Machine Learning in Critical care

Personal Bias

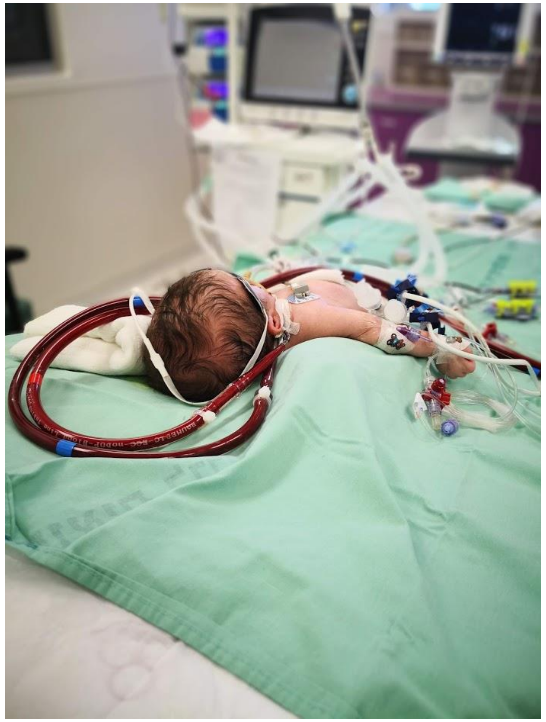
Danny Eytan

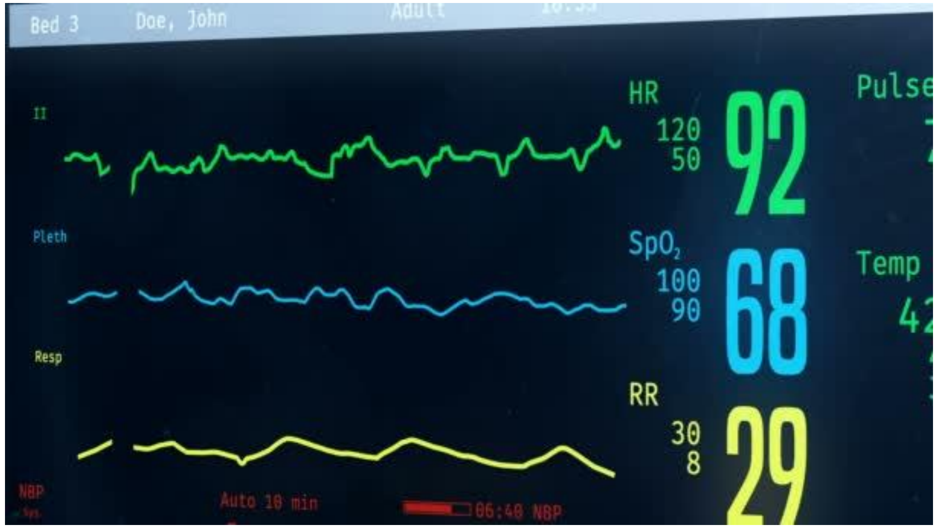
PICU – Rambam Medical Center

Technion – Israel Institute of Technology

The Hospital for Sick Children – Toronto Canada

Adapting **Humans, Technology & Data Science** into Pediatric Critical Care




Bed 3
Doe, John
Adult
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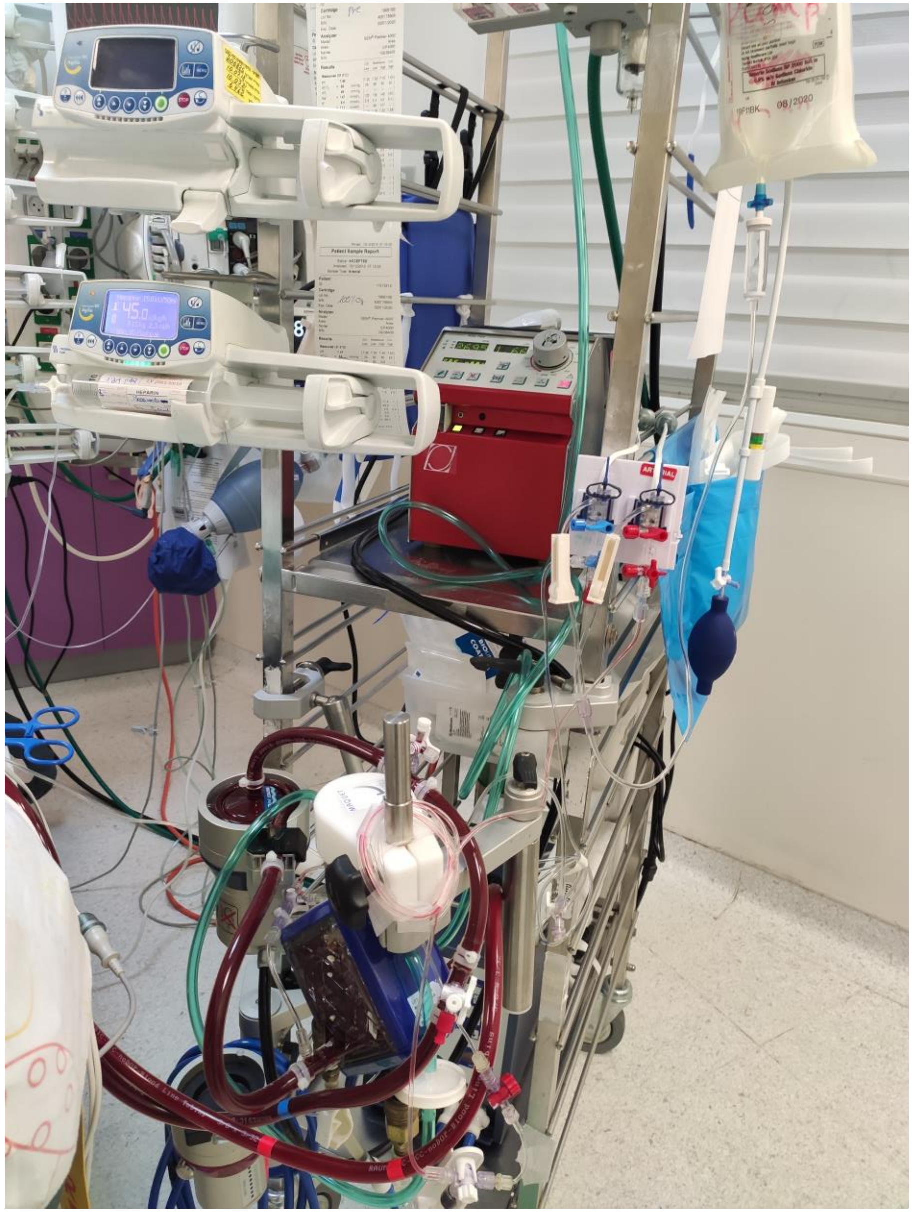


PDM
PICU-BED6
Inf 3-12mon
EtCO2
low
HR /min
ECG
113
PVC
0 /min
Art
LA/L lead off
P2 Art mmHg
99/56
(71)
P8 RAP mmHg Contrl
78/7
SpO2 %
95
CO2 mmHg
ET
23
FI
0
(63)
T2 °C
T2
37.1
SHOT ON MI 9T
AI TRIPLE CAMERA
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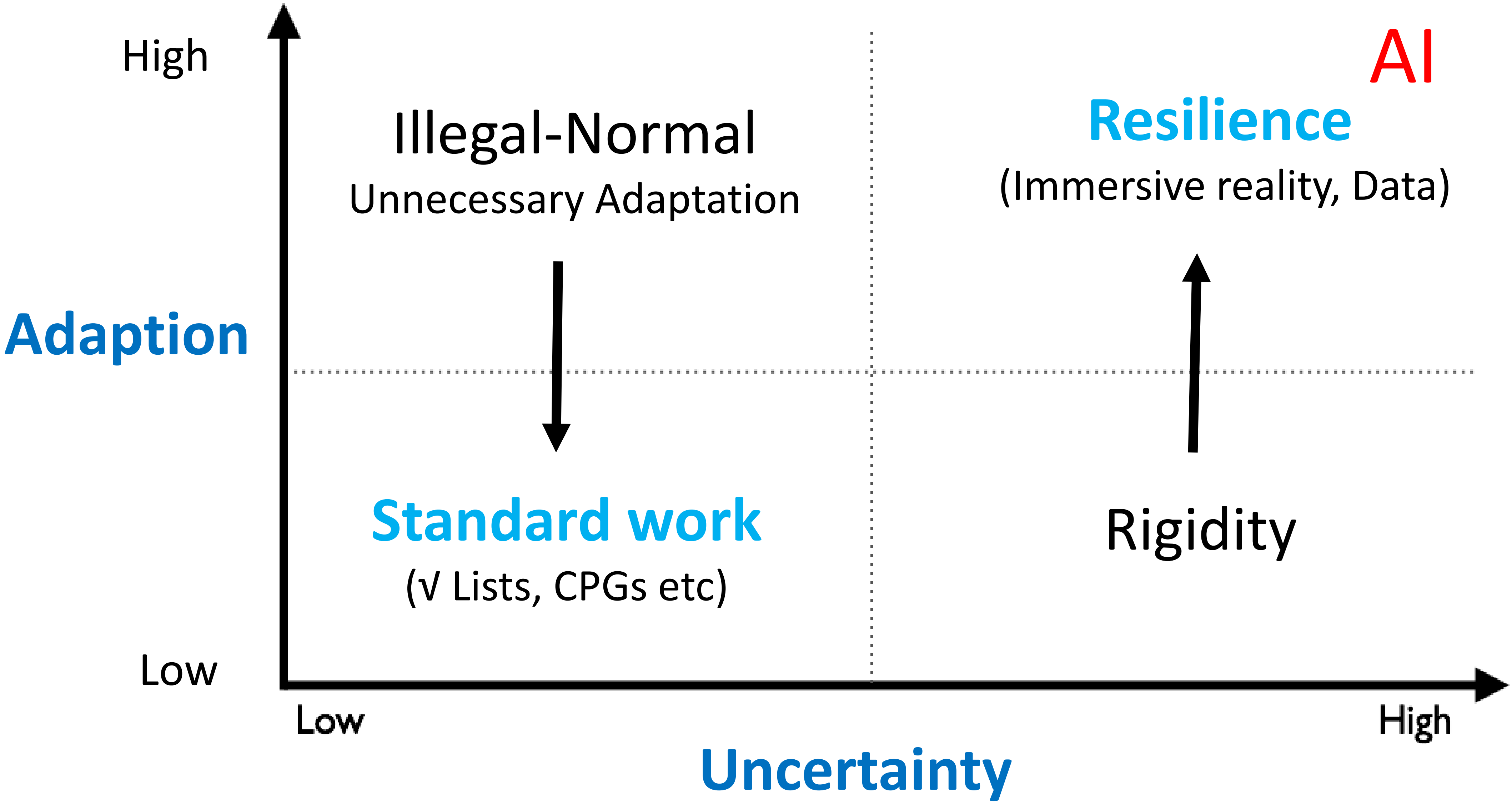
Understand how we work: our behaviors adapting to uncertainty



Trbovich P, Fan M, Pinkney S, Kolodzey L, Laussen PC, 2018

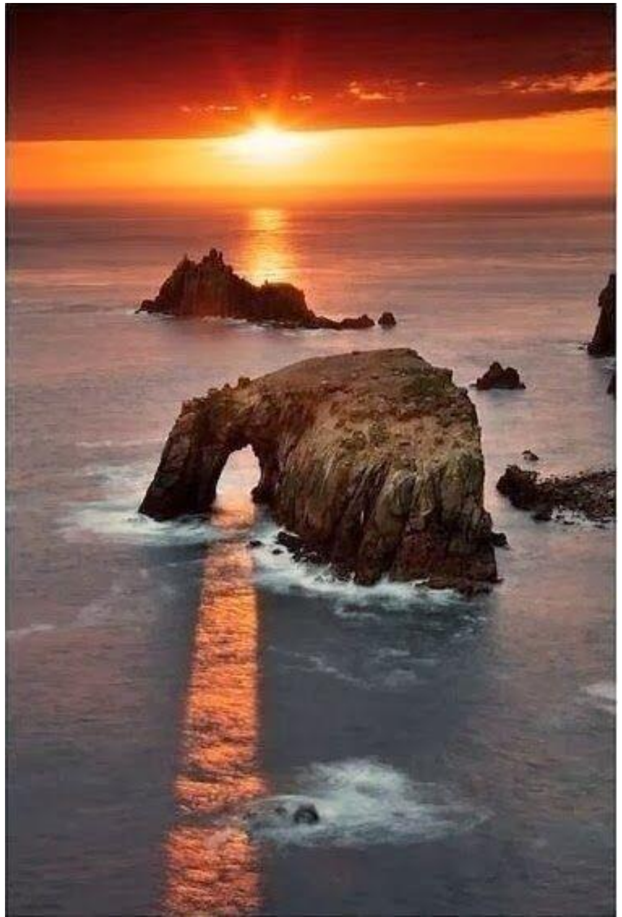
Where are the biggest opportunities today in ML for health?

Diagnosis

Where are the biggest opportunities today in ML for health?

Where are the biggest opportunities today in ML for health?

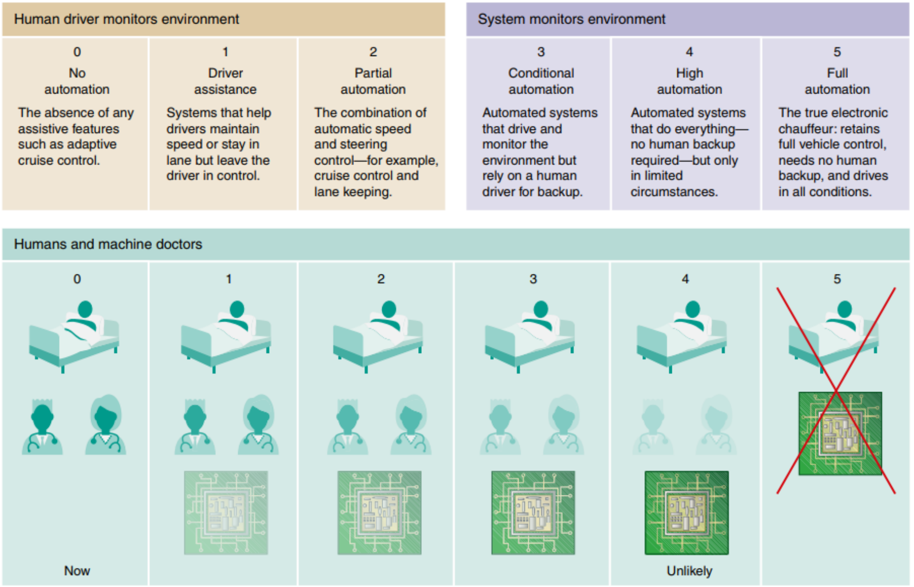
Insight on
disease process

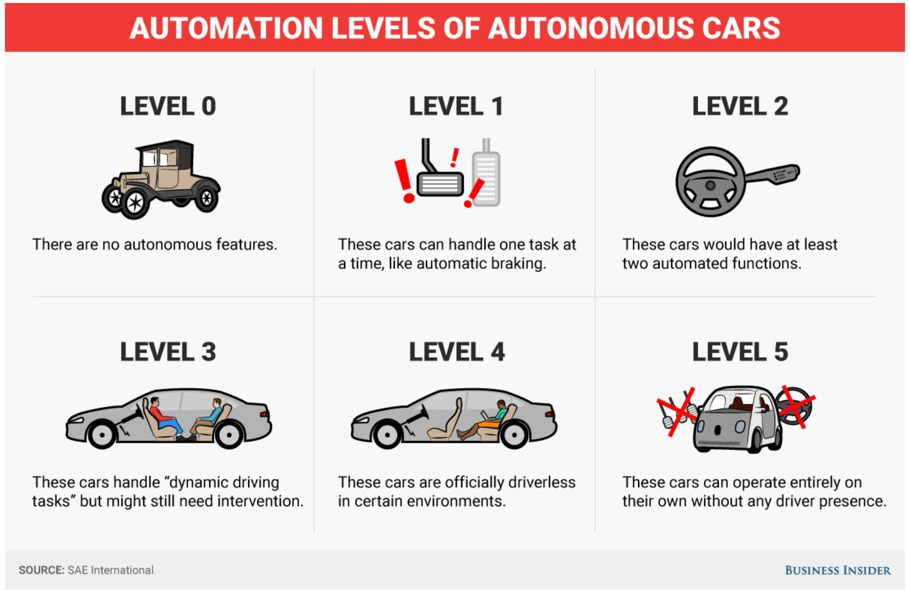


Where are the biggest opportunities today in ML for health?

Decision support

"The picture's pretty bleak, gentlemen. ... The world's climates are changing, the mammals are taking over, and we all have a brain about the size of a walnut."





Hierarchy of healthcare opportunities

1. Task automation
   - Medical imaging evaluation
   - Automating routine processes
2. Clinical support and augmentation
   - Ensuring standards of care
   - Identifying early warning signs
   - Complex diagnostics
3. Expanding clinical capacities
   - Precision medicine for individualized treatment
   - Generate new evidence – drugs and treatments, disease processes
   - Expand monitoring capacities – new sensors

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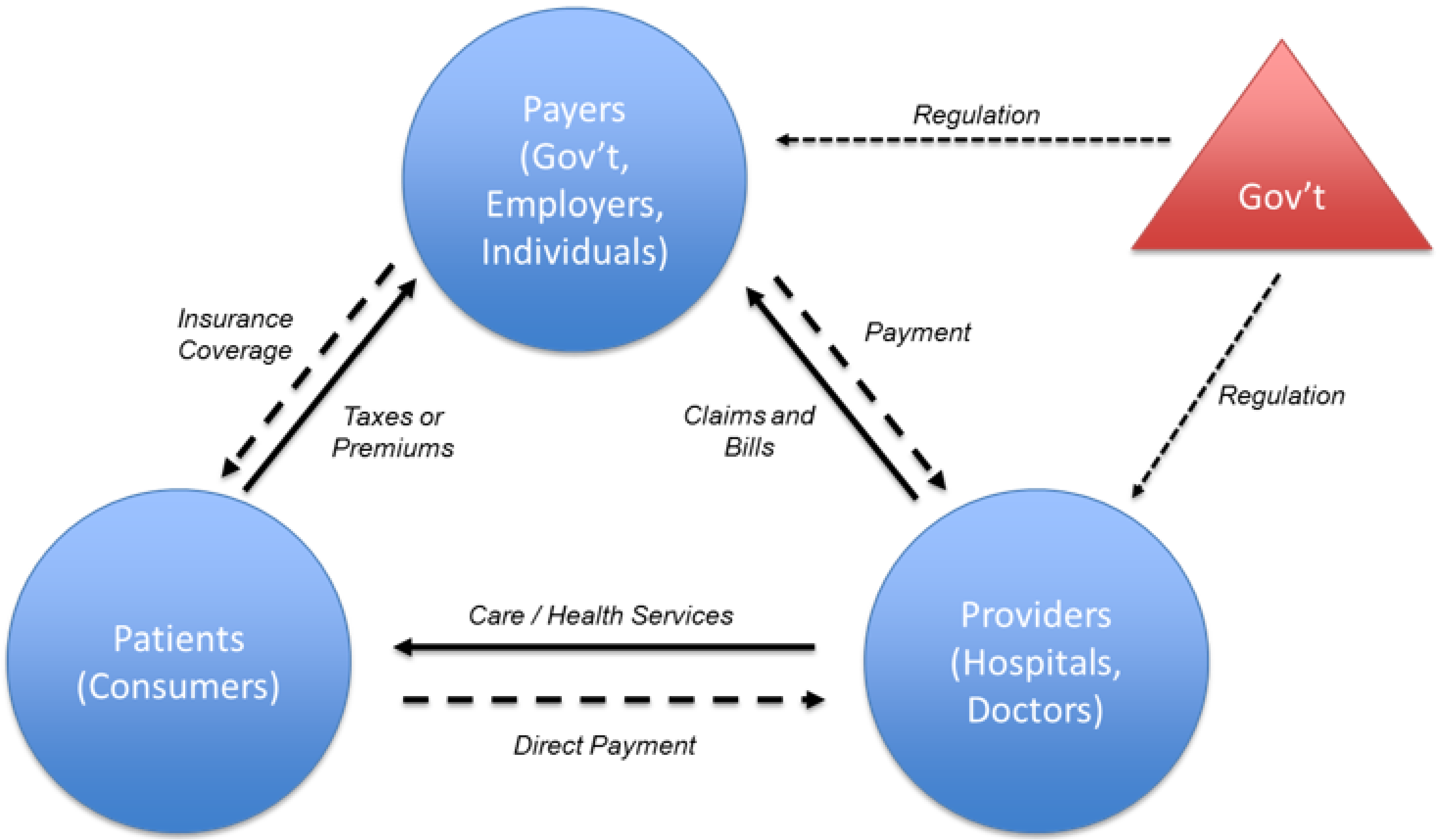
ML will affect all aspects and levels of healthcare



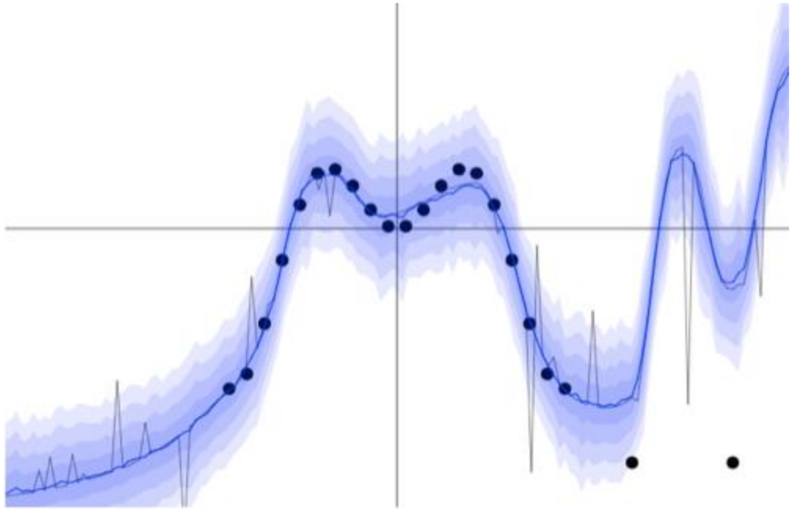
Unique aspects of ML in healthcare

- Life or death decisions
  - Need robust algorithms
  - Checks and balances built into ML deployment
  - Regulation
  - (Also arises in other applications of AI such as autonomous driving)
  - Need fair and accountable algorithms
- Many questions are about unsupervised learning
  - Discovering disease subtypes, or answering question such as “characterize the types of people that are highly likely to be readmitted to the hospital”?
- Many of the questions we want to answer are causal
  - Naïve use of supervised machine learning is insufficient

Label noise is the rule

- In many image and text tasks, we often have a nearly deterministic true mapping (features)→(label)
- However, no such mapping for predicting mortality
- Doctors often disagree on diagnoses

- Giving the confidence of the prediction is often crucial



Humans are *not* experts (even doctors!)

- Hard to validate models by inspection

Missing data is the rule

- Most lab tests are missing most of the time
  - Presence of lab test can be as informative as the value of the lab test itself! (we will see next week)
- Data collection is very incomplete
  - Heart rate monitor taken off when patient is moved

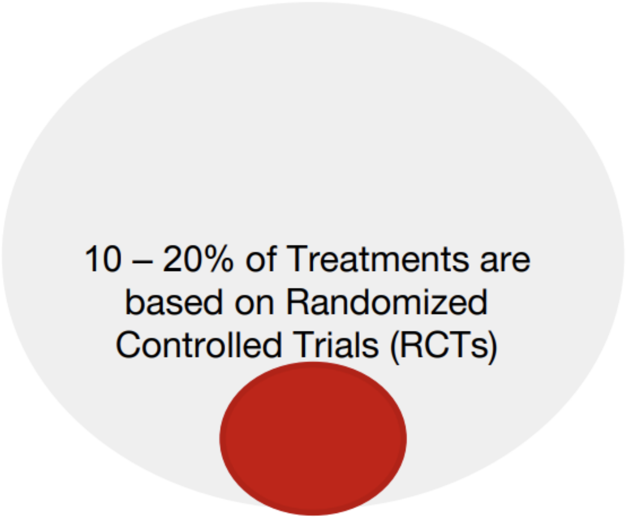
- Difficulty of deploying ML
  - Commercial electronic health record software is difficult to modify
  - Data is often in silos; everyone recognizes need for interoperability, but slow progress
  - Careful testing and iteration is needed

Need for interpretability

When dermatologists are looking at a lesion that they think might be a tumor, they'll break out a ruler—the type you might have used in grade school—to take an accurate measurement of its size. Dermatologists tend to do this only for lesions that are a cause for concern. So in the set of biopsy images, if an image had a ruler in it, the algorithm was more likely to call a tumor malignant, because the presence of a ruler correlated with an increased likelihood a lesion was cancerous. Unfortunately, as Novoa emphasizes,

Procedure for generating evidence in healthcare

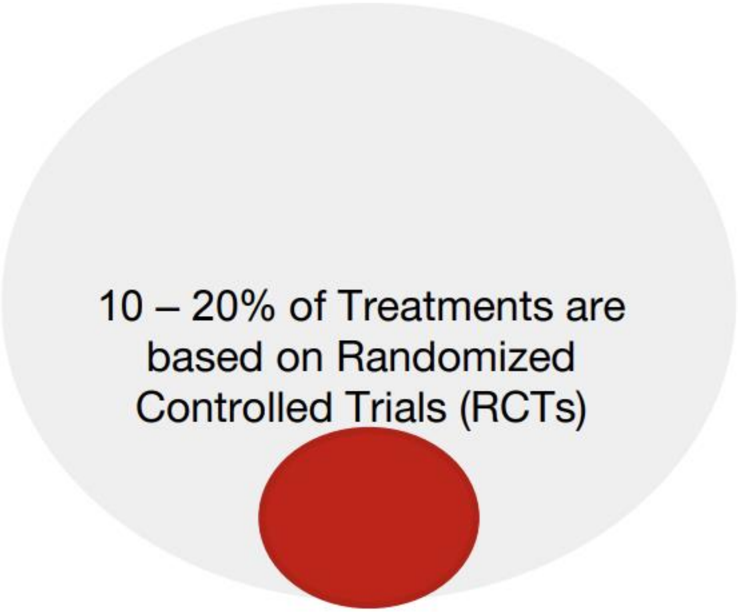
Randomized Controlled Trials (RCTs) are **rare and expensive**

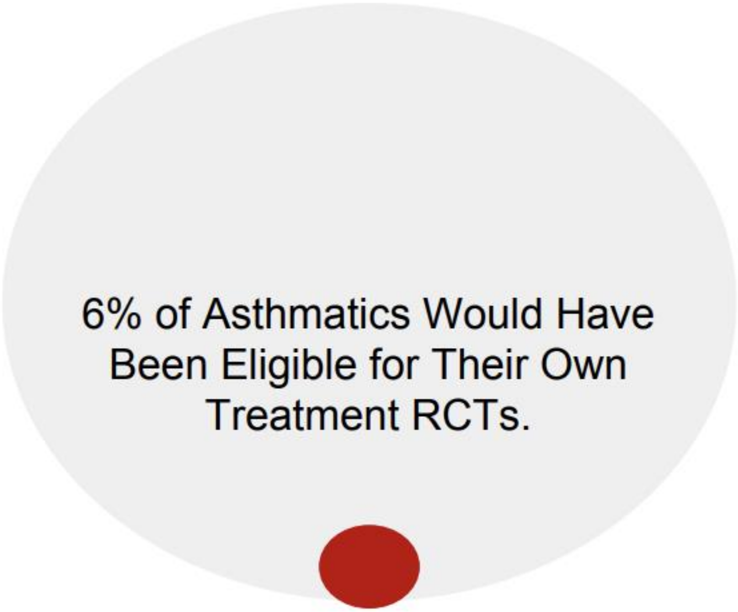


[1] *Smith M, Saunders R, Stuckhardt L, McGinnis JM, Committee on the Learning Health Care System in America, Institute of Medicine. Best Care At Lower Cost: The Path To Continuously Learning Health Care In America. Washington: National Academies Press; 2013..*

Procedure for generating evidence in healthcare

Randomized Controlled Trials (RCTs) are **rare and expensive**, and can encode **structural biases** that apply to very few people.





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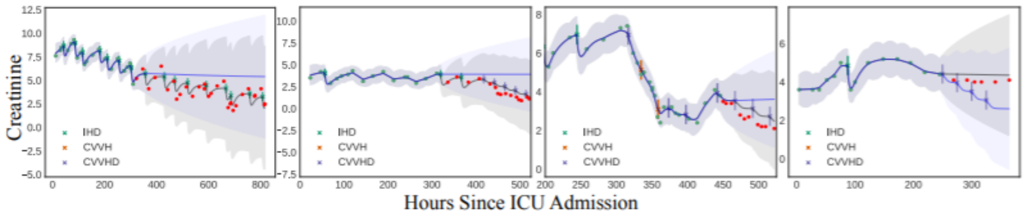
[2] Travers, Justin, et al. "External validity of randomised controlled trials in asthma: to whom do the results of the trials apply?." Thorax 62.3 (2007): 219-223.

Counterfactual prediction in healthcare

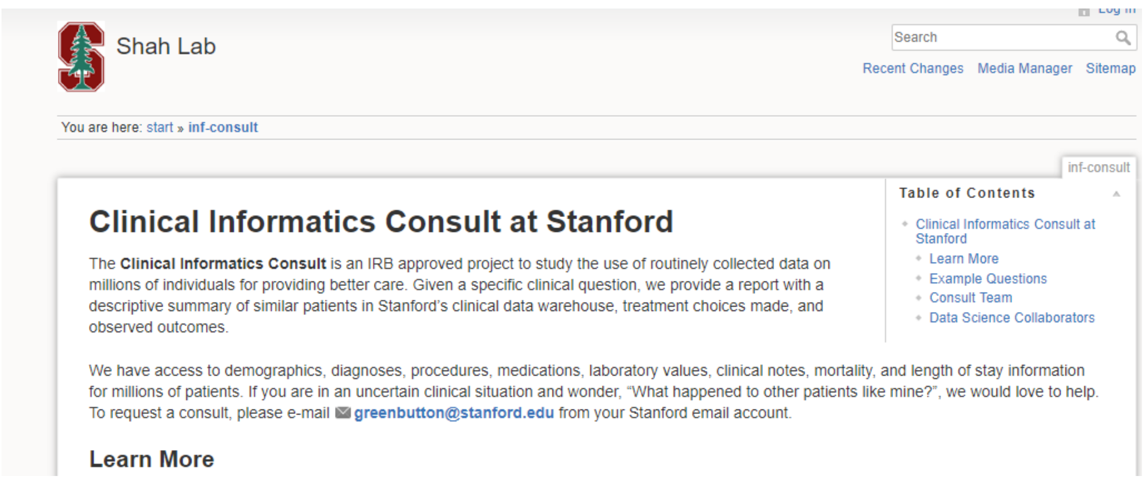
Reliable Decision Support using Counterfactual Models

Suchi Saria



Structured Inference Networks for Nonlinear State Space Models

Rahul G. Krishnan, Uri Shalit, David Sontag
Courant Institute of Mathematical Sciences, New York University
{rahul, shalit, dsontag}@cs.nyu.edu



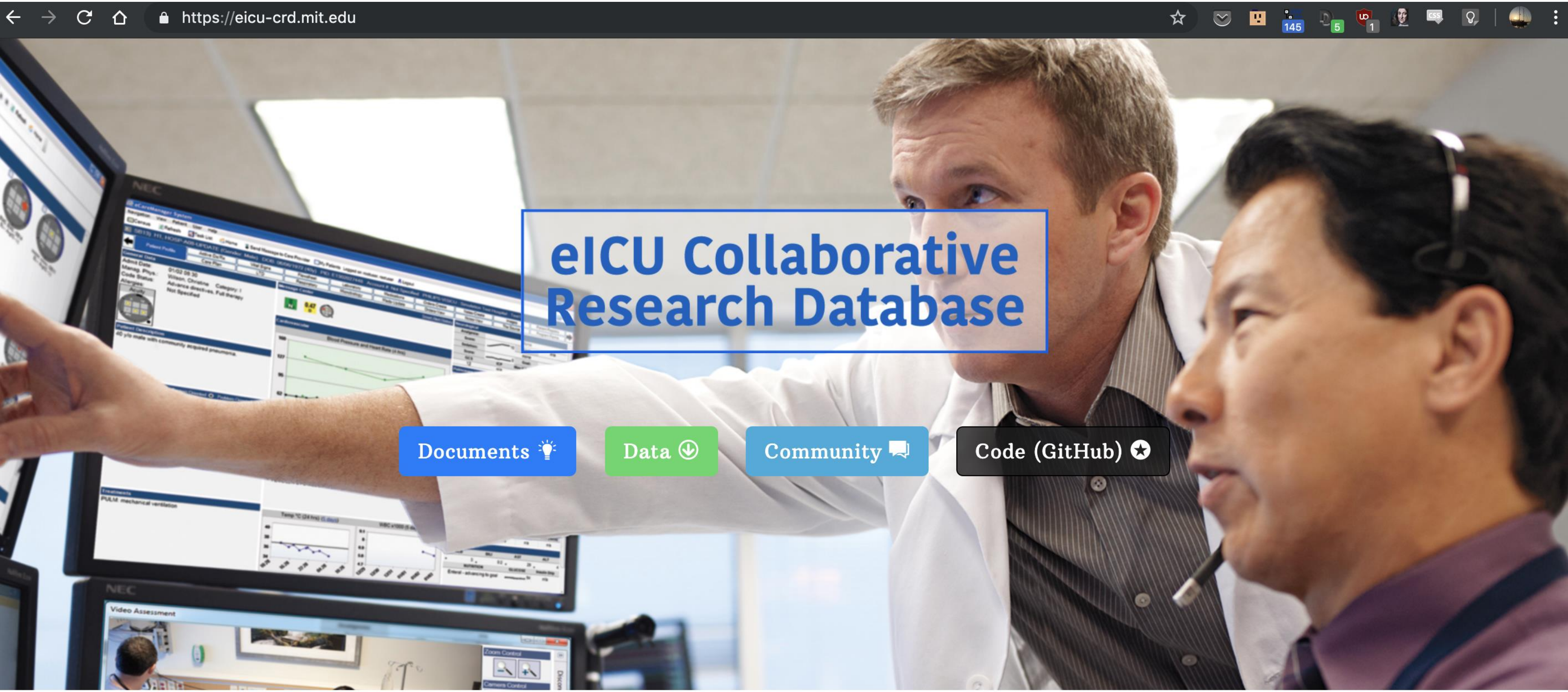
Massachusetts Institute of Technology

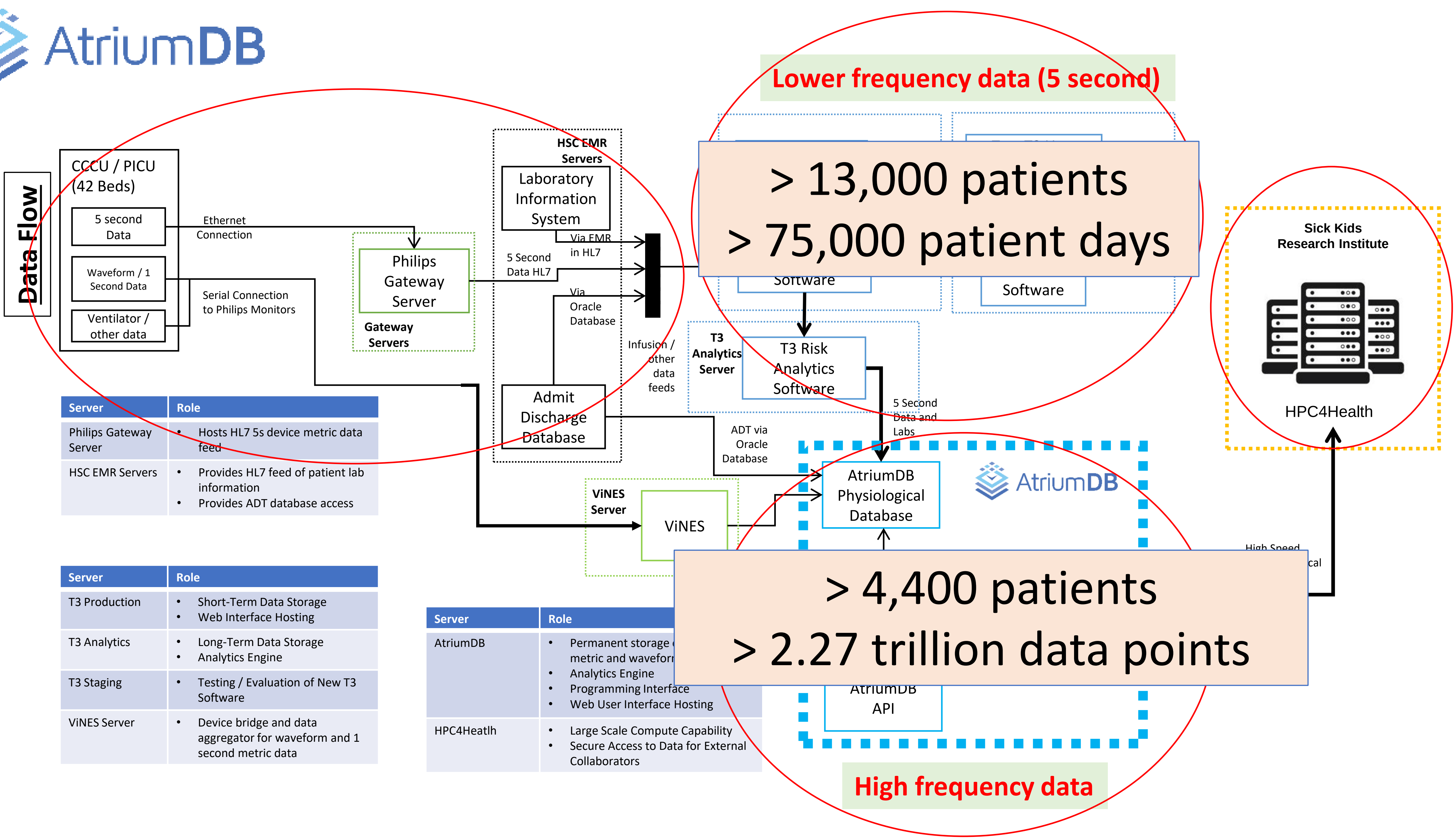
Laboratory for Computational Physiology

De-identified health data from ~40K critical care patients

Demographics, vital signs, laboratory tests, medications, notes, …

- eICU: 200,00 admission from 335 ICU unit
- less detailed than MIMIC





Server	Role
Philips Gateway Server	• Hosts HL7 5s device metric data feed
HSC EMR Servers	• Provides HL7 feed of patient lab information • Provides ADT database access

Server	Role
T3 Production	• Short-Term Data Storage • Web Interface Hosting
T3 Analytics	• Long-Term Data Storage • Analytics Engine
T3 Staging	• Testing / Evaluation of New T3 Software
ViNES Server	• Device bridge and data aggregator for waveform and 1 second metric data

Server	Role
AtriumDB	• Permanent storage metric and wavefor • Analytics Engine • Programming Interface • Web User Interface Hosting
HPC4Heatlh	• Large Scale Compute Capability • Secure Access to Data for External Collaborators

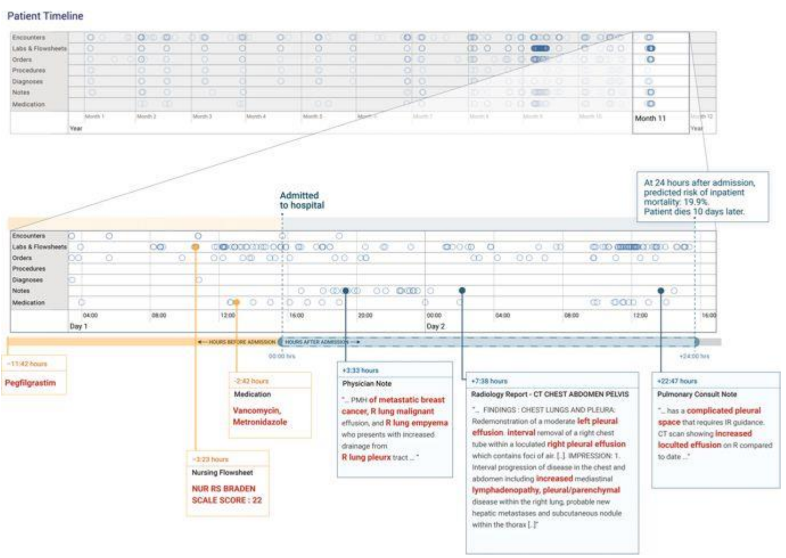
Prediction in ICU

Article | OPEN | Published: 08 May 2018

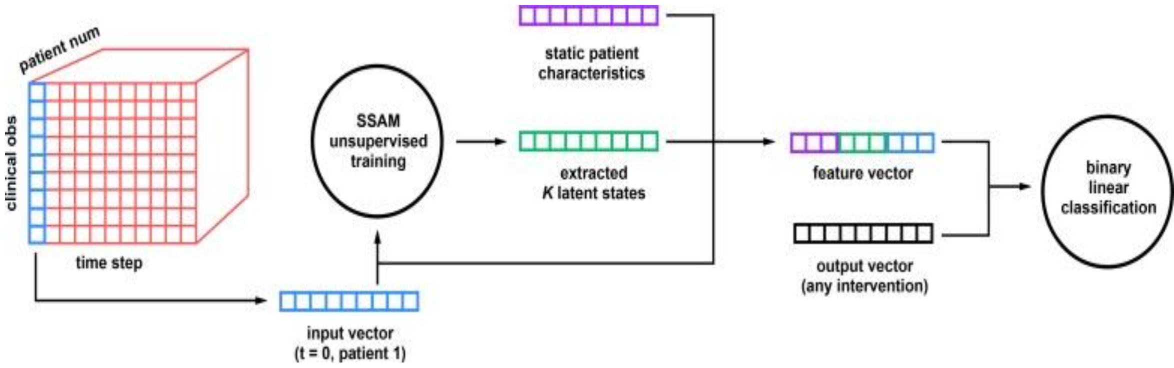
Scalable and accurate deep learning with electronic health records

Alvin Rajkomar, Eyal Oren, [...] Jeffrey Dean

npj Digital Medicine **1**, Article number: 18 (2018) | Download Citation



Predicting intervention onset in the ICU with switching state space models,
Marzyeh Ghassemi



Clinical Intervention Prediction and Understanding using Deep Networks

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Alistair Johnson AEWJ@MIT.EDU

Leo Anthony Celi LCELI@MIT.EDU

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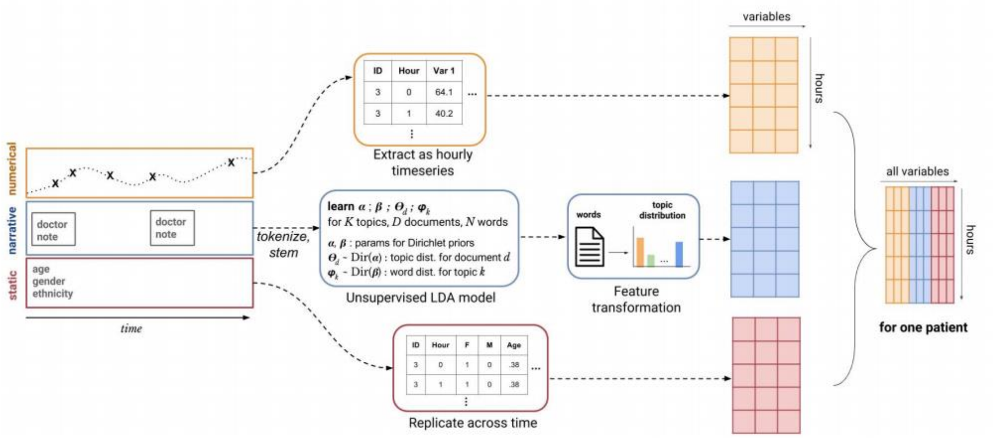
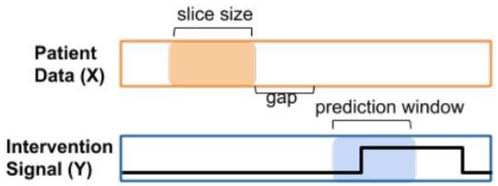
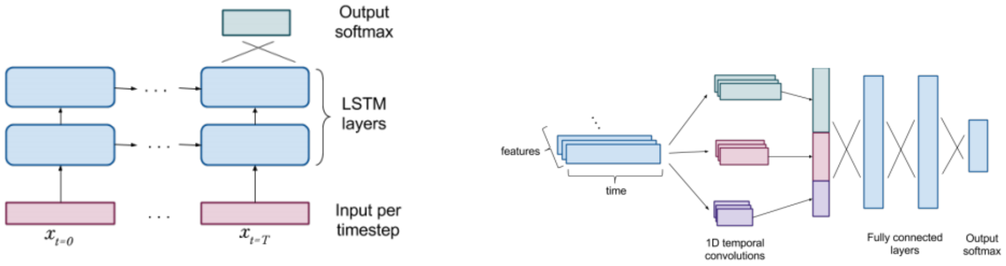


Figure 1: Data preprocessing and feature extraction with numerical measurements and lab values, clinical notes and static demographics.





(a) The LSTM consists of two hidden layers with 512 nodes each. We sequentially feed in each hour's data. At the end of the example window, we use the final hidden state to predict the output.

(b) The CNN architecture performs temporal convolutions at 3 different granularities (3, 4, and 5 hours), max-pools and combines the outputs, and runs this through 2 fully connected layers to arrive at the prediction.

Figure 3: Schematics of LSTM and CNN model architectures.

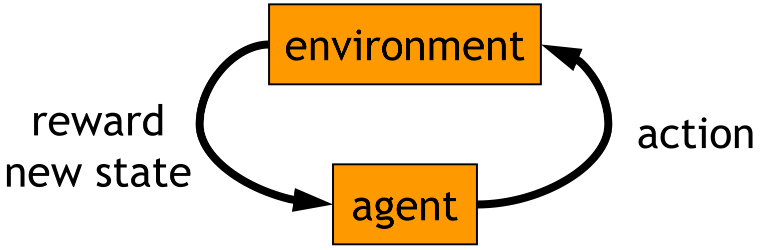
		Intervention Type				
Task	**Model**	VENT	NI-VENT	VASO	COL BOL	CRYS BOL
Onset AUC	Baseline	0.60	0.66	0.43	0.65	0.67
	LSTM Raw	0.61	0.75	**0.77**	0.52	0.70
	LSTM Words	**0.75**	**0.76**	0.76	**0.72**	**0.71**
	CNN	0.62	0.73	**0.77**	0.70	0.69
Wean AUC	Baseline	0.83	0.71	0.74	-	-
	LSTM Raw	0.90	0.80	**0.91**	-	-
	LSTM Words	0.90	**0.81**	**0.91**	-	-
	CNN	**0.91**	0.80	**0.91**	-	-
Stay On AUC	Baseline	0.50	0.79	0.55	-	-
	LSTM Raw	0.96	**0.86**	**0.96**	-	-
	LSTM Words	**0.97**	**0.86**	0.95	-	-
	CNN	0.96	**0.86**	**0.96**	-	-
Stay Off AUC	Baseline	0.94	0.71	0.93	-	-
	LSTM Raw	0.95	**0.86**	**0.96**	-	-
	LSTM Words	**0.97**	**0.86**	0.95	-	-
	CNN	0.95	**0.86**	**0.96**	-	-
Macro AUC	Baseline	0.72	0.72	0.66	-	-
	LSTM Raw	0.86	**0.82**	**0.90**	-	-
	LSTM Words	**0.90**	**0.82**	0.89	-	-
	CNN	0.86	0.81	**0.90**	-	-


ARTICLES
https://doi.org/10.1038/s41591-018-0213-5
nature medicine

The Artificial Intelligence Clinician learns optimal treatment strategies for sepsis in intensive care

Matthieu Komorowski[1,2,3], Leo A. Celi[3,4], Omar Badawi[3,5,6], Anthony C. Gordon[1*] and A. Aldo Faisal[2,7,8,9*]

- Supervised learning
  - classification, regression
- Unsupervised learning
  - clustering
- Reinforcement learning
  - more general than supervised/unsupervised learning
  - learn from interaction w/ environment to achieve a goal



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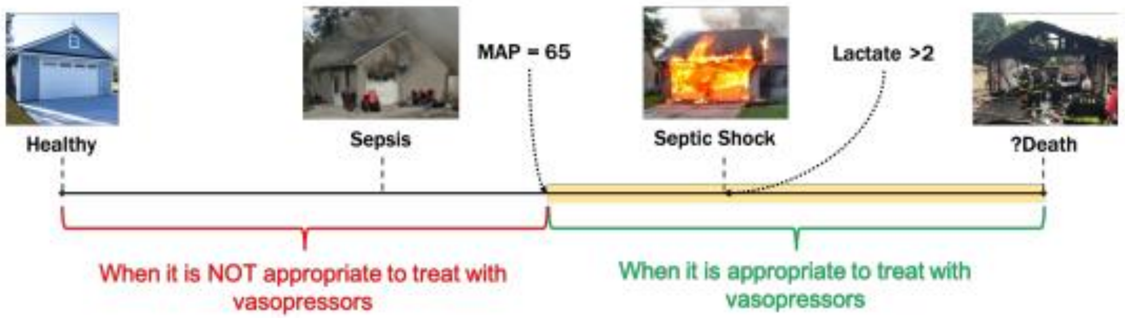
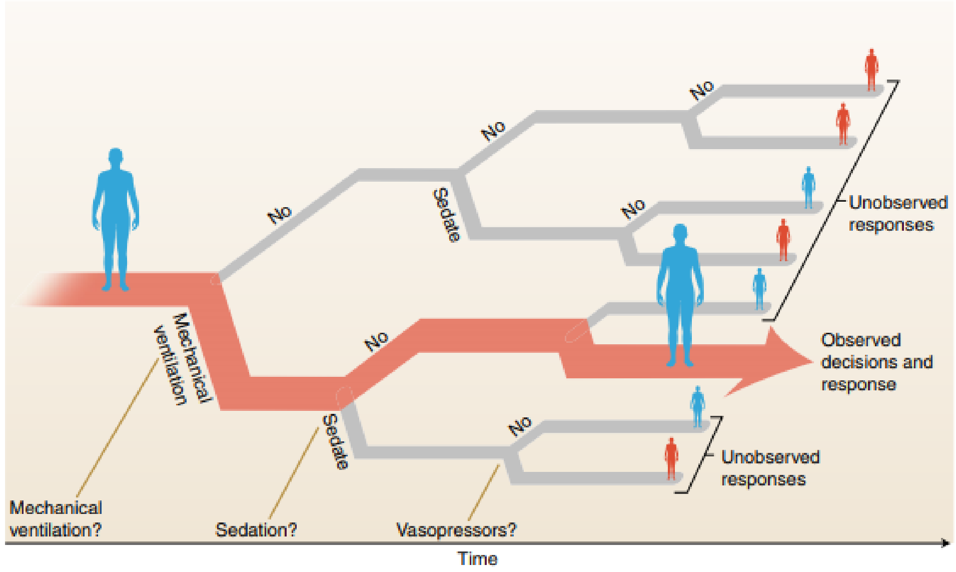


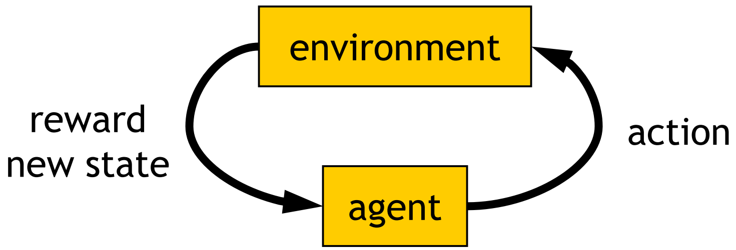


Markov Decision Process (MDP)

- Set of states S, set of actions A, initial state S_0
- transition model P(s,a,s')
  - P([1,1], up, [1,2]) = 0.8
- reward function r(s)
  - r([4,3]) = +1
- goal: maximize cumulative reward in the long run

- policy: mapping from S to A
  - $\pi(s)$ or $\pi(s,a)$ (deterministic vs. stochastic)

- reinforcement learning
  - transitions and rewards usually not available
  - how to change the policy based on experience
  - how to explore the environment



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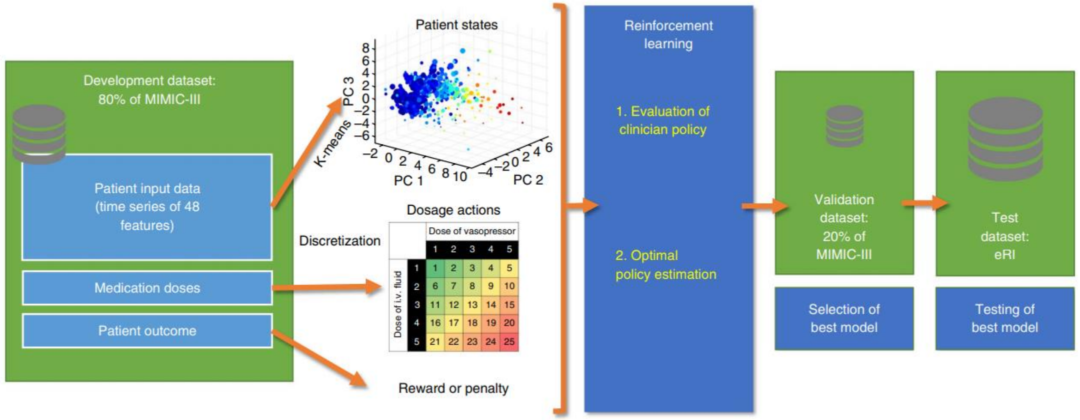

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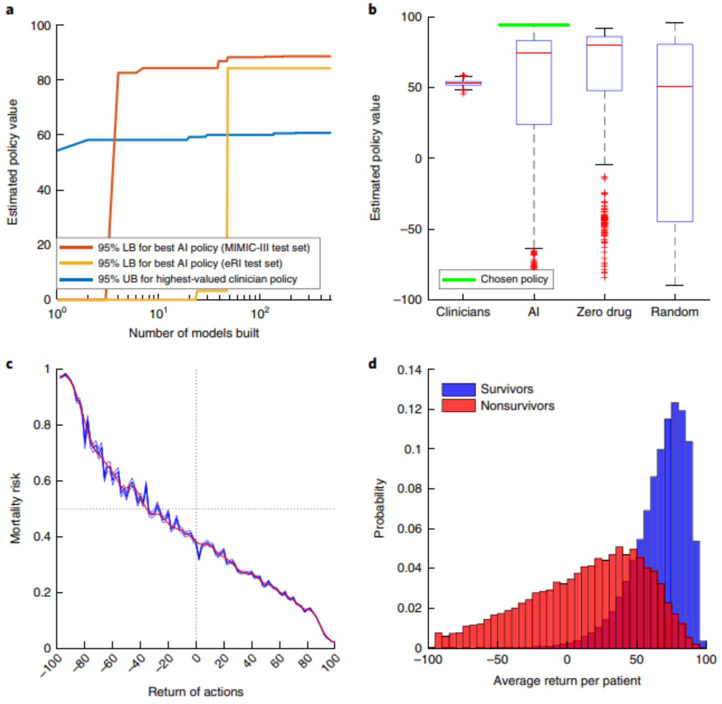

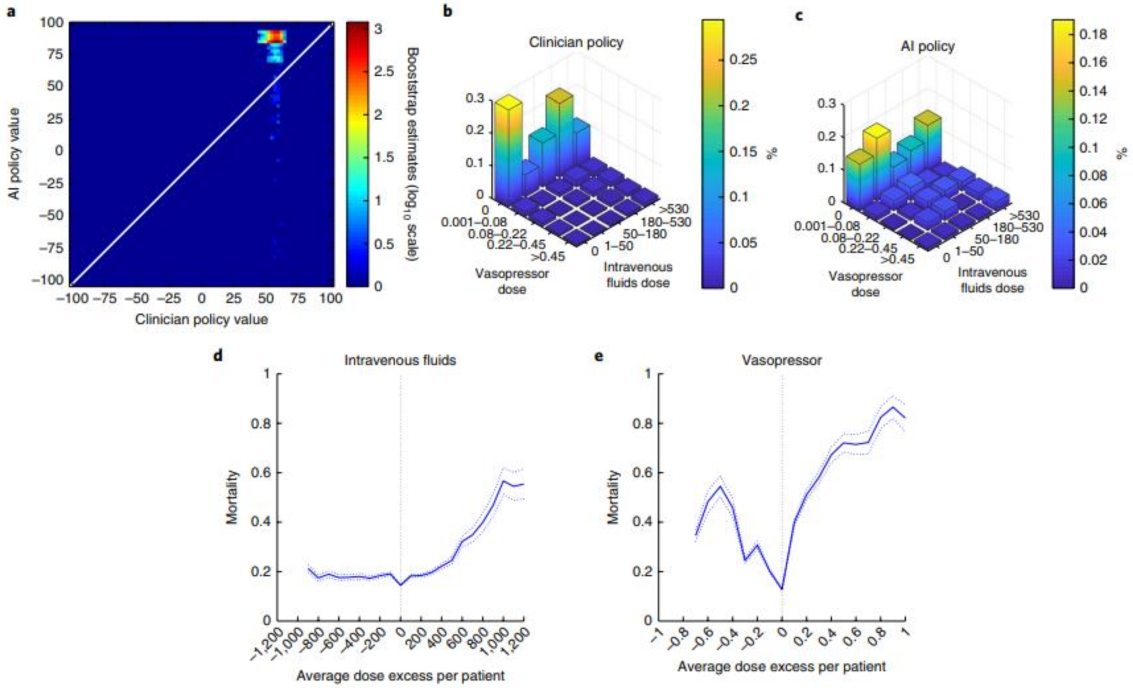

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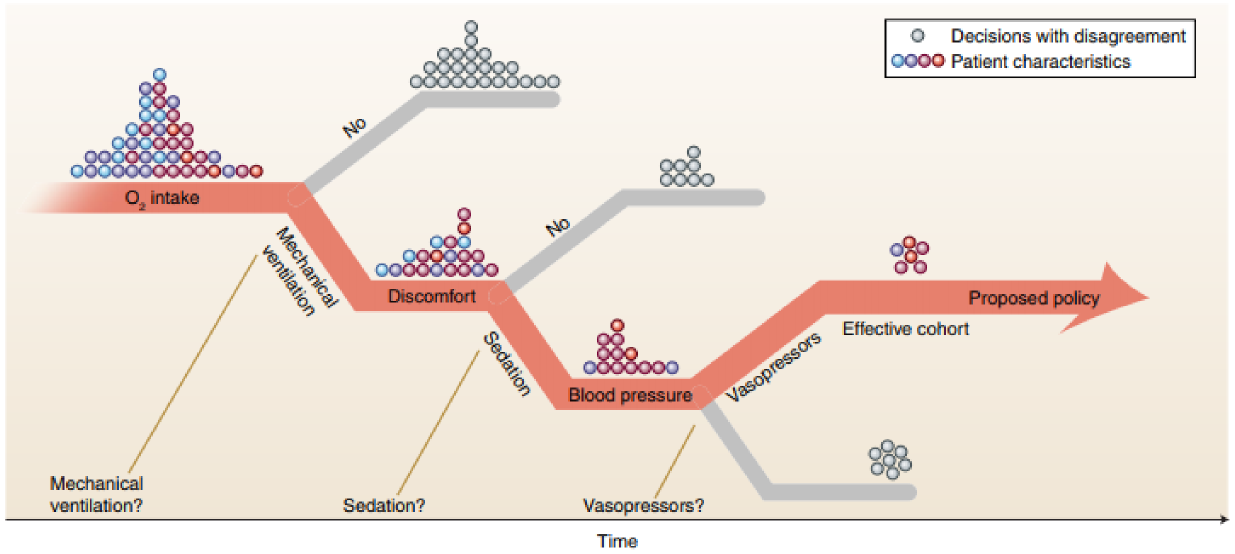


My personal biased challenge

The Critical Care Patient

Treatments

Ventilation
Infusions
Interventions
….

Continuous

Physiological Variables

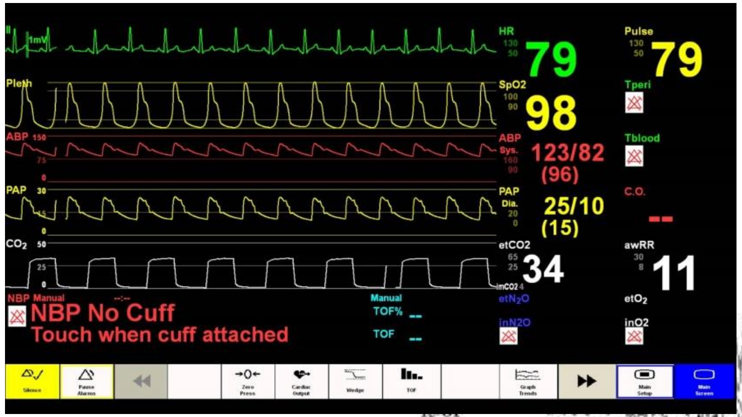
Heart rate (500Hz→1/3600)
Blood Pressure
Respiratory Rate
Urine Output
….

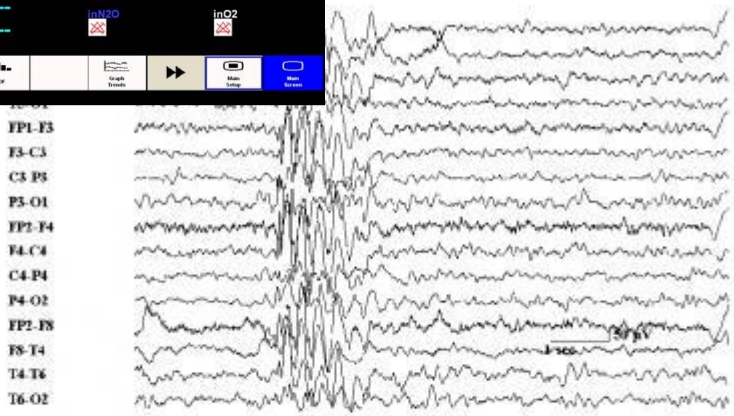
Complex Monitoring

EEG
R Index
NIRS
…

Intermittent Data

Lab Data
Genomics
Proteomic
Imaging
Notes
….

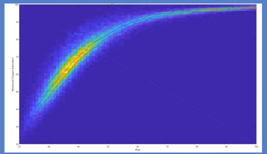


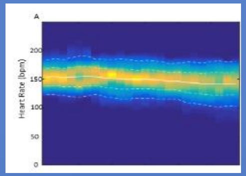


Modeling the critically-ill patient: combining systems physiology, big-data and machine learning

Patient's state and trajectory

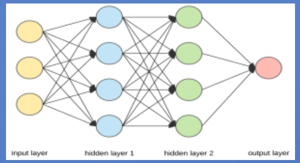
What's the course from admission to discharge?





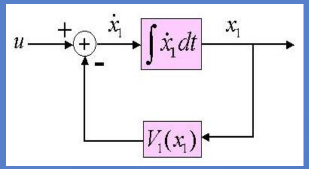
Prediction and Causal inference

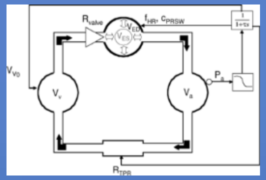
What's the future expected trajectory?
Treatment response?



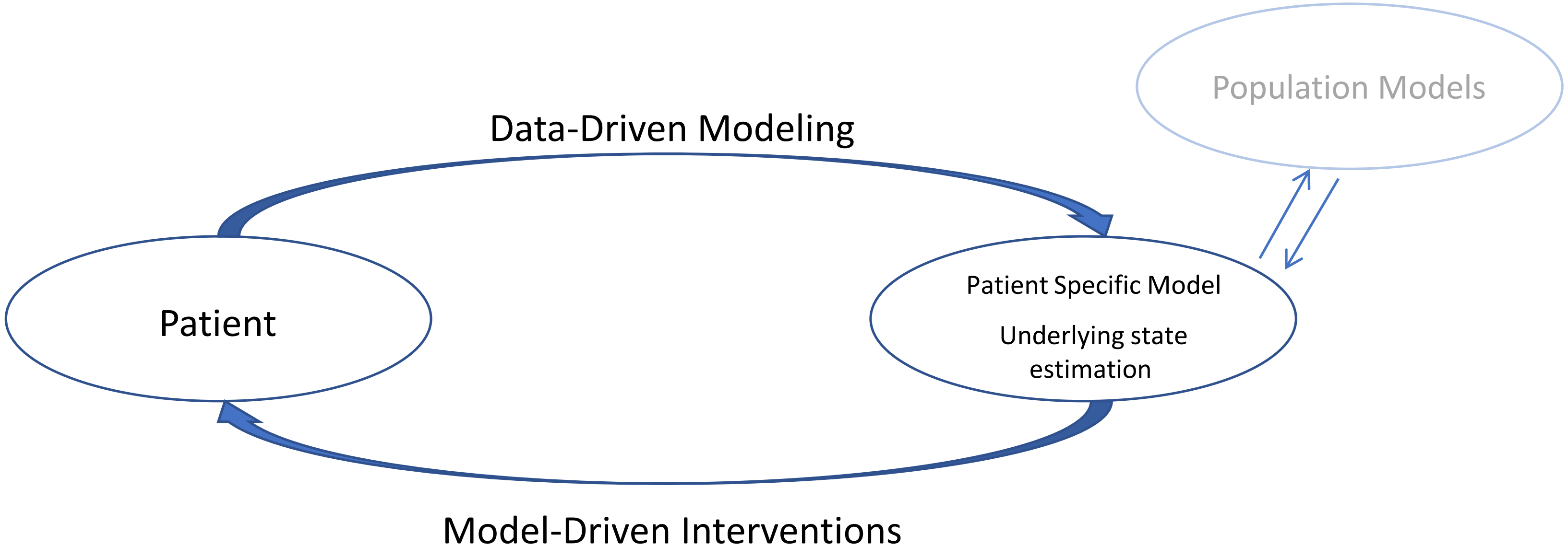
Physiological modeling

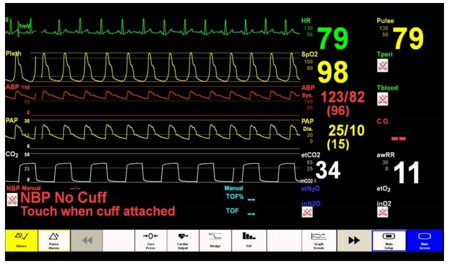
Mechanistic dynamical models

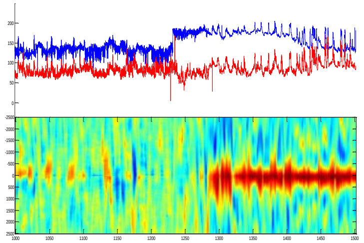


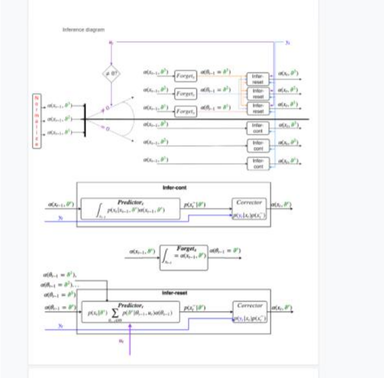


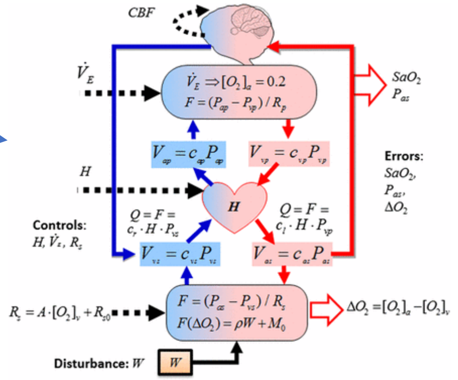
Combining mechanistic models and data driven estimation



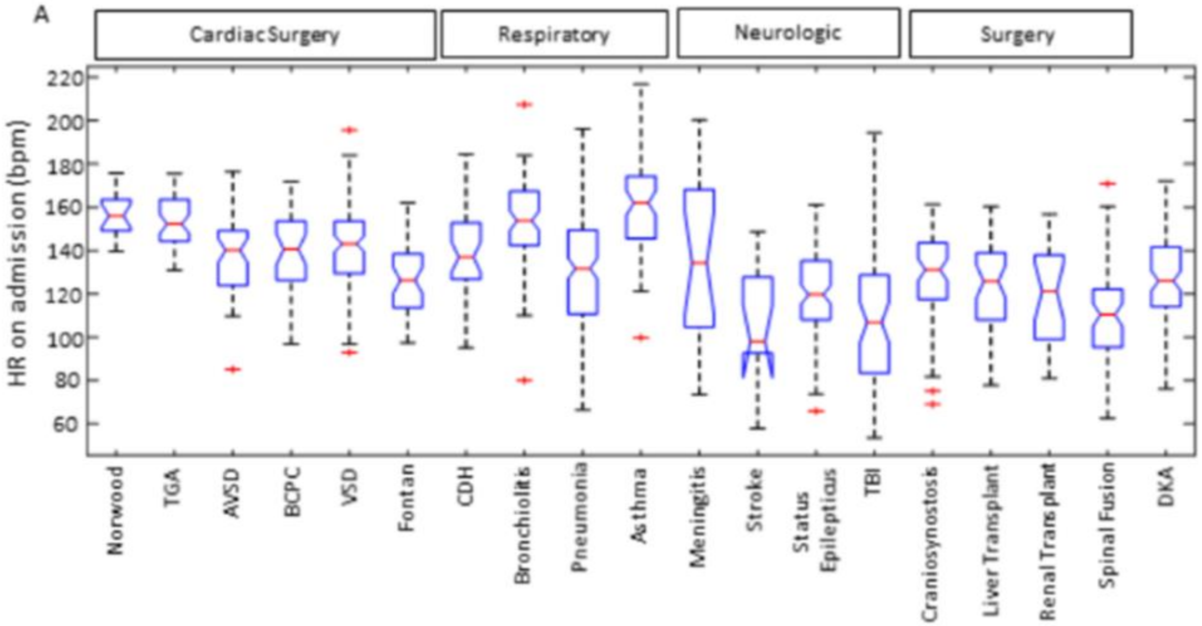


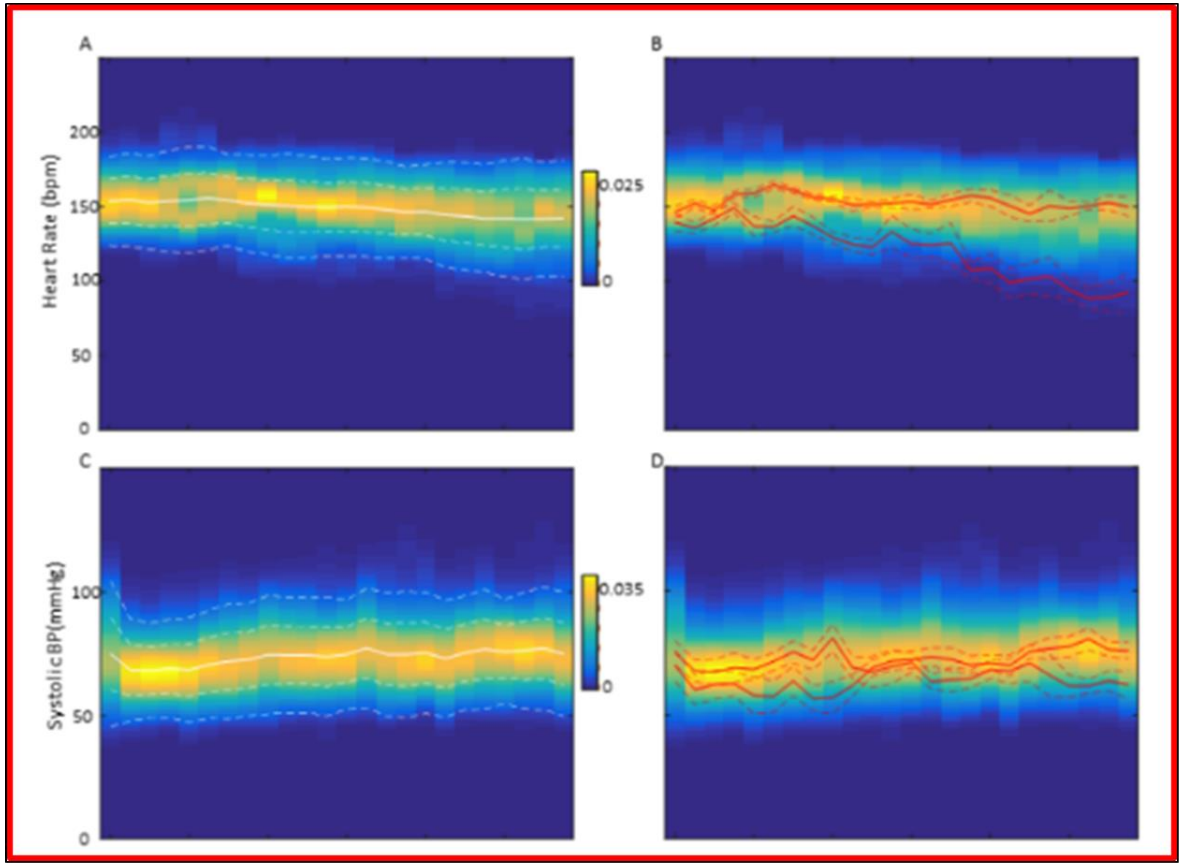






Using Big Data: Understanding the **physiologic** Phenotypes……



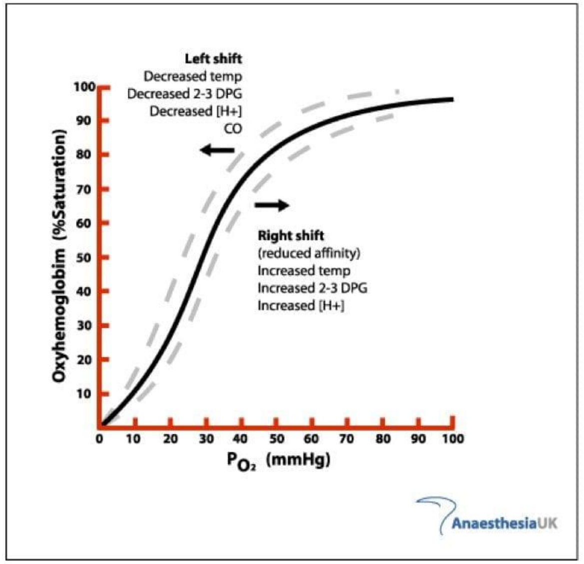


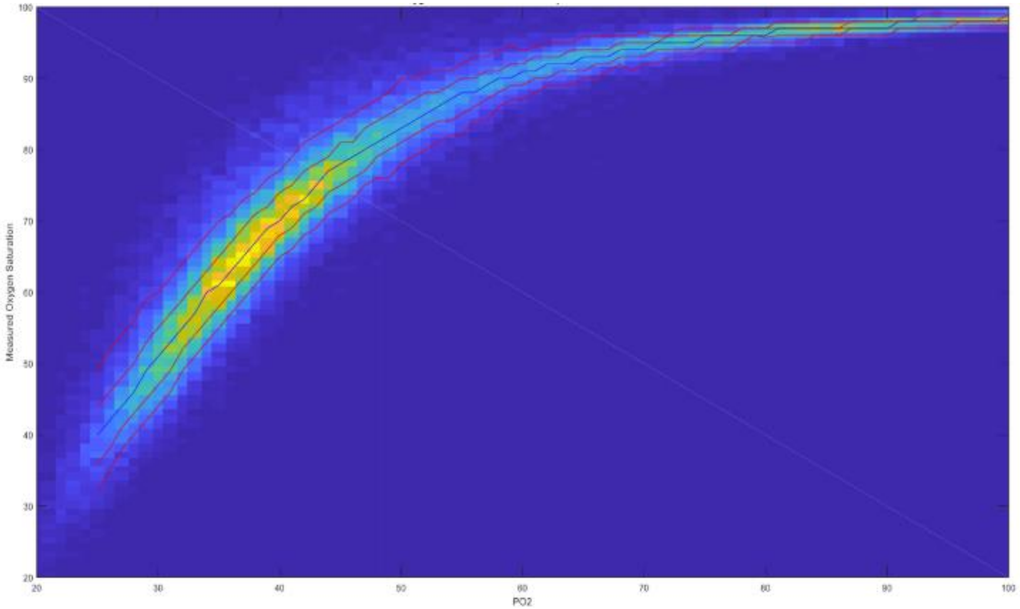
Individualized target ranges and boundaries

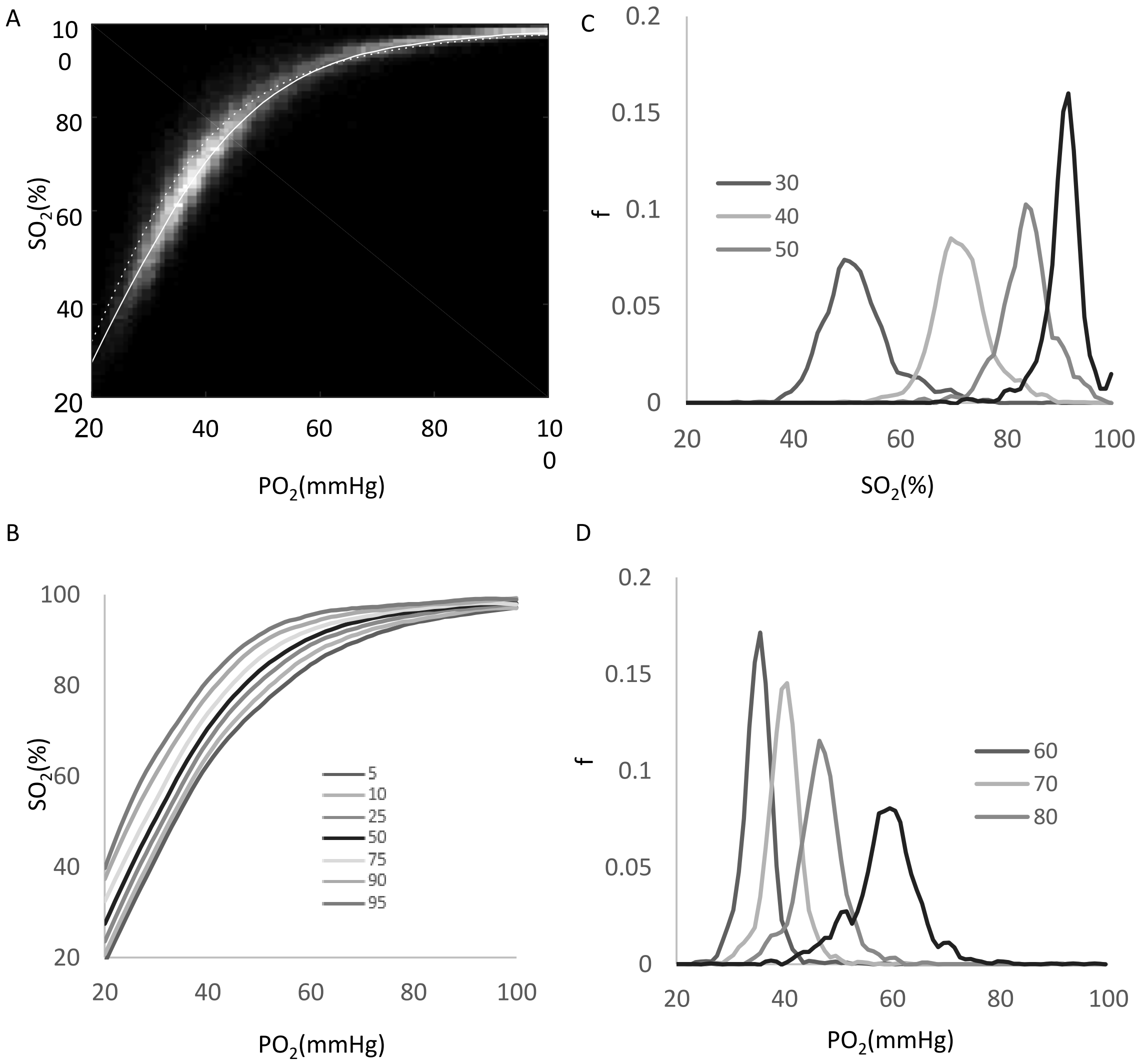
Eytan D, Goodwin AJ, Greer R, Guerguerian AM, Mazwi M, Laussen PC. Distributions and behavior of vital signs in critically ill children by admission diagnosis. Pediatric Critical Care Medicine. 2018 Feb;19(2):115-124.

Eytan D, Goodwin AJ, Greer R, Guerguerian AM, Laussen PC. Heart rate and blood pressure centile curves and distributions by age of hospitalized critically ill children. Frontiers in Pediatrics. 2017 Mar;17(5):52.

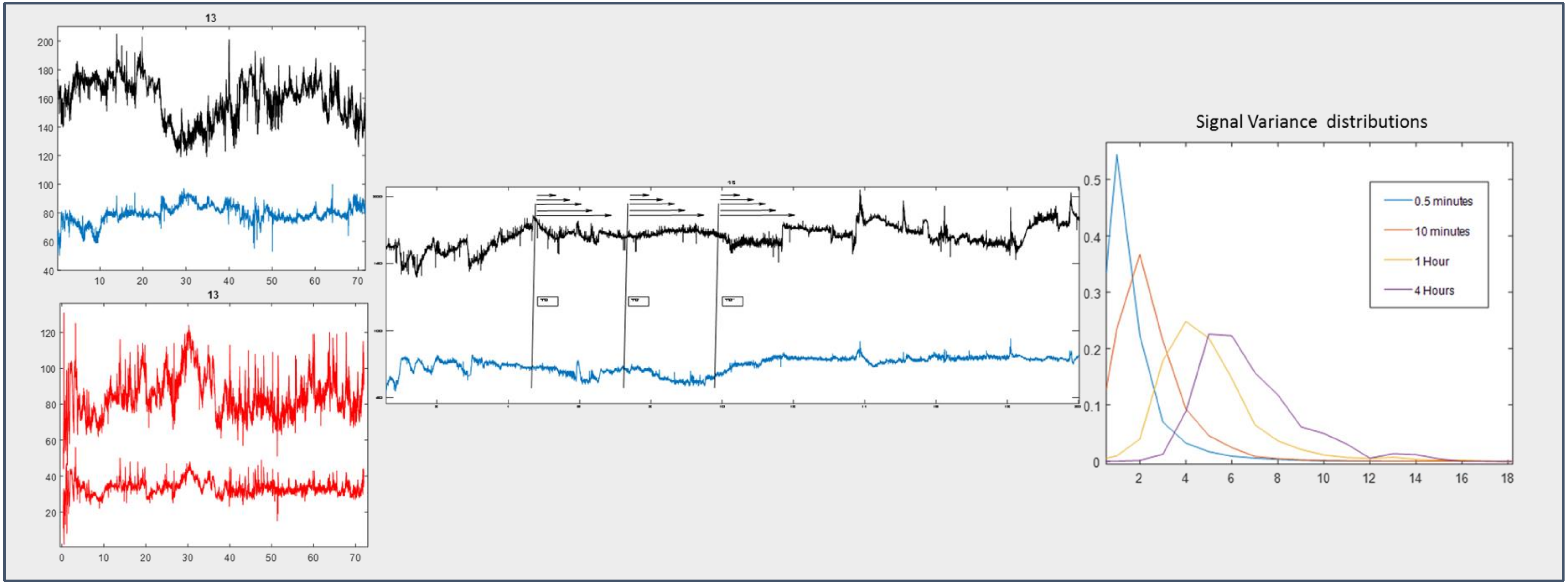
Using Big Data: Understanding the **laboratory Phenotypes……**





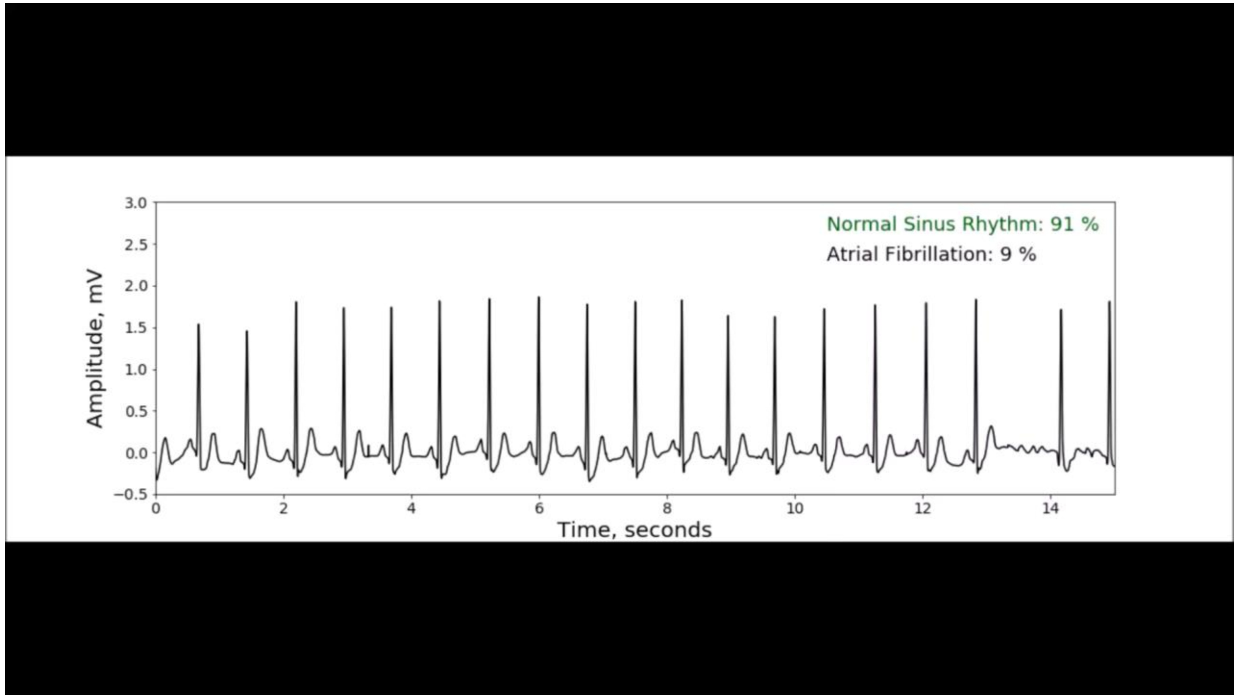


It is about TIME.....

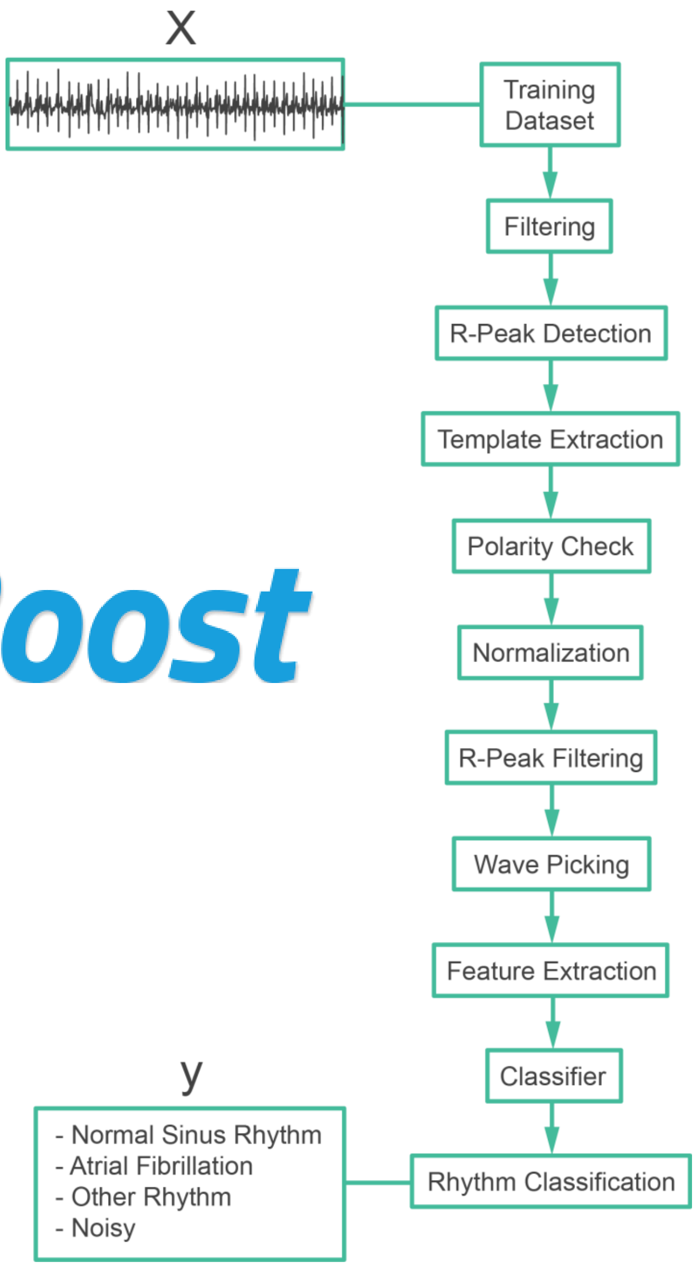


- (SD) is α size of the window

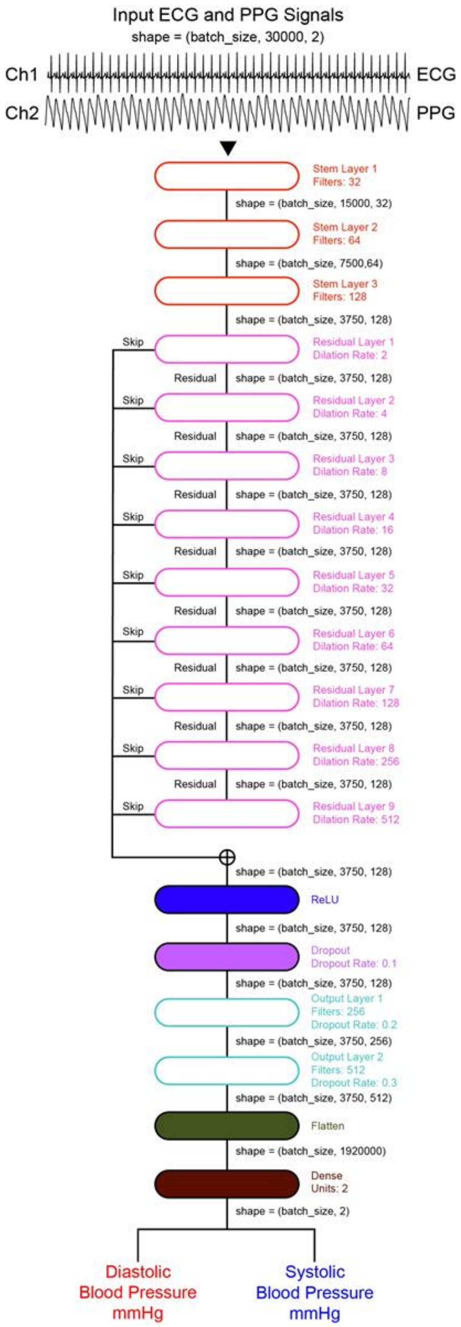
ECG Classification

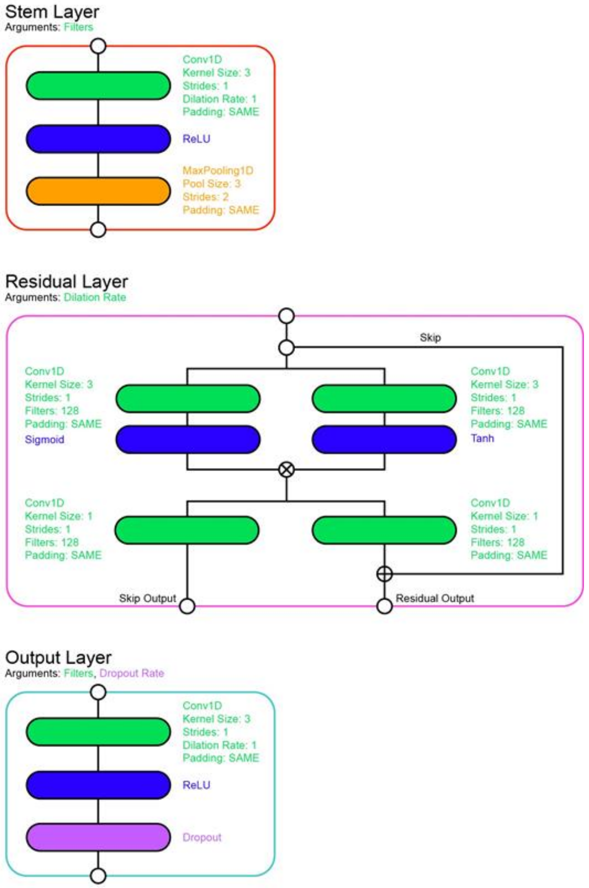


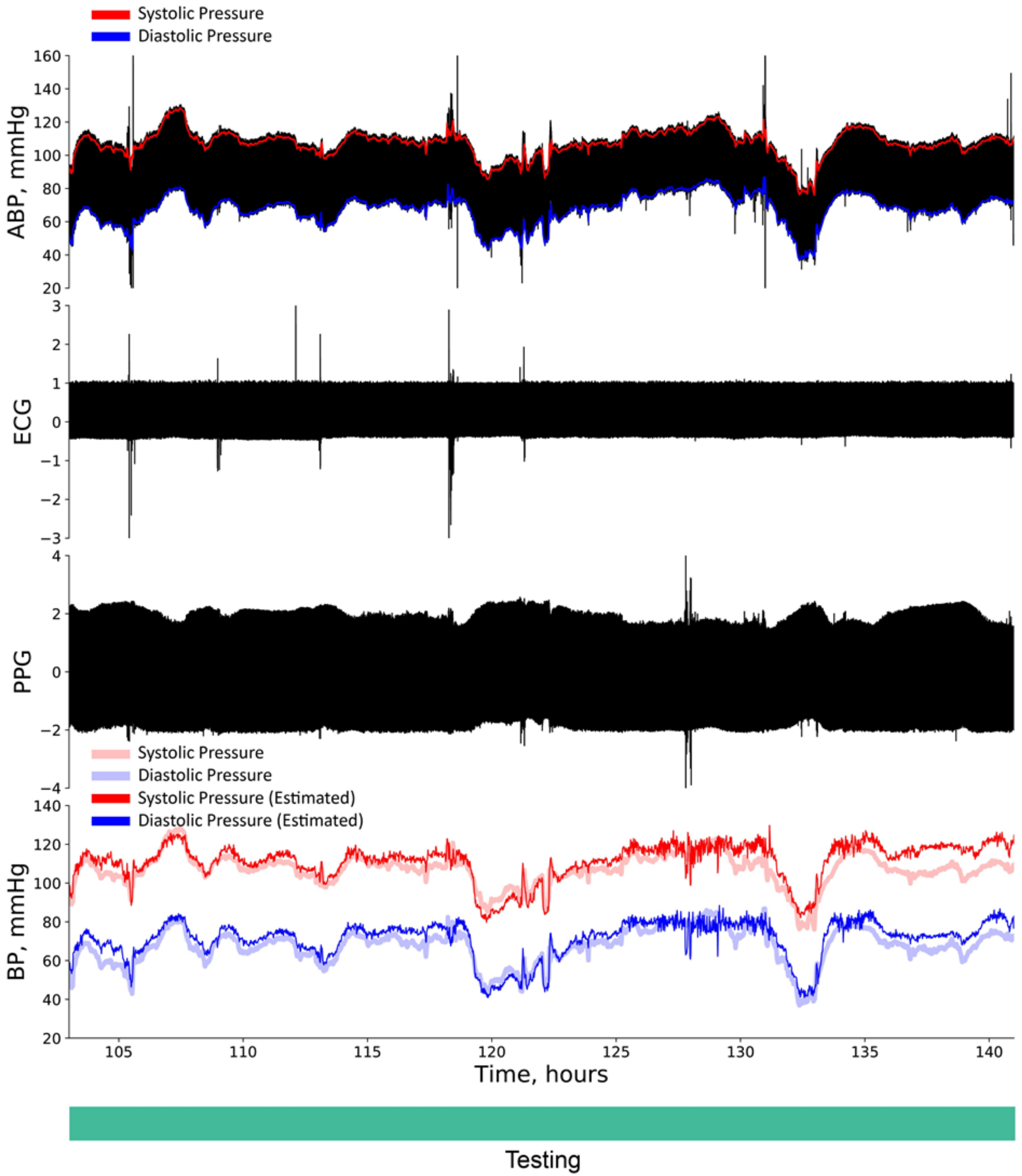
"Atrial Fibrillation Classification Using Step-By-Step Machine Learning".
Goodfellow, Sebastian; Goodwin, Andrew; Greer, Robert; Laussen, Peter; Mazwi, Mjaye; Eytan, Danny. Biomedical Physics & Engineering Express 2018



Sebastian Goodfellow







Sebastian Goodfellow

ML: Prediction of cardiac arrest in the CCU

Prediction of Cardiac Arrest from Physiological Signals in the Pediatric ICU

Sana Tonekaboni[1,2] STONEKABONI@CS.TORONTO.EDU
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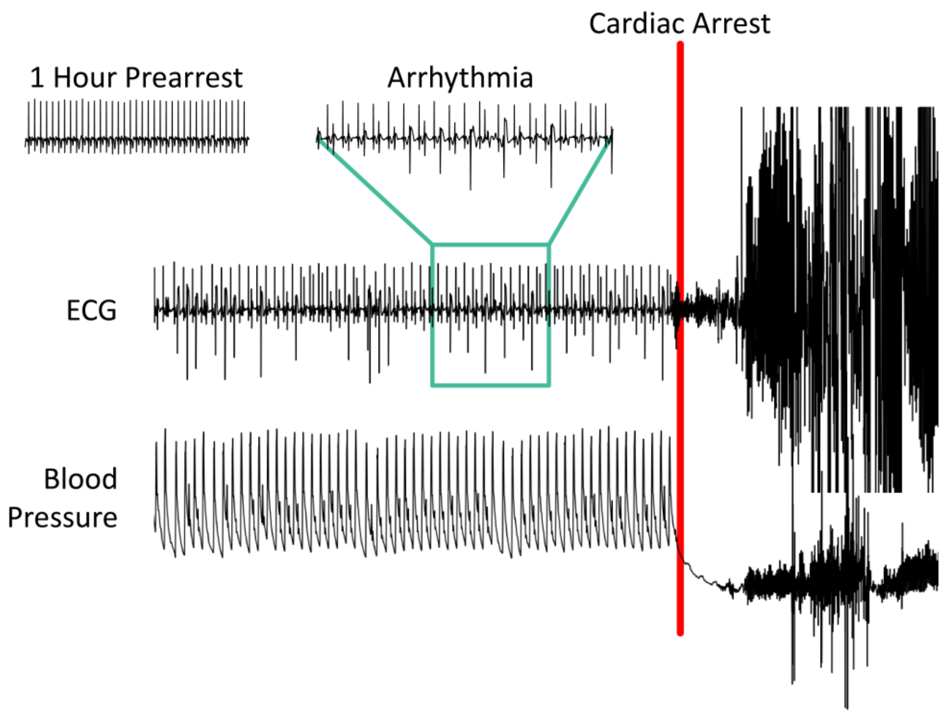
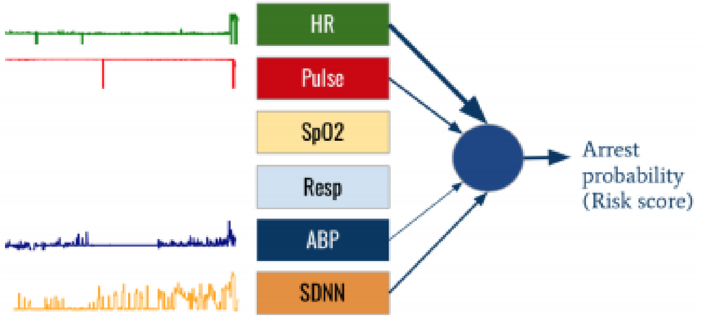
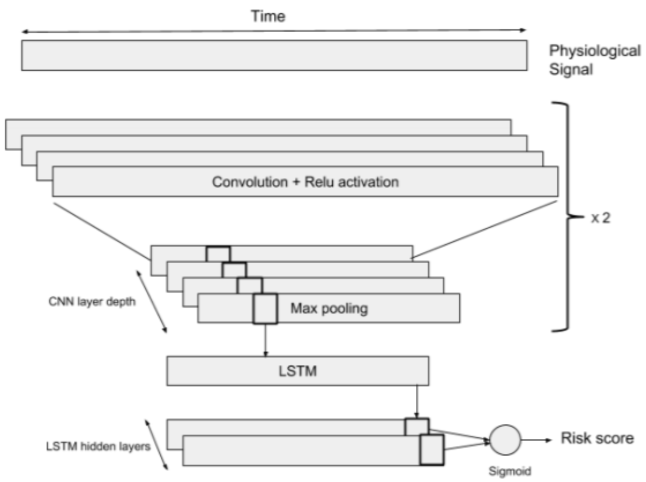
Anna Goldenberg[1,2] ANNA.GOLDENBERG@VECTORINSTITUTE.AI





6: Risk score prediction using the ensemble model with existing physiological



0.83 average F1

Sana Tonekaboni

ML: Prediction of cardiac arrest in the CCU

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0.83
average F1

ronto's SickKids announces first-of-its-kind artificial intelligence position

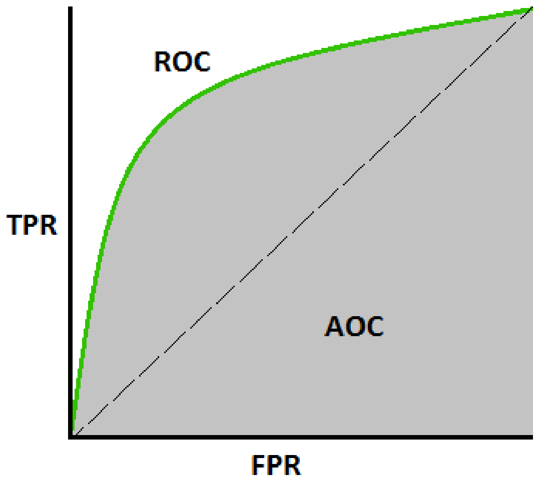
heart defect.

CHRIS DONOVAN/THE GLOBE AND MAIL

SickKids is now preparing to test the early-warning system at the bedside, Dr. Laussen said during an interview inside the pediatric ICU, where between 40 and 50 different physiological signals an hour were streaming from an infant boy named Mason. Less than a week earlier, Mason had undergone two open-heart surgeries to correct a congenital heart defect.

If the model works as planned, doctors would be able to use the five minutes of lead time to change medications or make other interventions to prevent a cardiac arrest. In cases in which prevention is not possible, at least the medical team would have time to prepare.

"Instead of it being a sudden event and we're rushing to the scene, we [will have] people there, ready, organized and responding," Dr. Laussen said. "That response is critical."



< Previous Abstract | Next Abstract >

Clinician Perception of a Machine Learning–Based Early Warning System Designed to Predict Severe Sepsis and Septic Shock

Ginestra, Jennifer C. MD[1]; Giannini, Heather M. MD[1]; Schweickert, William D. MD[2,3]; Meadows, Laurie RN, CCRN[4]; Lynch, Michael J. RN, CEN[4]; Pavan, Kimberly MSN, CRNP[5]; Chivers, Corey J. PhD[3]; Draugelis, Michael , BS[3]; Donnelly, Patrick J. RN, MS[6]; Fuchs, Barry D. MD, MS[2,3]; Umscheid, Craig A. MD, MS[3,7,8]

Critical Care Medicine: May 24, 2019 - Volume Online First - Issue - p
doi: 10.1097/CCM.0000000000003803
Feature Article: PDF Only

SDC PAP

Abstract | Author Information | Article Metrics

Objective: To assess clinician perceptions of a machine learning–based early warning system to predict severe sepsis and septic shock (Early Warning System 2.0).

Design: Prospective observational study.

Setting: Tertiary teaching hospital in Philadelphia, PA.

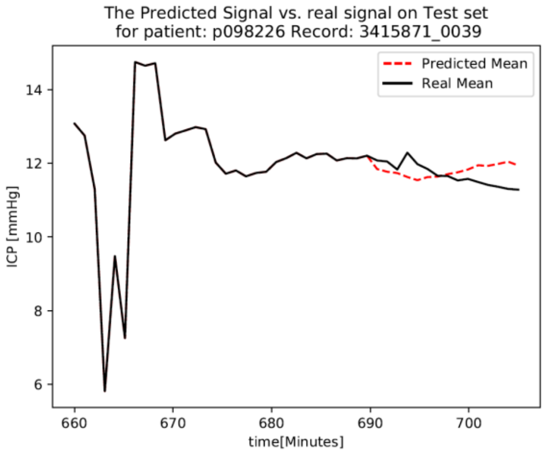
Patients: Non-ICU admissions November–December 2016.

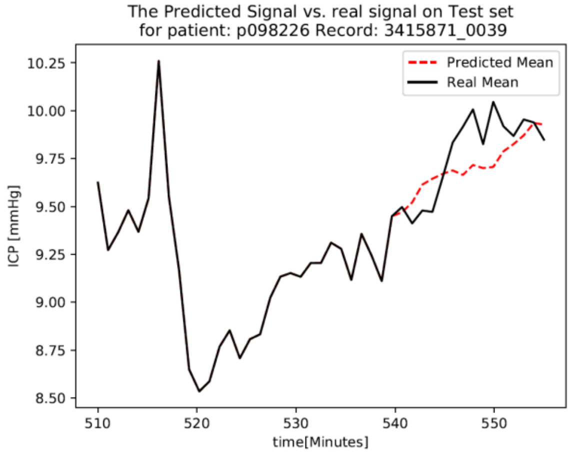
Interventions: During a 6-week study period conducted 5 months after Early Warning System 2.0 alert implementation, nurses and providers were surveyed twice about their perceptions of the alert's helpfulness and impact on care, first within 6 hours of the alert, and again 48 hours after the alert.

Measurements and Main Results: For the 362 alerts triggered, 180 nurses (50% response rate) and 107 providers (30% response rate) completed the first survey. Of these, 43 nurses (24% response rate) and 44 providers (41% response rate) completed the second survey. Few (24% nurses, 13% providers) identified new clinical findings after responding to the alert. Perceptions of the presence of sepsis at the time of alert were discrepant between nurses (13%) and providers (40%). The majority of clinicians reported no change in perception of the patient's risk for sepsis (55% nurses, 62% providers). A third of nurses (30%) but few providers (9%) reported the alert changed management. Almost half of nurses (42%) but less than a fifth of providers (16%) found the alert helpful at 6 hours.

Conclusions: In general, clinical perceptions of Early Warning System 2.0 were poor. Nurses and providers differed in their perceptions of sepsis and alert benefits. These findings highlight the challenges of achieving acceptance of predictive and machine learning–based sepsis alerts.

Short-term prediction of Intracranial pressure (ICP) signals in the ICU





Results Summary Page:

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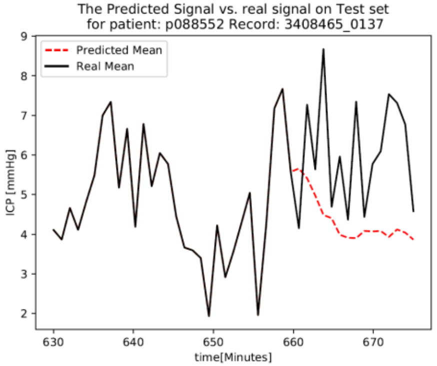
std mae: 1.42
mean mae of mean label: 1.68
std mae of mean label: 1.42
mean rmse: 2.45
std rmse: 1.93



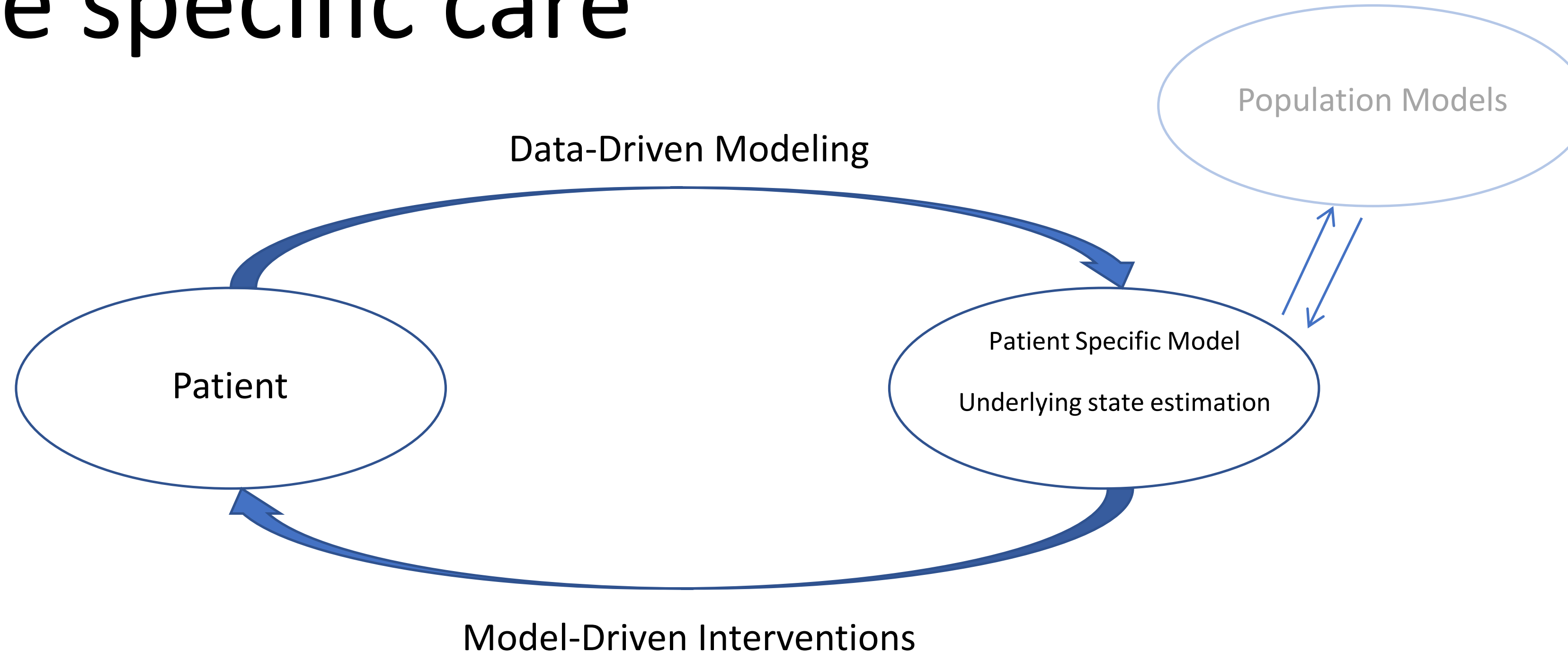
Evgeny Kamenetsky

Gil Caspi

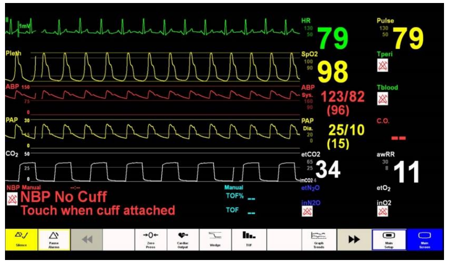
ANDREW AND ERNA VITERBI FACULTY OF ELECTRICAL ENGINEERING

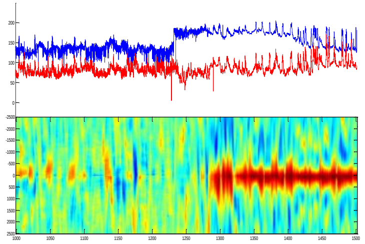
Technion Israel Institute of Technology

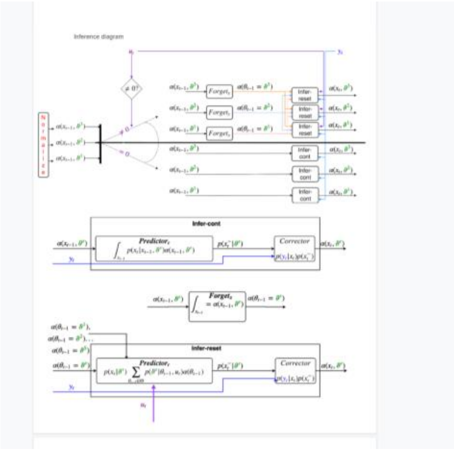
Patient-state specific care

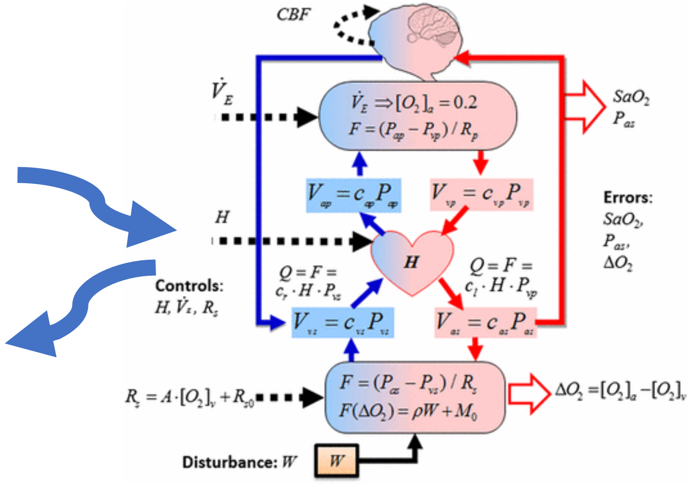


Combining mechanistic models and data driven estimation



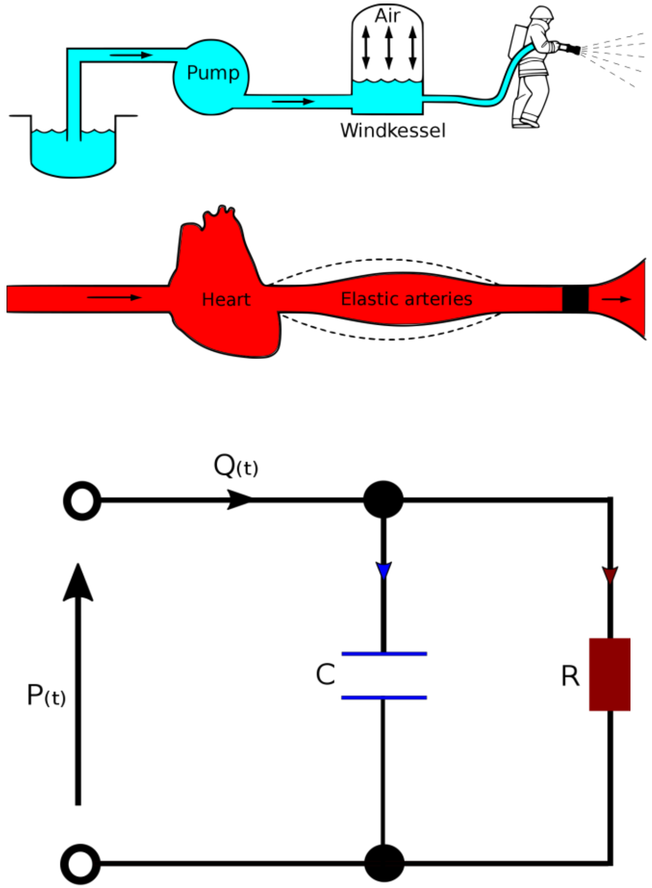


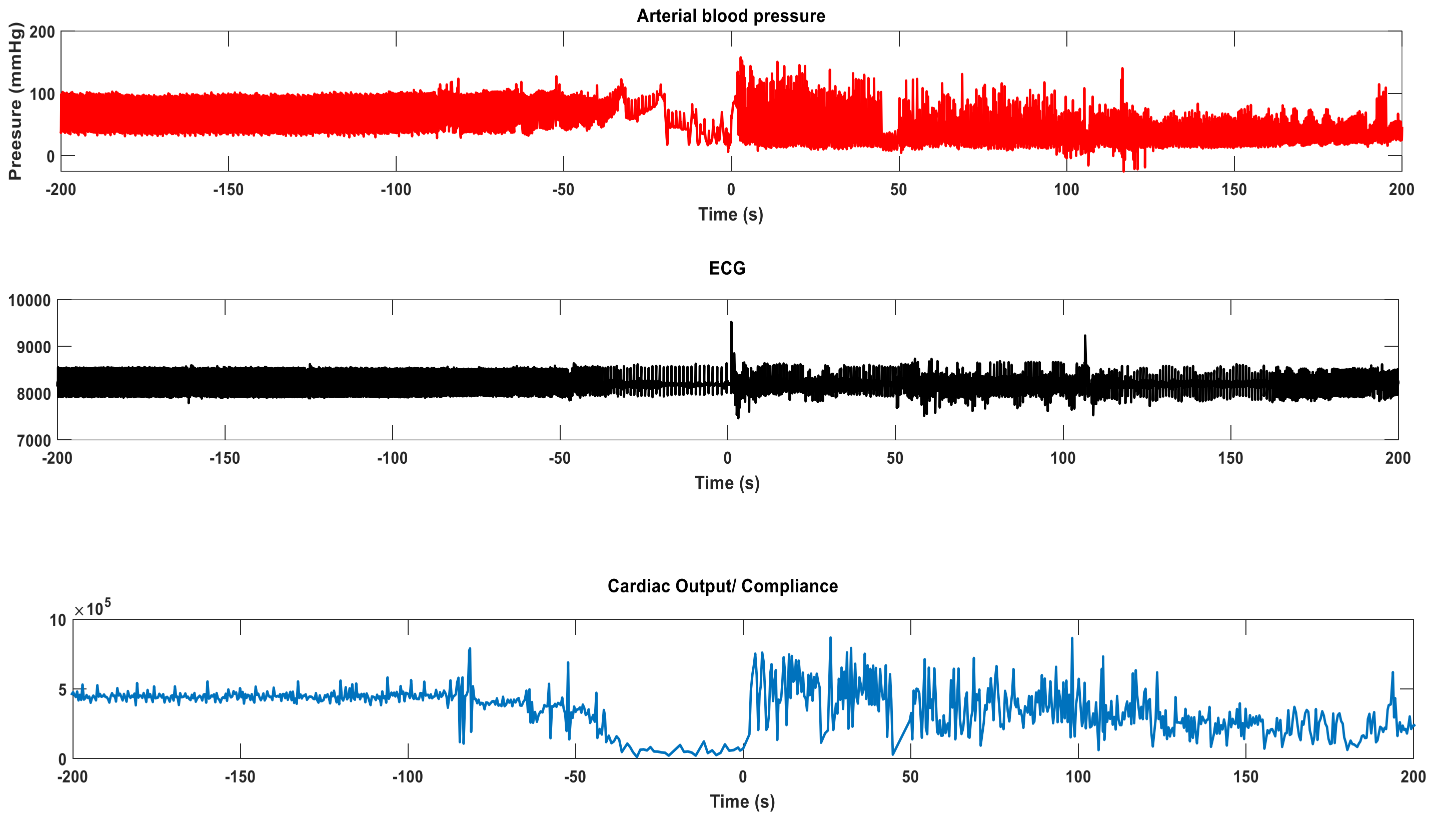




- Ron Teichner
- Neta Ravid

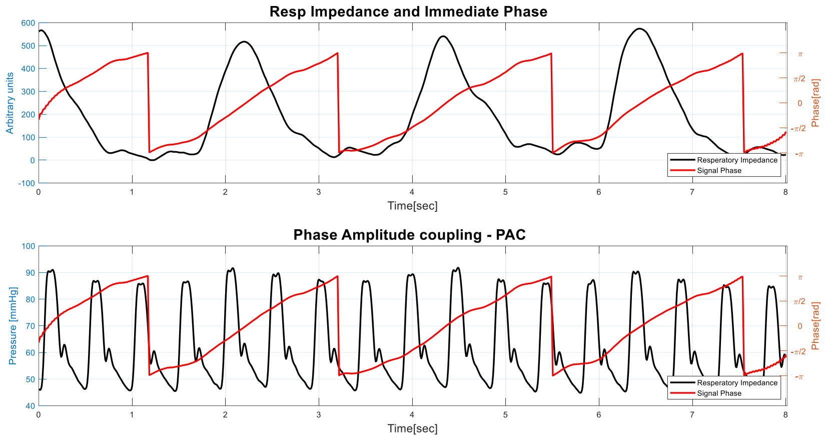
Combining mechanistic models and data driven estimation

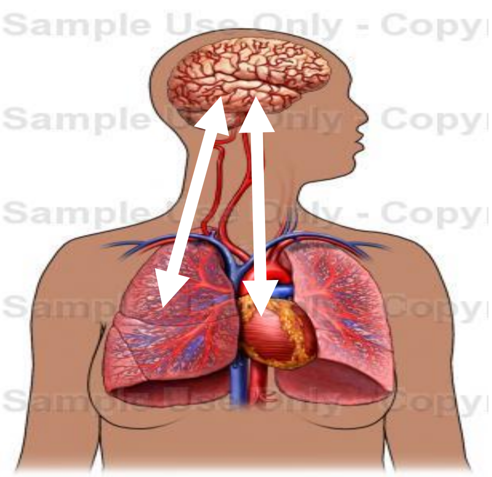


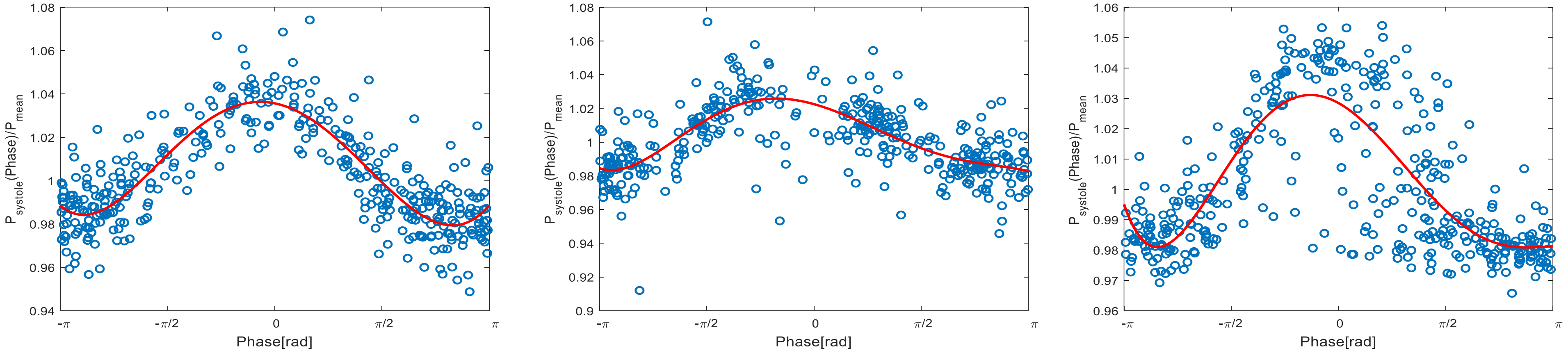


- Ely Erez

Cardio-pulmonary interactions







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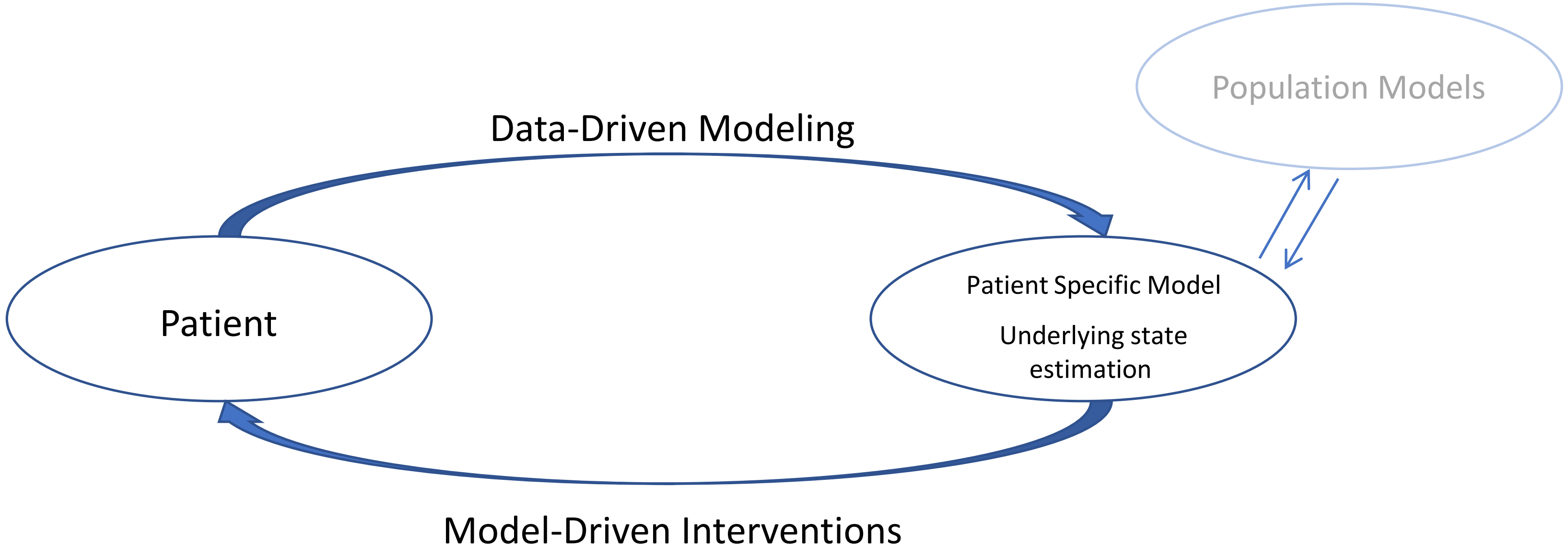
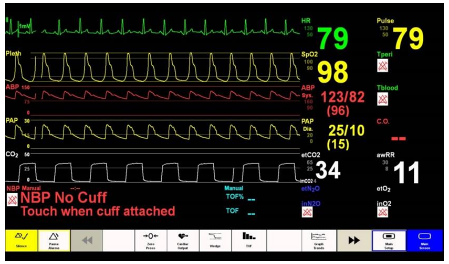
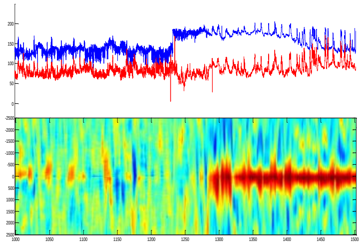
- Yonathan Prat
- Yuval Barzilai

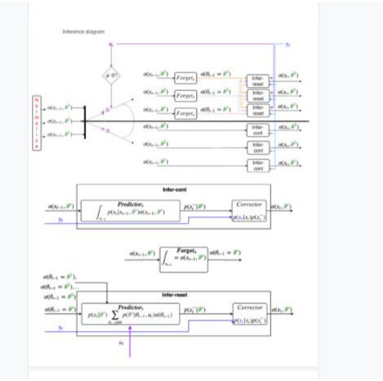
Technion
Israel Institute of Technology

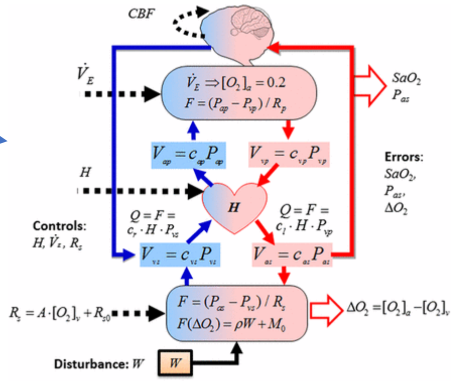
Combining mechanistic models and data driven estimation



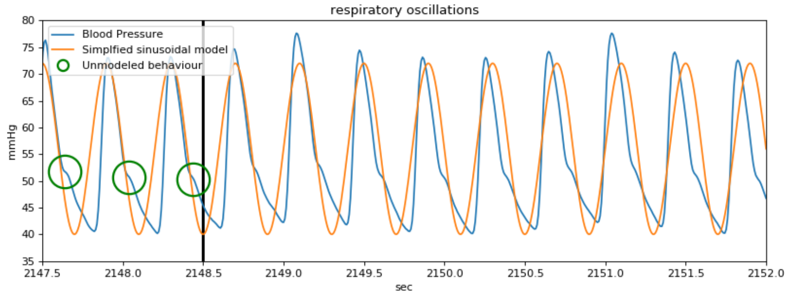


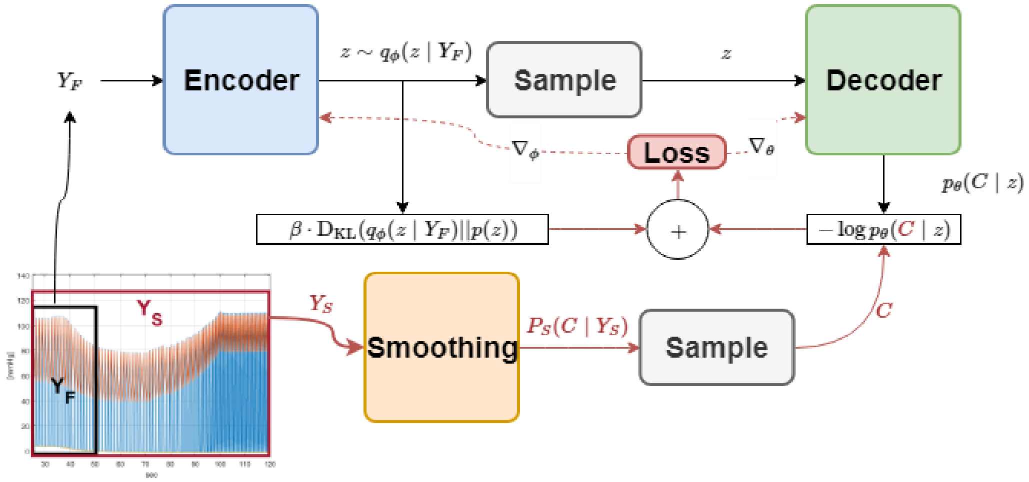






Improved online estimation of mechanistic models of the cardiovascular system using off-line data recorded from a patient population





AI needs teams……..

Sickkids

Peter Laussen
Mjaye Mazwi
Andrew Goodwin
Anusha Jegatheeswaren
Azzadeh Assadi
Robert Greer

Anna Goldenberg
Sebastian Goodfellow
Sana Tonekaboni

Technion

Uri Shalit
Ron Meir
Ronen Talmon
Ron Teichner
Neta Ravid
Ely Erez
Yonathan Prat
Yuval Barzilai
Gil Caspi
Evgeny Kamenetsky

Rambam

Josef Benari
Amir Hadash
Ori Attias
Amir Bar