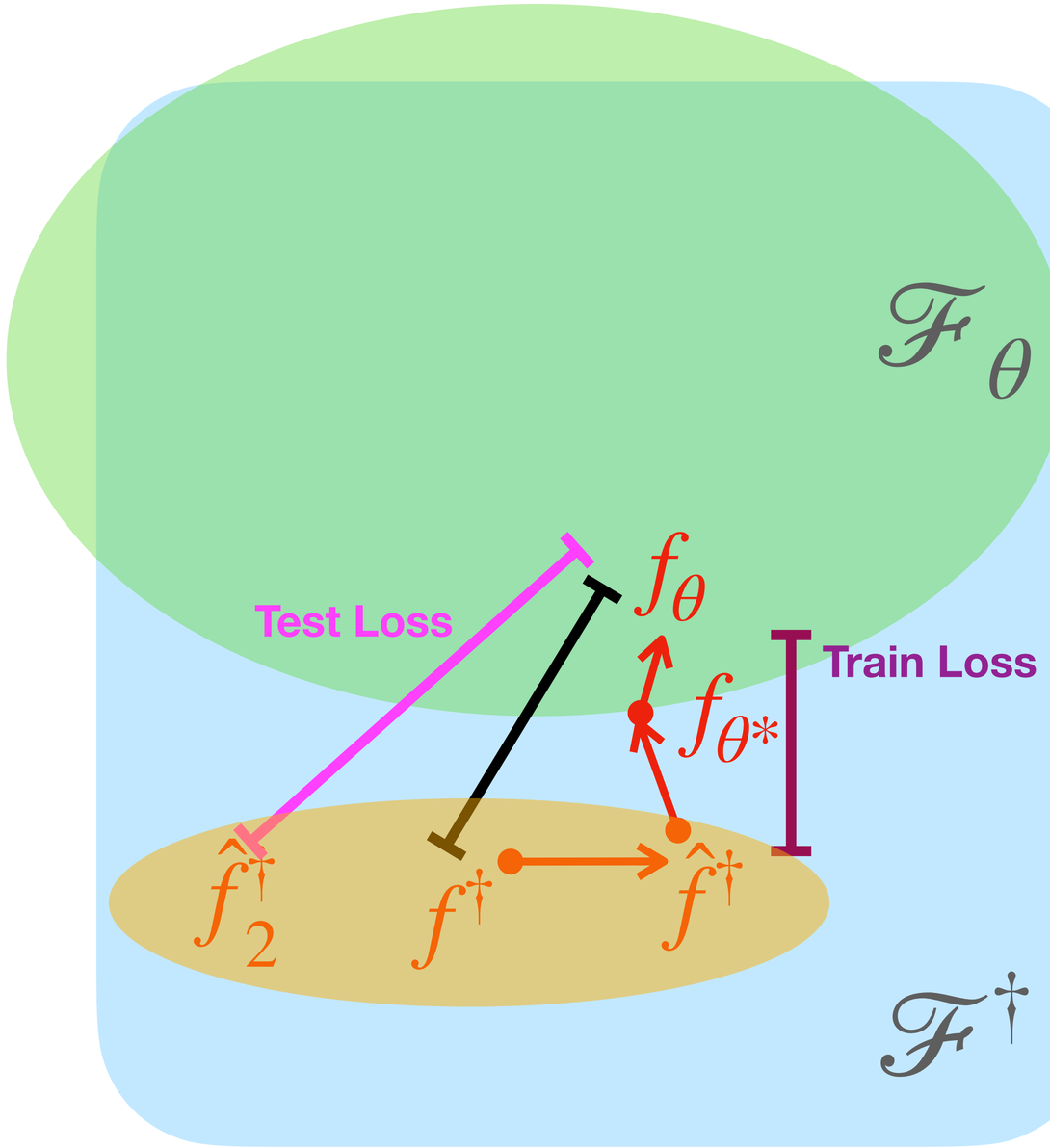


Standard “Problems w/ Solutions” in “AI”

machine learning



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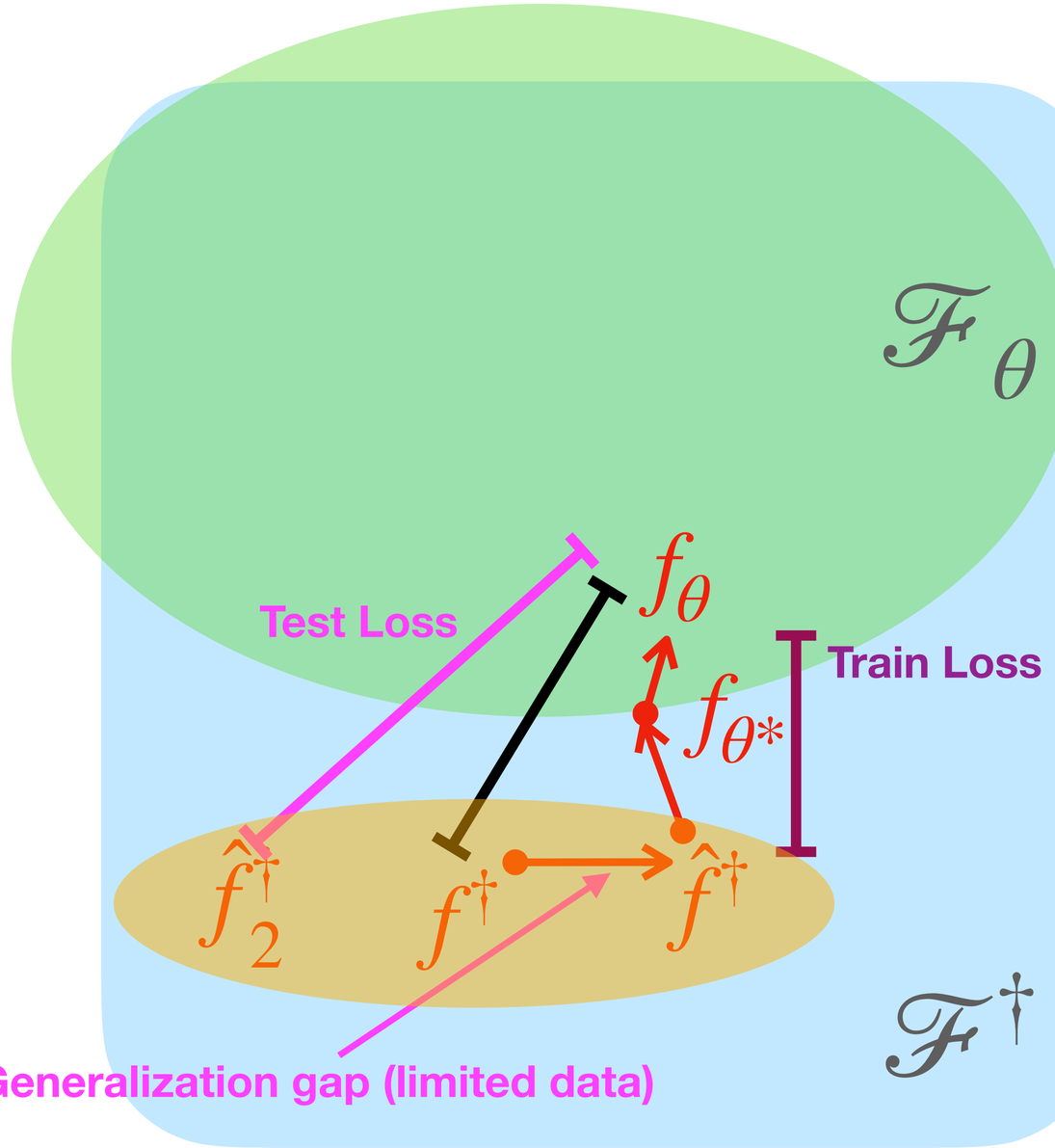

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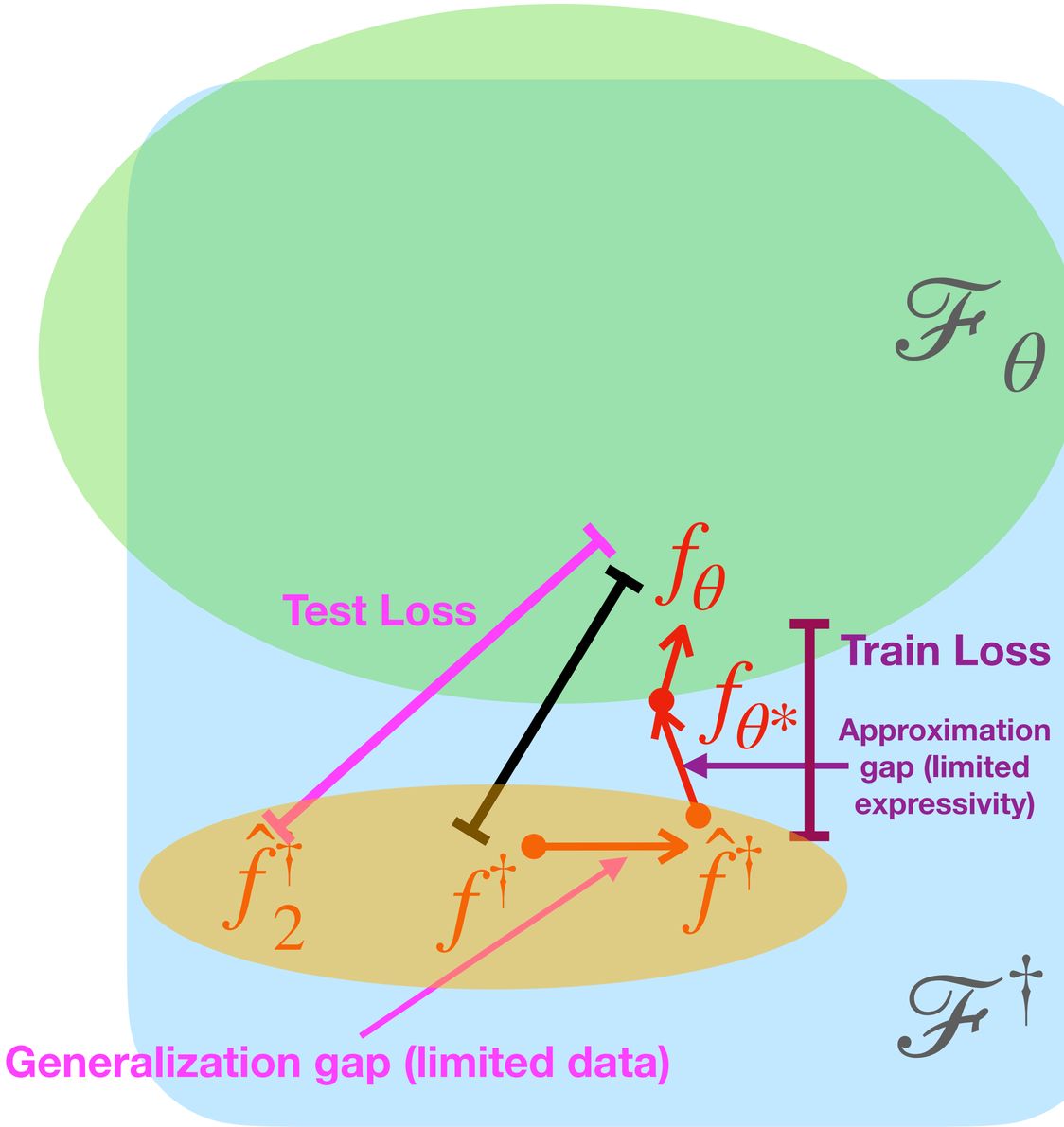
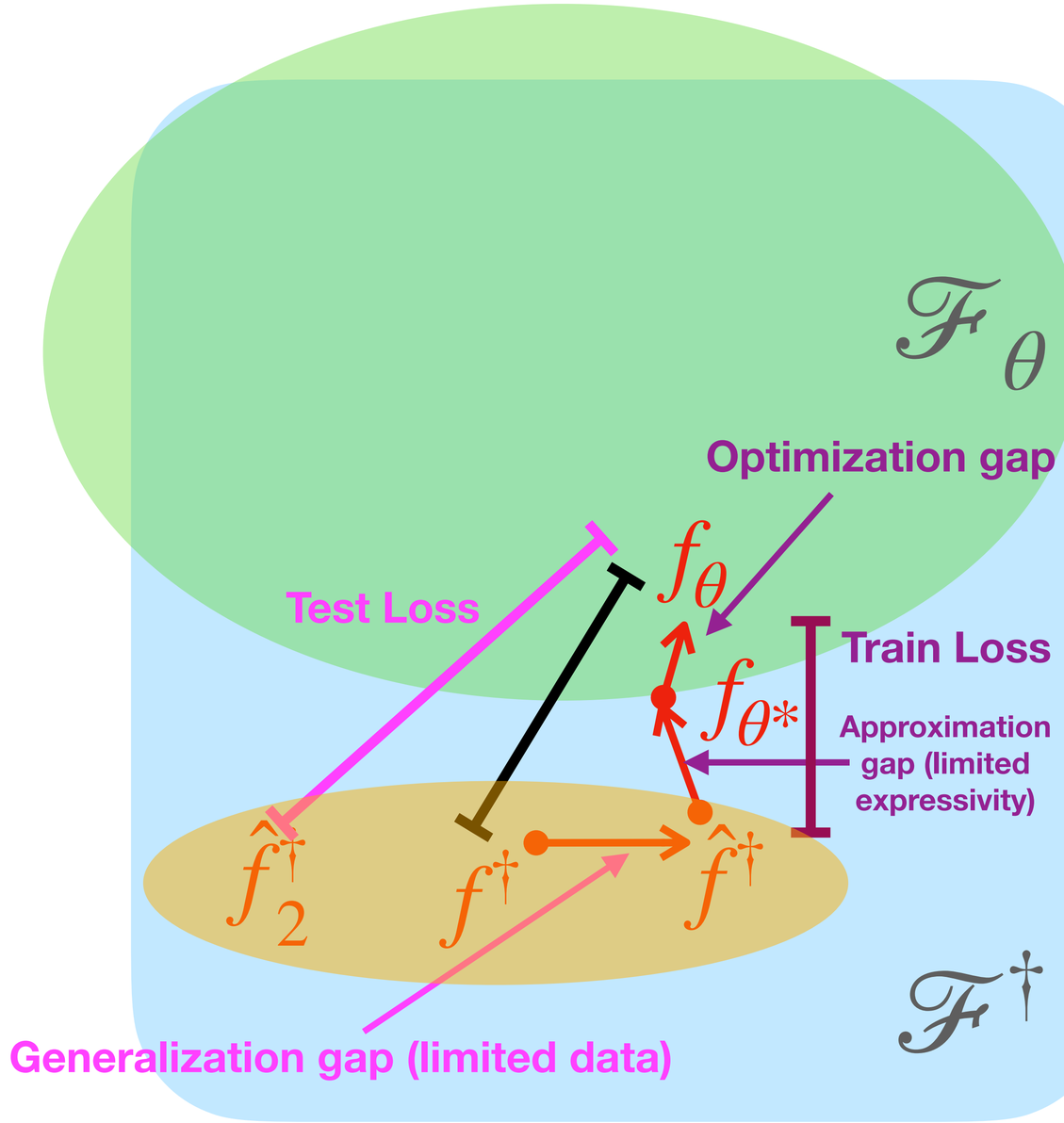


Standard “Problems w/ Solutions” in “AI”

machine learning

1. Generalization Gap
    1. Tons of data!
2. Approximation Gap
    1. More parameters!
3. Optimization Gap
    1. SGD (and variants) with lots of tunings/ hacks
    2. More parameters!
        1. Over-parametrization seems to convexify loss surfaces



Small Data Challenges

machine learning

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    1. e.g. be sure the learnt function is very boring away from data!

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Don’t be afraid of expressive models—just learn how to regularize!

Other challenges

machine learning

Other challenges

machine learning

1. Latent variables
    1. Hypothesize $f^{\dagger} : X \mapsto Y$, but our input space $U_{\text{inputs}} \subset X$
    2. Need to discover or account for hidden/latent variables!

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machine learning

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2. Noisy inputs
    1. For non-linear functions, input noise does not “cancel out”
        1. $f(x) \not\approx \mathbb{E}_{\eta}[f(x+\eta)]$ even for mean-zero noise η
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3. Non-stationarity
    1. Shifting data-distribution
    2. Shifting map $f^\dagger$

RL Introductory Discussion

Eric B. Laber

Duke University

Banff, June 2022

Acknowledgments

Thanks to

- Esteban and Matt
- Duke/UNC AI and Precision Medicine Lab
- National Science Foundation
- National Institutes of Health

Joint work with

- Alex Cloud*
- Michael Kosorok

On choices

Dad always thought laughter was the best medicine, which I guess is why several of us died of tuberculosis.
—Jack Handy

What is reinforcement learning (RL)?

- Subfield of ML focused on decision making under uncertainty
- Goal is to efficiently generate and use information to inform decision making to maximize some long term measure of utility
- Encompasses ideas from a wide range of disciplines
  - Experimental design
  - Statistical efficiency theory
  - Causal inference
  - Optimization
  - ...

RL in the news

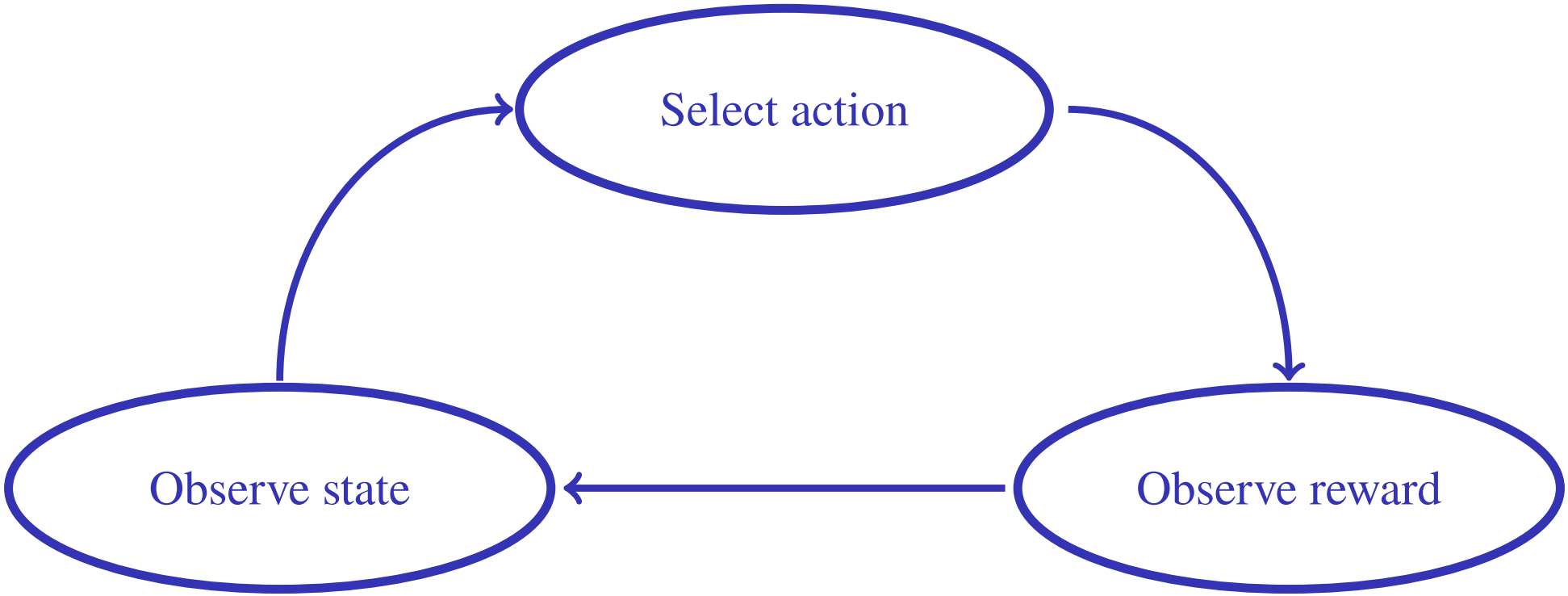
- Many recent high-profile examples of RL
  - Games
  - Robotics
  - Protein structure prediction

RL in the wild[1]

- Precision medicine
  - Adaptive clinical trials
  - Dynamic treatment regimes and just-in-time adaptive interventions (mHealth)
  - System-level (triage, adaptive team-based care, recall, etc.)
  - Public health (messaging, resource allocation, etc.)
- Retail
  - Advertising, recommender systems, pricing, etc.
  - Assortment selection
  - Fraud detection
  - Site selection

[1] Heavily biased by my own experience.

Reinforcement learning (RL) model of decision making



- Learn from experience $\Rightarrow$ action selection balance info and reward
- Examples
  - Randomized clinical trial: explore than exploit
  - Batched learning: alternating phases of learning and optimization
  - Fully online: jointly learn and optimization

Formalizing a batch one-stage decision problem

- Observe $\{(\boldsymbol{X}_i, A_i, Y_i)\}_{i=1}^n$ iid from P
  - $\boldsymbol{X} \in \mathcal{X} \subseteq \mathbb{R}^p$ covariates (decision context)
  - $A \in \mathcal{A}$ action (treatment, intervention, decision, etc.)
  - $Y \in \mathbb{R}$ utility (outcome, output, reward, etc.) higher is better
- Goal: select actions to maximize expected utility

Policies

- $\psi : \mathcal{X} \to 2^{\mathcal{A}}$ is set of allowable actions, i.e., $\psi(\boldsymbol{x}) \subseteq \mathcal{A} \setminus \emptyset$
- Policy $\pi : \mathcal{X} \to \mathcal{A}$ such that $\pi(\boldsymbol{x}) \in \psi(\boldsymbol{x})$ for all $\boldsymbol{x} \in \mathcal{X}$
  - Under π decision maker will select action $\pi(\boldsymbol{x})$ in context $\boldsymbol{x}$
  - Define $V(\pi) \triangleq \mathbb{E}^{\pi} Y$ to be expected utility if actions are selected according the policy π
  - Optimal policy satisfies $V(\pi^{\text{opt}}) \geq V(\pi)$ for all π

Approaches to estimation in batch one-stage setting

- Regression
  - Define $Q(\boldsymbol{x}, a) \triangleq \mathbb{E}(Y \big| \boldsymbol{X} = \boldsymbol{x}, A = a)$
  - Construct estimator $\widehat{Q}_n$ of Q using observed data
  - Estimated optimal policy $\widehat{\pi}_n(\boldsymbol{x}) = \arg\max_{a \in \psi(\boldsymbol{x})} \widehat{Q}_n(\boldsymbol{x}, a)$
- Policy search
  - For any policy π construct estimator[2] $\widehat{V}_n(\pi)$ of $V(\pi)$
  - Given class of policies Π compute $\widetilde{\pi}_n = \arg\max_{\pi \in \Pi} \widehat{V}_n(\pi)$

[2]Common approaches include augmented inverse probability weighting, marginal structural models, and G-computation. See Tsiatis et al. (2019) for review.

Considerations and open problems in one-stage batch case

- Scale and complexity
  - High-dimensional action spaces, e.g., assortment selection has $O(n^k)$ actions where n is catalog size and k is selection size
  - High-dimensional and complex feature spaces, e.g., txt recommendation from functional, imaging, and/or genetic data
- Experimental design
  - Assign actions to maximize efficiency of $\widehat{\pi}_n$
  - Ensure power for model diagnostics, secondary analyses, etc.
- Multiple outcomes and preference heterogeneity
  - Efficacy vs. side effects
  - Stated vs. revealed preferences

Formalizing an online one-stage decision problem

- Consider contextual bandit setting
- Observe $\{(\boldsymbol{X}_i, A_i, Y_i)\}_{i=1}^n$
  - Contexts $\boldsymbol{X}$ from fixed but unknown distn $P_{\mathbf{x}}$
  - Utility Y given $\boldsymbol{X} = \boldsymbol{x}, A = a$, from fixed but unknown distn $P_{y|\mathbf{x},a}$
  - Actions A_i drawn from distn which is allowed to vary over time and to depend on entire previous history $\overline{\boldsymbol{X}}_i, \overline{\boldsymbol{A}}_{i-1}, \overline{\boldsymbol{Y}}_{i-1}$
- Goal: adaptively select actions to maximize cumulative reward[3]

[3] I'm using reward here as a generic quantity which may mean utility, information, or some composite outcome.

Batch vs. online one-stage problems

- Learn from accumulating information
  - Generate information efficiently
  - Improve models $\Rightarrow$ more utility
  - Much more flexibility
- Inference more complicated
  - (Martingale) CLT may not apply directly
  - Standard tests and confidence intervals invalid with modification

Approaches to estimation in contextual bandit

- Perturbation-based methods
  - ϵ-greedy: estimate $\widehat{\pi}_n$ as in batch setting, follow $\widehat{\pi}_n$ with probability $(1 - \epsilon)$ and draw A_n from some 'exploration distribution' otherwise
  - Sample from posterior distribution of optimal posterior (Thompson Sampling)
- Deterministic approaches
  - Upper confidence bound selection: choose action with larger upper confidence bound on mean reward
  - Penalize reward with information gain (e.g., info-directed sampling)
- Many variant and nuances

Considerations and open problems in contextual bandits

- Same problems of scale and complexity as one-stage batch case
- Experimental design problem becomes much richer
  - Interim updates to estimated optimal designs
  - Sequential designs (enrichment, optimal, etc.)
- Study planning
  - Sample size and power analyses
  - Interim analyses, stopping criteria, etc.
- Indefinite deployment $\Rightarrow$ non-stationarity

Markov decision processes (MDPs)

- Ubiquitous model for RL
- Observe $\left\{\boldsymbol{S}_i^1, A_i^1, \ldots, \boldsymbol{S}_i^T, A_i^T, \boldsymbol{S}^{T+1}\right\}_{i=1}^n$ drawn i.i.d. from P
  - T observation period, e.g., trial follow-up
  - $\boldsymbol{S}^t \in \mathcal{S} \subseteq \mathbb{R}^p$ state at time t
  - $A \in \mathcal{A}$
- Utility $U^t = u(\boldsymbol{S}^t, A^t, \boldsymbol{S}^{t+1})$, higher is better
- Assume homogeneous MDP $\rightarrow$ focus on deterministic stationary policies $\pi : \mathcal{S} \rightarrow \mathcal{A}$

Notions of cumulative utility

- Discounted utility

$$V_\gamma(\boldsymbol{s};\pi) \triangleq \mathbb{E}^\pi \left\{ \sum_{k\geq 0} \gamma^k U^{t+k} \middle| \boldsymbol{S}^t = \boldsymbol{s} \right\}$$

- Average utility[4]

$$\overline{V}(\boldsymbol{s};\pi) \triangleq \lim_{T\to\infty} \mathbb{E}^\pi \left(\frac{1}{T} \sum_{k=1}^{T} U^{t+k} \middle| \boldsymbol{S}^t = \boldsymbol{s} \right)$$

- Given some measure $V(\boldsymbol{s};\pi)$ of the 'goodness' of π, optimal policy satisfies $V(\boldsymbol{s};\pi^{\text{opt}}) \geq V(\boldsymbol{s};\pi)$ for all π

[4]Under mild regularity conditions $\overline{V}$ doesn't depend on the starting state.

Estimation (of π^{opt}) in MDPs

- Model-based: system dynamics model + simulation optimization
- Model-free: construct estimating functions for optimal policy
  - Typically derived from Bellman equations
  - Only model part of dynamics, e.g., moments
- Bias-variance trade-off in model-free vs. model-based

Considerations and open problems in MDPs

- Scalability and complexity
- Experimental design is still more complicated
  - Need to ensure sufficient exploration of state space
  - Need to consider delayed effects
- Feature construction to ensure Markov (approx) holds
- Need principled methods for optimally combing model-based and model-free methods

We're excited to chat about these problems!

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