The Challenges and Opportunities for Healthcare Recommendation Systems in a Rapidly Evolving Health Data Ecosystem.

Mohammad M. Ghassemi, Ph.D.

ghamut

About Me

Education:

- PhD, Computer Science, MIT

Occupation:

- Founder, Ghamut Corp.
- Prof. Michigan State Uni.

http://ghassemi.xyz

More Importantly

Introduction

1967: 1MB = $1 Million

2017: 1MB = $0.02

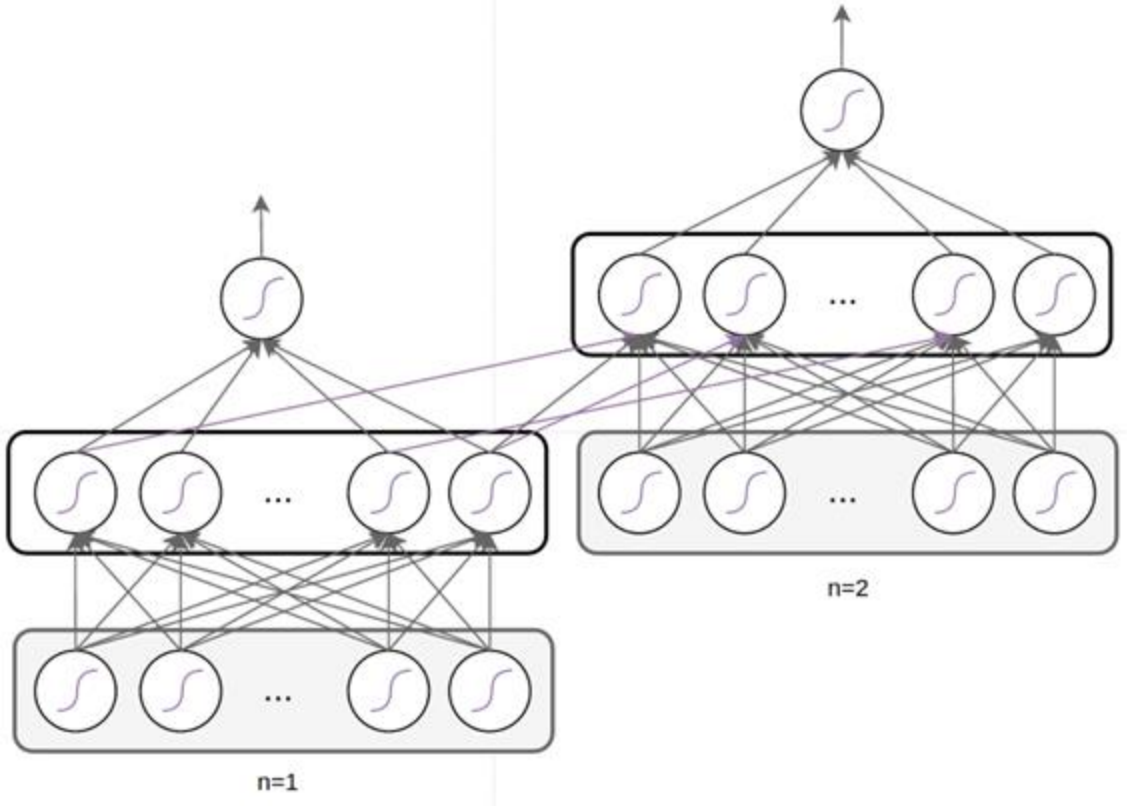
As costs diminished, storing data became more cost-effective than managing or curating it and modern-day "Big Data" was born

https://www.computerworld.com/article/3182207/data-storage/cw50-data-storage-goes-from-1m-to-2-cents-per-gigabyte.html

Introduction

More data and computation power led to resurgence of neural network approaches ("Deep Learning")

Deep methods proved capable of automatically learning data representations that out-performed feature-engineering approaches in key areas: vision, speech, translation



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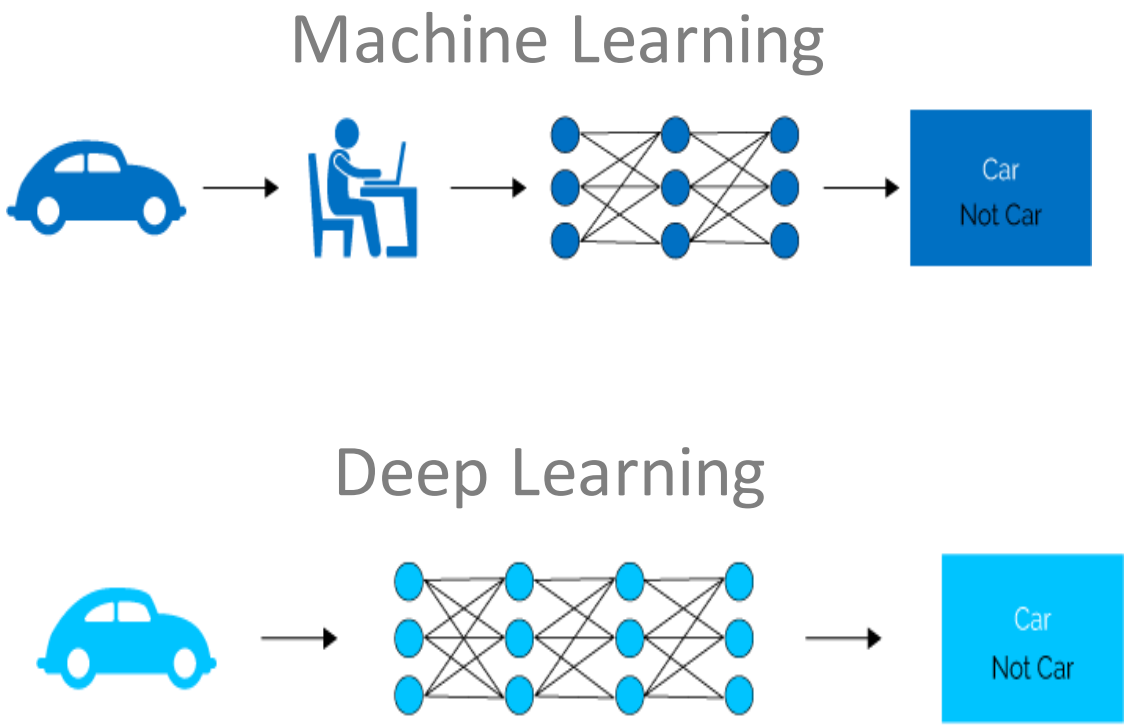
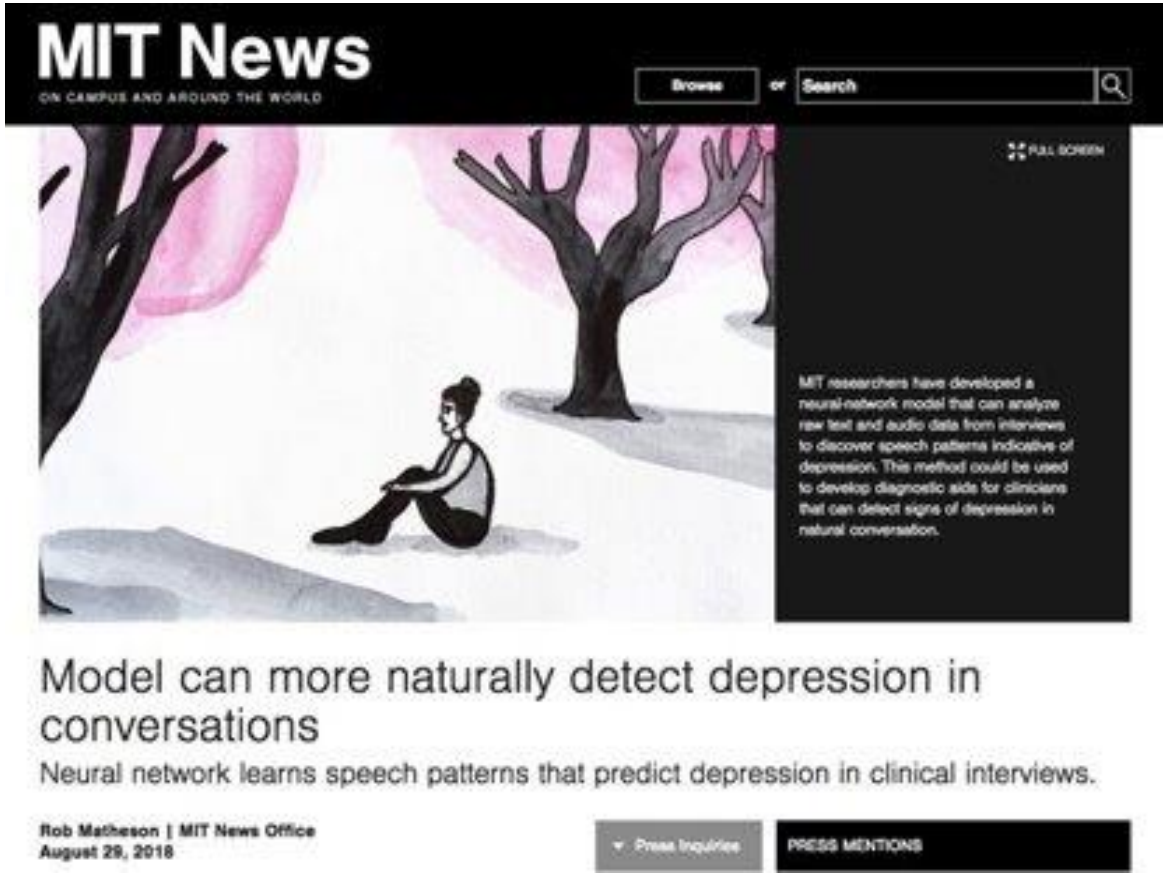


https://www.xenonstack.com/blog/log-analytics-with-deep-learning-and-machine-learning

Introduction

There is increasing interest in *Big Data*, *Machine Learning* and *Artificial Intelligence* in the health and behavior contexts



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Health data is being collected at a unprecedented scale and resolution.

If you use MIMIC data or code in your work, please cite the following publication:

MIMIC-III, a freely accessible critical care database. Johnson AEW, Pollard TJ, Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, and Mark RG. Scientific Data (2016). DOI: 10.1038/sdata.2016.35. Available from: http://www.nature.com/articles/sdata201635

Technical Challenges

For health/behavioral applications methods must be: Interpretable, generalizable and support (not control) decisions

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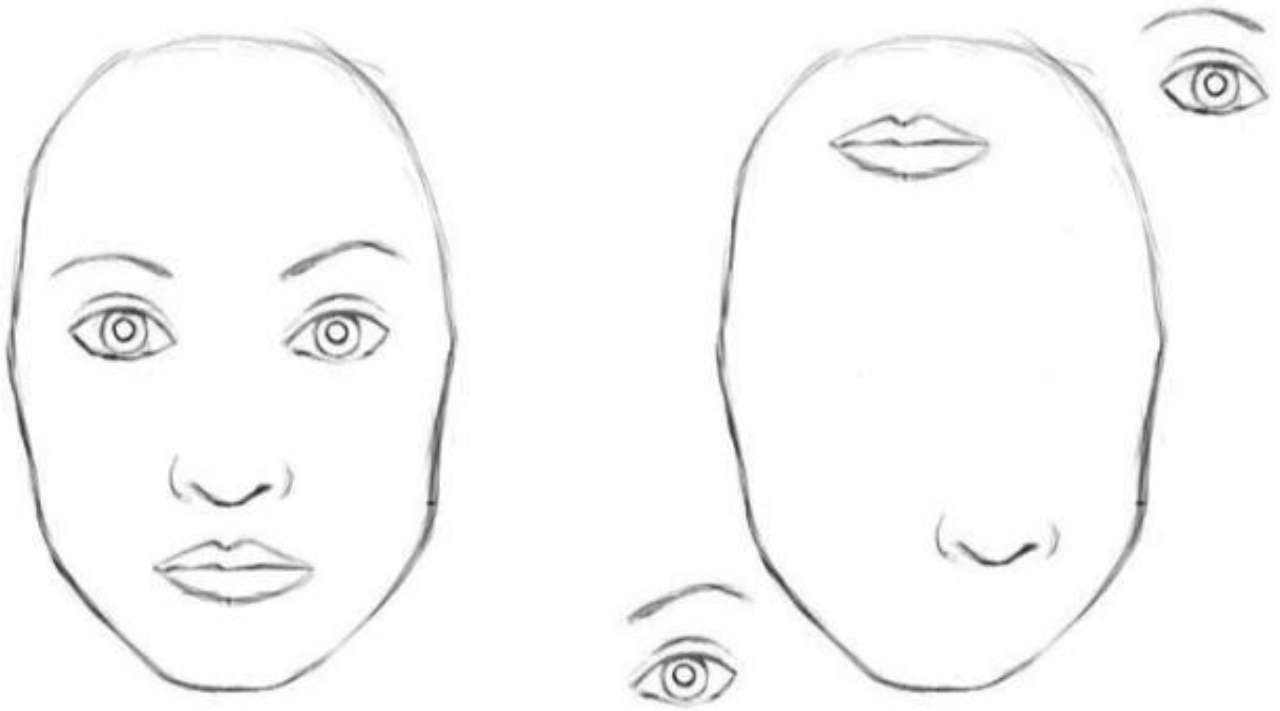

Practical Opportunities

Current health data enable *reactionary* optimization of care

Using data outside the hospital (social + wearable), we may clarify causal factors of disease, and allow for *proactive* approaches

Today's Talk

1. Data collection:
Tool to translate paper data from hospital spreadsheets into digital form

2. Decision support:
Method to prognosticate coma outcomes after cardiac arrest

3. Optimal Control:
AI for passive monitoring of narrative mood during conversations

4. Moving Forward
Future directions, and opportunities for collaboration

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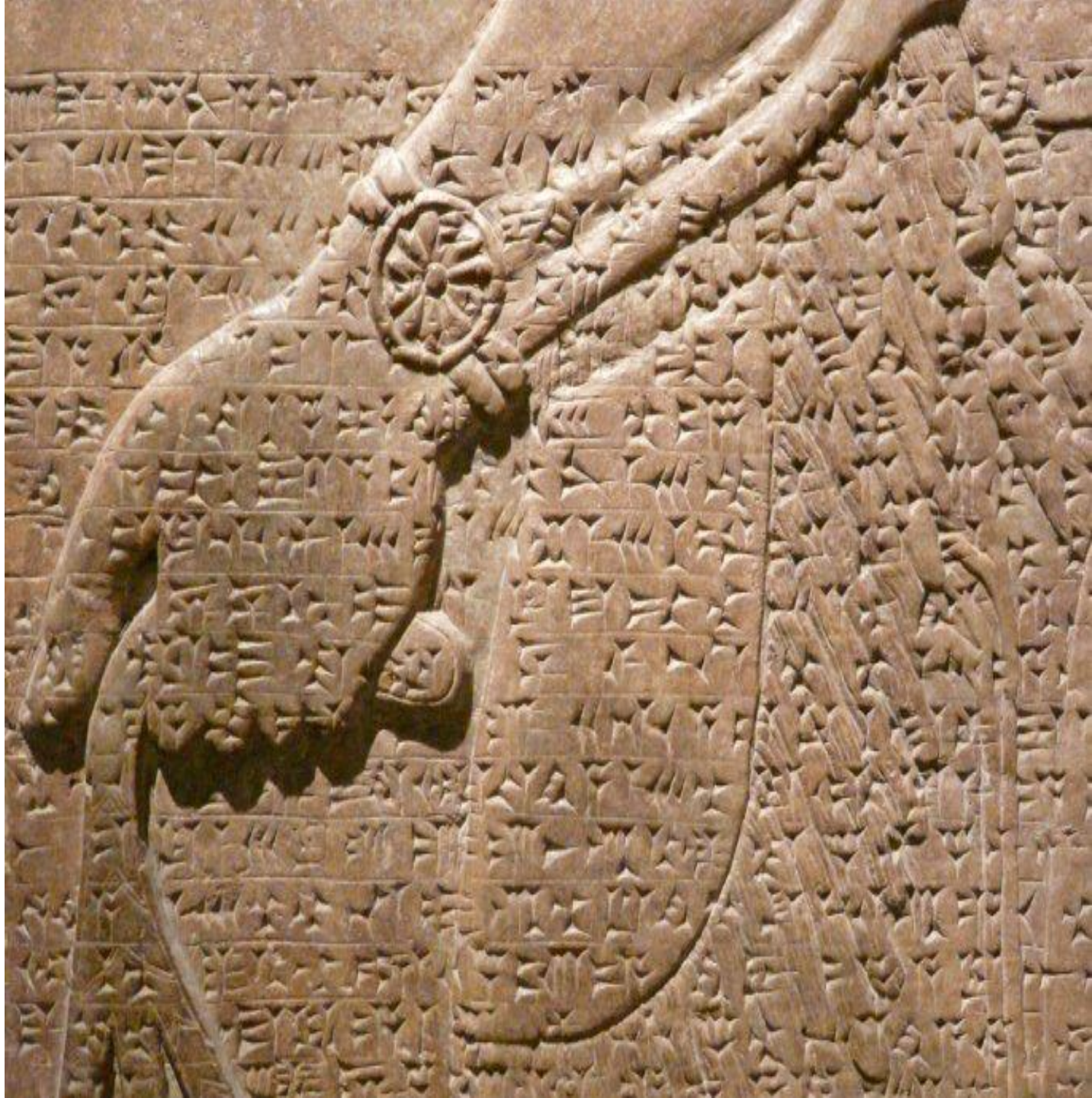
An Open-Source Tool for the Automated Transcription of Paper Spreadsheet Data

As presented in IEEE Big Data 2017

Data collection:
A 5,000 year tradition

3000 B.C.: Sumerians kept clay records on property, transactions, and marriages



Data collection:
A 5,000 year tradition

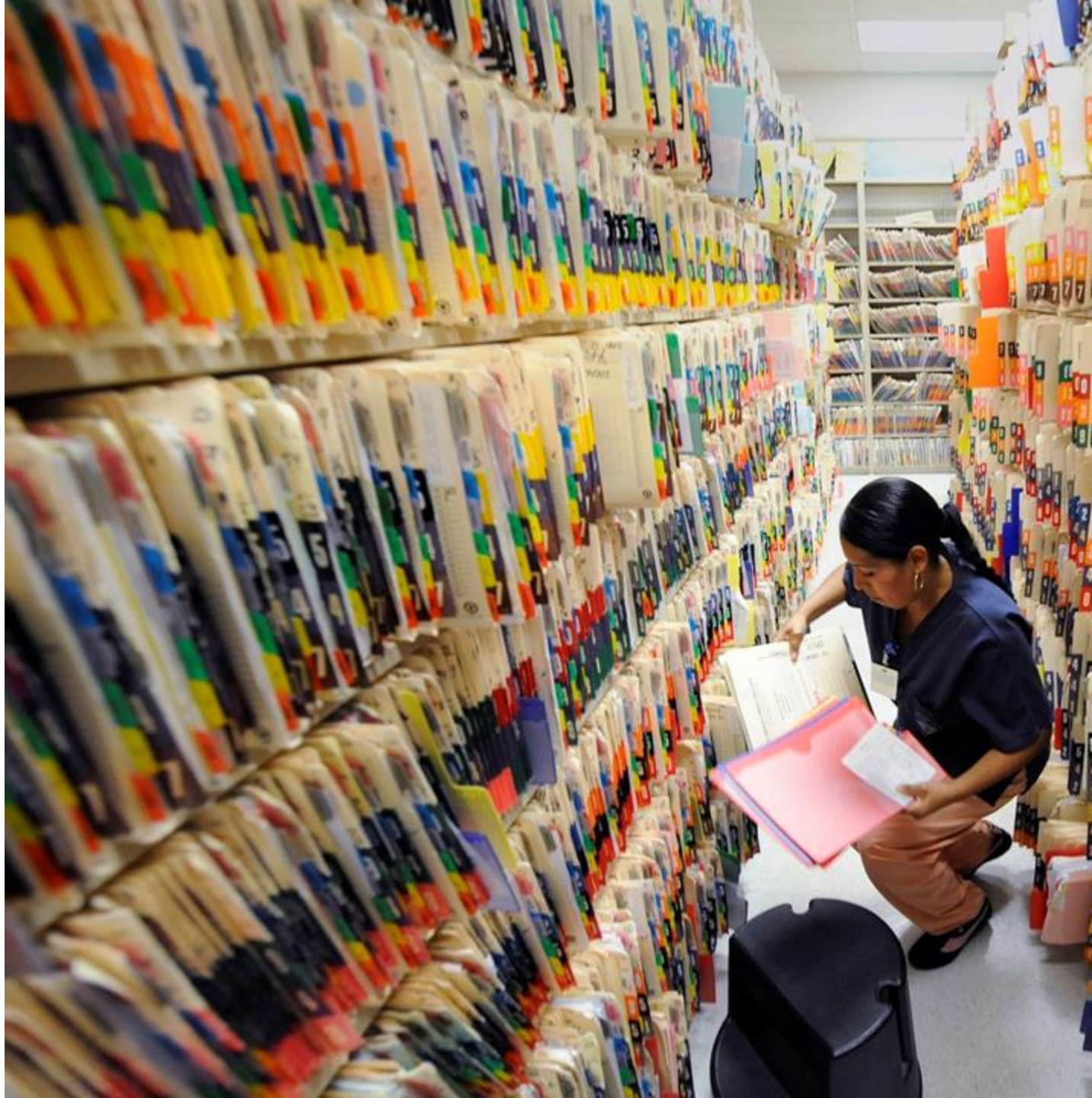
1600 B.C.: Egyptians kept medical records on prominent patients

Data collection:
A 5,000 year tradition

2017 AD: Hospitals keep records on just about everything

Data collection:
A 5,000 year tradition

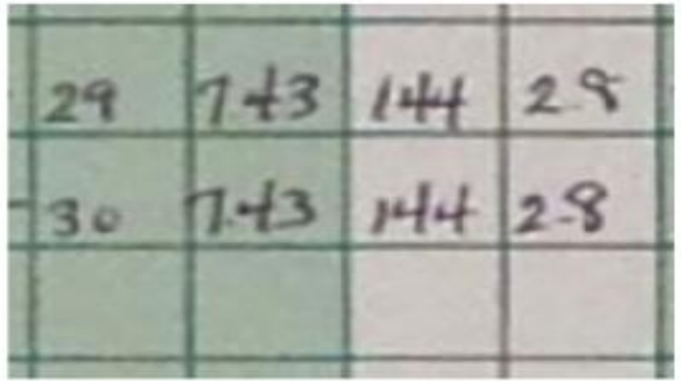
2017 AD: So much interesting information is still locked within paper records

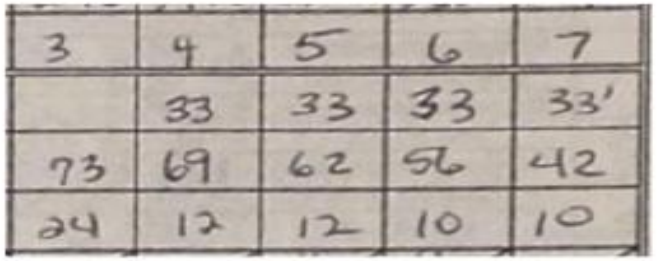


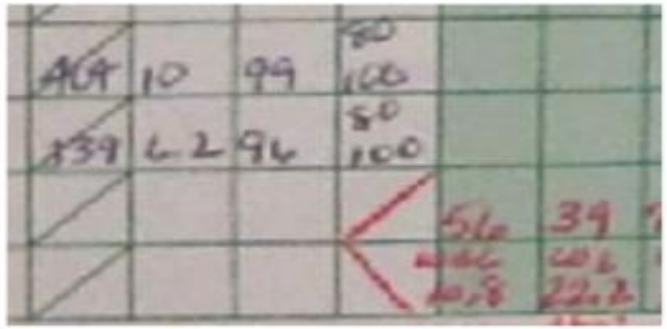
Importance:

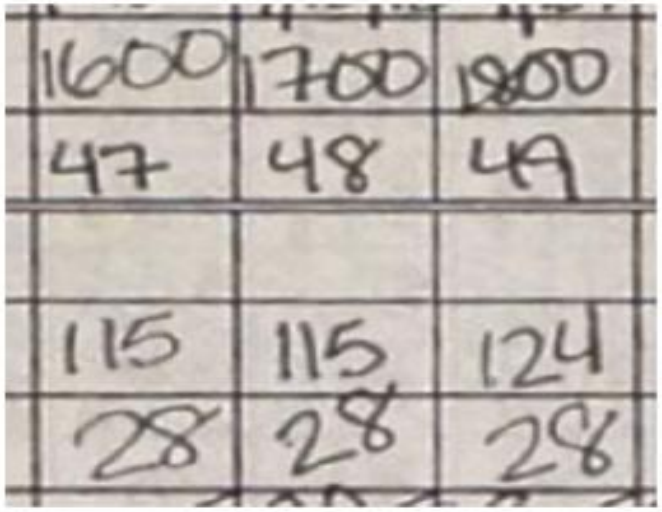
90% of US hospitals still maintain paper archives

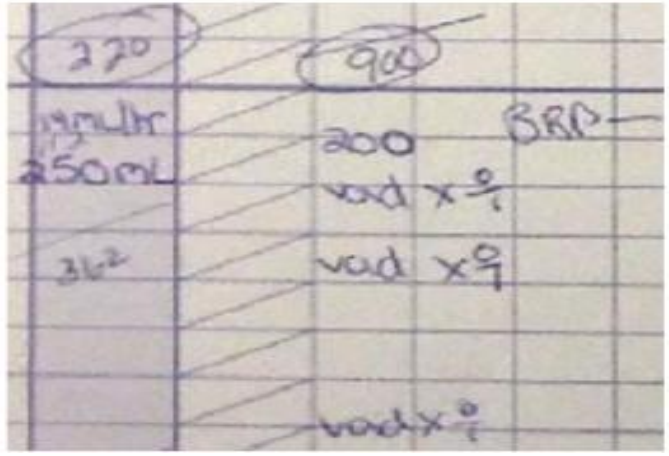
Data transcription costs time and money, and transcribing sensitive patient data costs **even more**





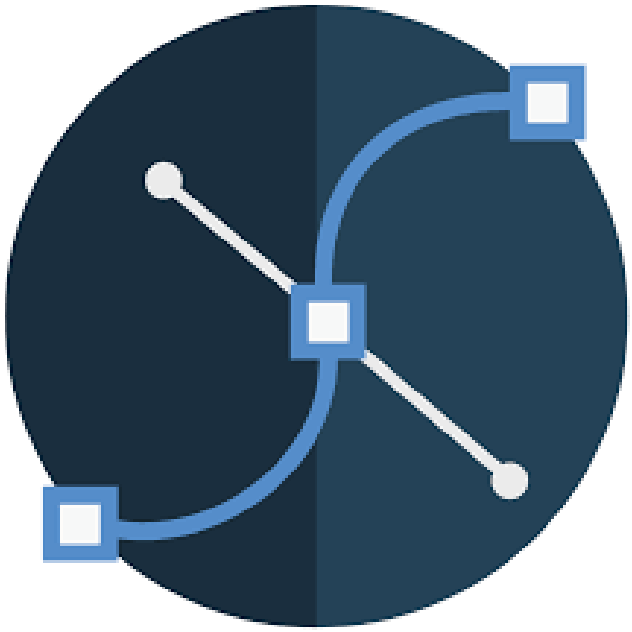






A.I. is an ideal solution:

1. Cheap
2. Scalable
3. Maintains privacy



Challenges:

1. data is heterogeneous *within* spreadsheets: different ink, cell colors, handwriting

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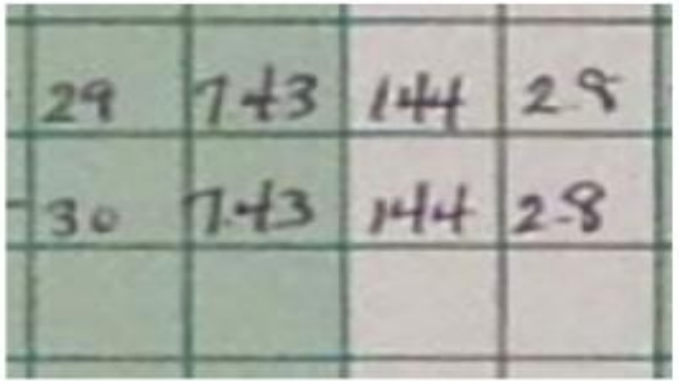
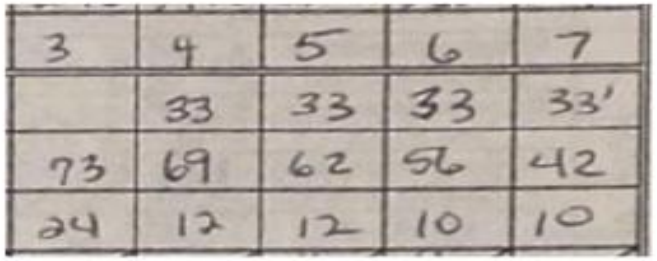
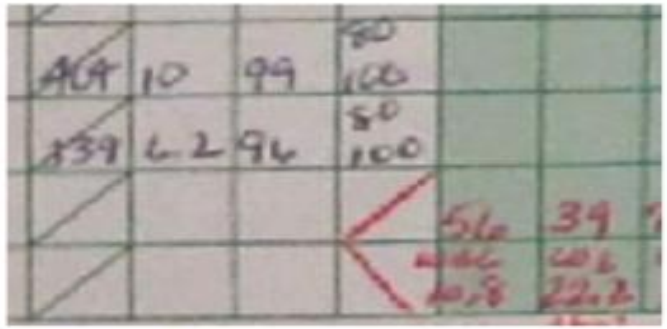
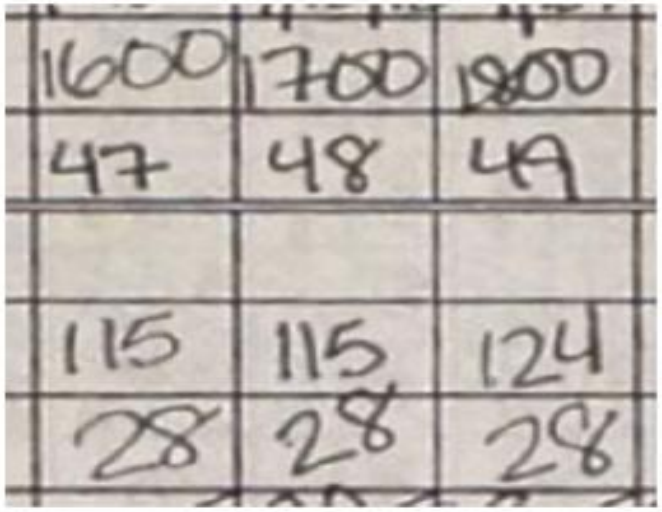
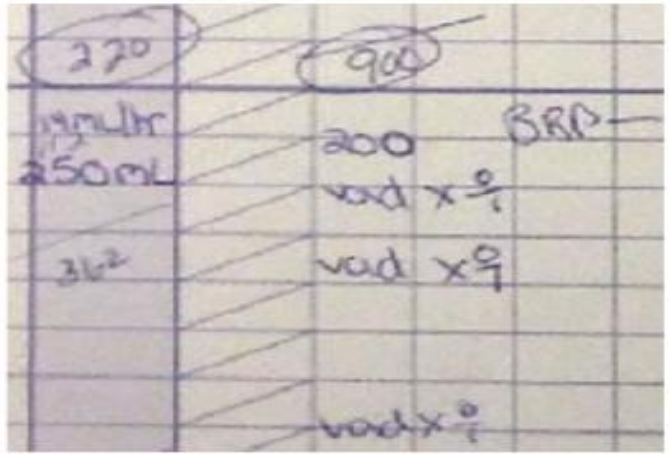
3. data often breaks ‘rules’: circling, cross through, underlining, spilling outside borders, etc.











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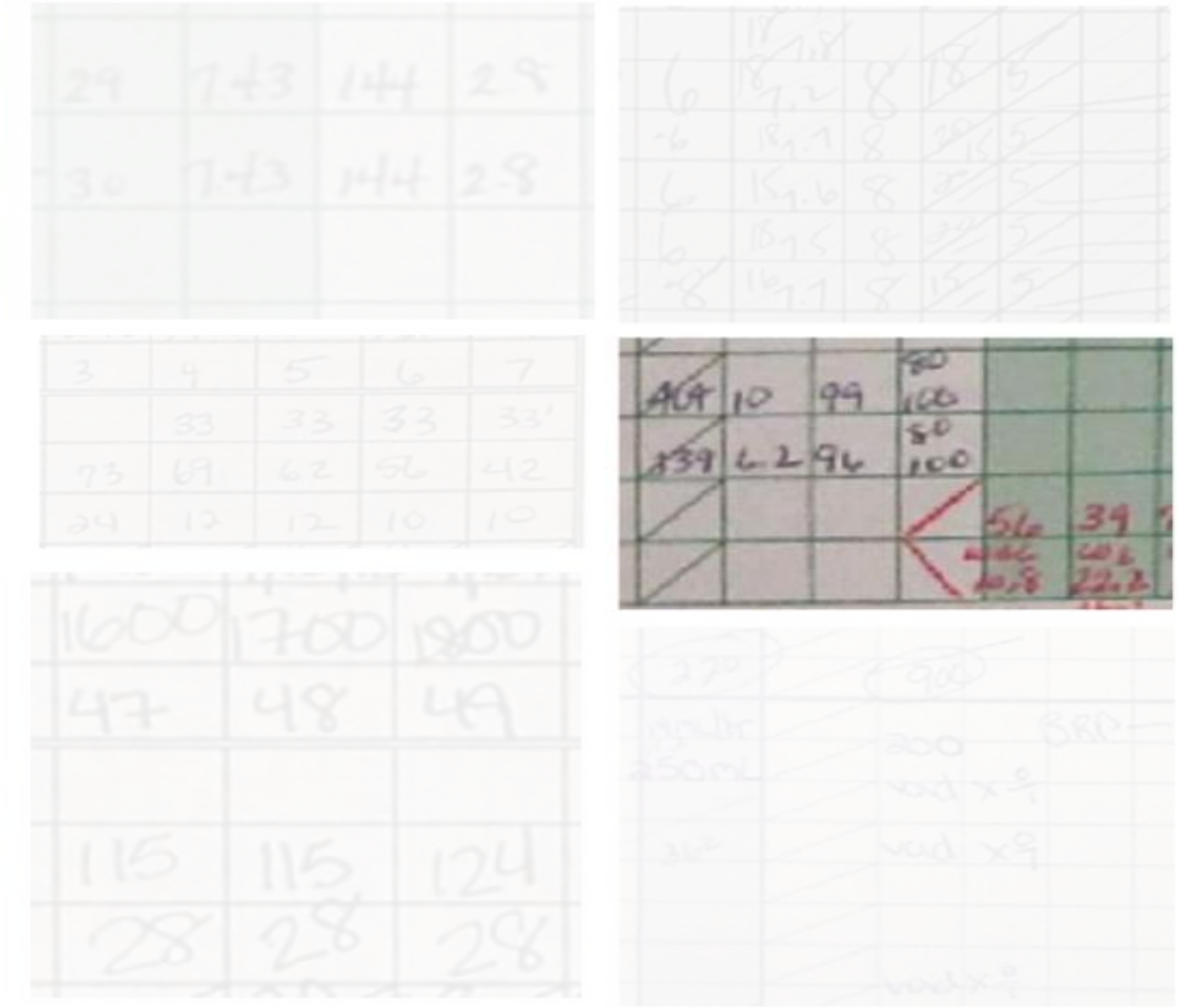

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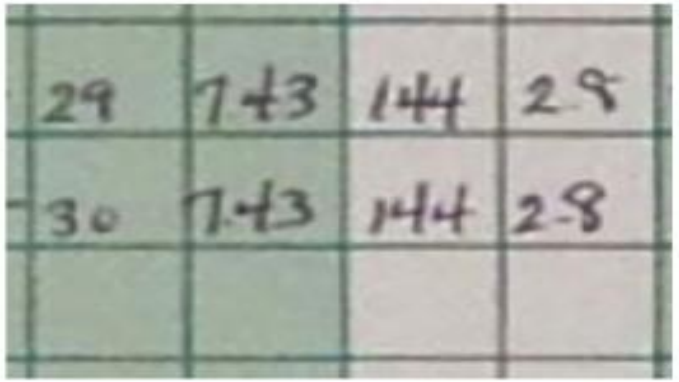

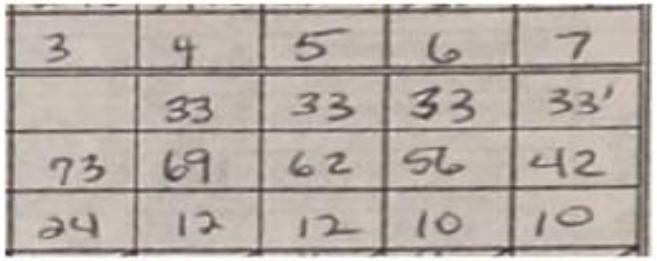

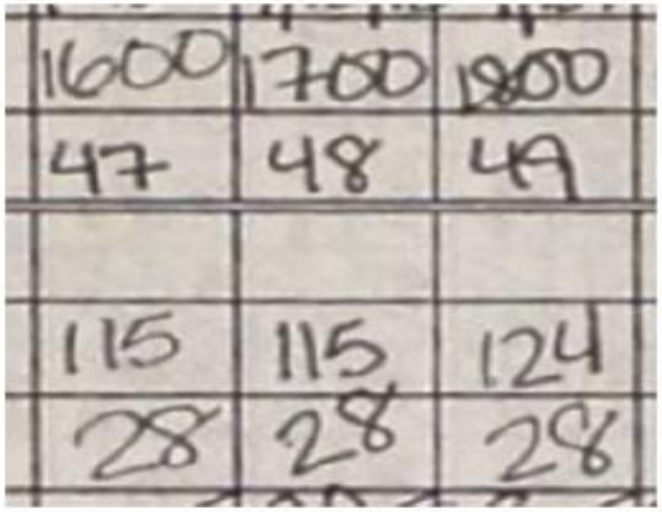

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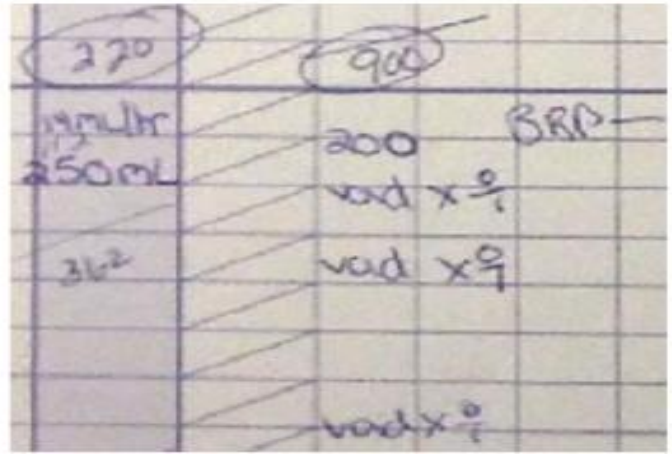
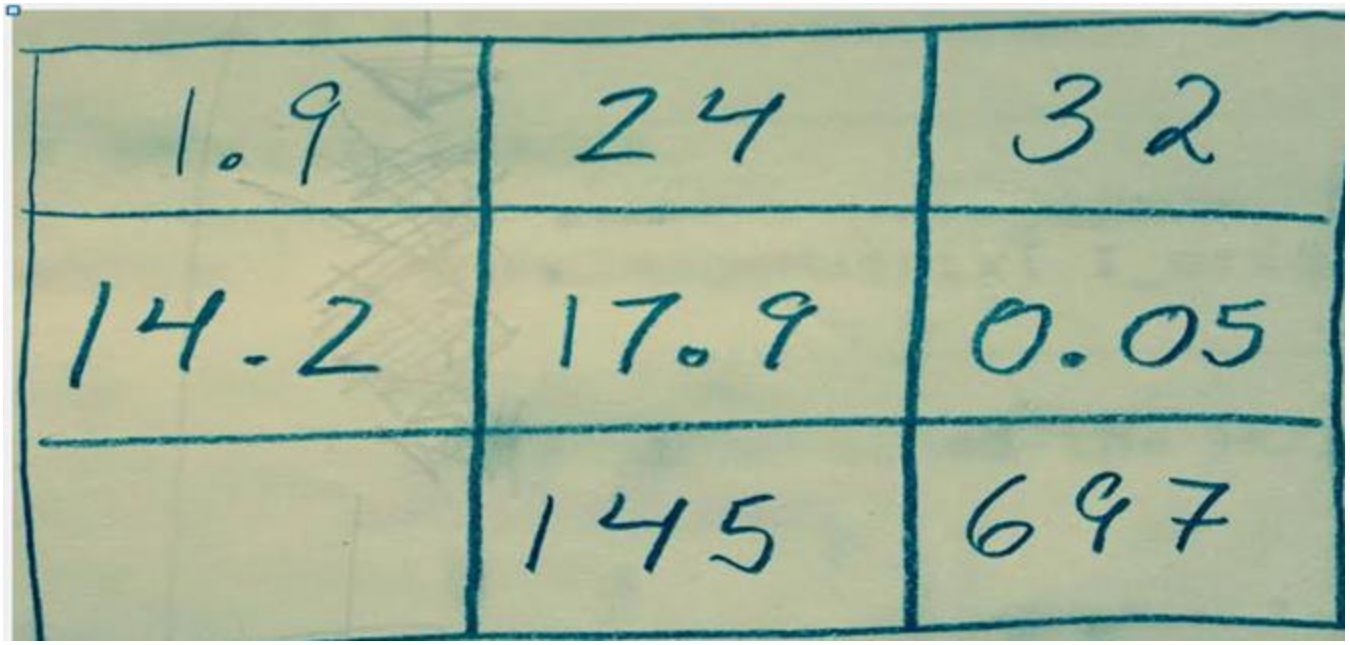


Objectives:

1. Build an open source tool to extract data using crowd-sourcing and machine-learning

2. Test our tool on a heterogeneous set of 139 medical flowsheets, containing ~36K cells of data

3. Work with collaborators to improve the tool



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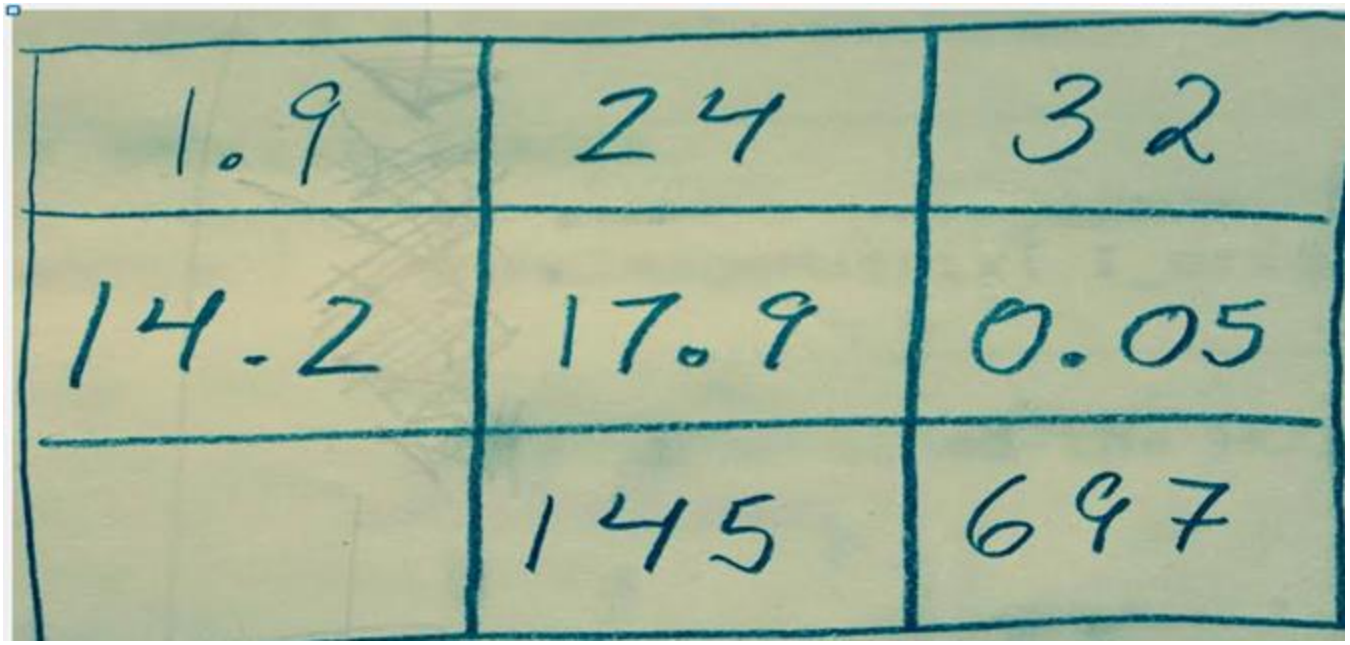

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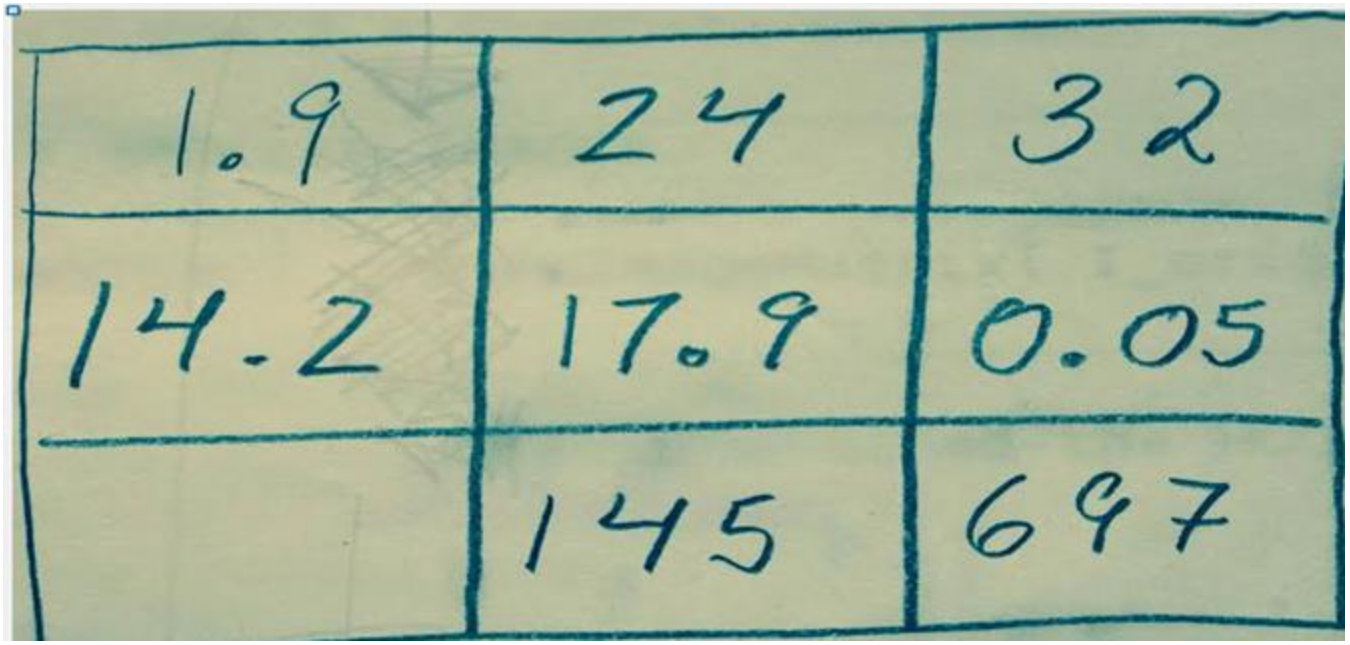

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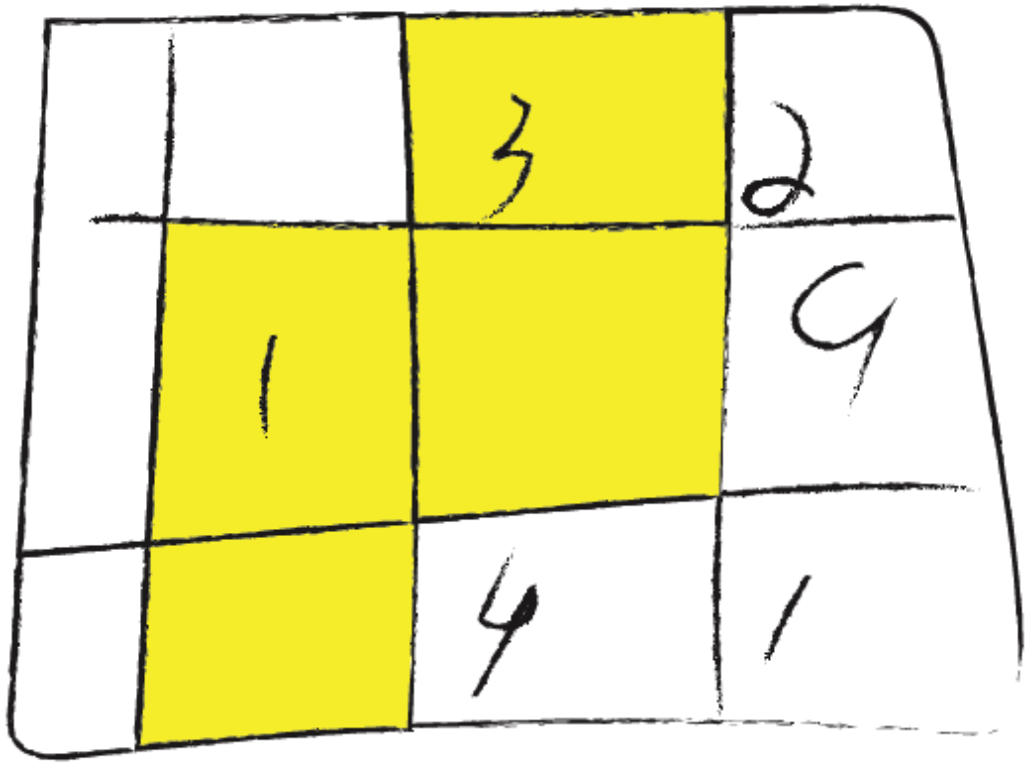

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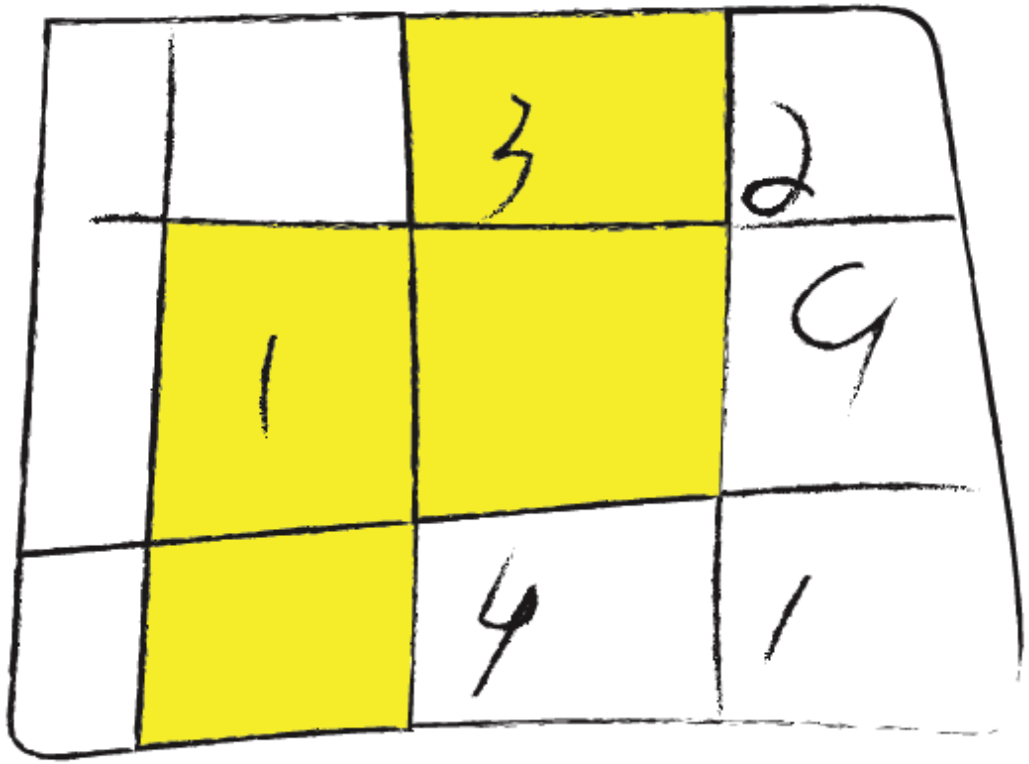
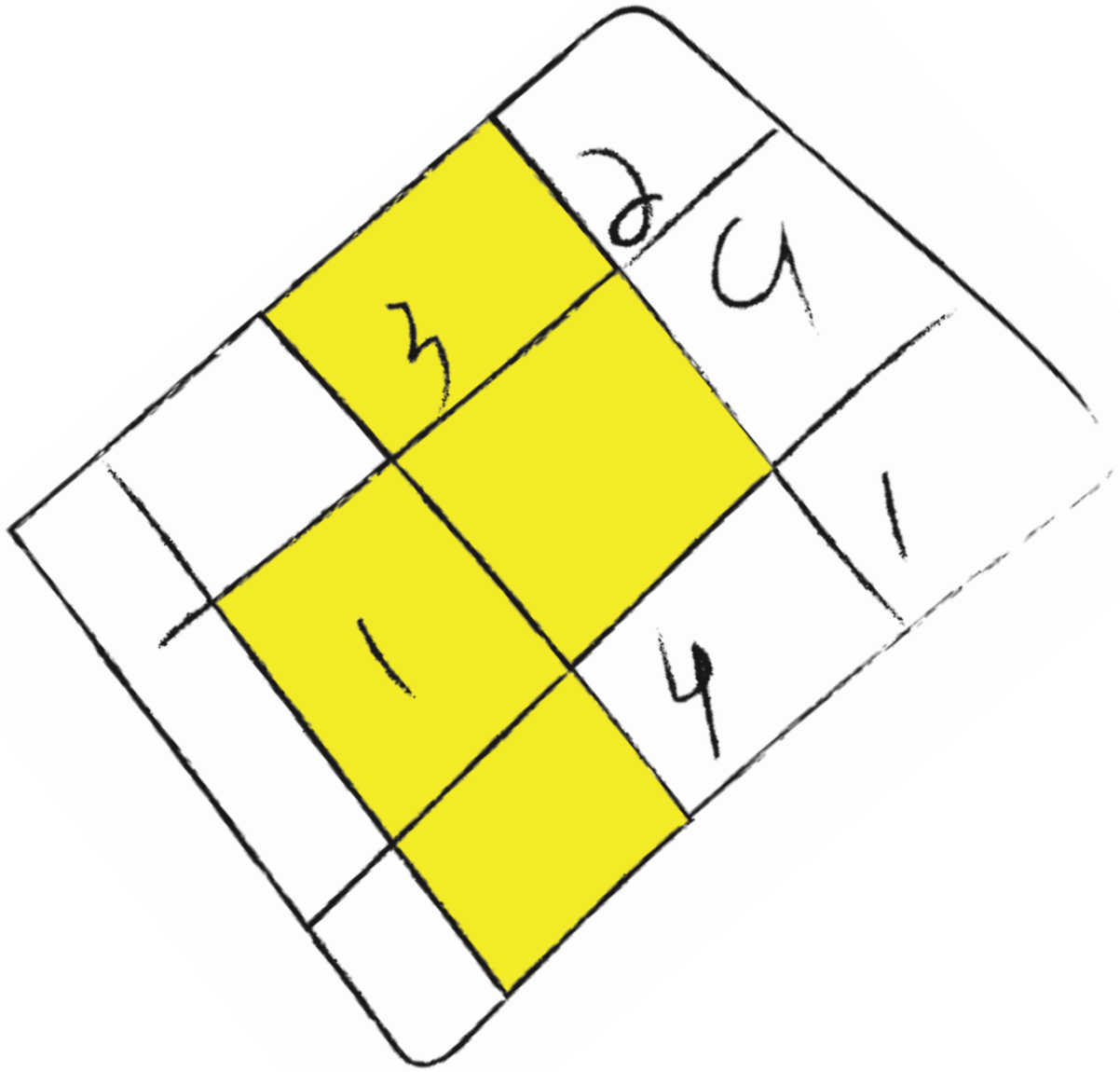
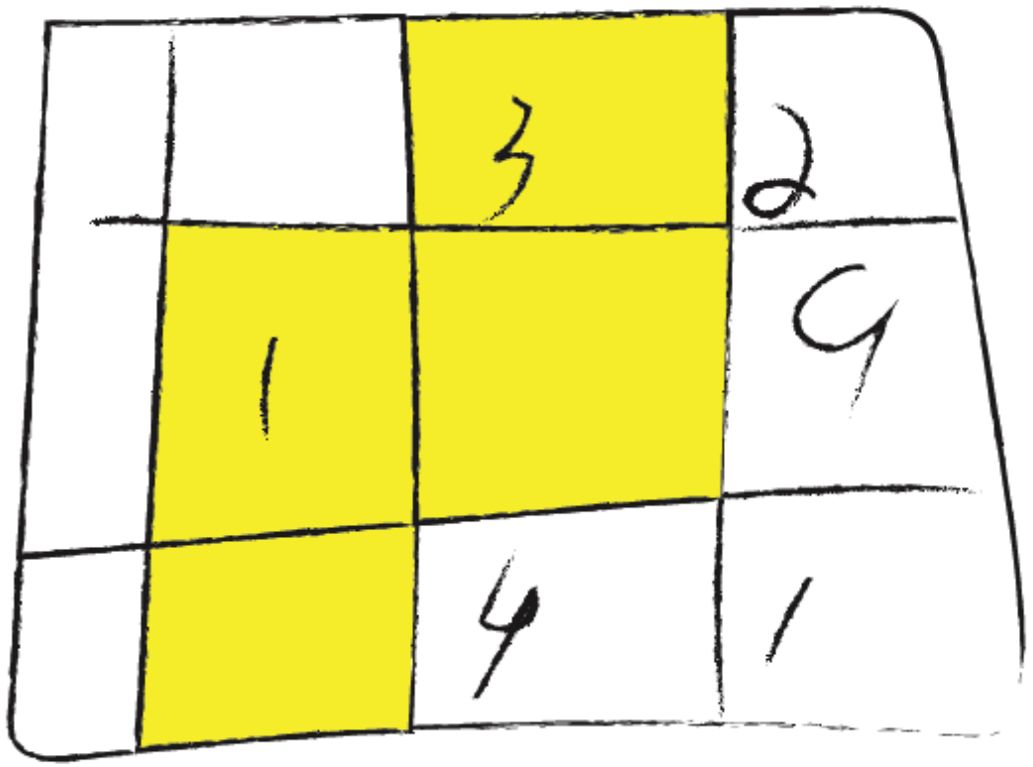
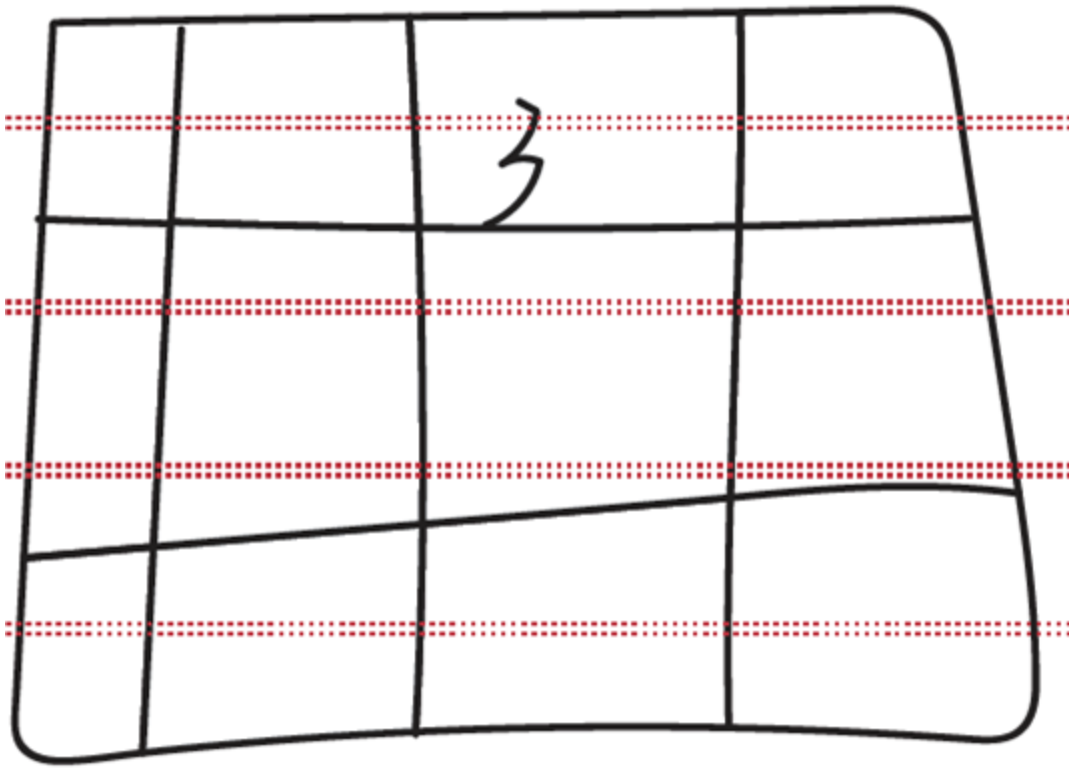




The user takes a photo of a spreadsheet they wish to transcribe

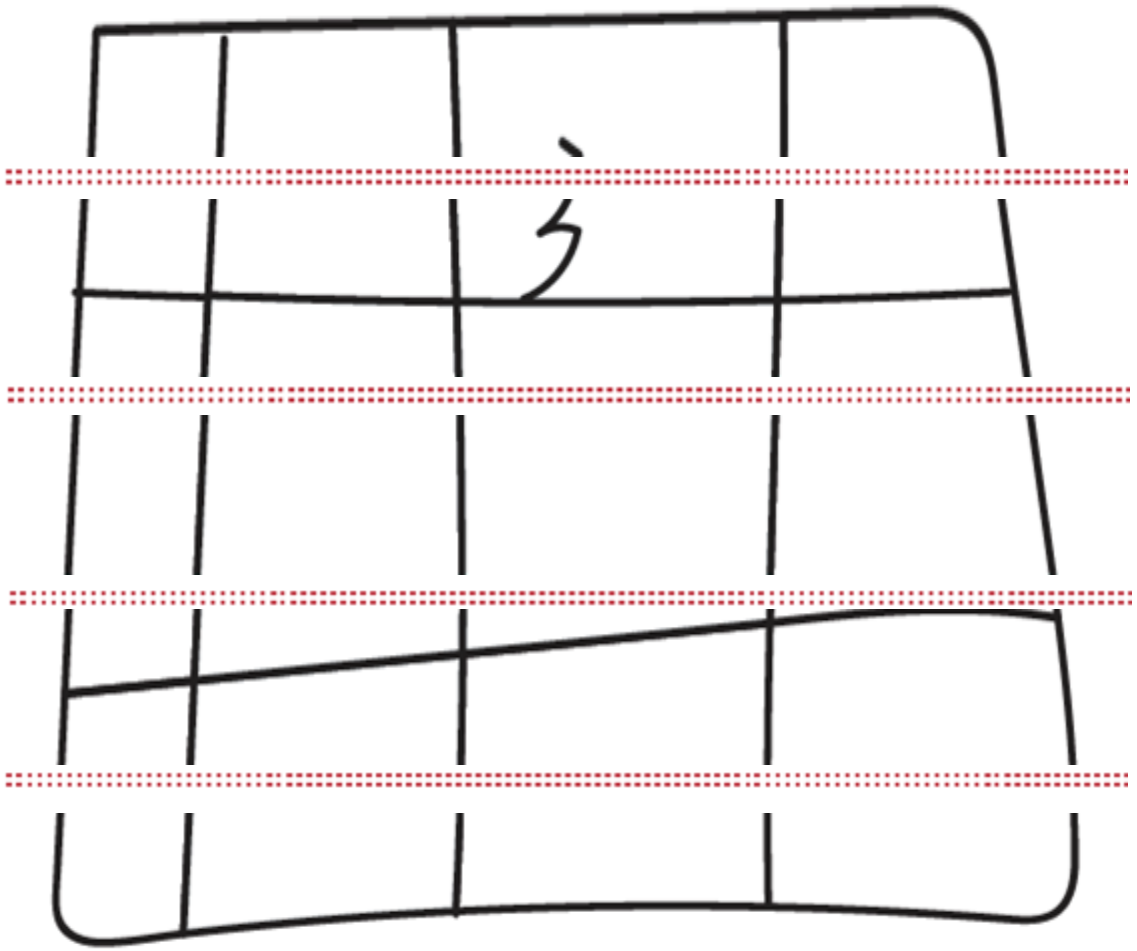


The software assumes that images are aligned

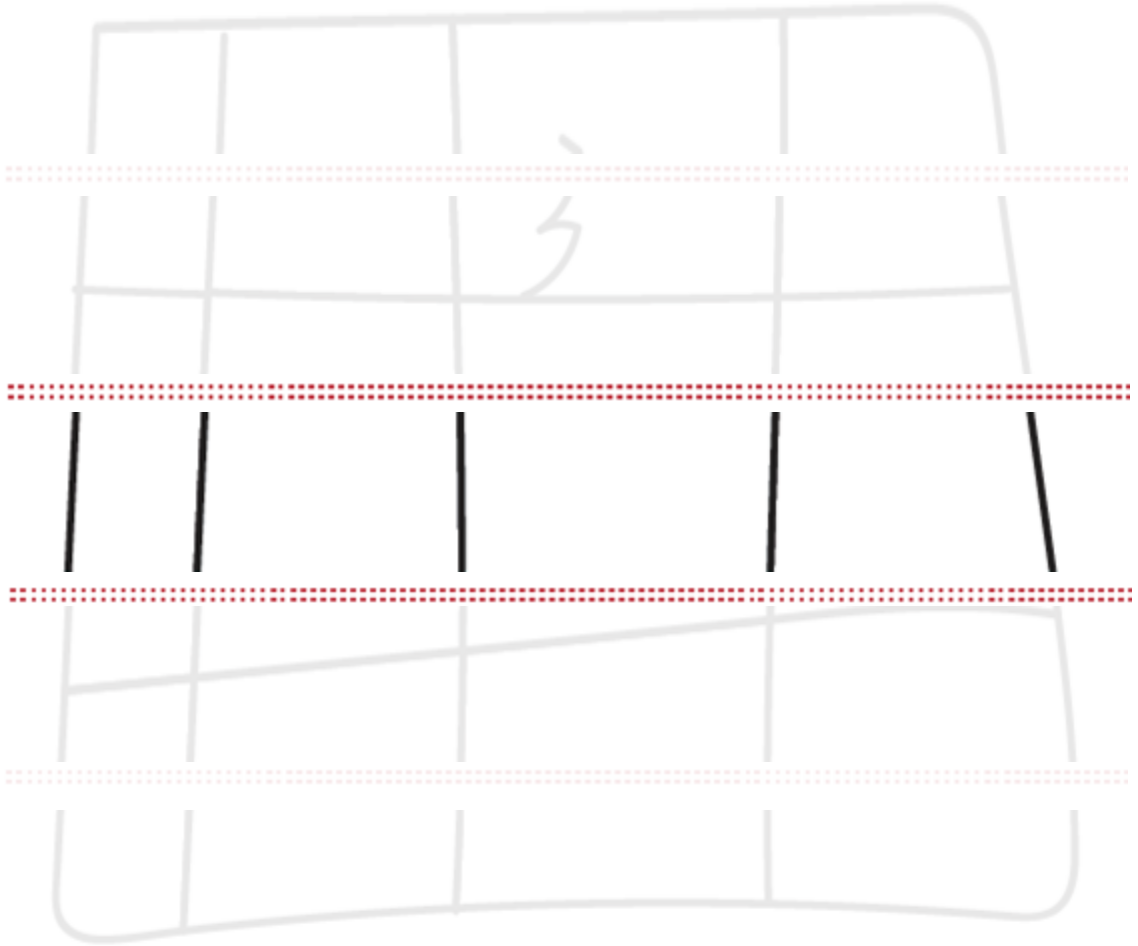


The images are adaptively filtered to remove color and shading

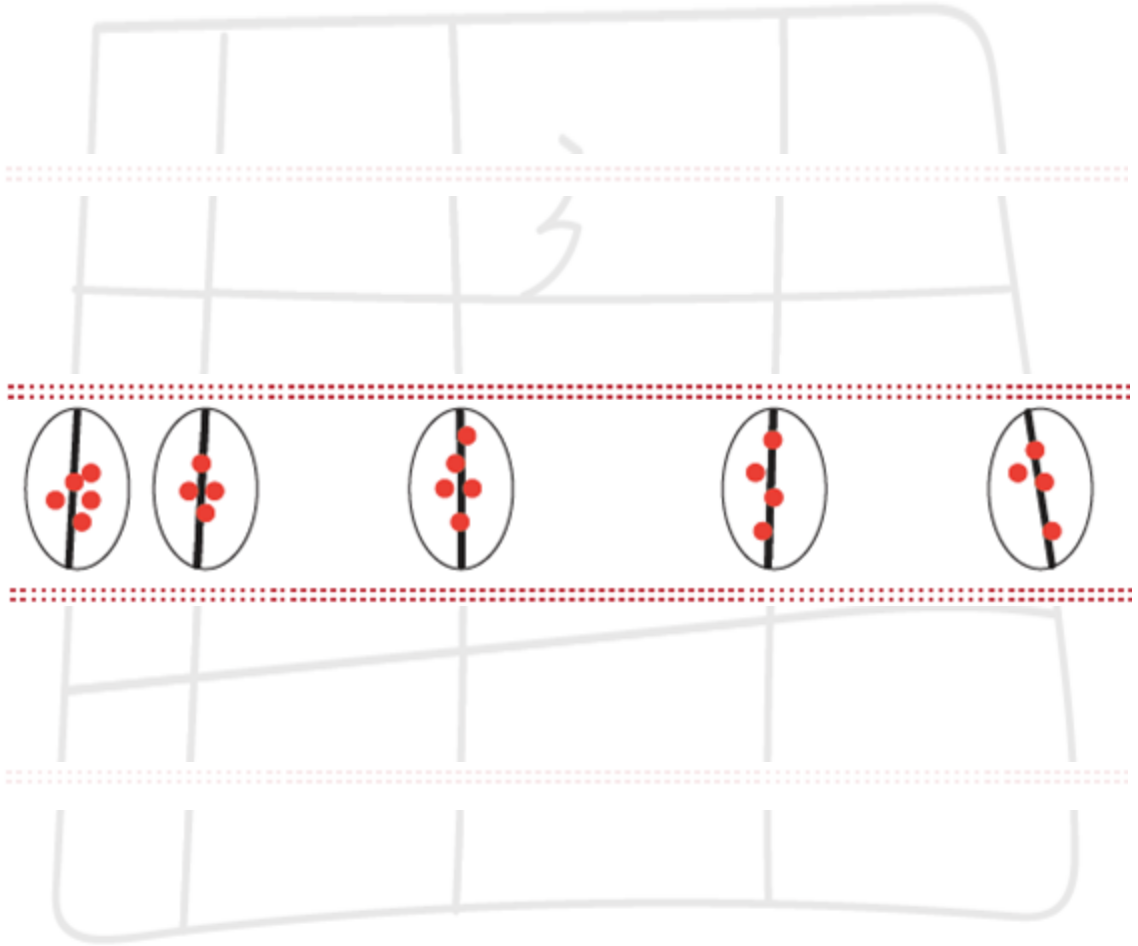
Retain the largest connected component (the gridlines)



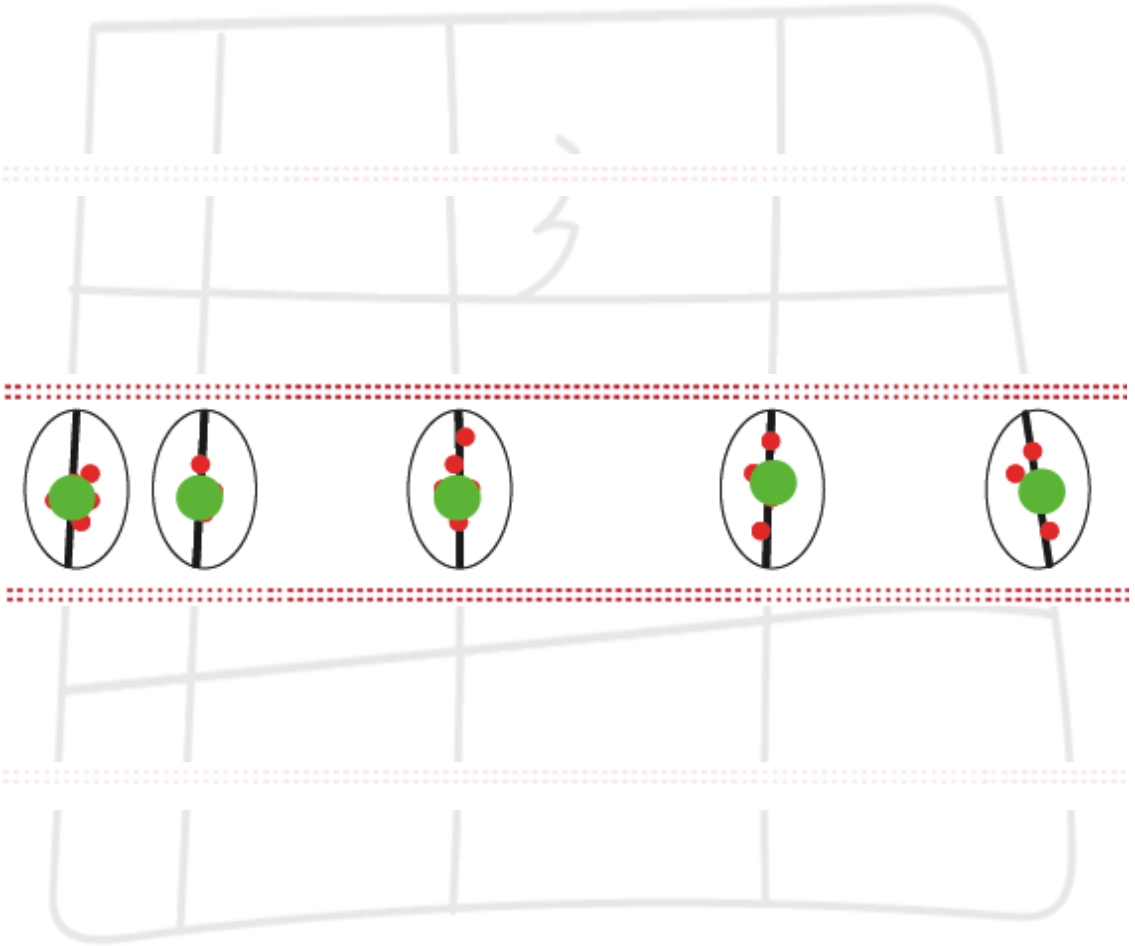
The image is then cut into strips



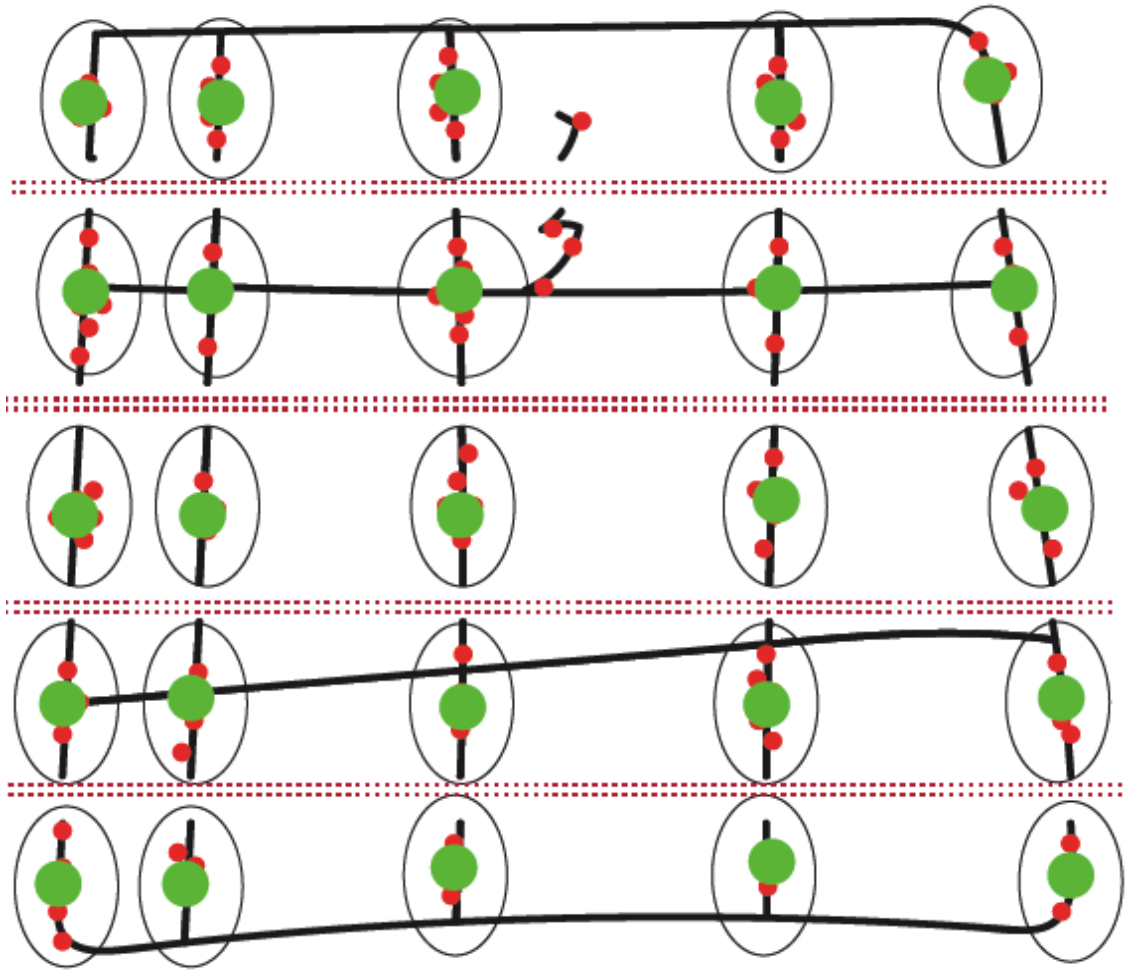
Within a given strip, the Hough image transform is applied to identify the location of near vertical line segments



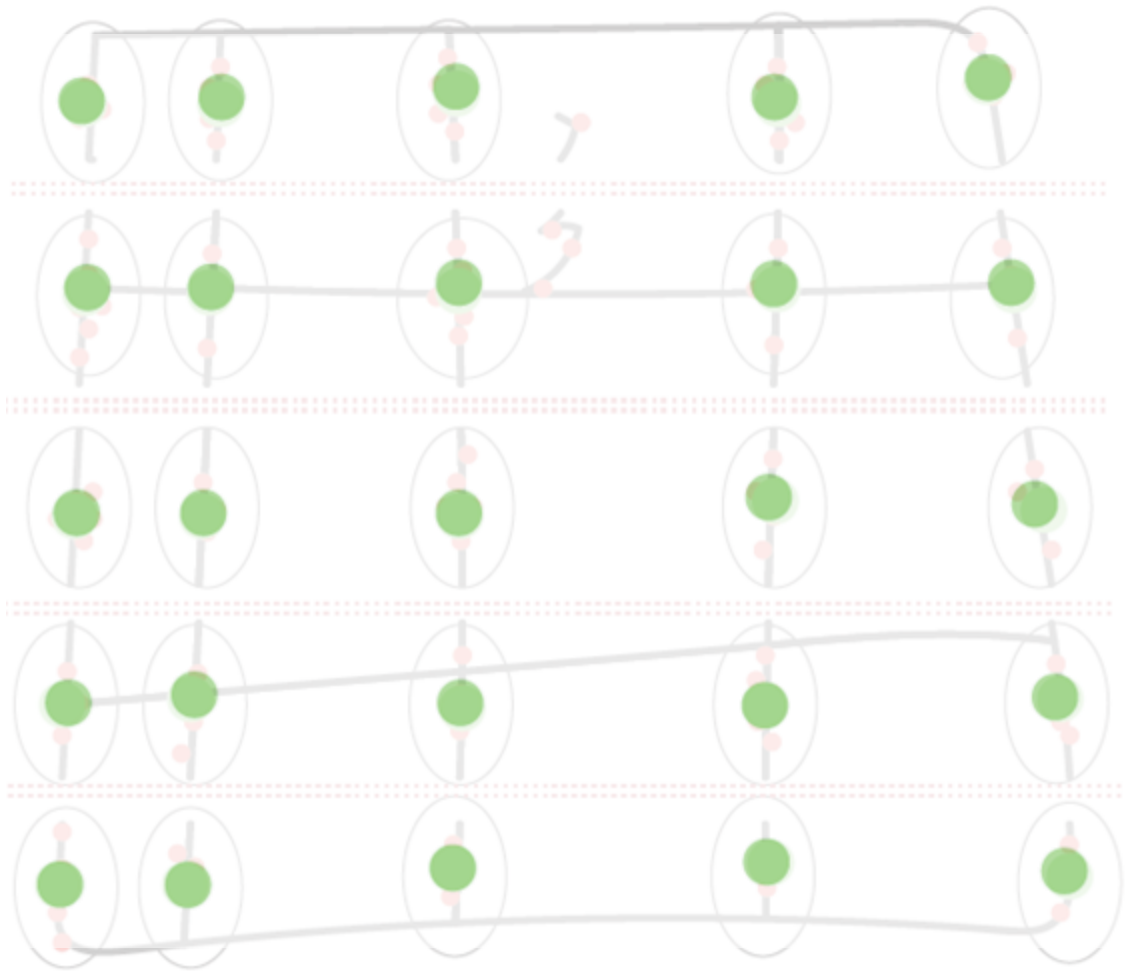
The number of spreadsheet columns are estimated based on the number of Hough peak clusters



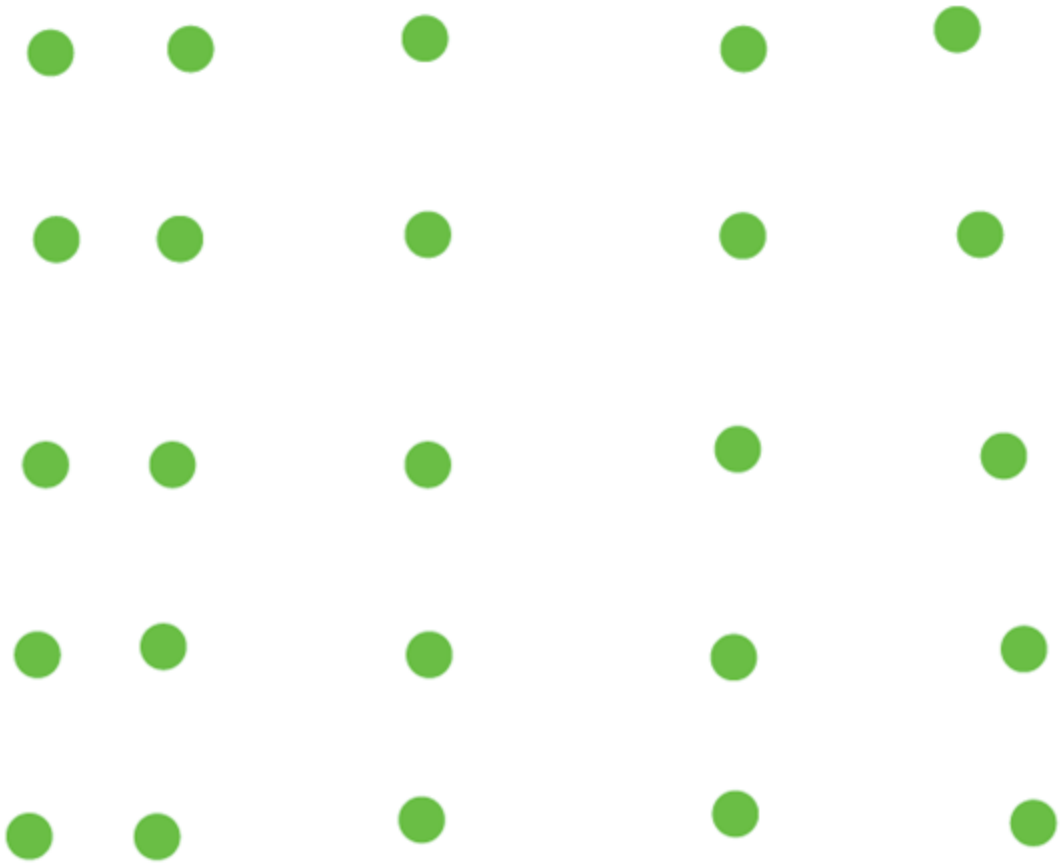
K-mediods is applied to the Hough peaks to identify the location of the column-lines, within the strip



This process is repeated for all strips



This leaves us with a set of points that represent the location of the line within each strip



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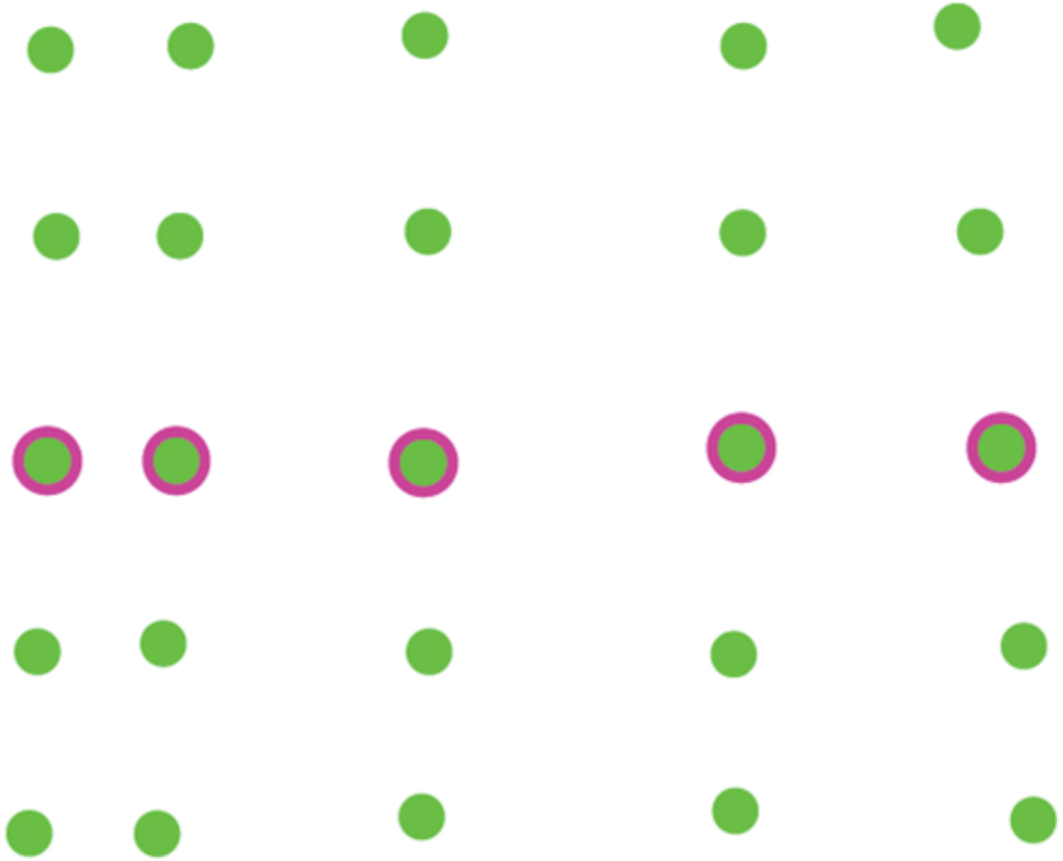
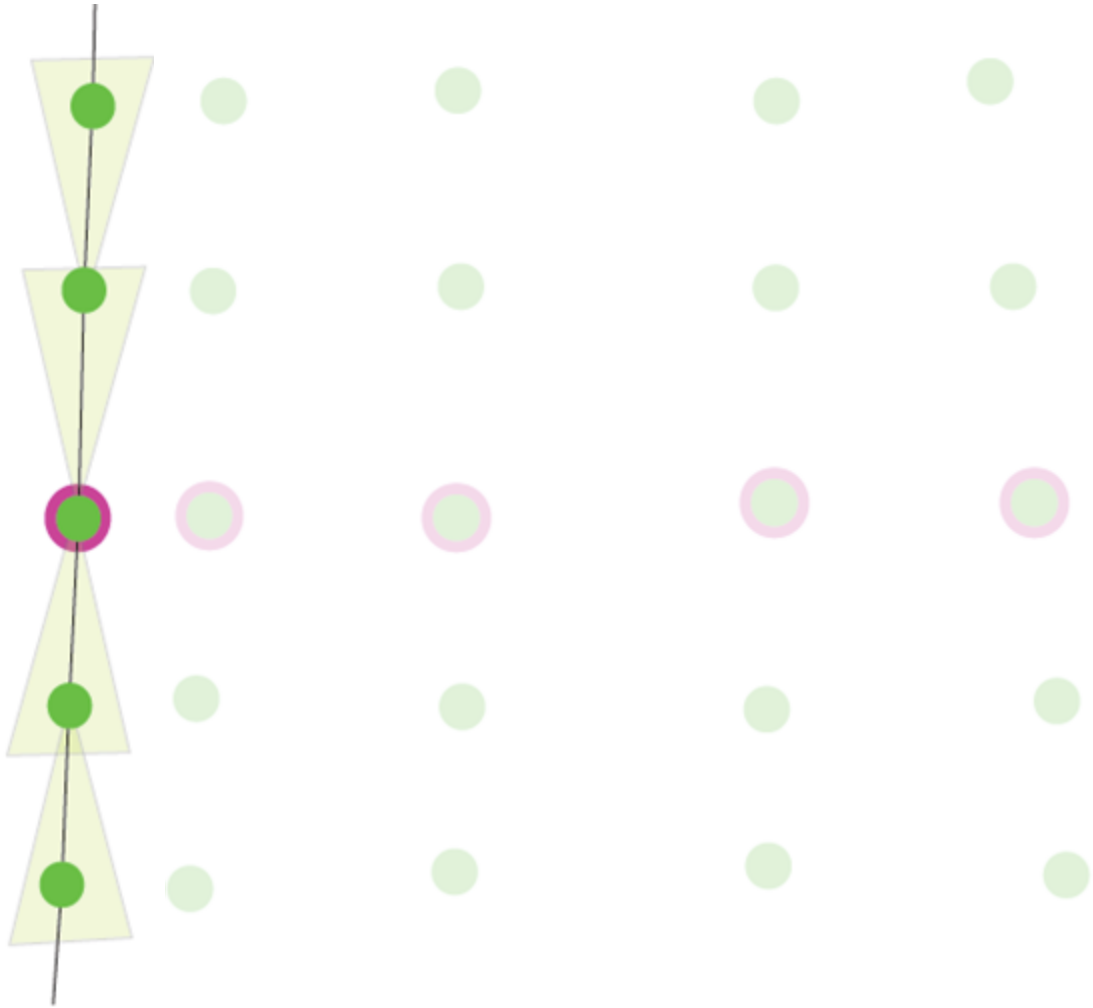
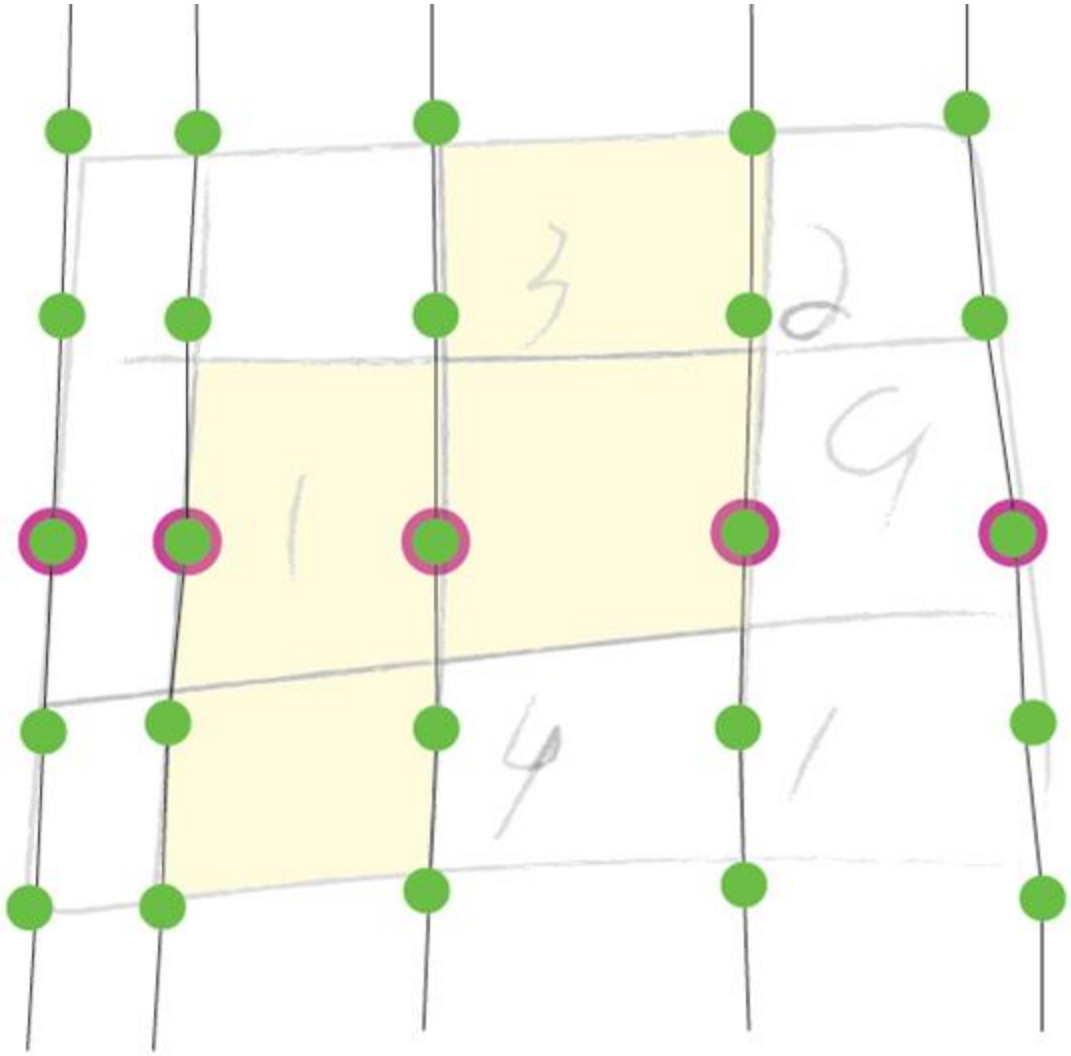


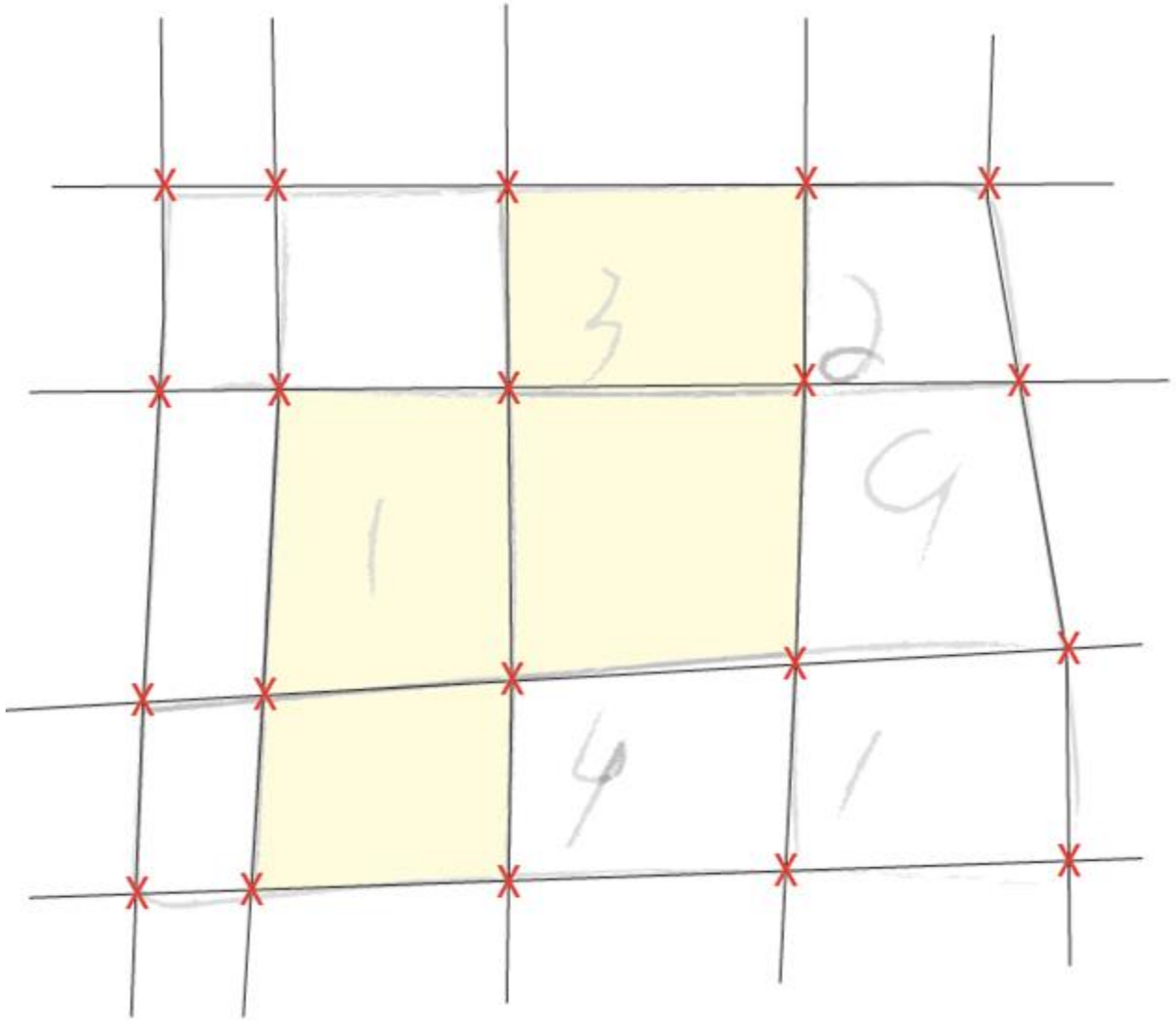
Starting from the center-most strip



We identify the closest neighboring points above, and below, within a search window

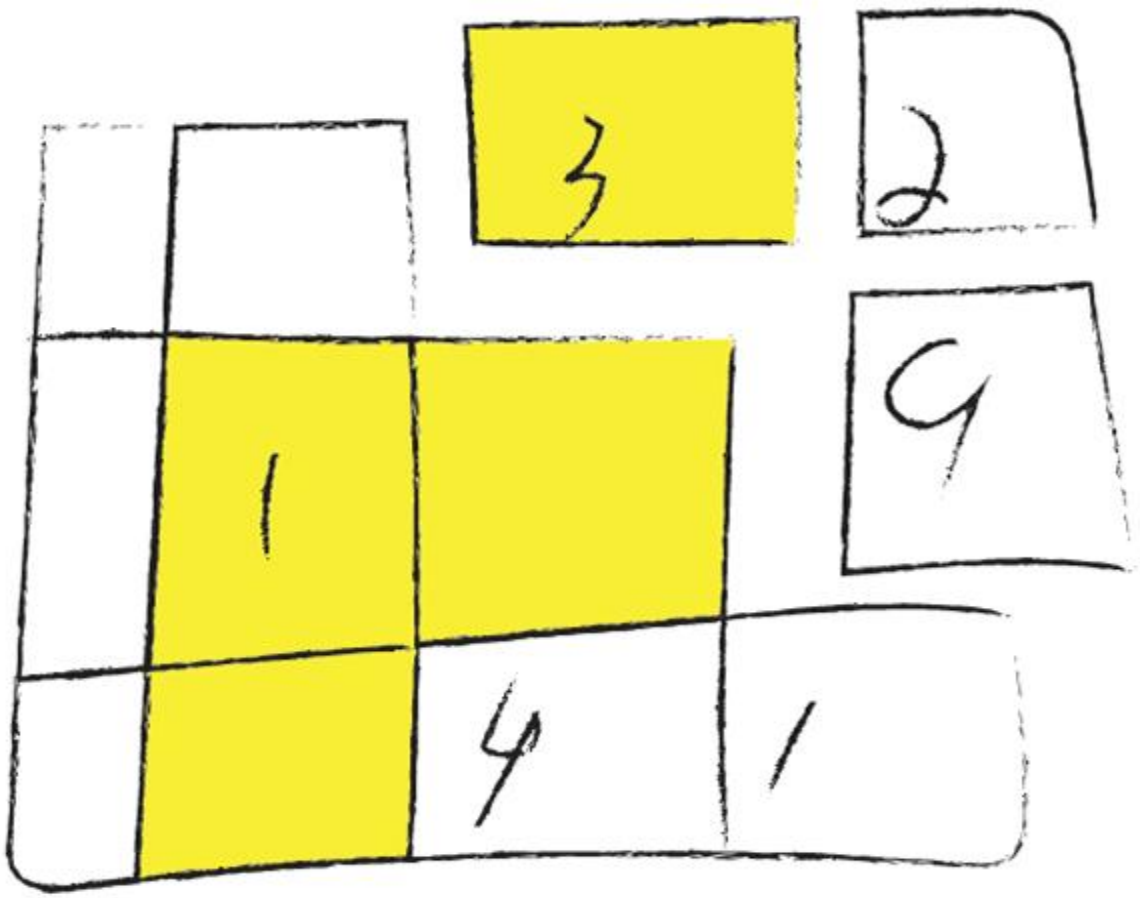


This allows us to approximate the location of the column lines



The same process may be performed to estimate the location of the row lines

The intersection of the row and column lines identify the borders of each cell image



Allowing us to extract the images, for further processing

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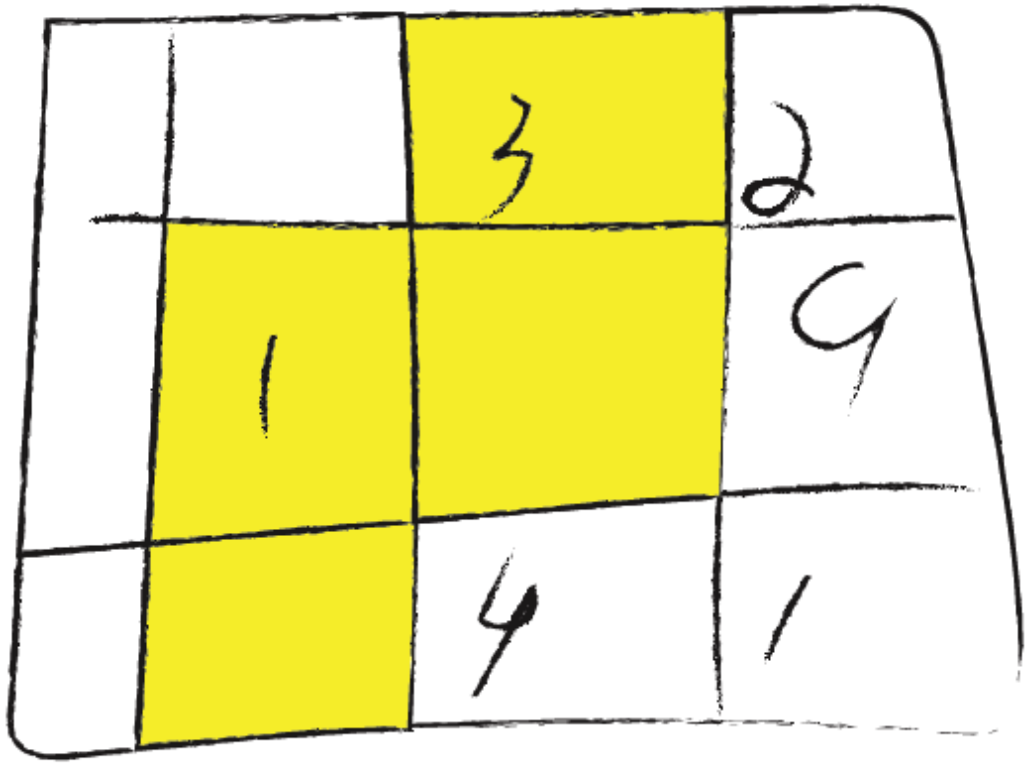

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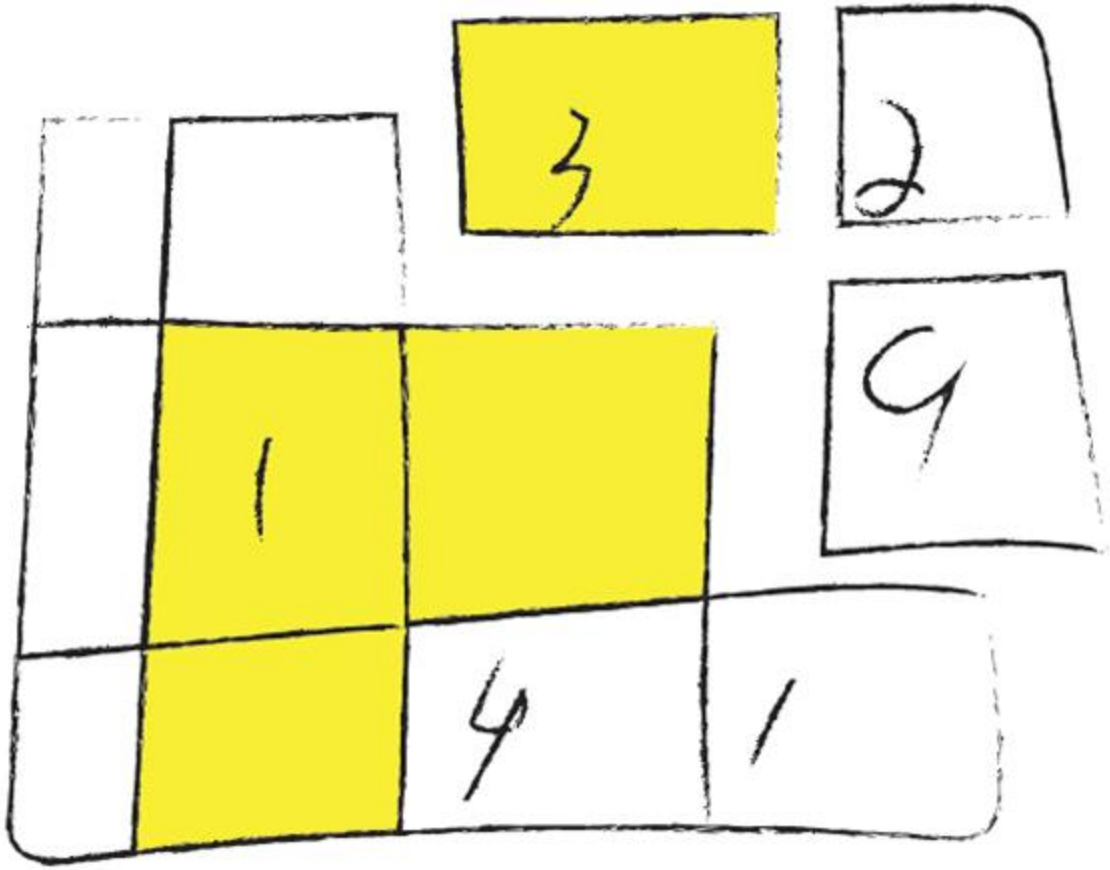

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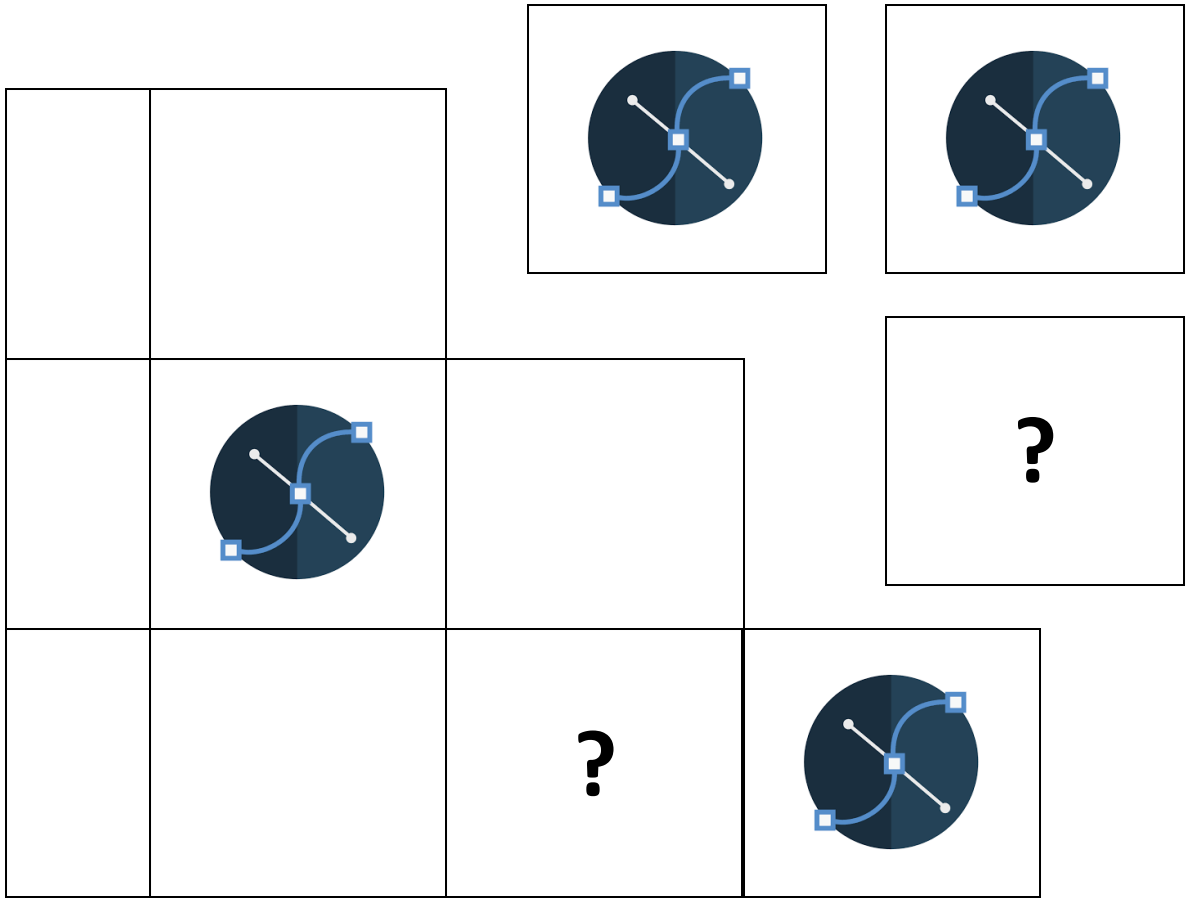
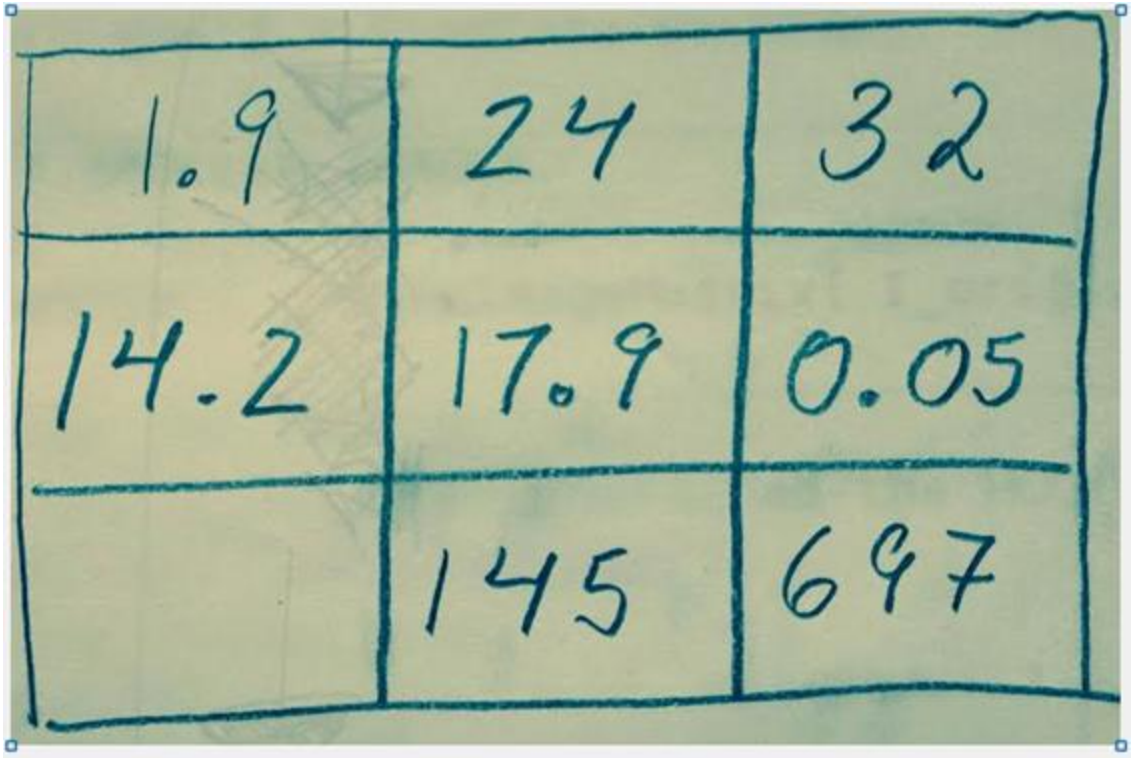


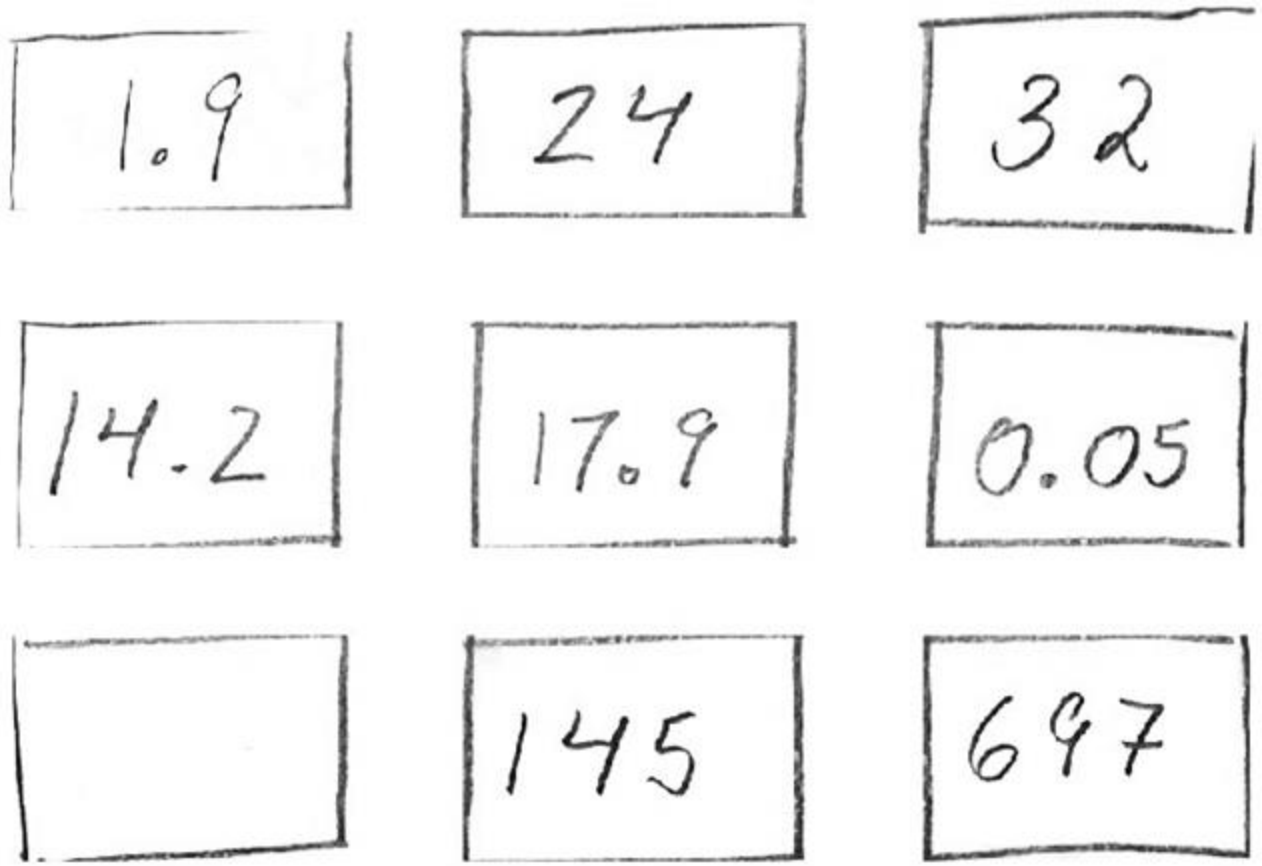
Digit Extraction

Once the cells are extracted, we classify their contents



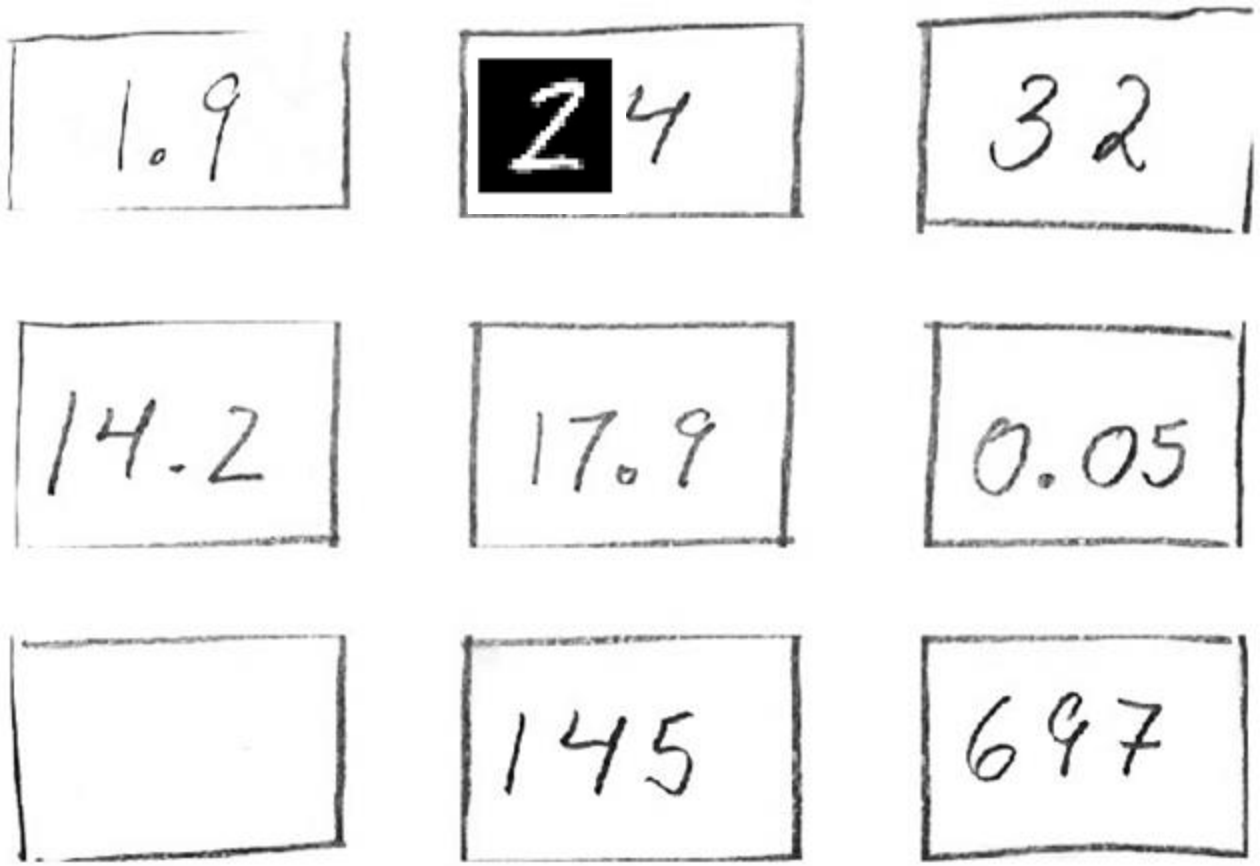
Digit Extraction

To do this, we extract digits from the cells



Digit Extraction

Digits are extracted to be uniformly sized, so they are compatible with popular machine learning approaches



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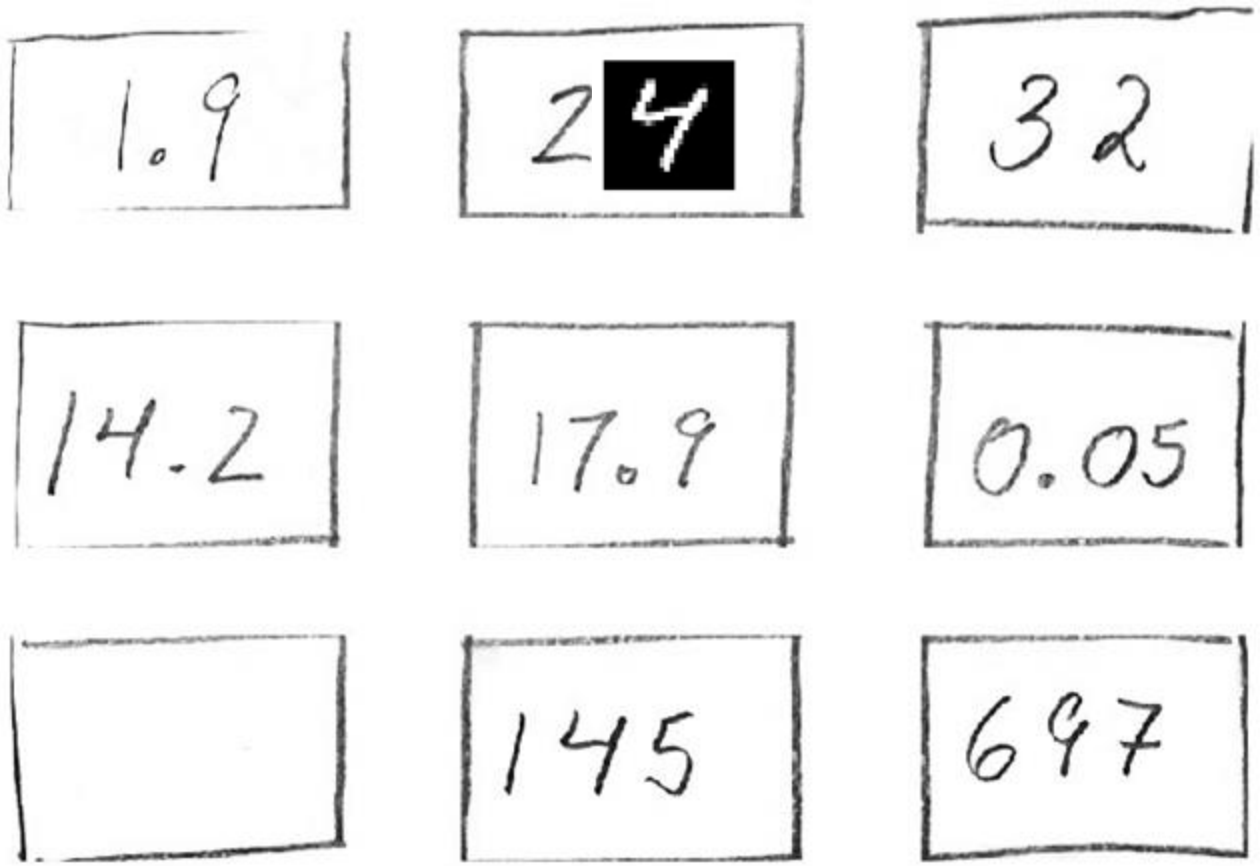
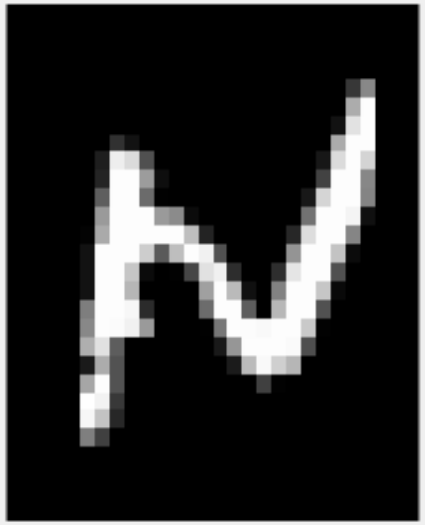
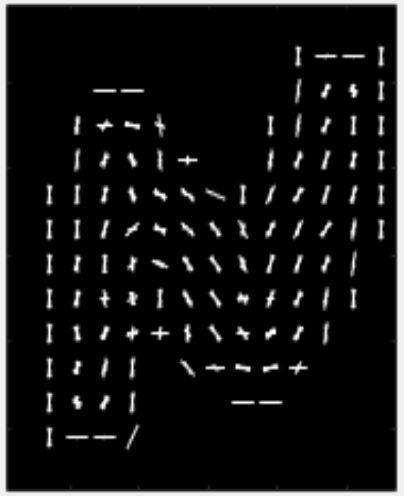


Digit Classification

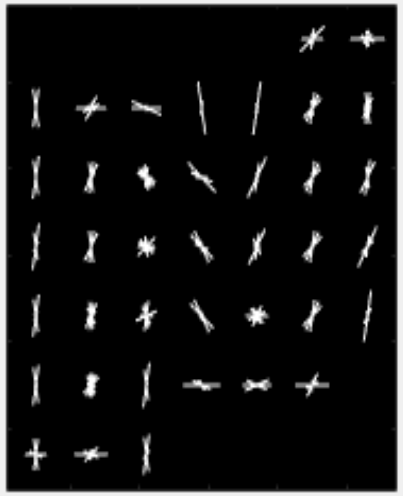
After digits are extracted, we deploy a Multinomial Support Vector Machine with histogram of oriented gradient features (HoG) for classification



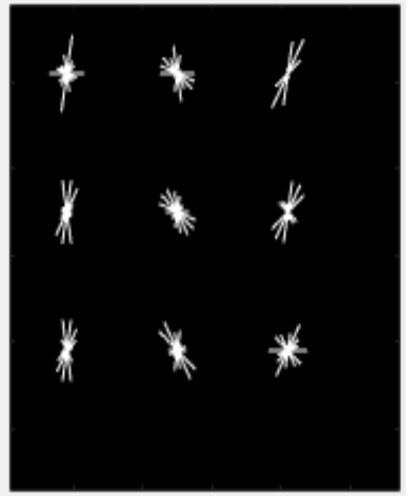
CellSize = [2 2]
Feature length = 6084



CellSize = [4 4]
Feature length = 1296



CellSize = [8 8]
Feature length = 144



Digit Classification

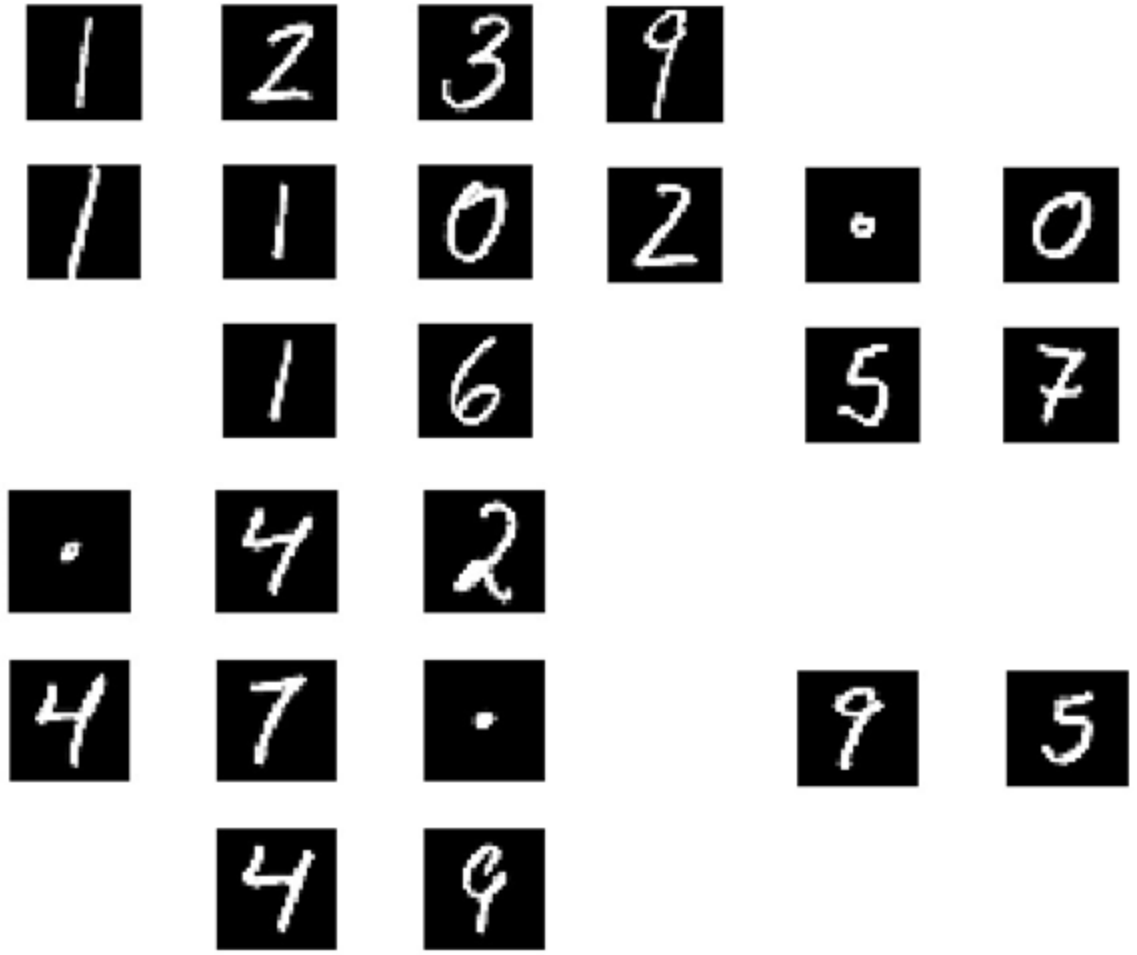
The algorithm was trained using the MNIST dataset

Confusion matrix

digit	0	1	2	3	4	5	6	7	8	9
0	0.94	0.00	0.00	0.00	0.00	0.02	0.01	0.00	0.00	0.02
1	0.00	0.99	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00
2	0.00	0.00	0.94	0.01	0.00	0.00	0.01	0.02	0.00	0.03
3	0.00	0.00	0.01	0.95	0.00	0.04	0.00	0.00	0.00	0.00
4	0.00	0.01	0.00	0.00	0.88	0.00	0.00	0.00	0.01	0.10
5	0.00	0.00	0.00	0.00	0.00	0.98	0.00	0.01	0.01	0.00
6	0.03	0.00	0.00	0.00	0.00	0.00	0.95	0.00	0.01	0.00
7	0.00	0.01	0.02	0.01	0.00	0.00	0.00	0.93	0.00	0.03
8	0.03	0.00	0.02	0.00	0.01	0.00	0.01	0.02	0.84	0.06
9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.96

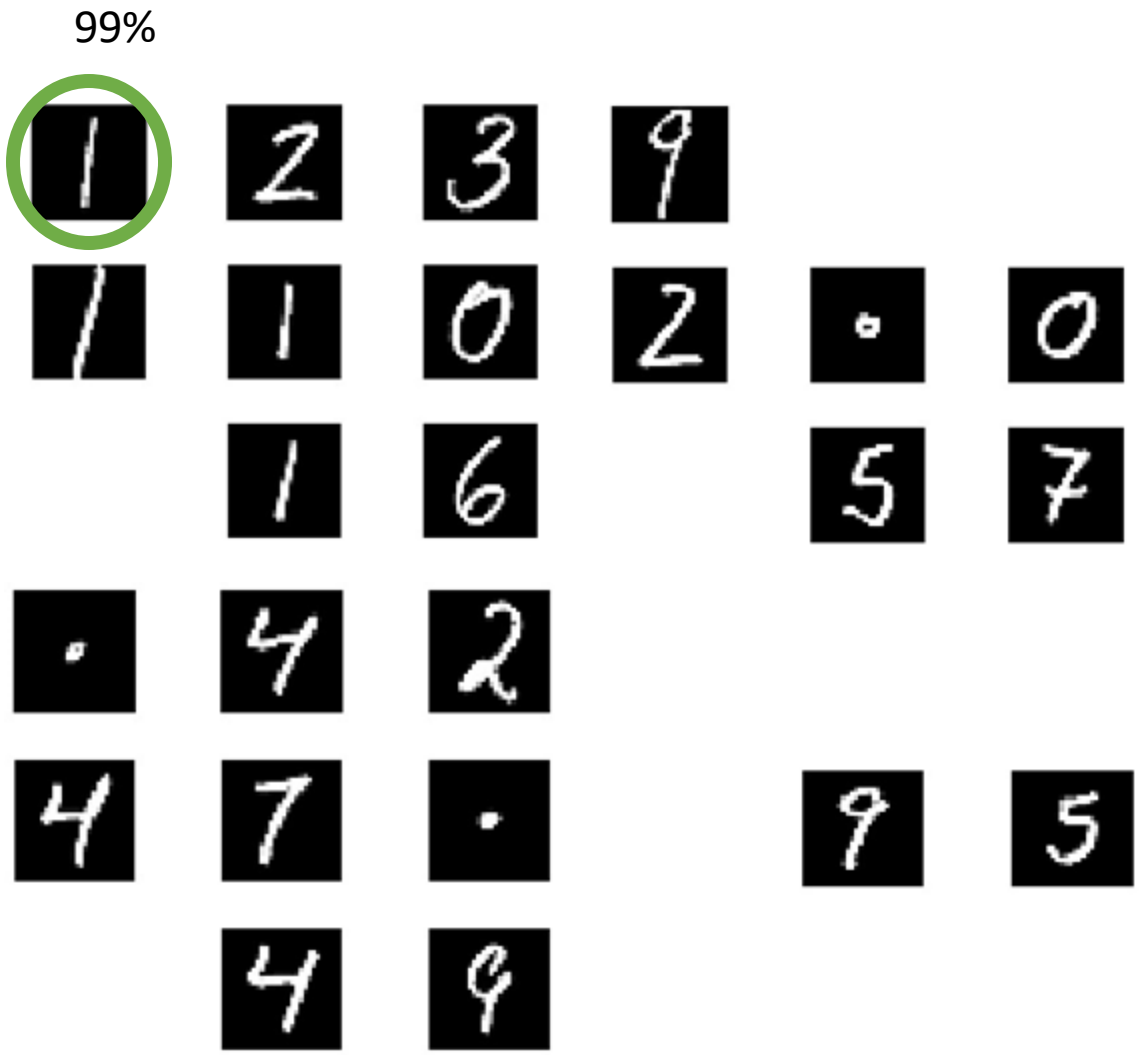
Digit Classification

The algorithm classifies digits, according to their multinomial probability



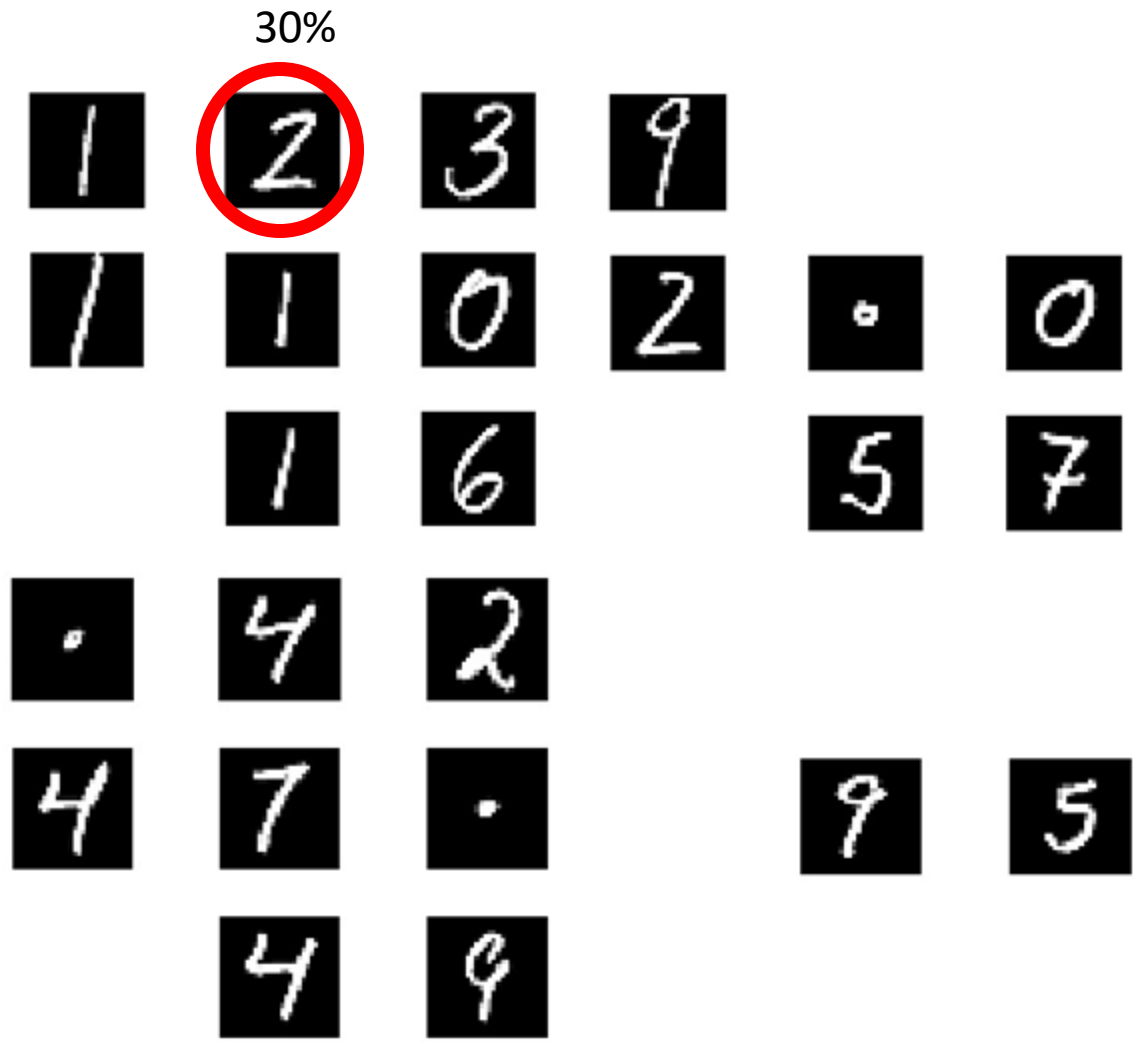
Digit Classification

For some digits, it will have high confidence



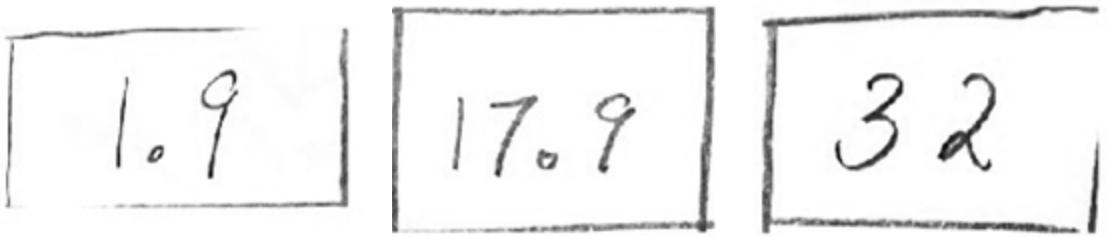
Digit Classification

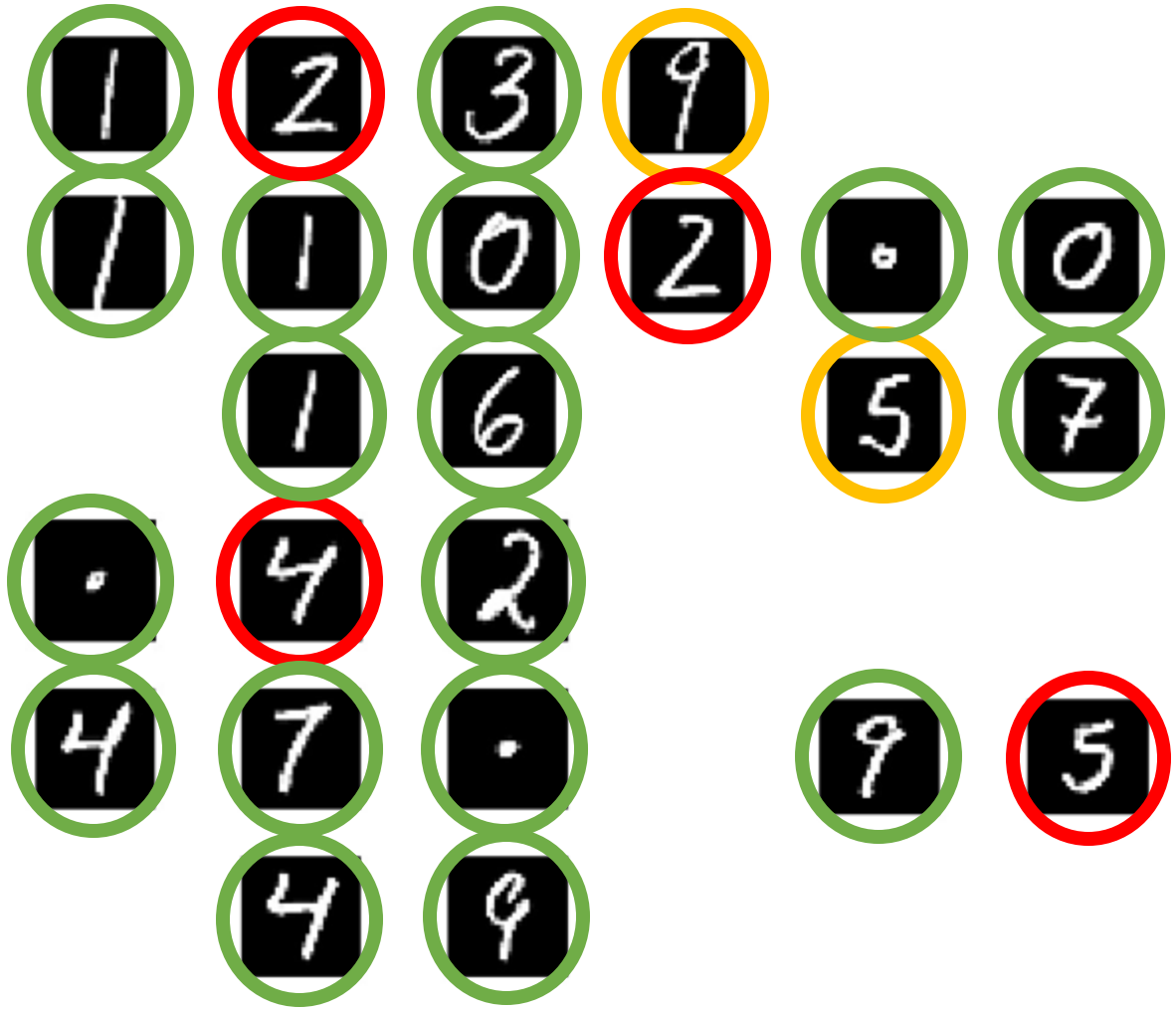
For other digits, it will have low confidence



Digit Classification

Cells containing digits above the confidence threshold are transcribed by the machine





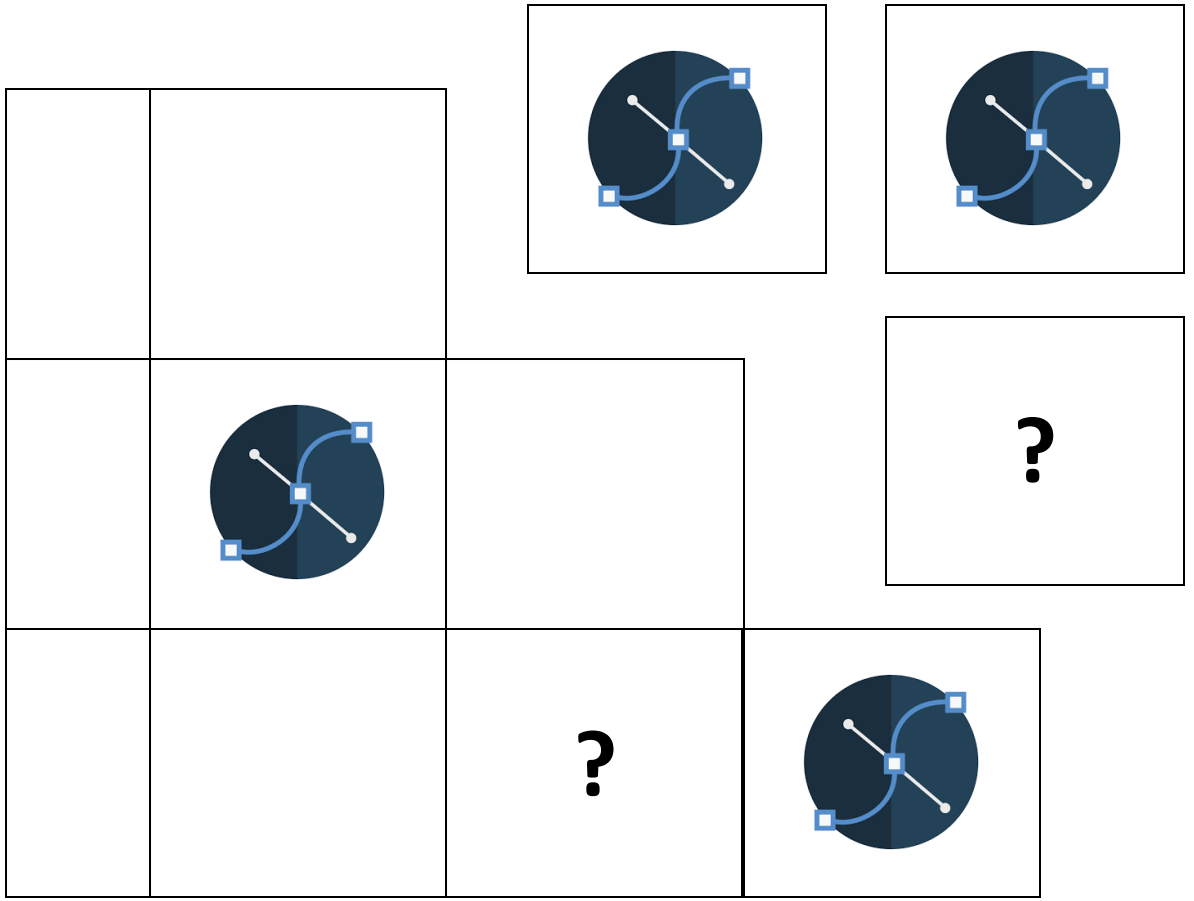
How the Tool Works: 4 Steps

Step 1: the extraction of cell images from the spreadsheet grid

Step 2: machine recognition of digits within the cells

Step 3: human transcription of cells with challenging content

Step 4: feedback of human transcription results to the machine



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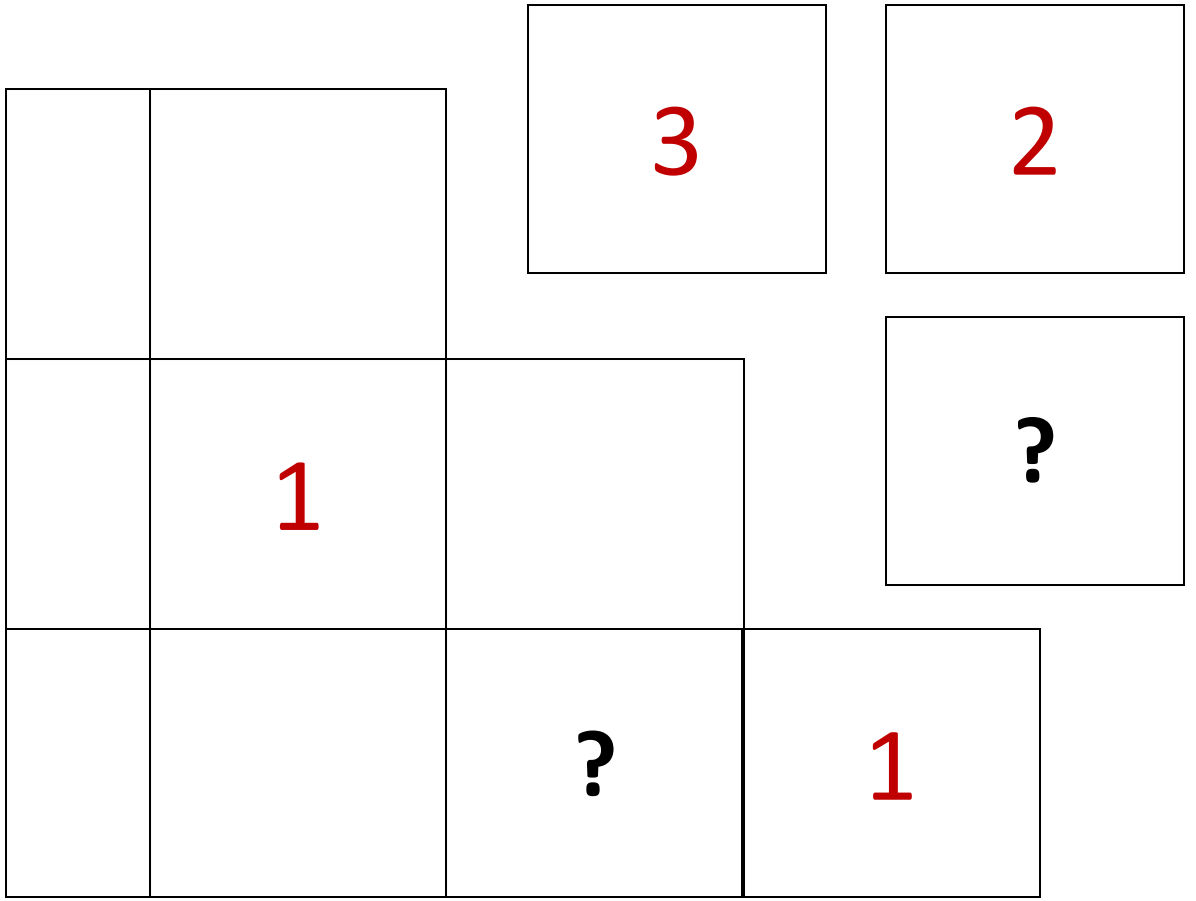

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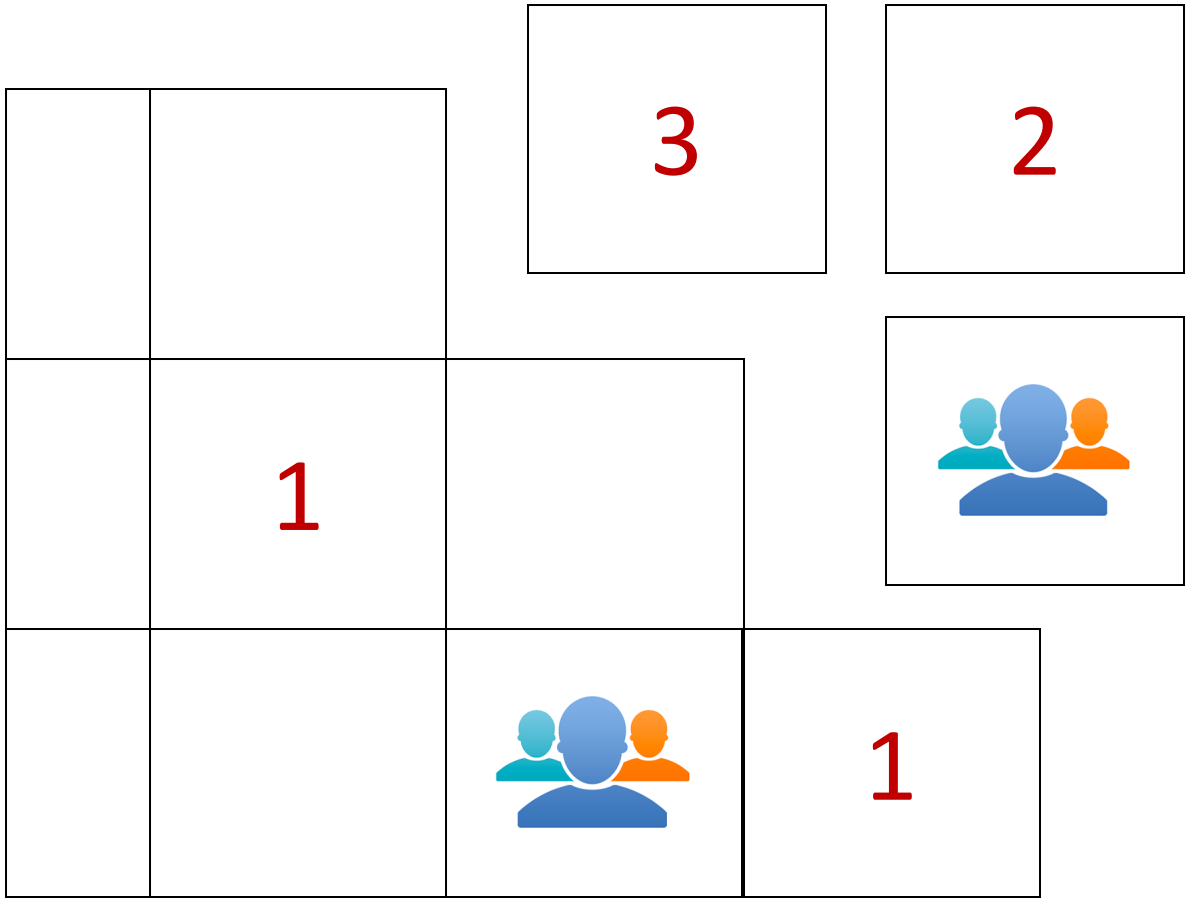
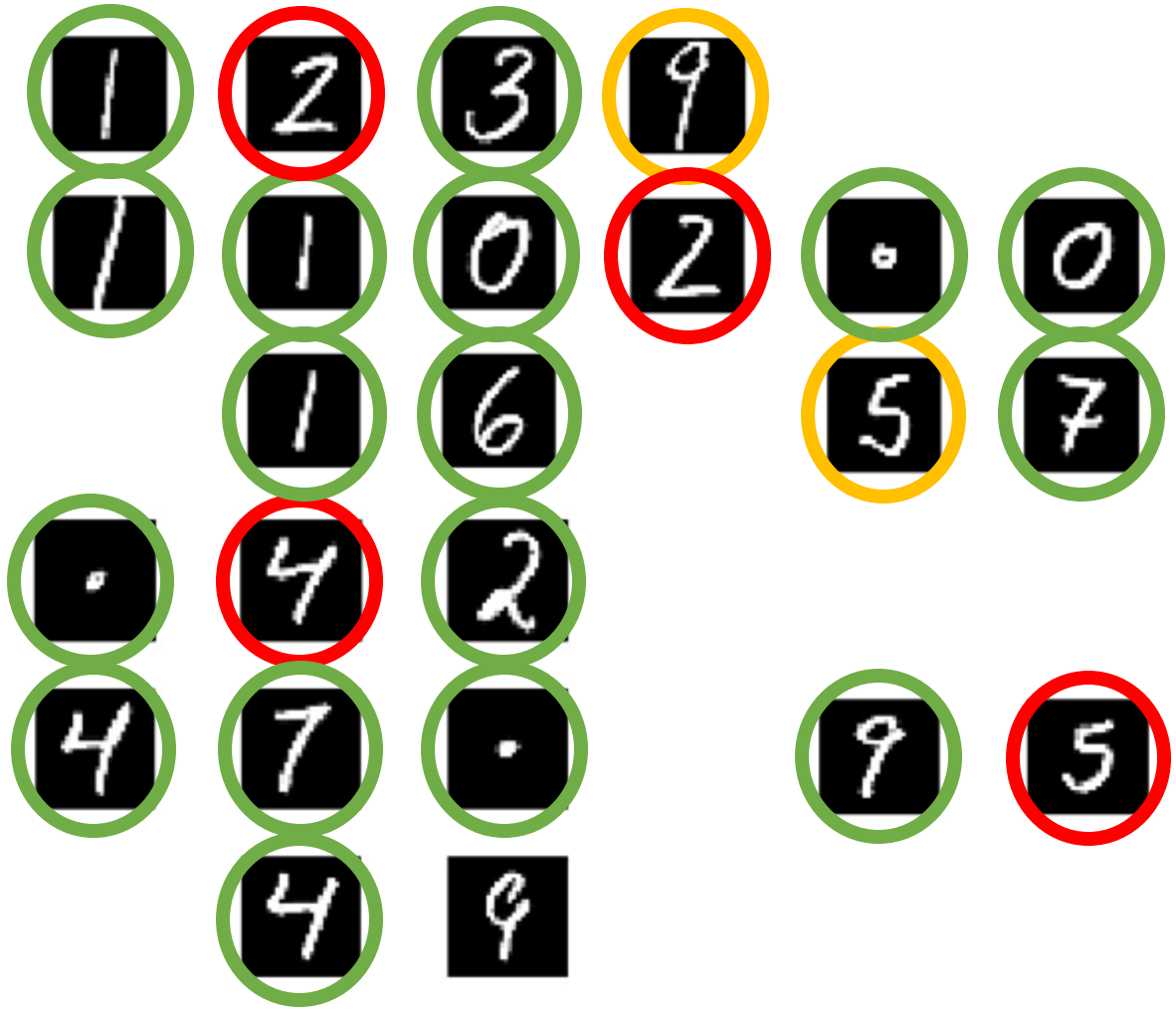


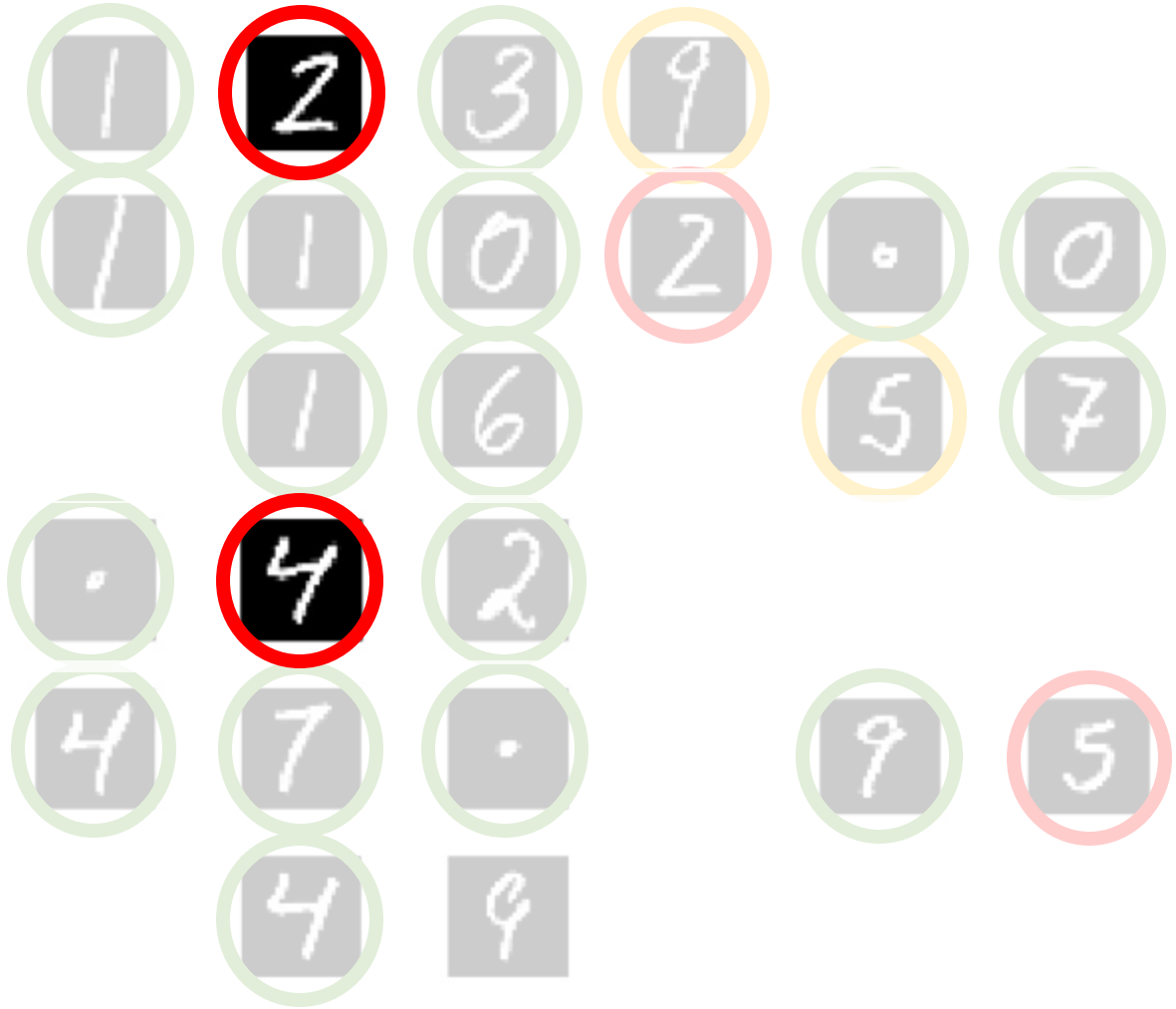
Human Transcription

Cells that contained digits beneath a confidence threshold are marked for the crowd annotation



Human Transcription

By doing crowd annotation one cell at a time, patient privacy is protected!



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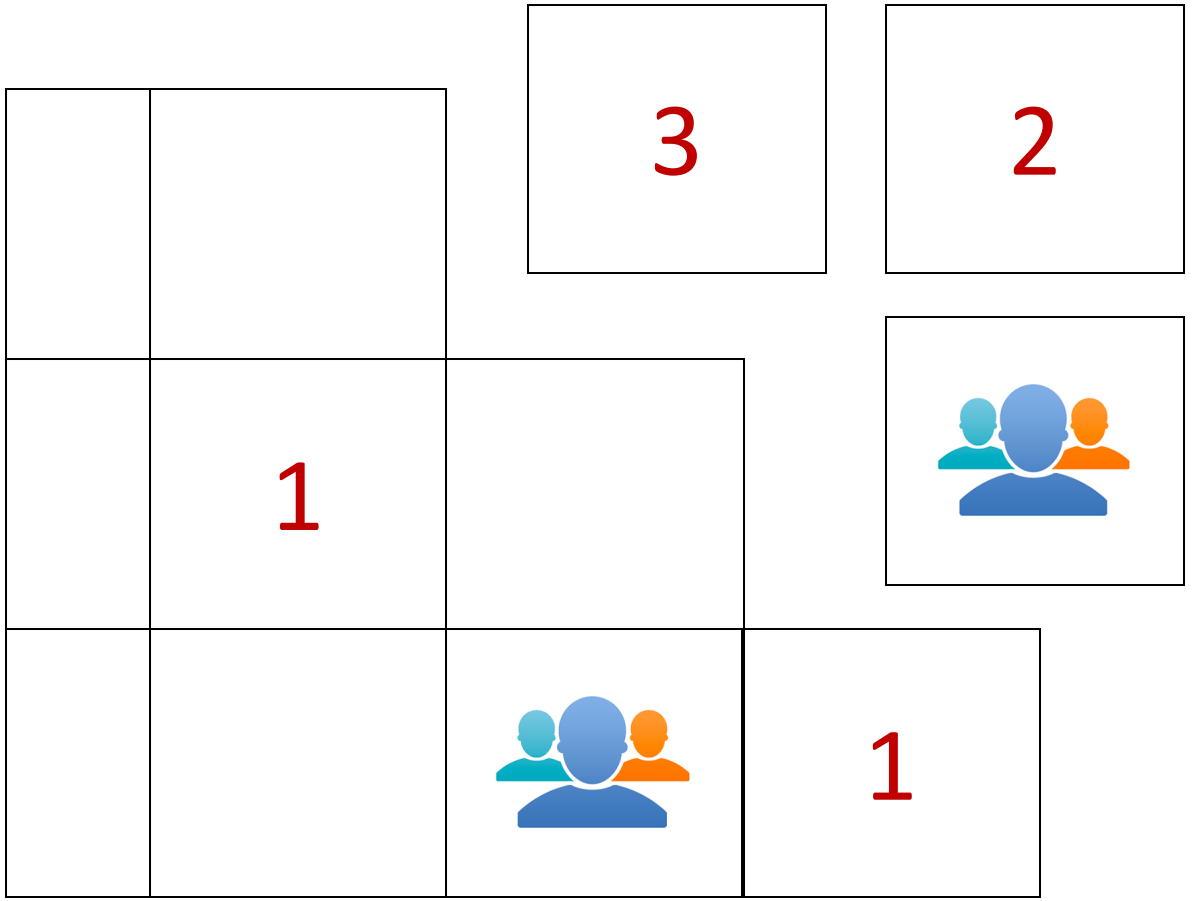

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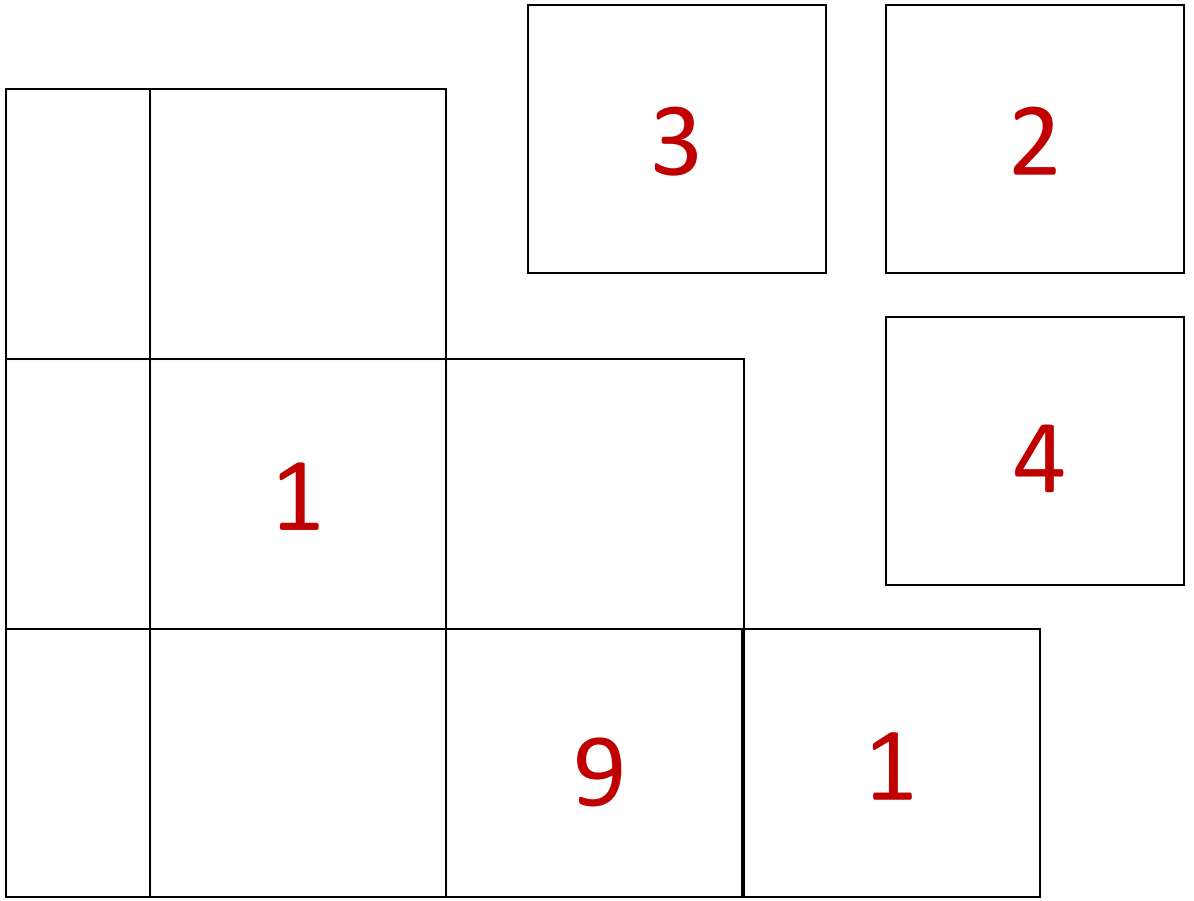

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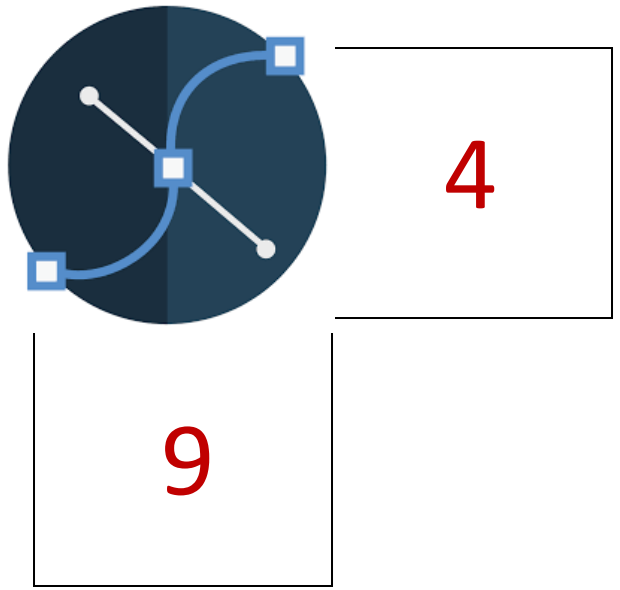
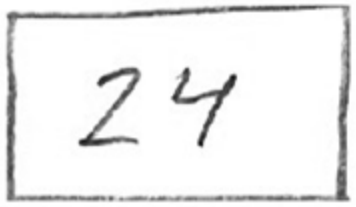
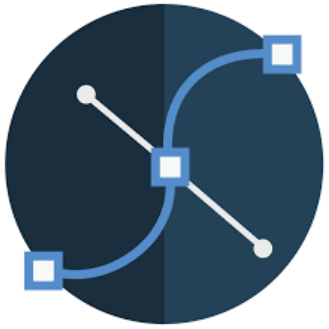
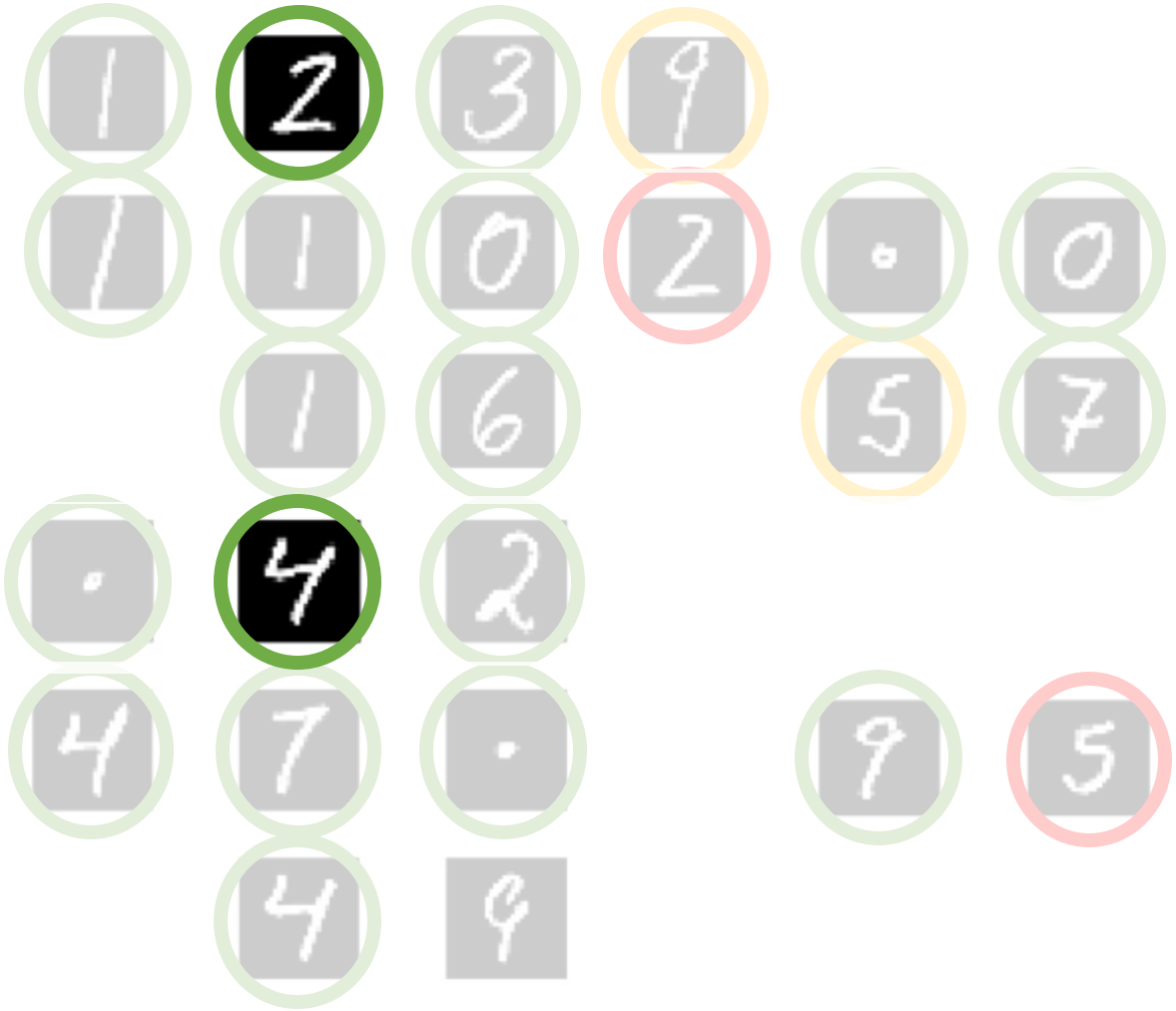


Digit Classification

The algorithm is then retrained using the new annotations from the crowd workers



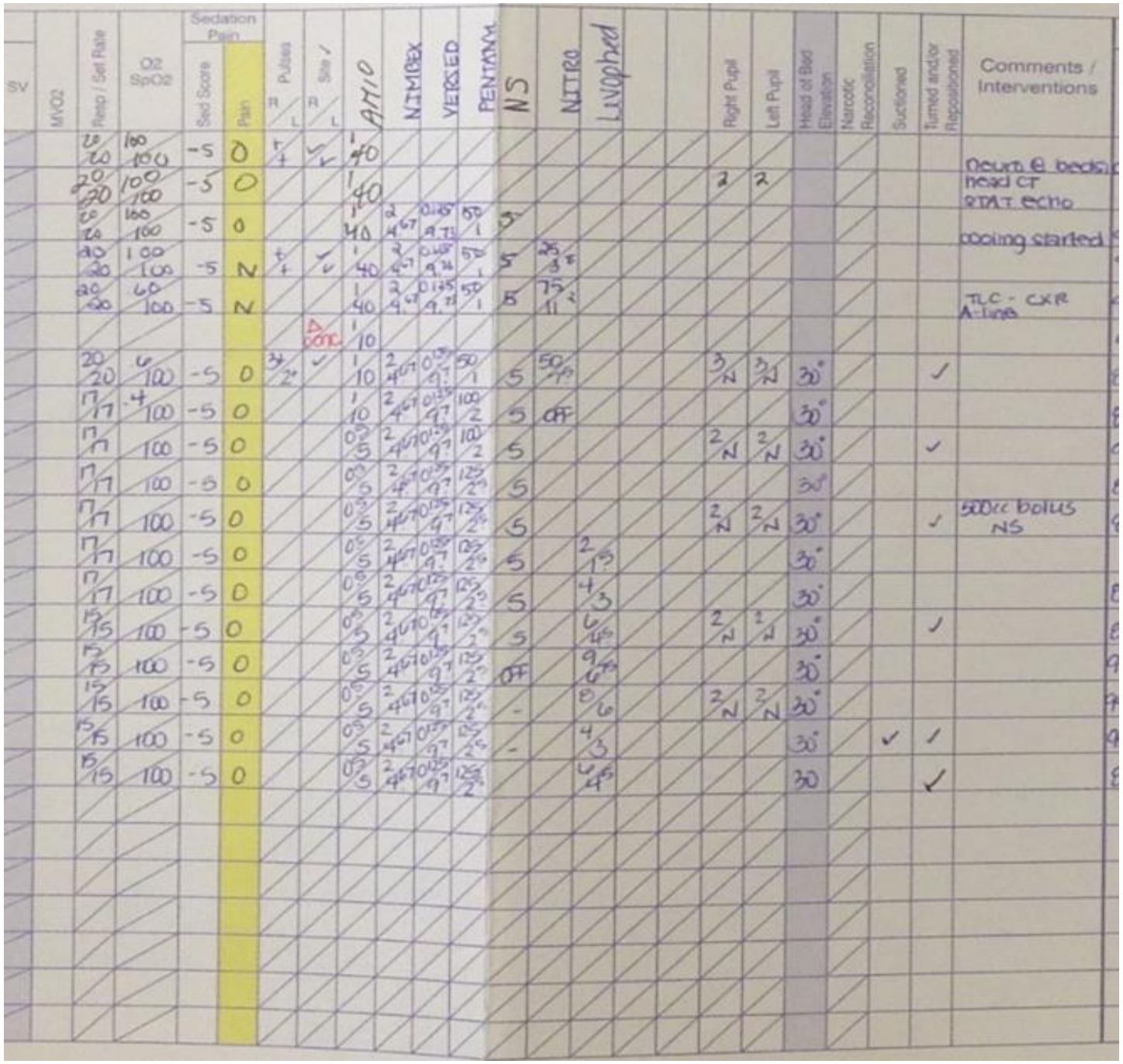




Key Results + Cost Comparison

Grid Line Extraction

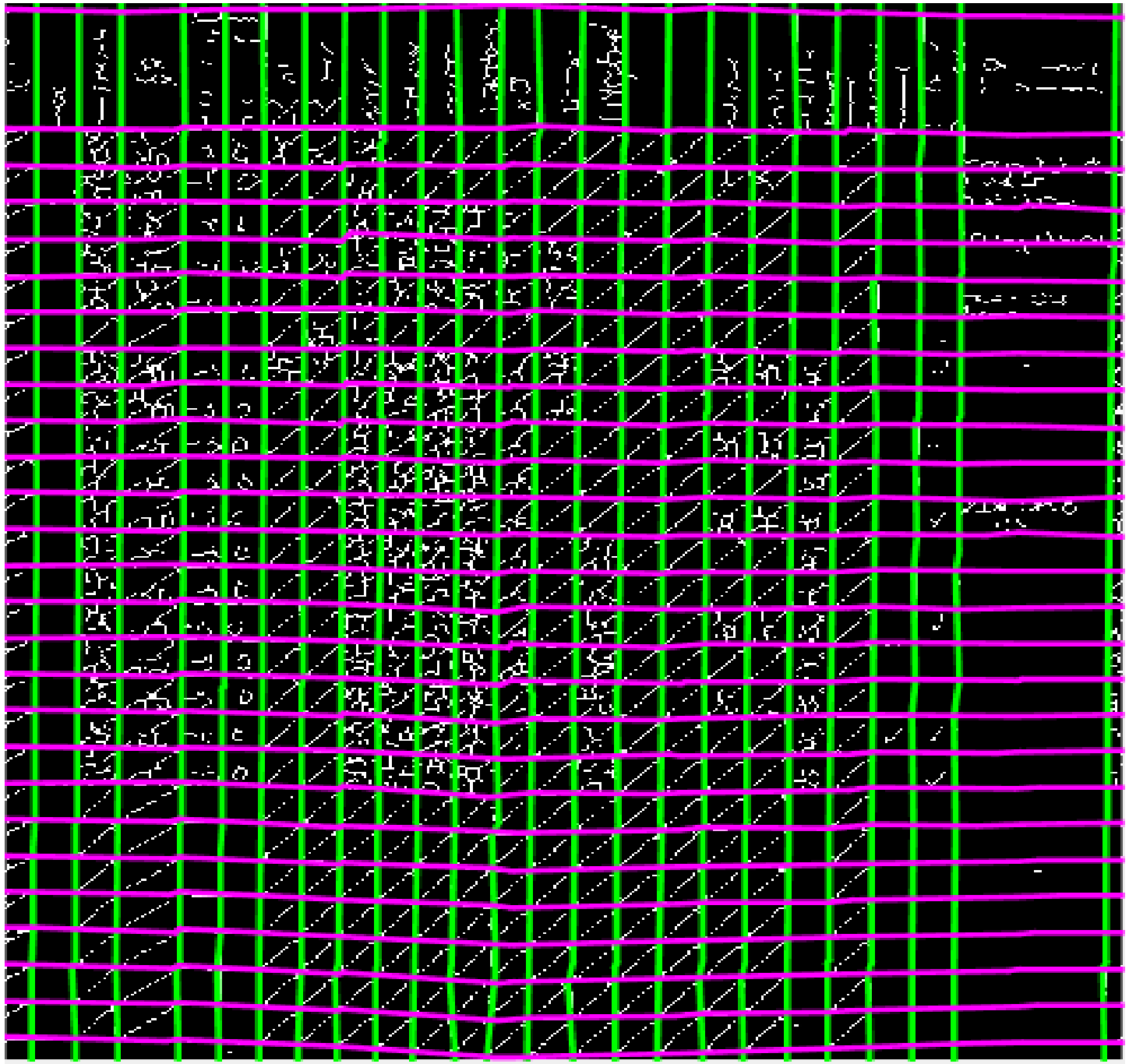
An example of a spreadsheet image transcribed by the software

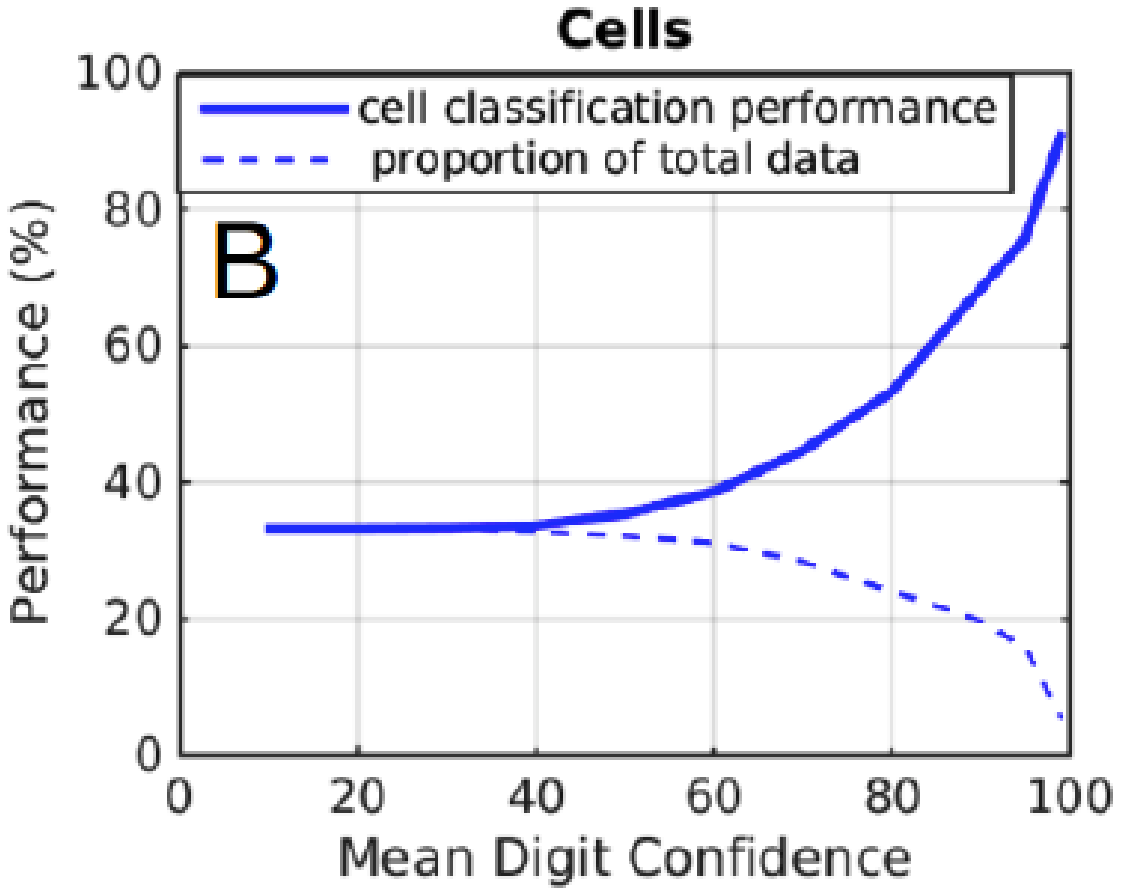


Grid Line Extraction

The grid-line extraction accounts for non-uniformities in: lighting, bends in paper, cell size, etc.

In our collected data, 93% of grid lines were accurately identified

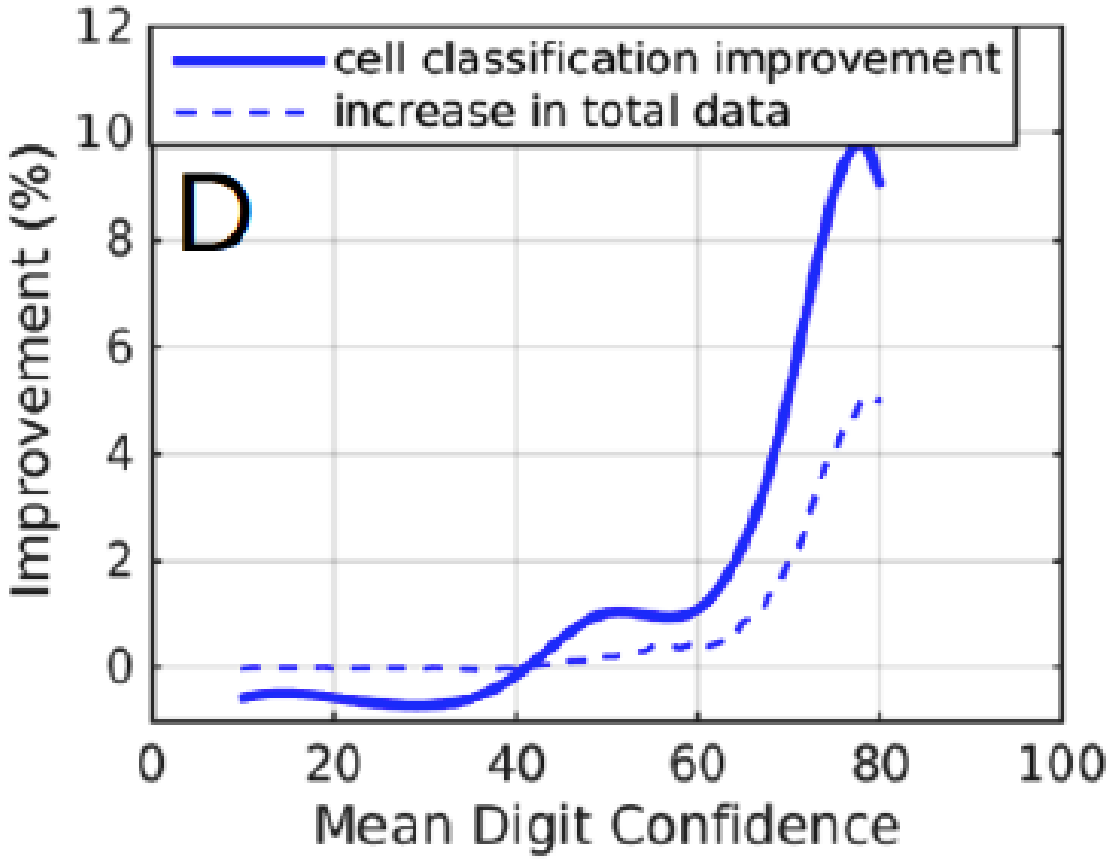




At a digit confidence threshold of 99%, cell contents are correctly classified in 90% of cases

Our tool was half the price and 11.4 times faster than a clinical research assistant

A lower bound for savings using this approach is 5.6%



After crowd feedback, the tool's classification performance improved further

At the 80% confidence threshold, we observed a 10% improvement in accuracy

The lower bound for savings using this approach was 10%

Todays Talk:

~~**1. Data collection:**~~
~~Tool to translate paper data from hospital spreadsheets into digital form~~

2. Decision support:
Method to prognosticate coma outcomes after cardiac arrest

3. Optimal Control:
AI for passive monitoring of narrative mood during conversations

4. Moving Forward
Future directions, and opportunities for collaboration

Life After Death: Techniques for the rapid prognostication of post-anoxic coma patients

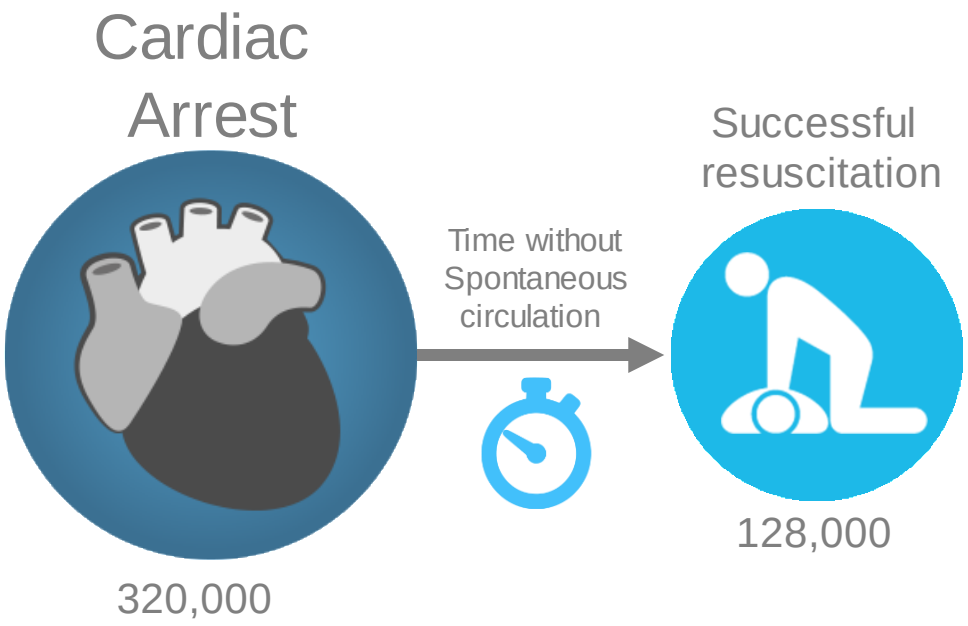
MIT Press (2018)

Cardiac arrest affects 320K people in the US annually

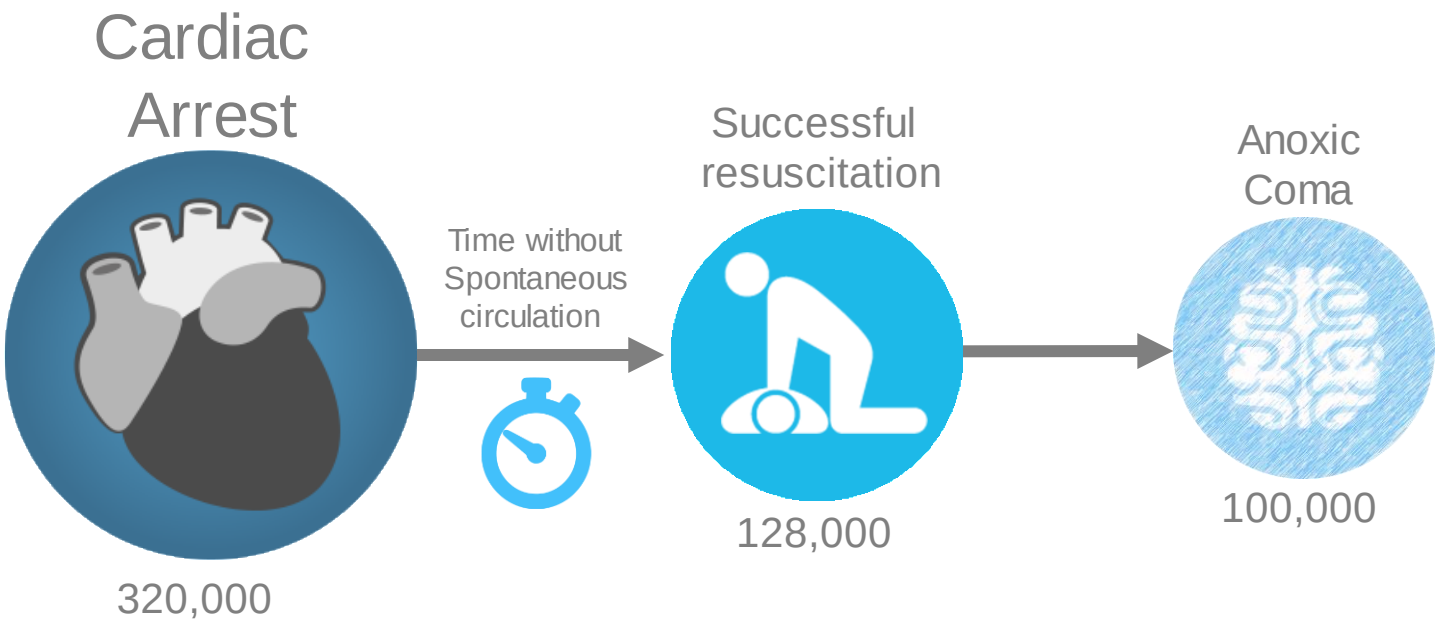
Cardiac Arrest

320,000

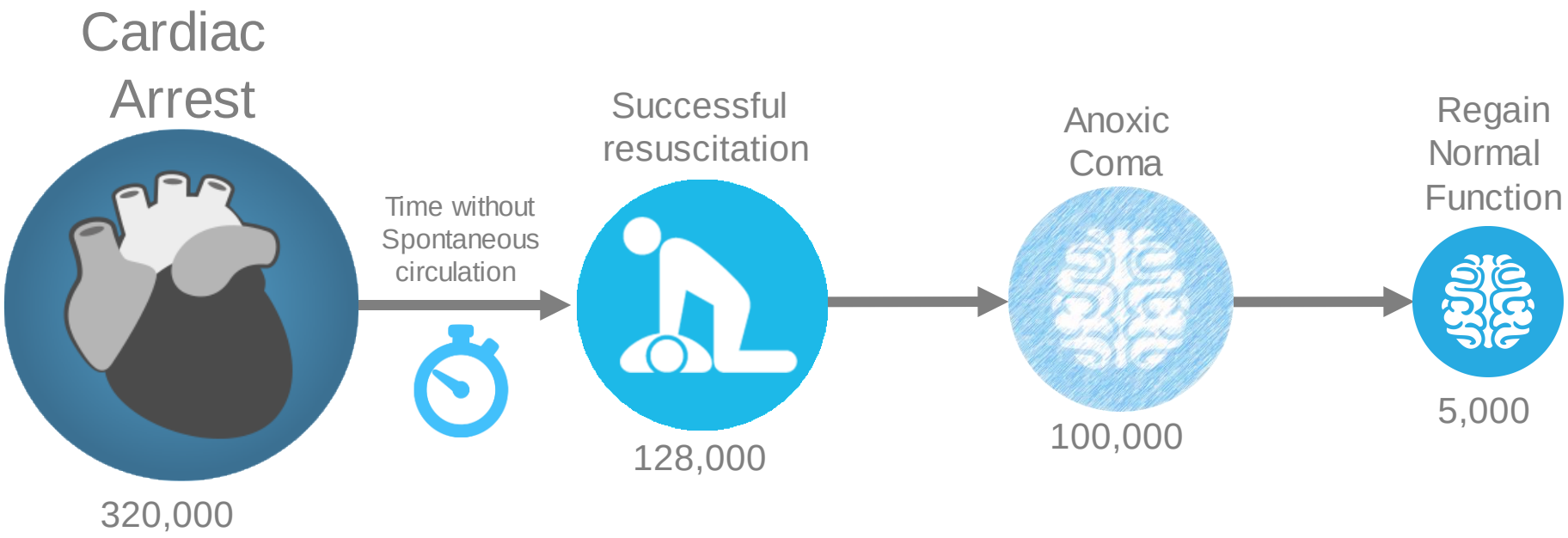
128K patients are successfully resuscitated



100K enter an indefinite, anoxia-induced coma



10K will survive, but only 5K will regain normal function



Outcome metric

Cerebral Performance Category	Conscious (Y/N)	Cerebral Disability	Consequences
1	Y	Mild	May resume independent activities with minimal complications
2	Y	Moderate	May resume independent activities while requiring some assistance
3	Y	Severe	Will require assistance to perform activities and may involve paralysis, or dementia.
4	N	Vegetative	Requires assistance to survive and will be minimally aware/responsive
5	N	Brain-Death	Requires assistance to survive and will be totally unaware/response

Outcome metric

Cerebral Performance Category	Conscious (Y/N)	Cerebral Disability	Consequences	
1	Y	Mild	May resume independent activities with minimal complications	Good
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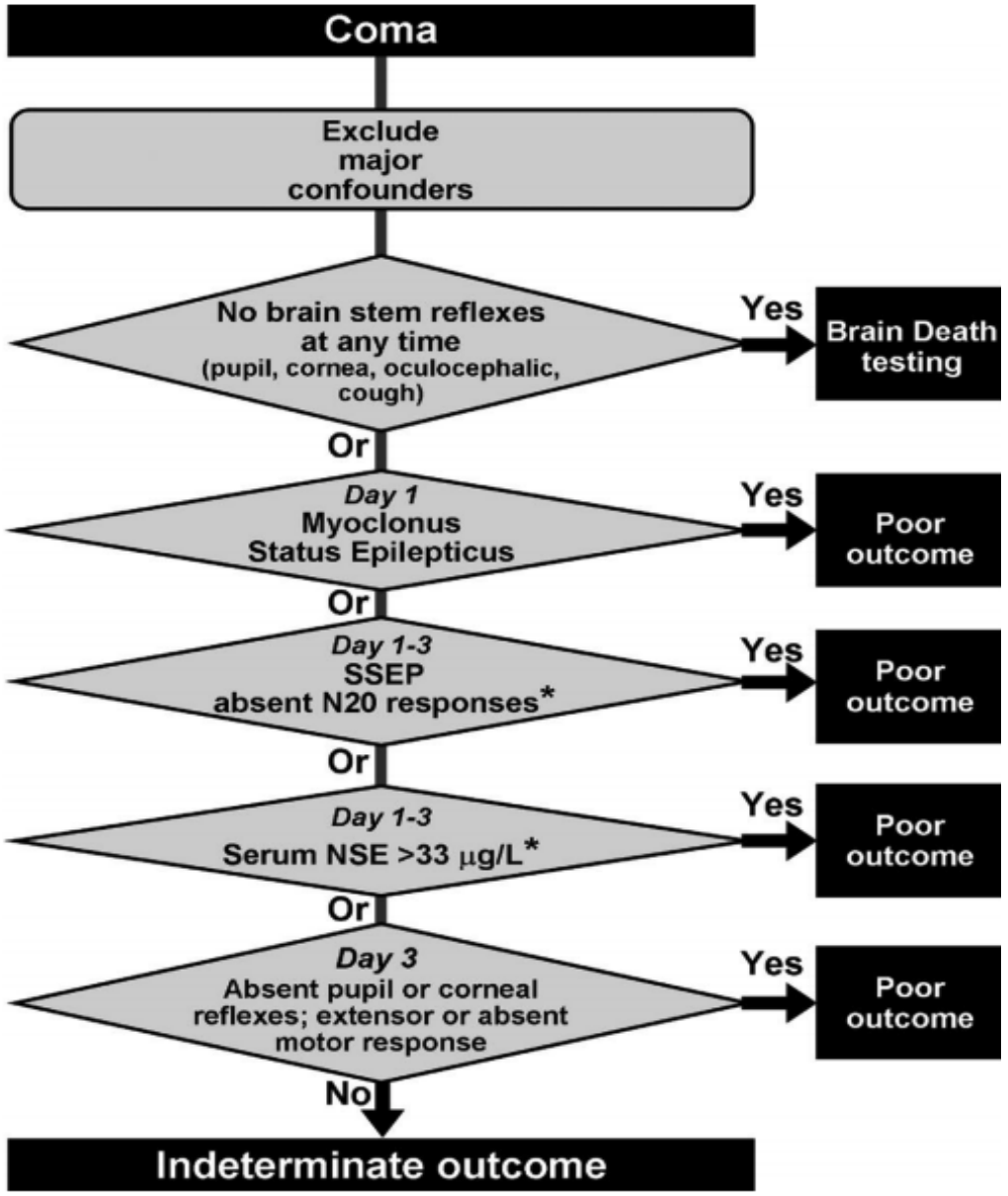
3	Y	Severe	Will require assistance to perform activities and may involve paralysis, or dementia.	Bad
4	N	Vegetative	Requires assistance to survive and will be minimally aware/responsive	
5	N	Brain-Death	Requires assistance to survive and will be totally unaware/response	

Goals of prognostication

- **Primary:** Prevent premature withdrawal care
- **Secondary:** Prevent unnecessary care
  (up to $20,000 per day in ICU)

Current Prognostic Guidelines

- A sequence of clinical observations and auxiliary tests performed at specific time points following cardiac arrest
- Accurate in predicting poor neurological outcomes when severe deficits are present (FPR < 1%)
- No guidance in cases where such clear-cut signs are lacking, or under varying protocols (e.g. therapeutic hypothermia)



The American Academy of Neurology

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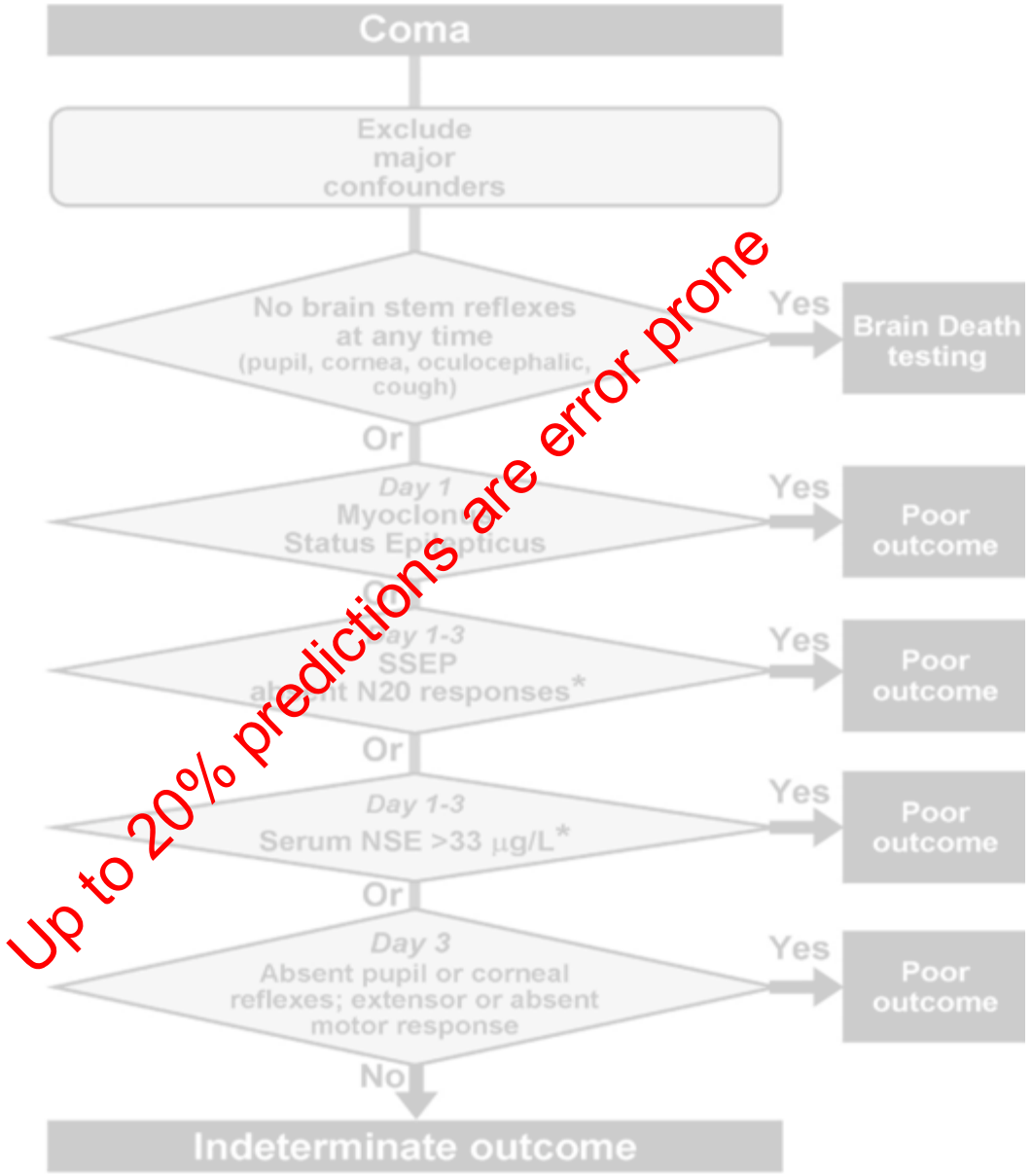

The American Academy of Neurology

Review of the Literature

EEG Features
Tjepkema-Cloostermans, 2017
AUC = 0.94 at 24 hours
N = 283

Pain-related SSEP
Zanatta, 2015
AUC = 0.84 at 72 hours
N = 167

NSE
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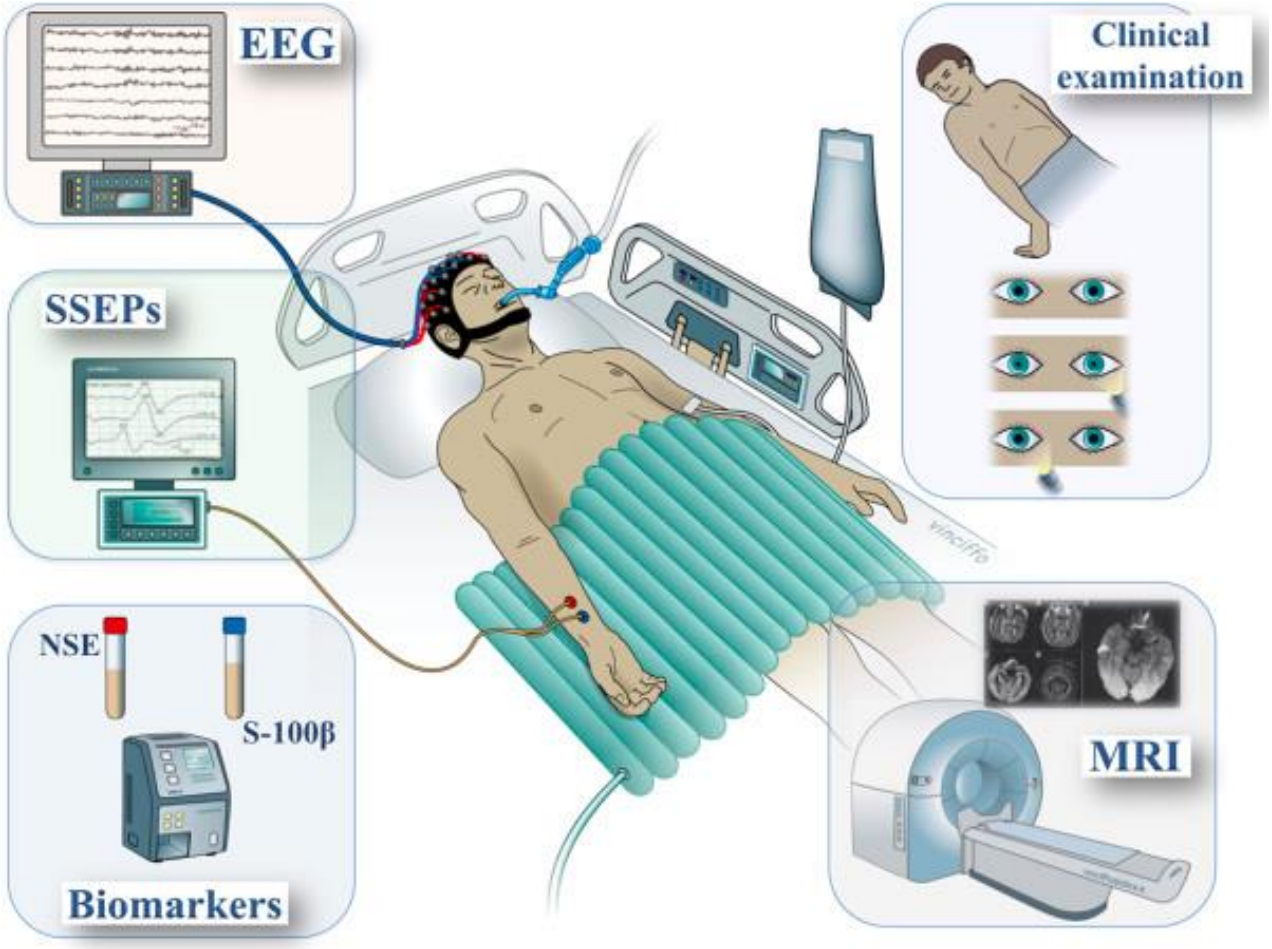
AUC = 0.77 at 24 hours
N = 153



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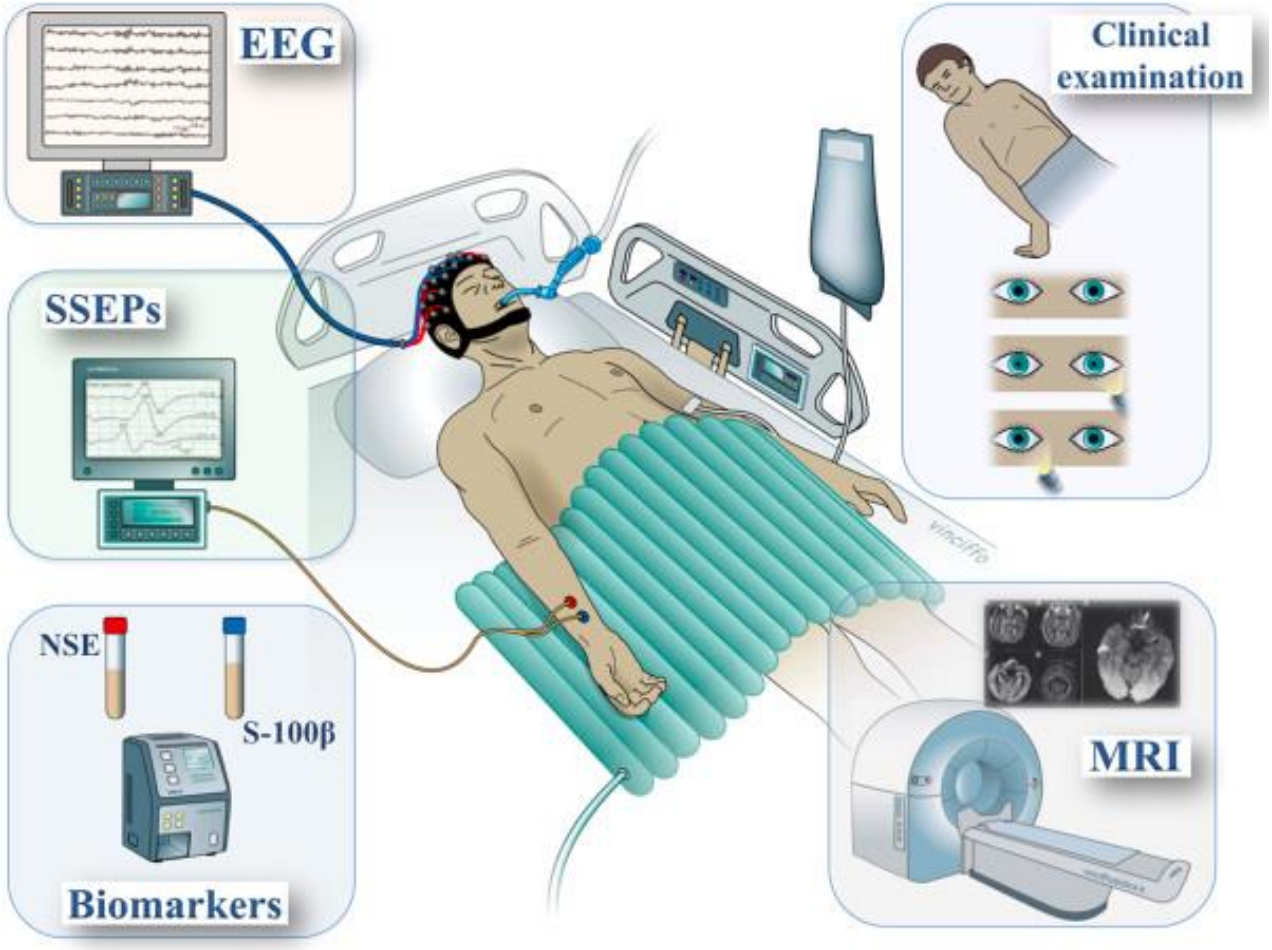

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Conclusions

- **Limited Sample Sizes:** larger samples are needed

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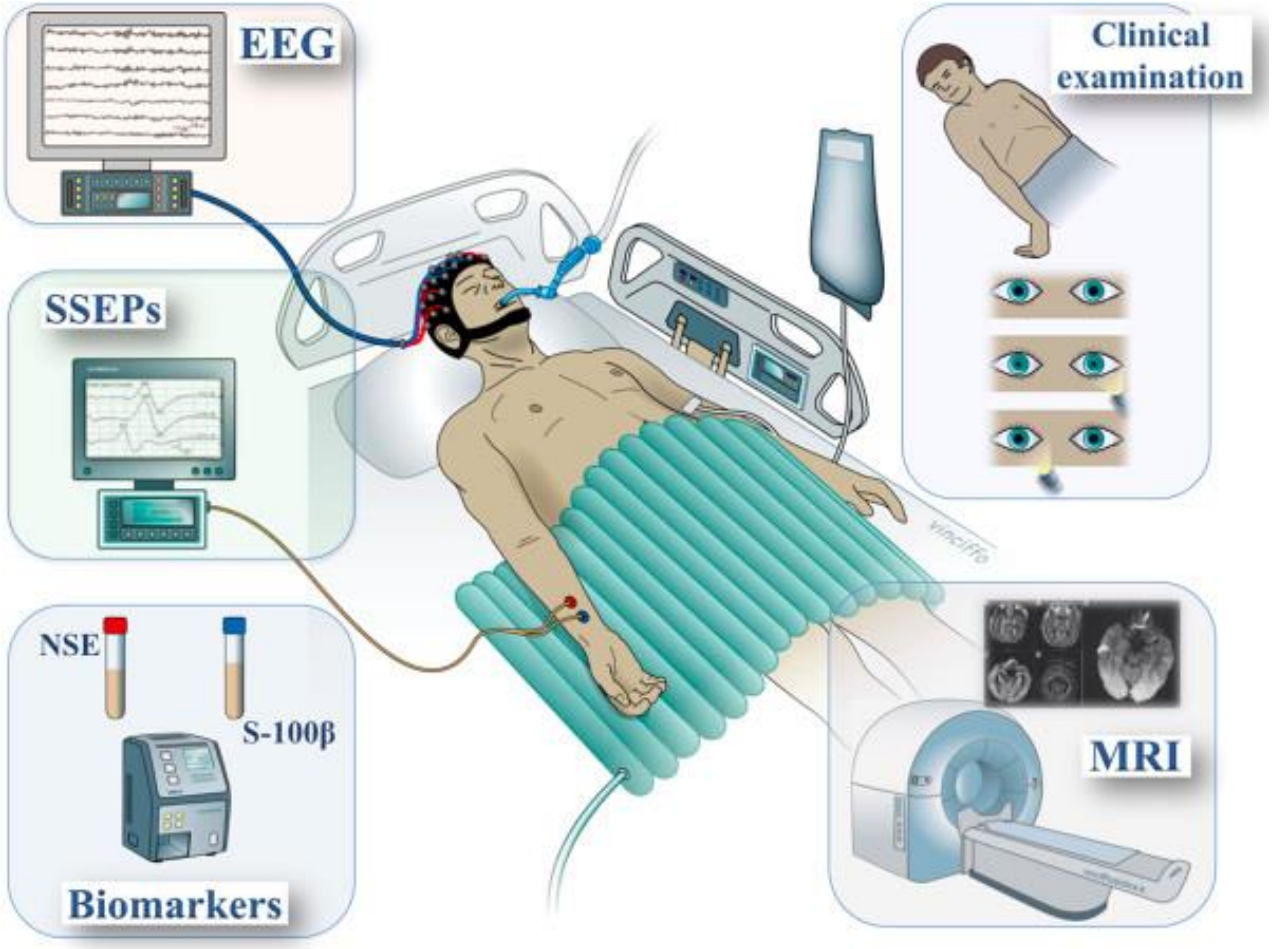

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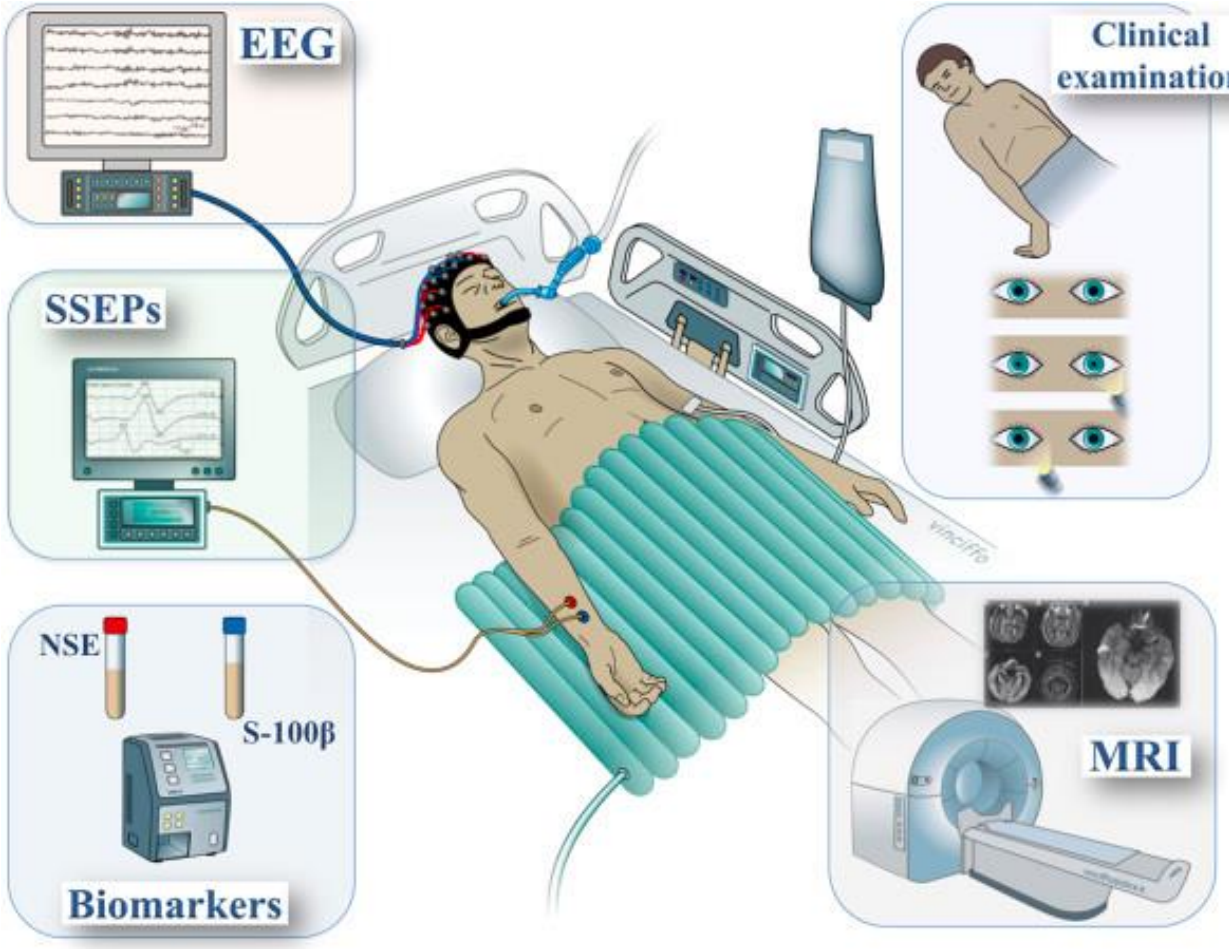

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- **Limited Sample Sizes:** larger samples are needed
- **Time Specific:** prediction should be possible at all points in time

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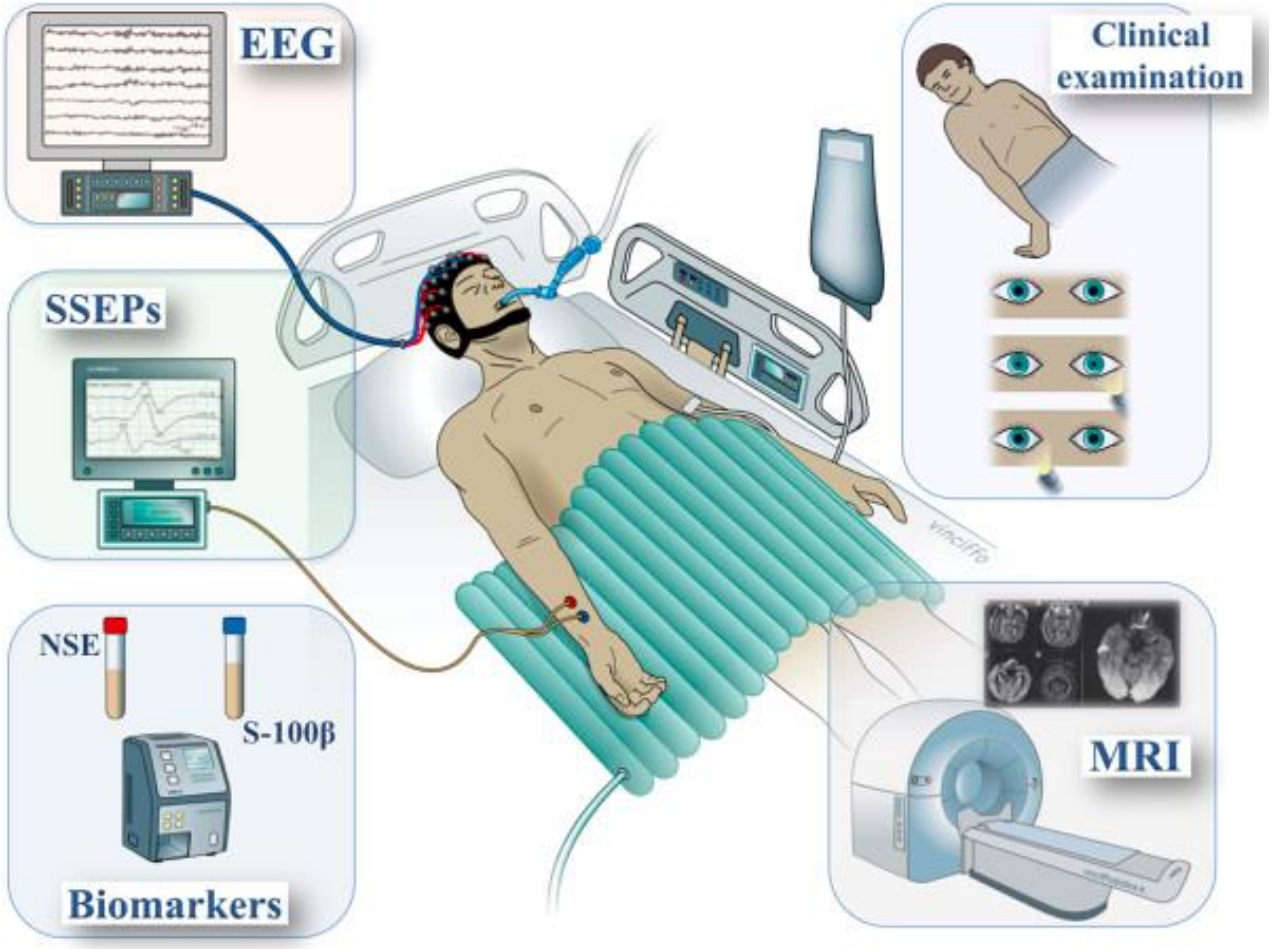

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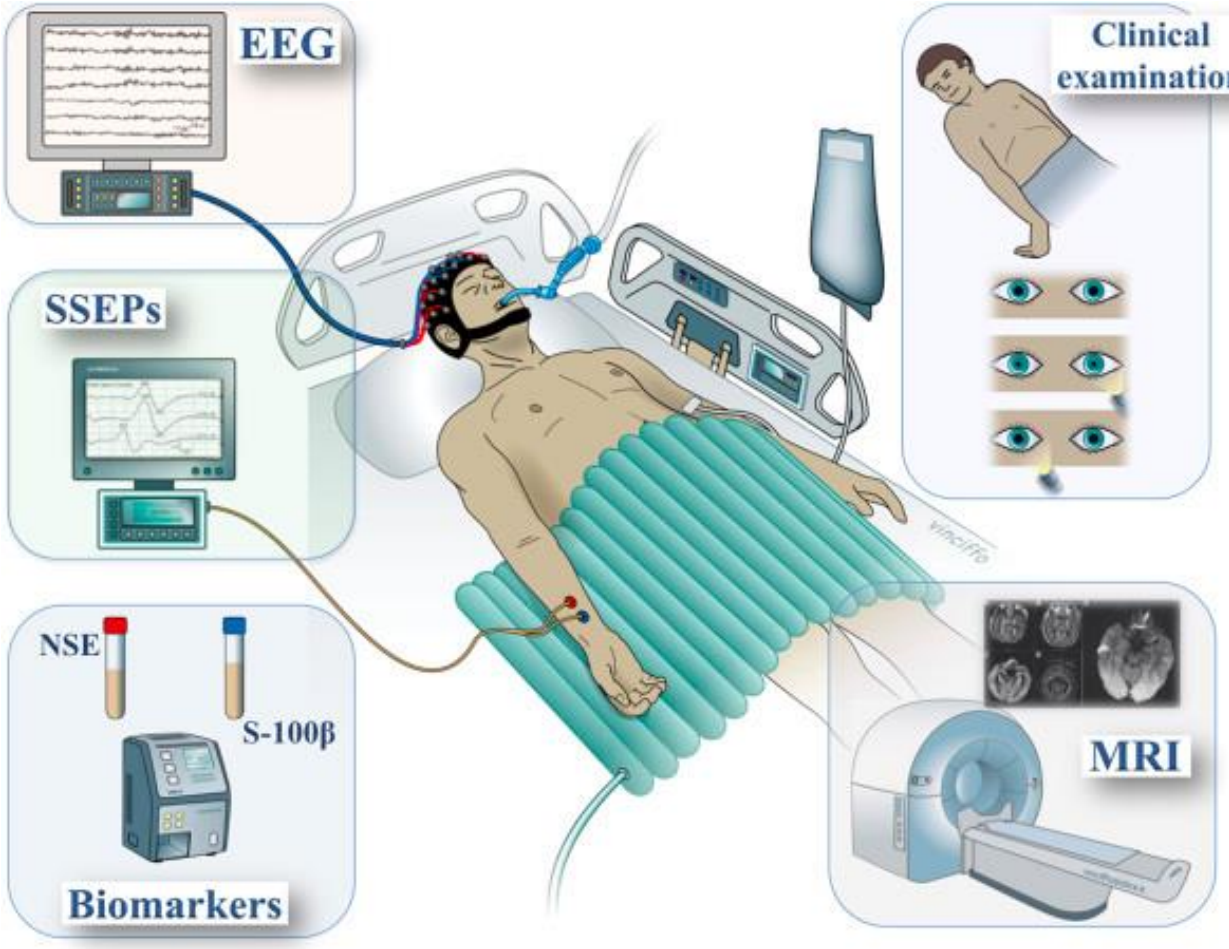

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- **Limited Sample Sizes:** larger samples are needed
- **Time Specific:** prediction should be possible at all points in time
- **Classification focused:** risk scoring may be better

Review of the Literature

EEG Features
Tjepkema-Cloostermans, 2017
AUC = 0.94 at 24 hours
N = 283

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NSE
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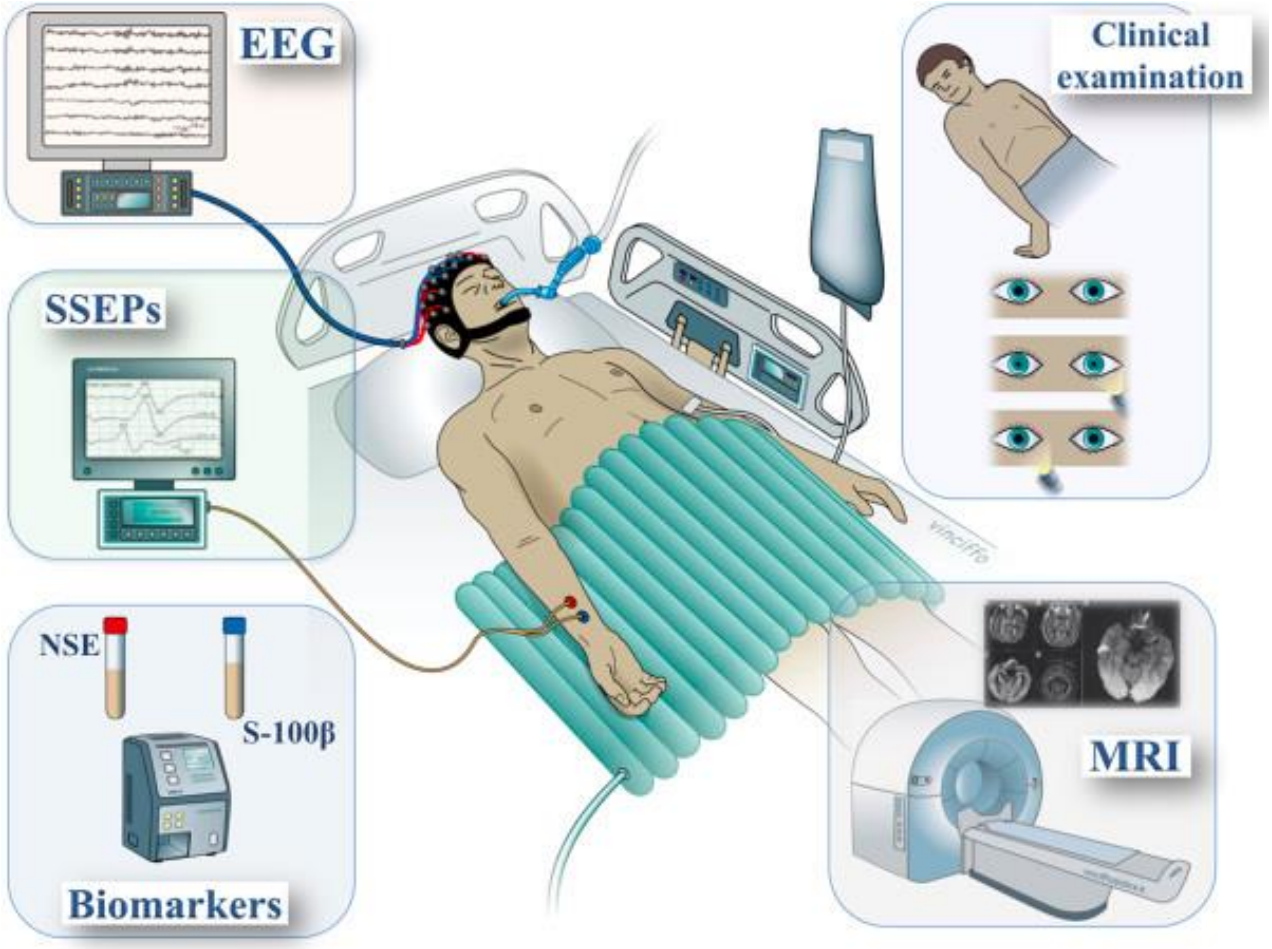

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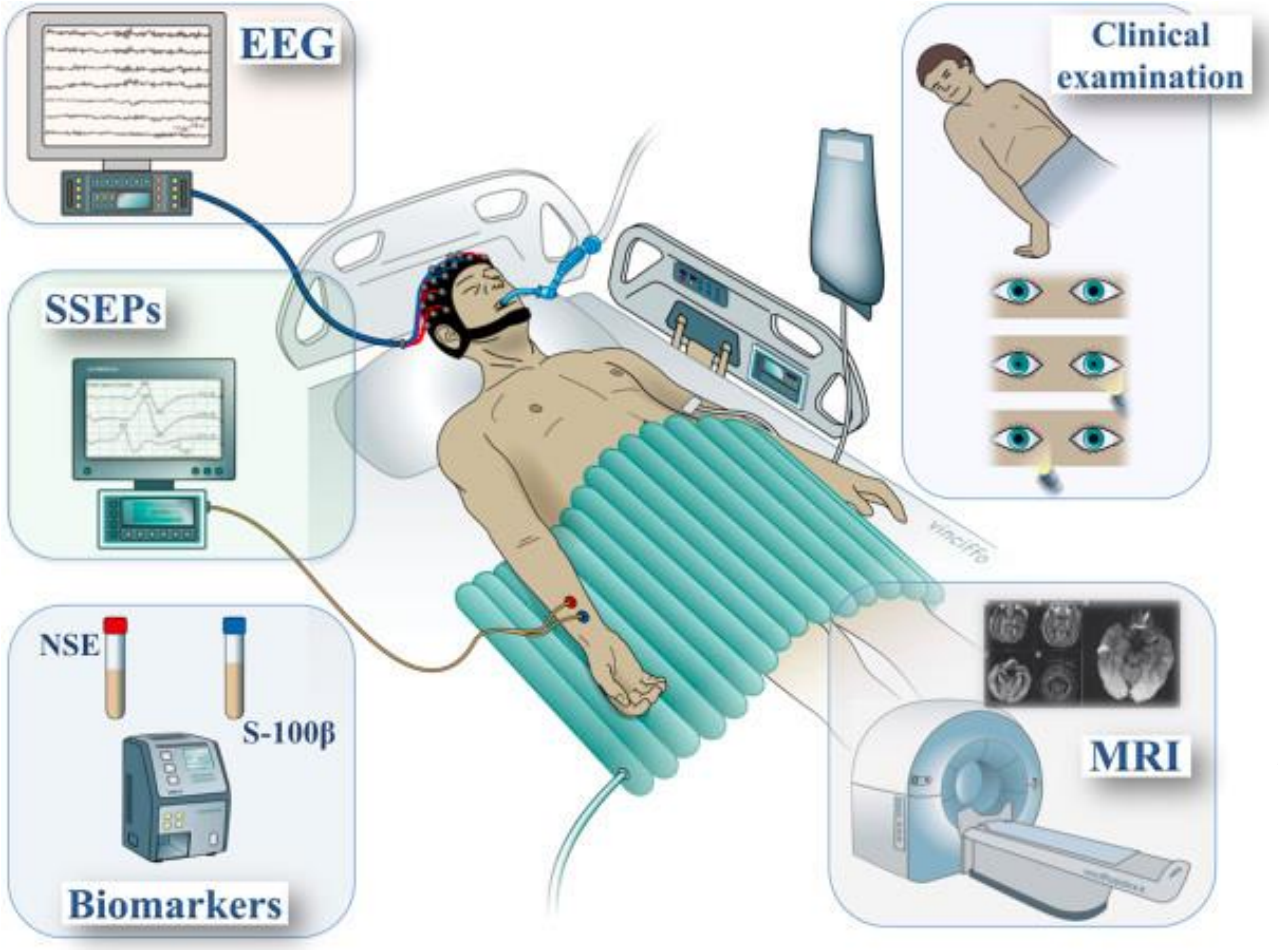

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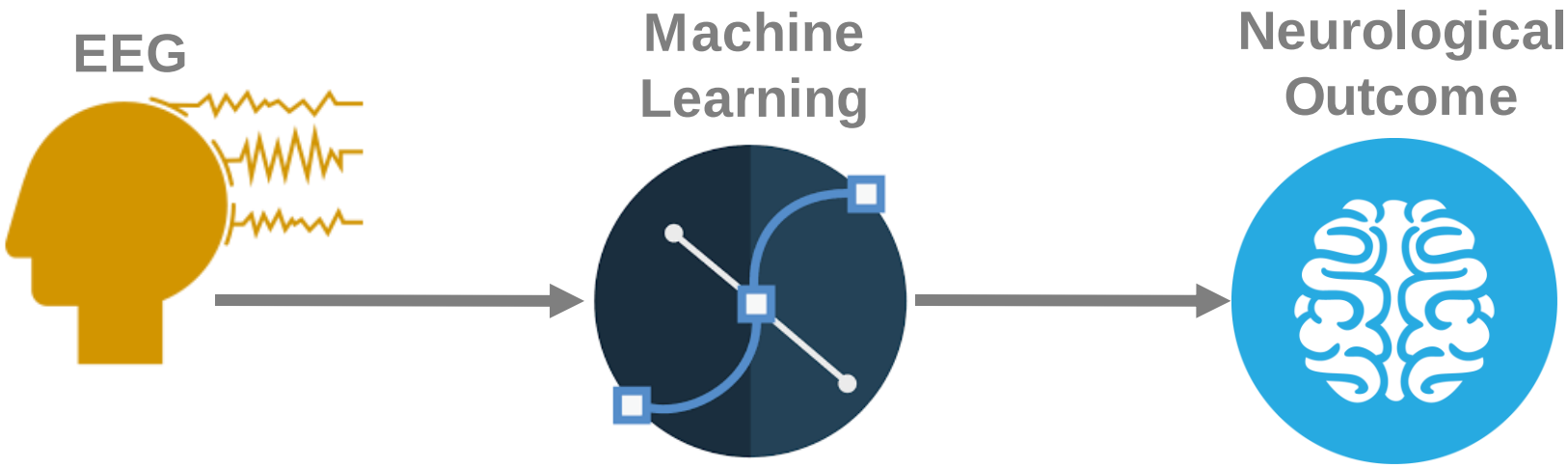
Conclusions

- **Limited Sample Sizes:** larger samples are needed
- **Time Specific:** prediction should be possible at all points in time
- **Classification focused:** risk scoring may be better
- **EEG alone can provide state-of-the-art performance**

Our Goal: Build a better prognostication algorithm



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2. Time-sensitive

3. Models that assess risk

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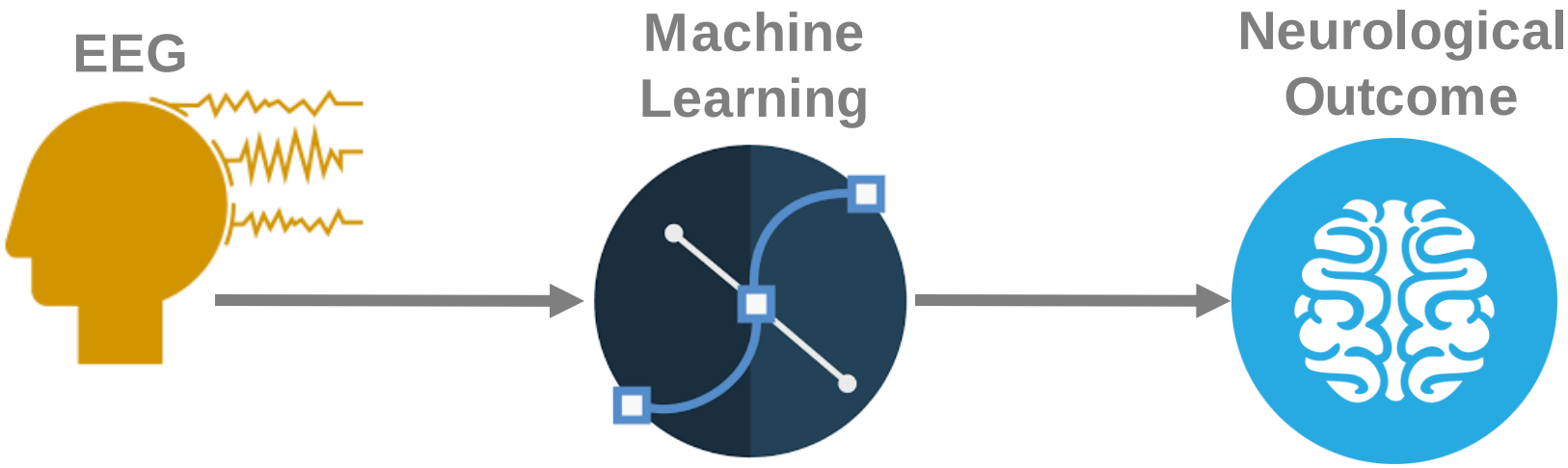

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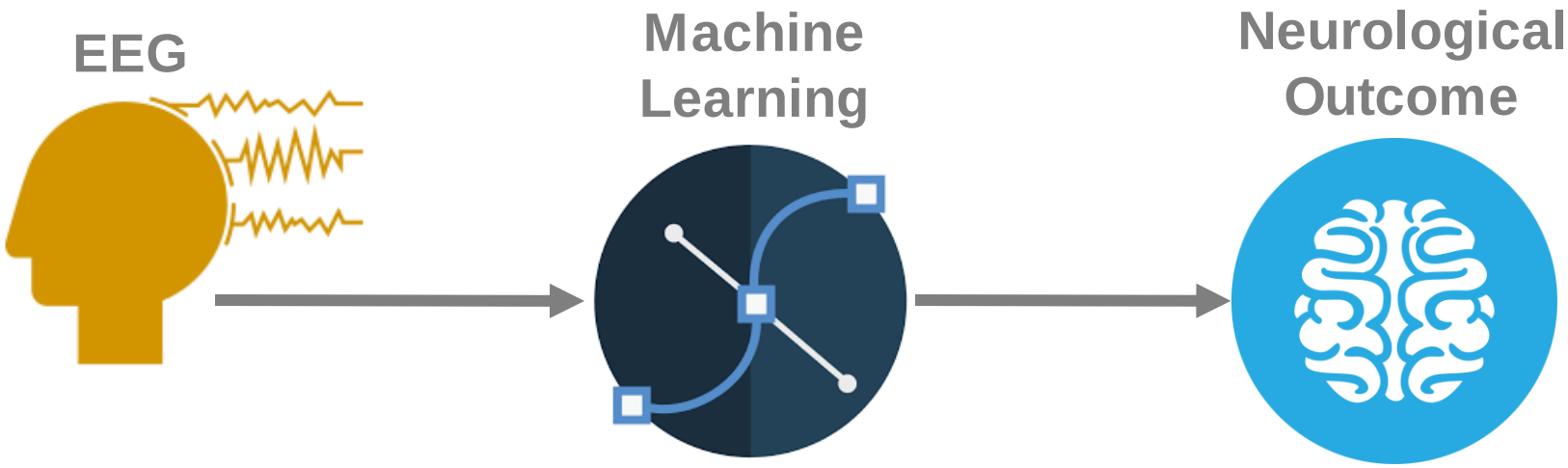

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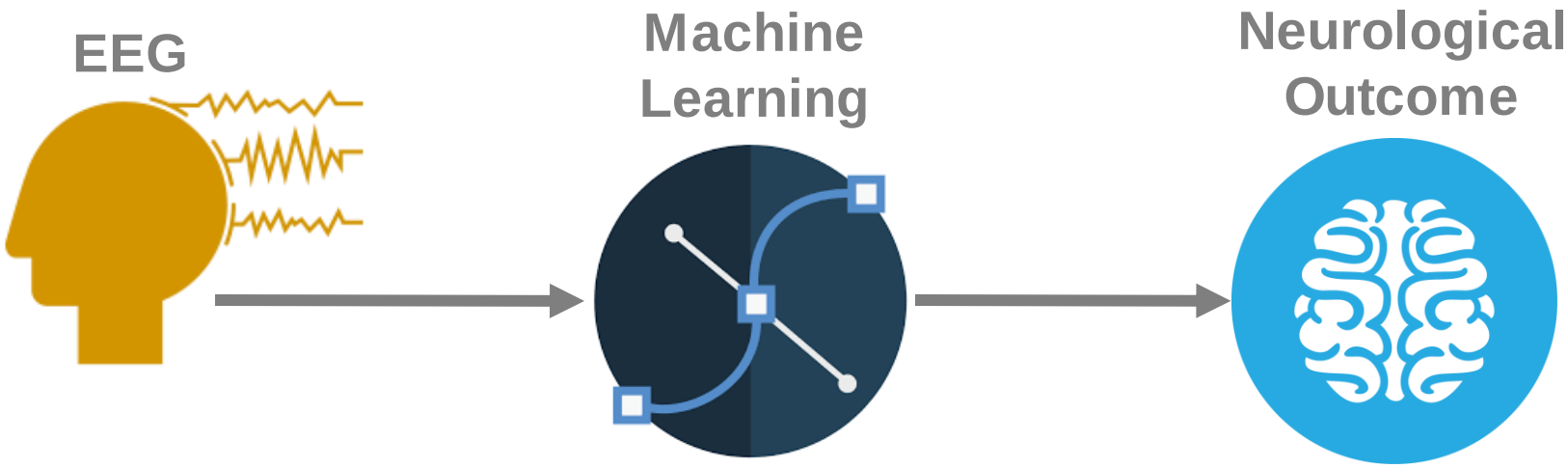

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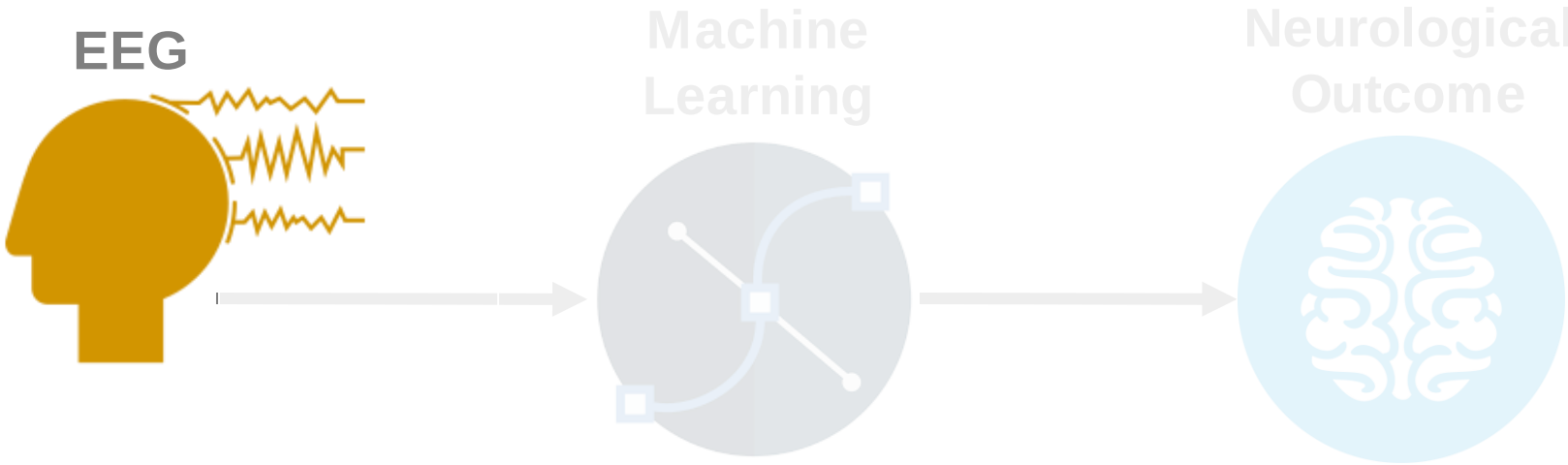

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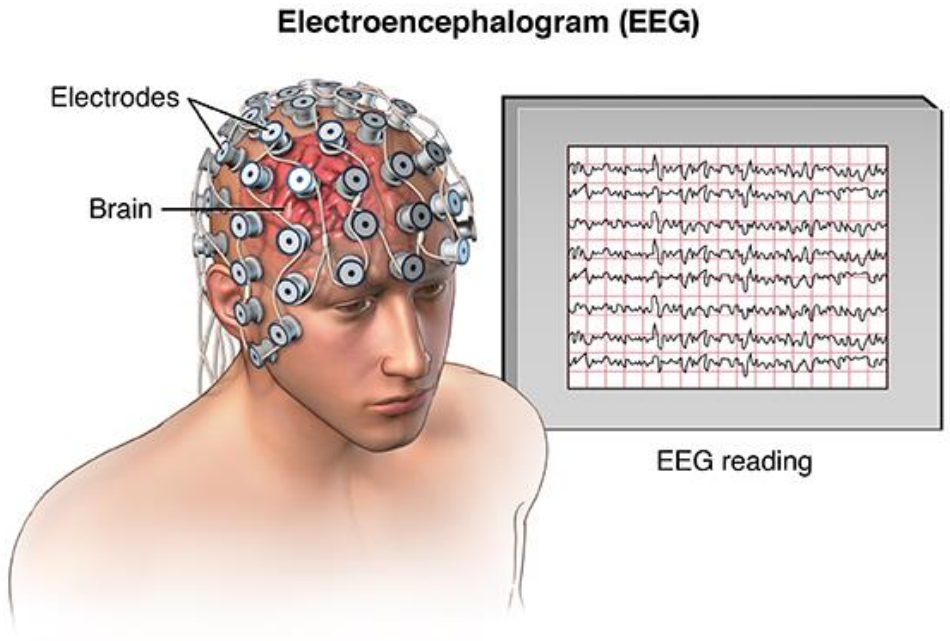
EEG Collection and Interpretation

- Each EEG electrode records an **ensemble** of cellular activity near the location of the electrode

- Electrode Placement was in accordance with the International 10-20 system



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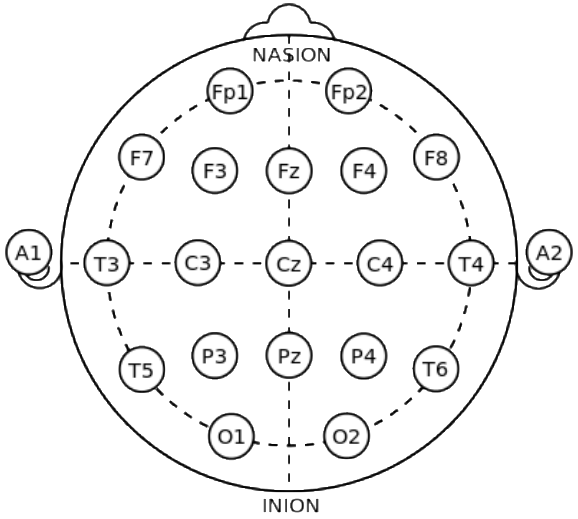
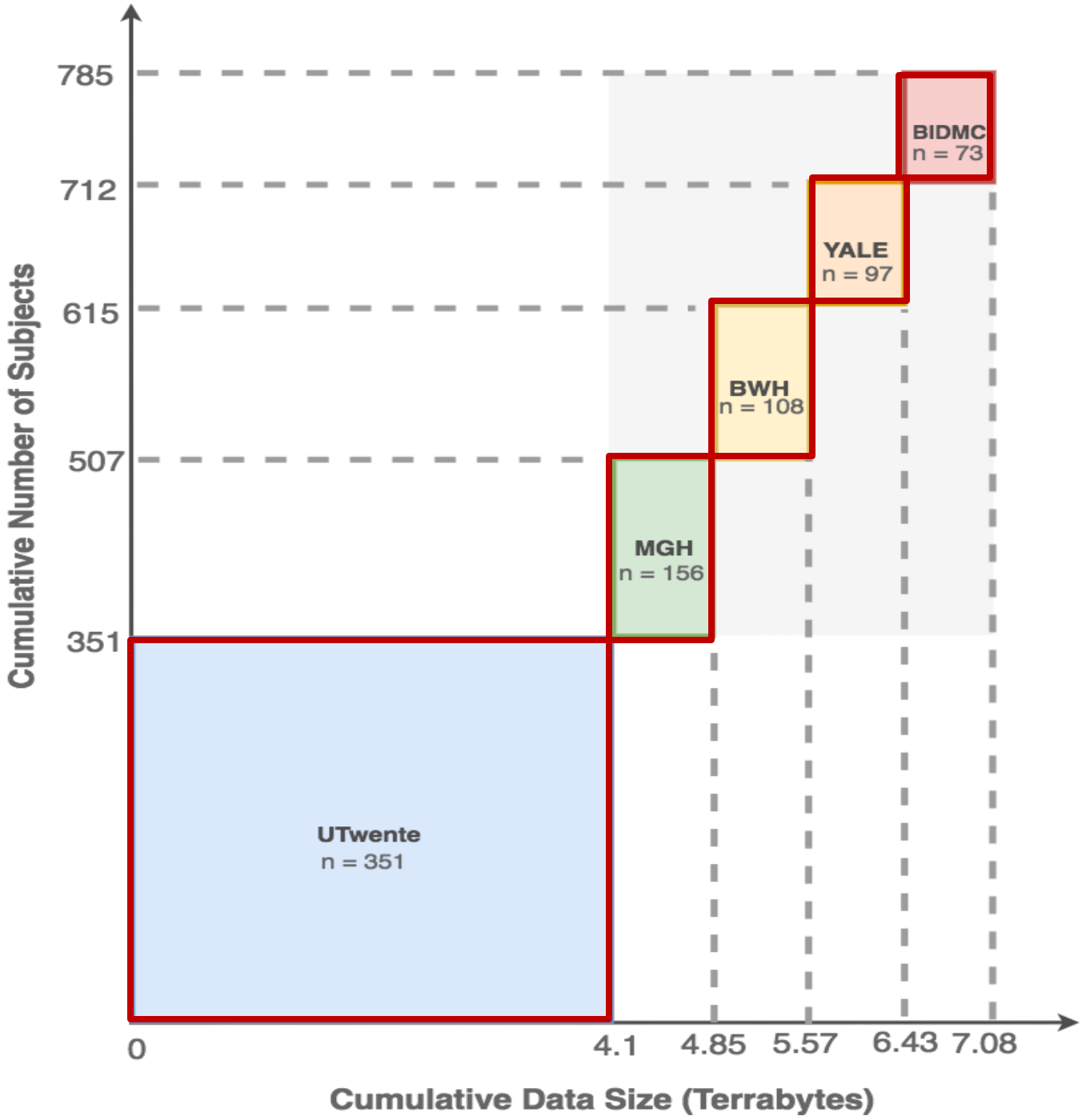


EEG data

- 5 contributing institutions
- 785 unique patients
- 7 terabytes of data



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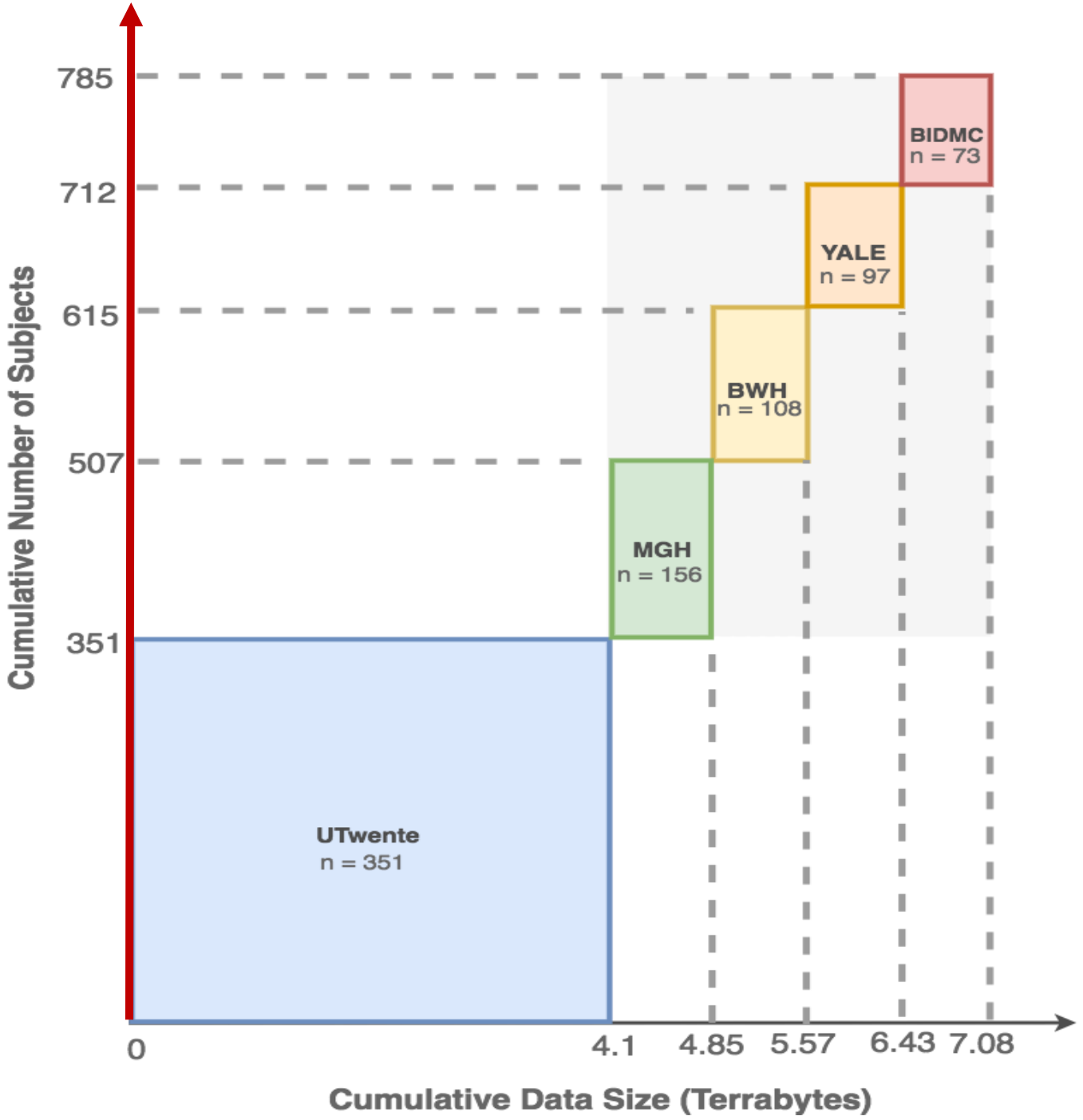

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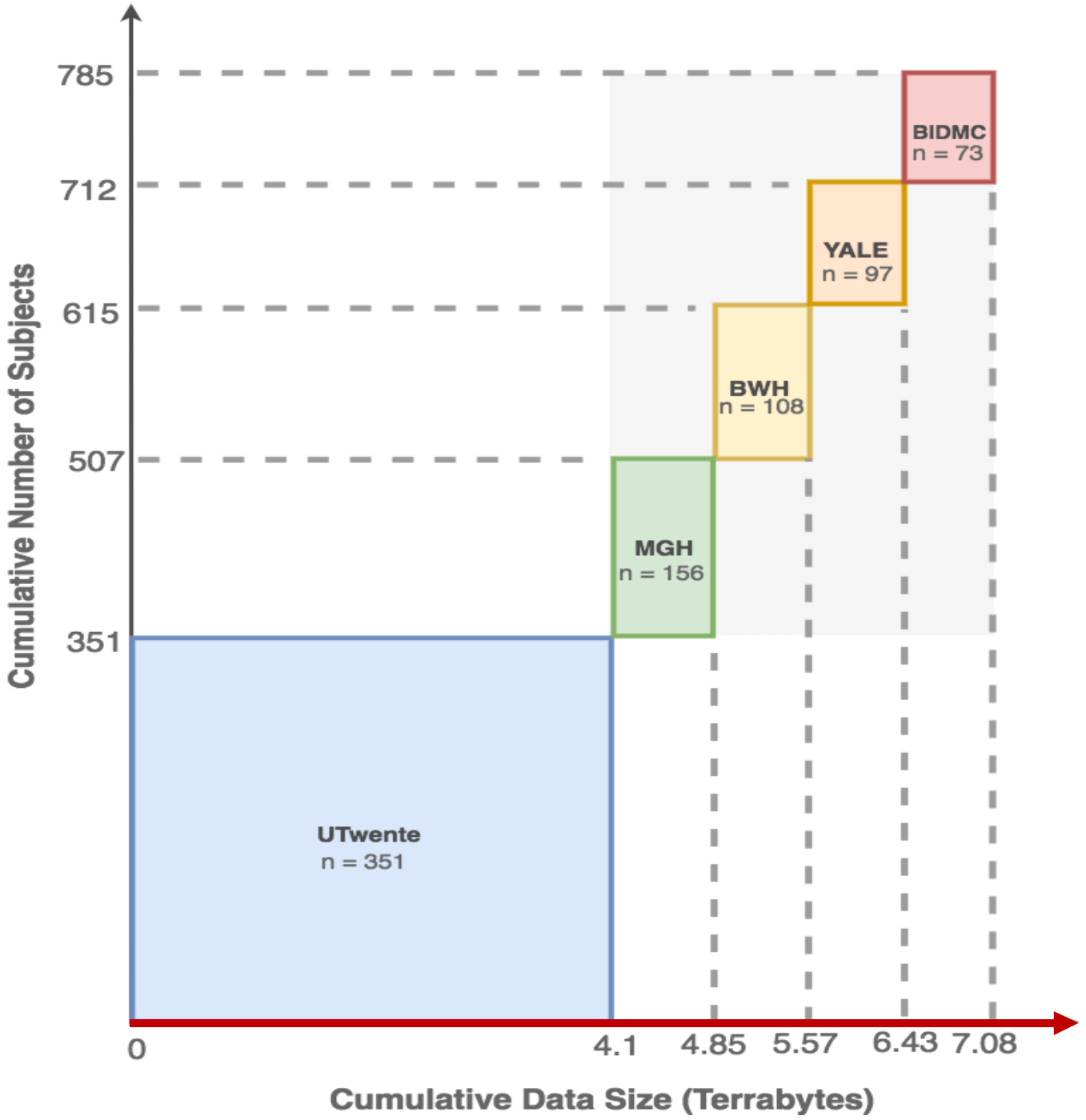

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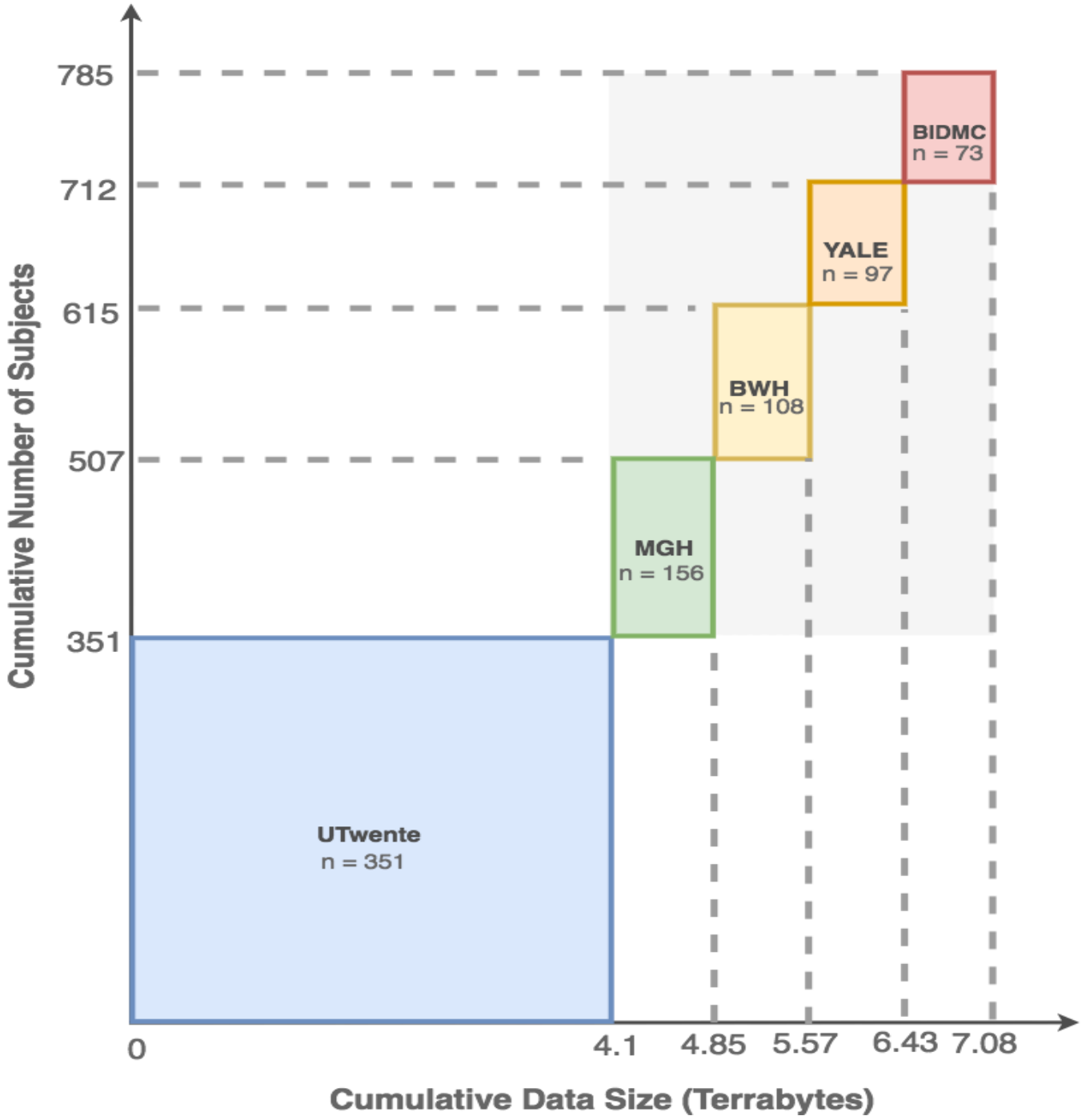
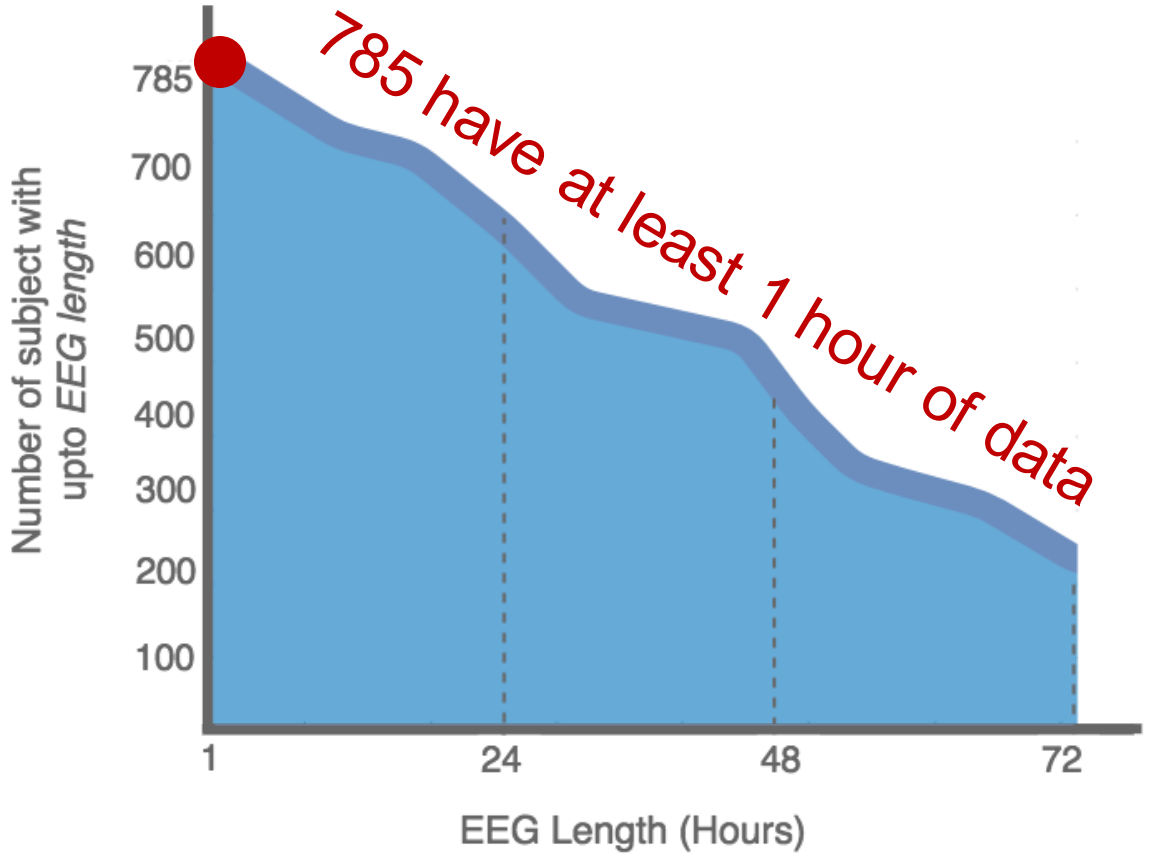


EEG temporal properties

- Data densities linearly decrease over time
- EEG withdrawal is assessed approximately once every 24 hours



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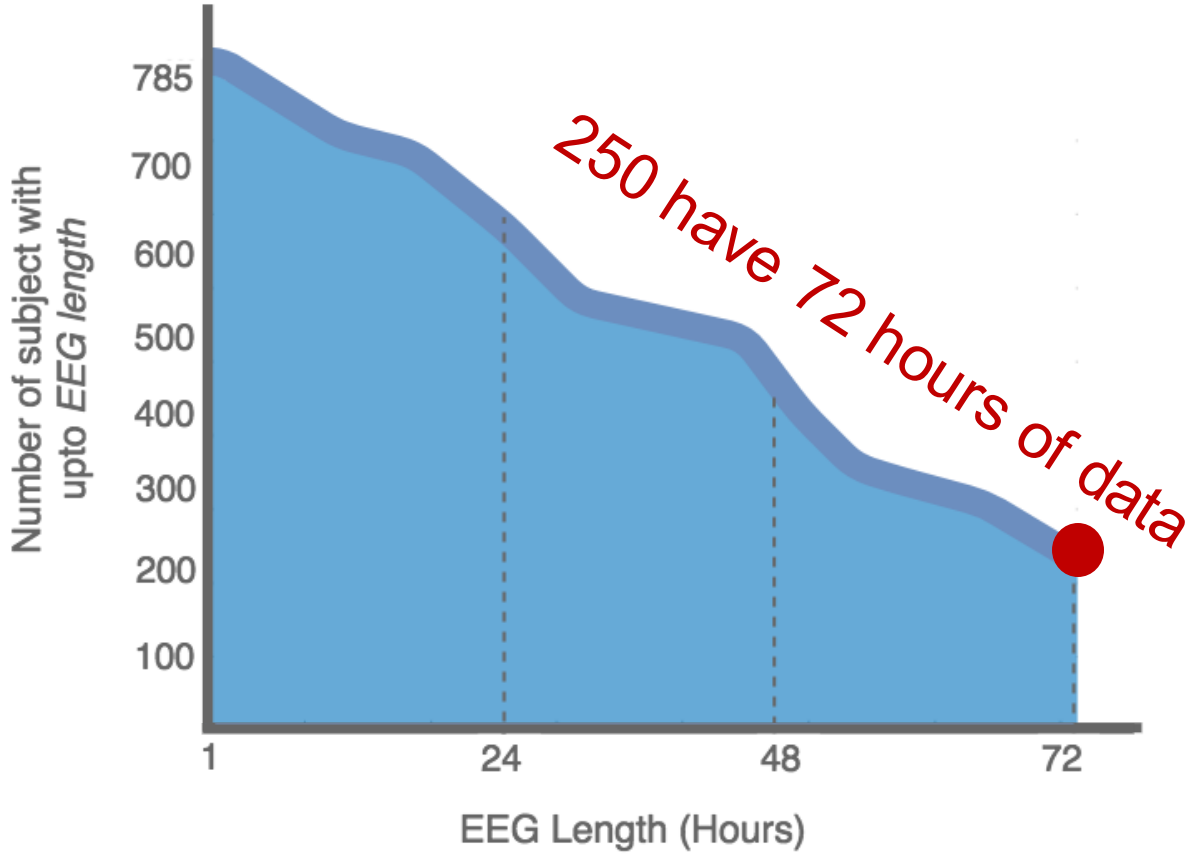

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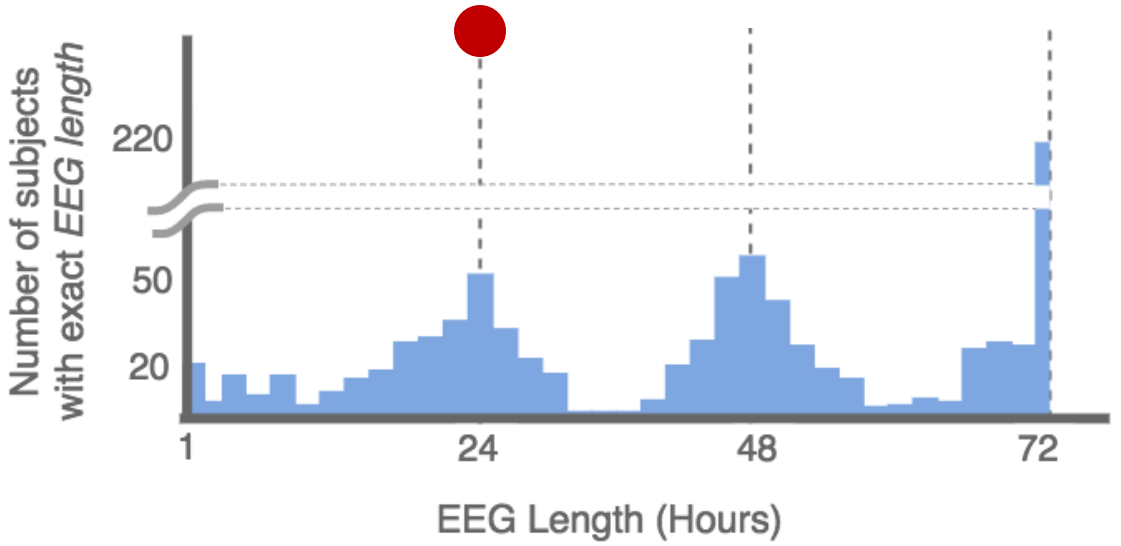

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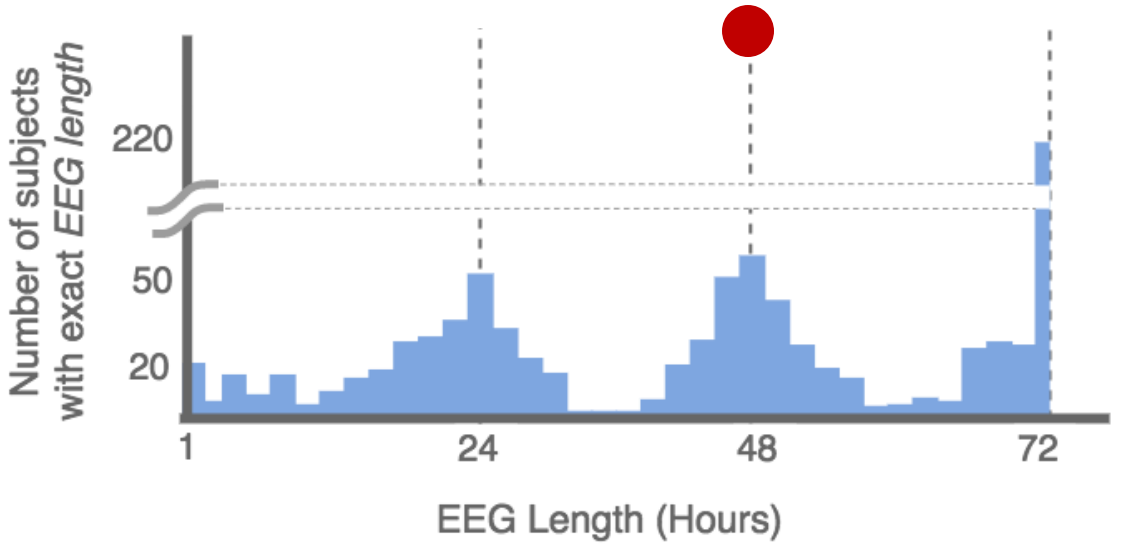

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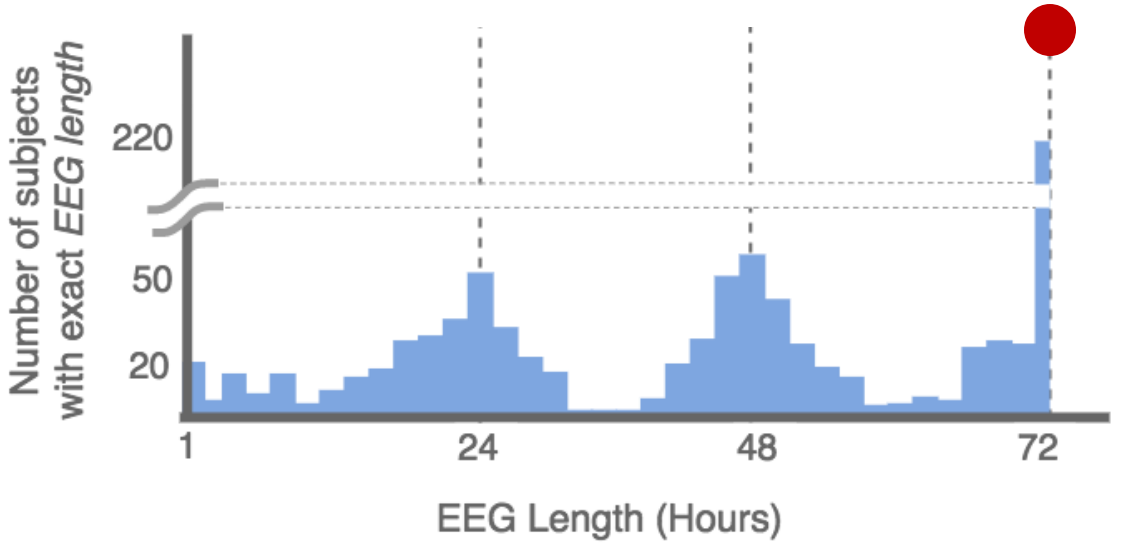
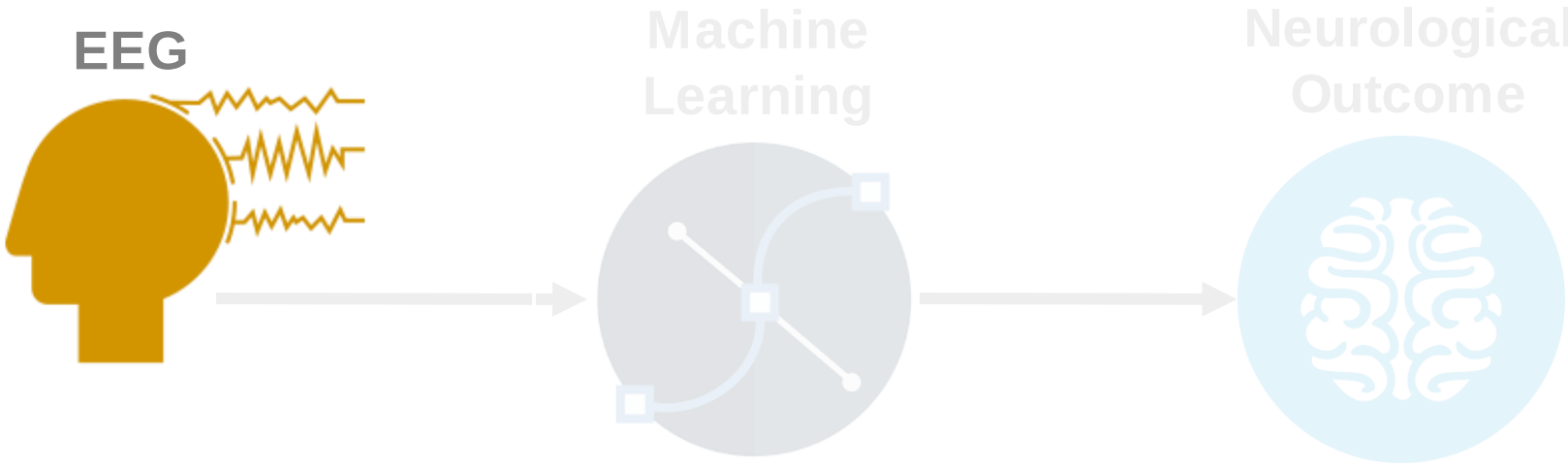


What about the clinical data?

Clinical Characteristics

Clinical Feature (Mean)	Good Outcomes	Bad Outcomes
Age (Years)	57	63
Gender (% Male)	68	68
ROSC (Mins)	19.47	25.7
Rhythm at Arrest (%)		
VFib	69	34
Other (PEA / Asystole)	25	61
Unknown	*6*	*5*
Cause of Arrest (%)		
Pulmonary	50	34
Anesthesia	3.6	8.5
Neurologic	9.6	13.8
Other/Unknown (%)	*36.8*	*43.7*
Arrest Location		
In Hospital (%)	9	11
Out of Hospital (%)	63	56
Unknown (%)	28	33

Data Collection



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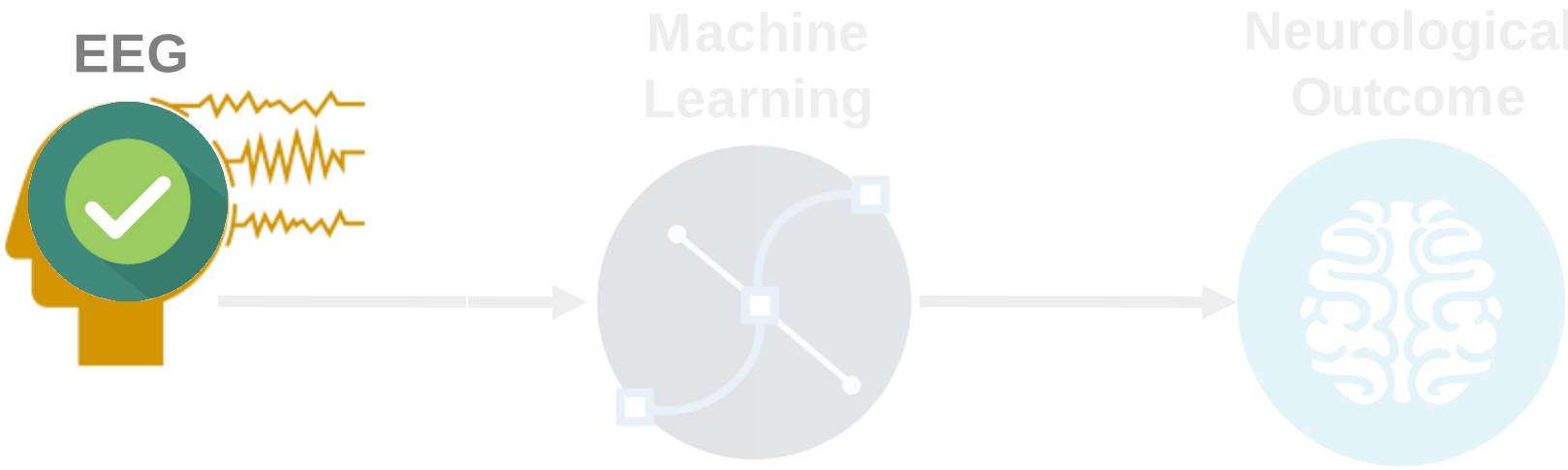

1. Collected an EEG archive 2x larger than largest set previously described in the literature

2. Time-sensitive

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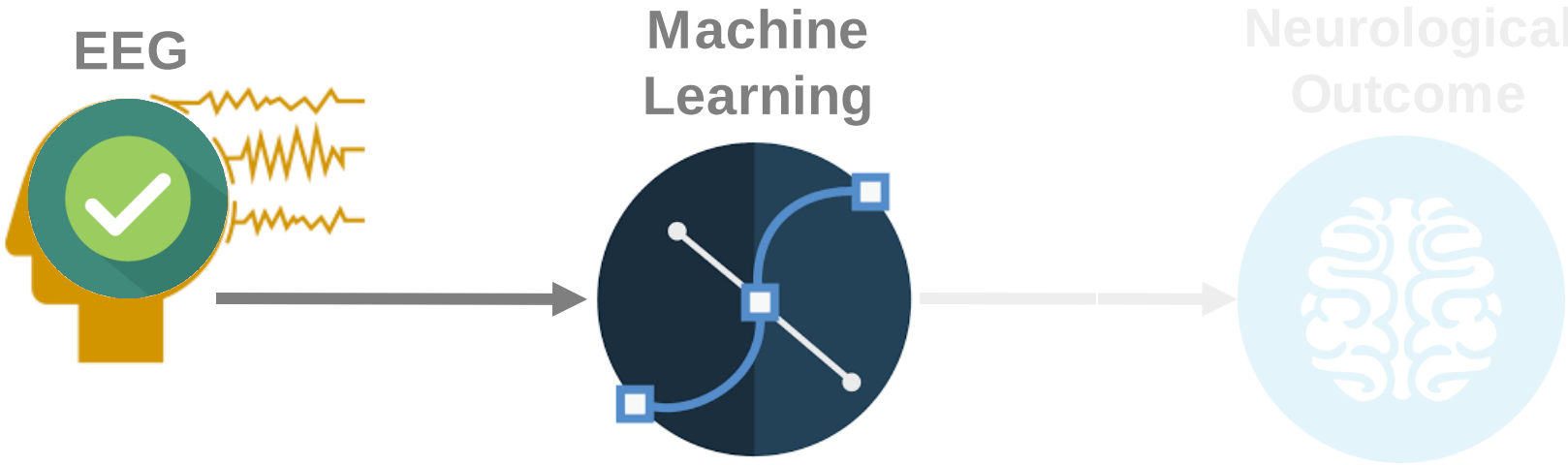
Deploy *time-sensitive* modeling approaches



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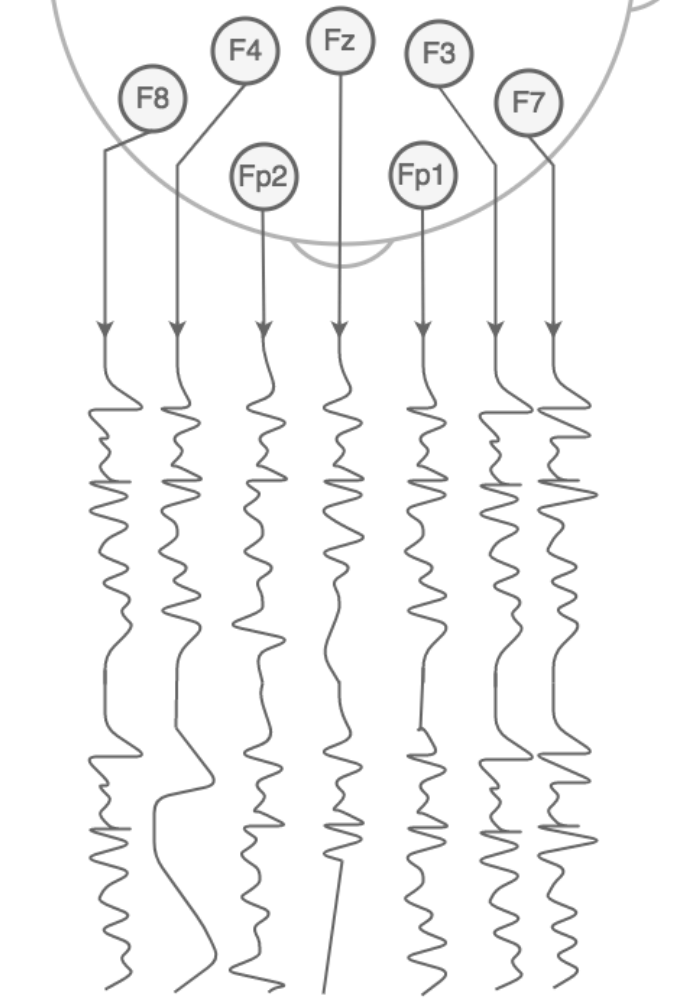

2. Identify artifacts in five second epochs

2.1 Disconnects and saturation

2.2 Eye and muscle artifact

2.3 Moment-based artifacts

3. Choose five minute epochs with minimal artifact

3.1 Generate artifact score

3.2 Identify cleanest epochs in each hour of data

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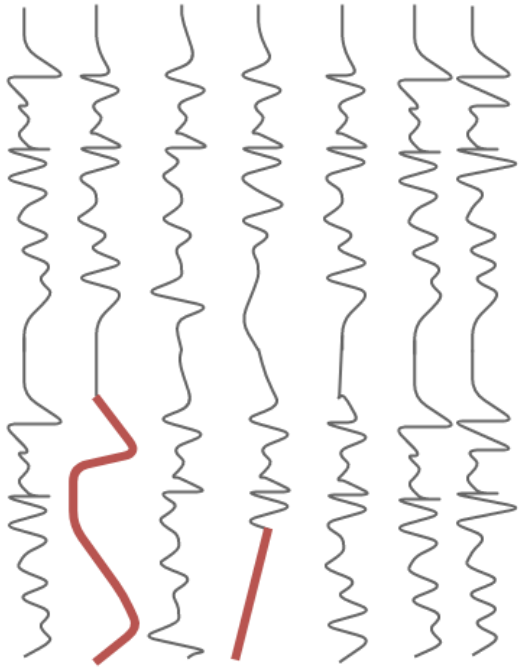

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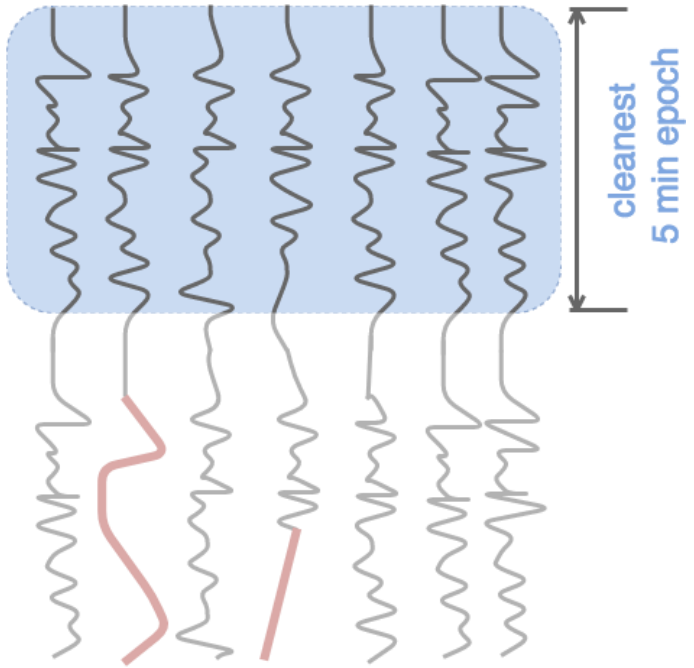
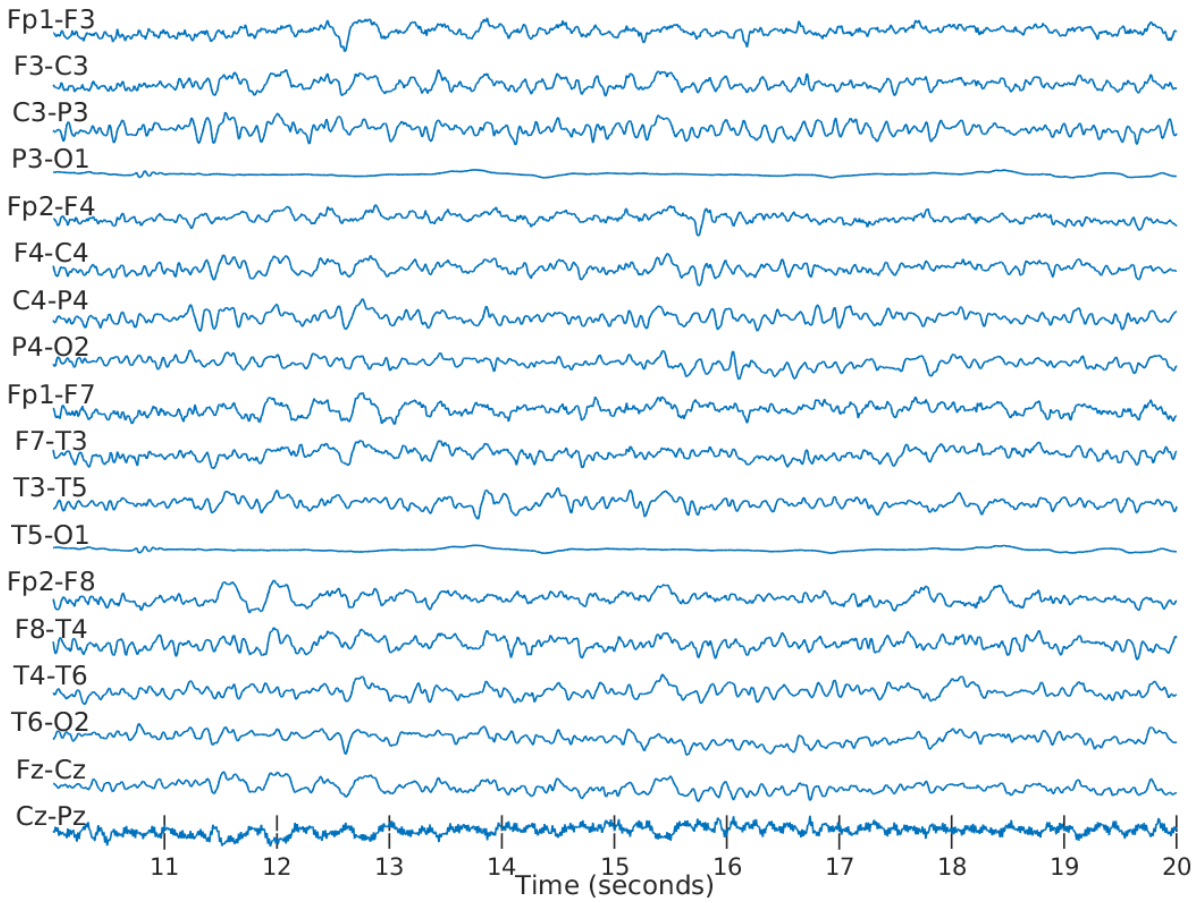


52 features to describe three signal qualities

- Complexity (21 features)
- Category (24 features)
- Connectivity (7 features)



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  e.g. Shannon Entropy

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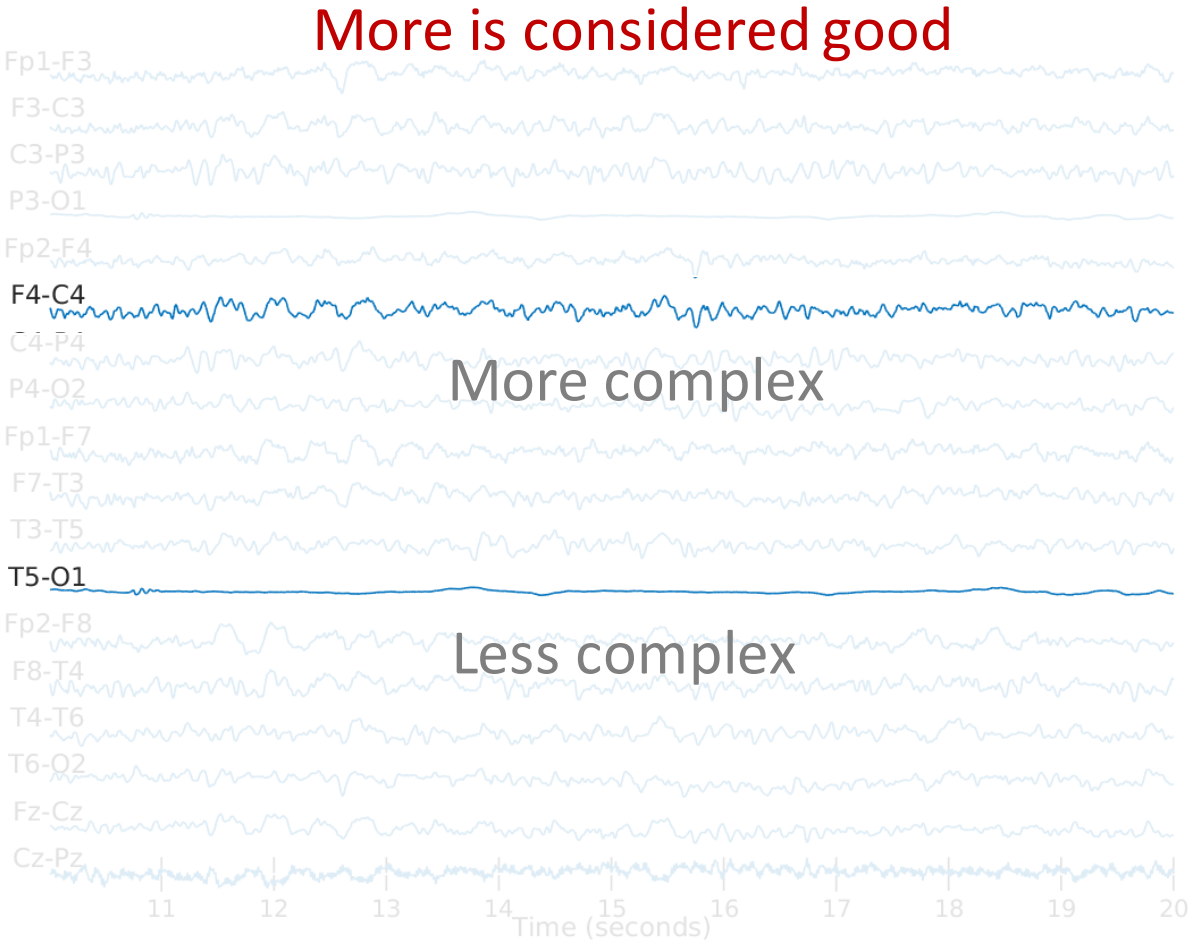

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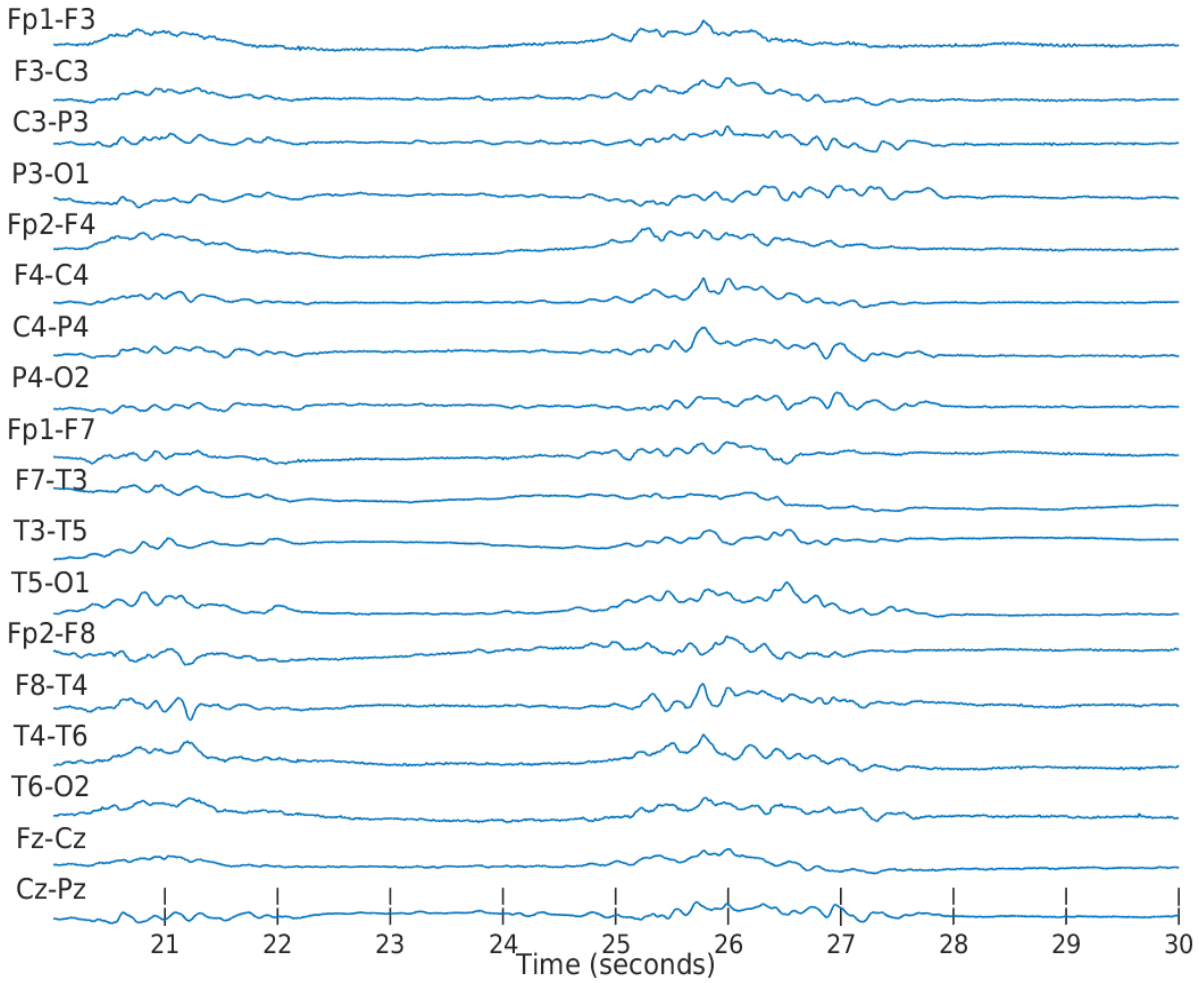

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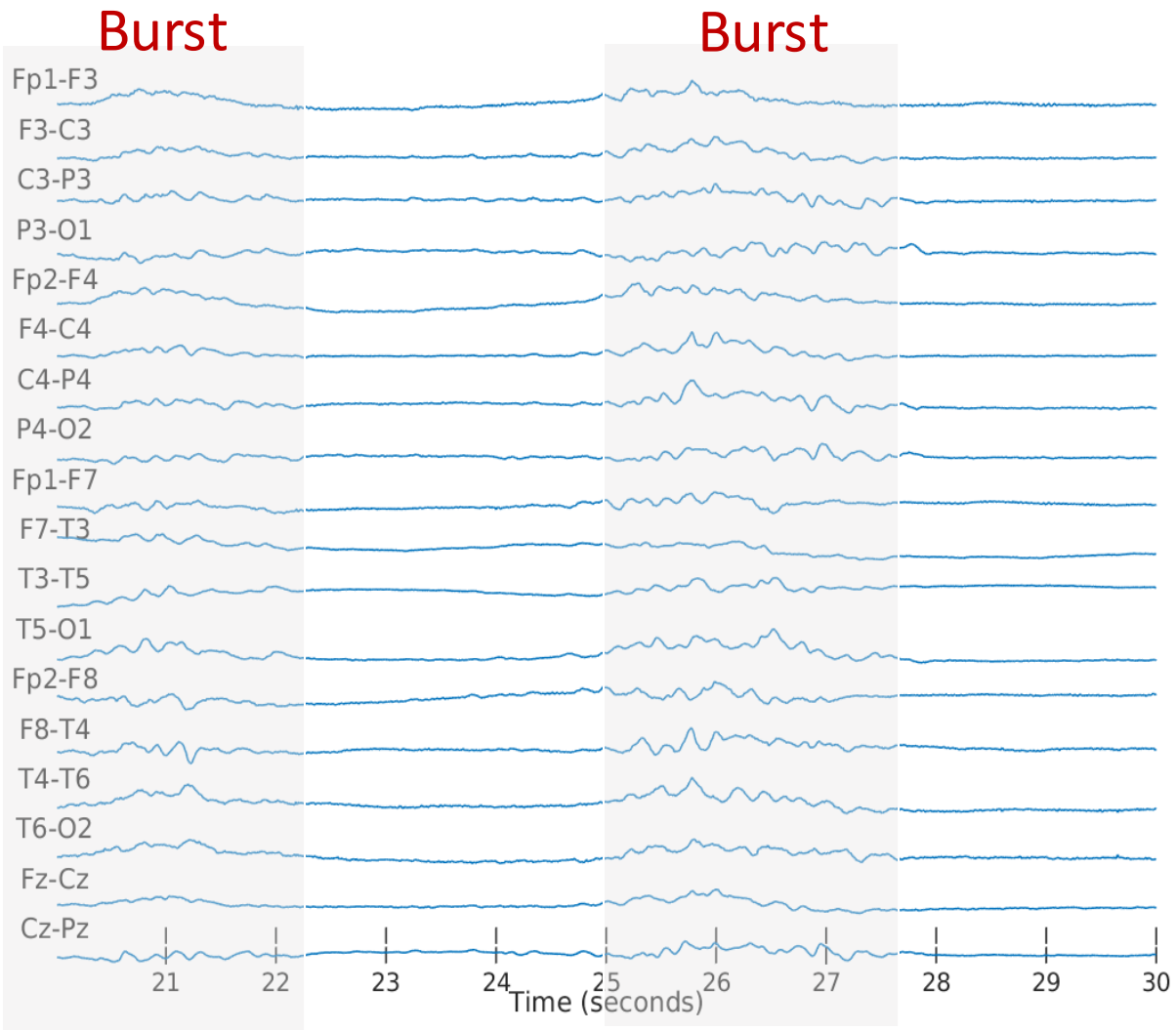

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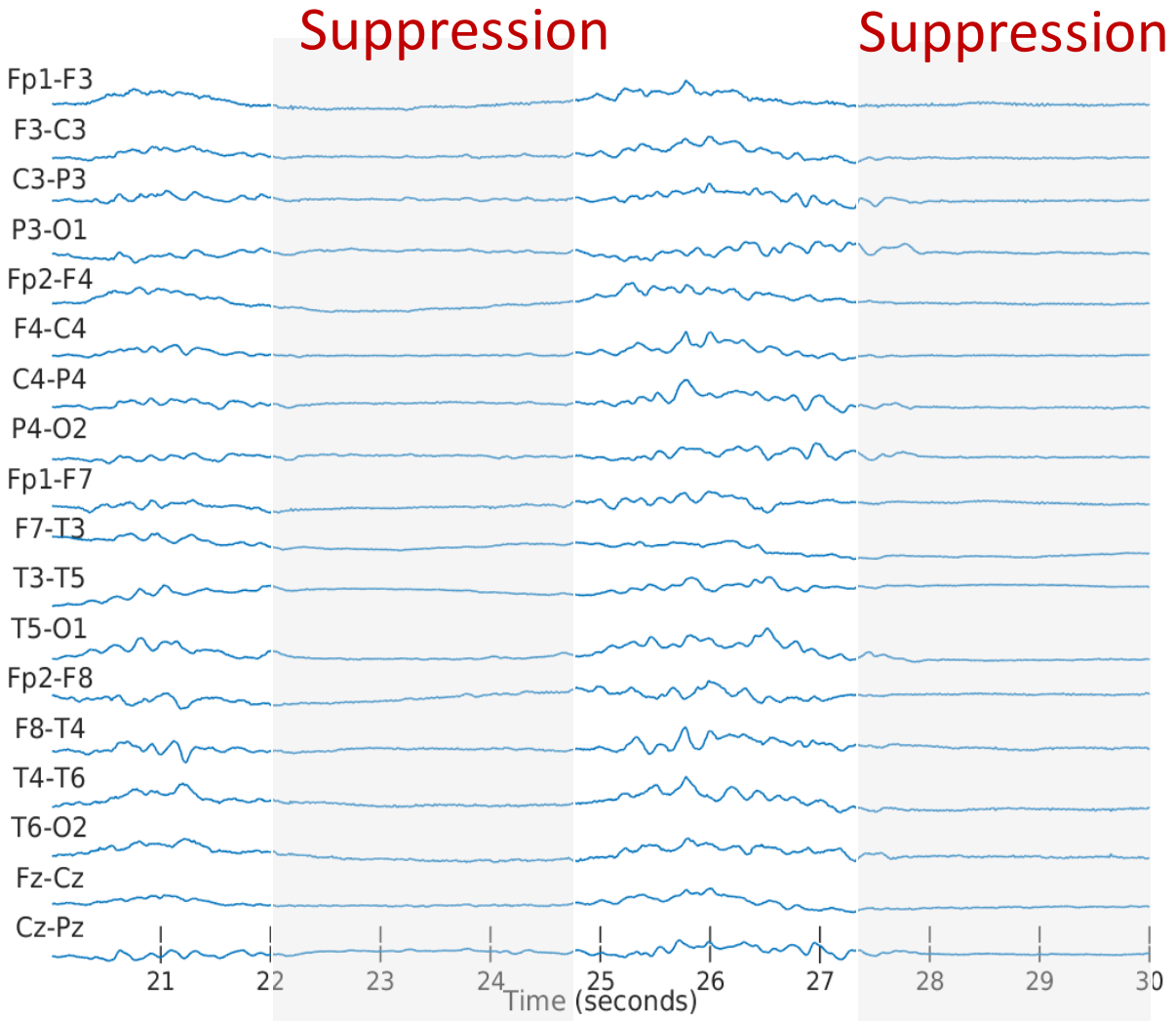

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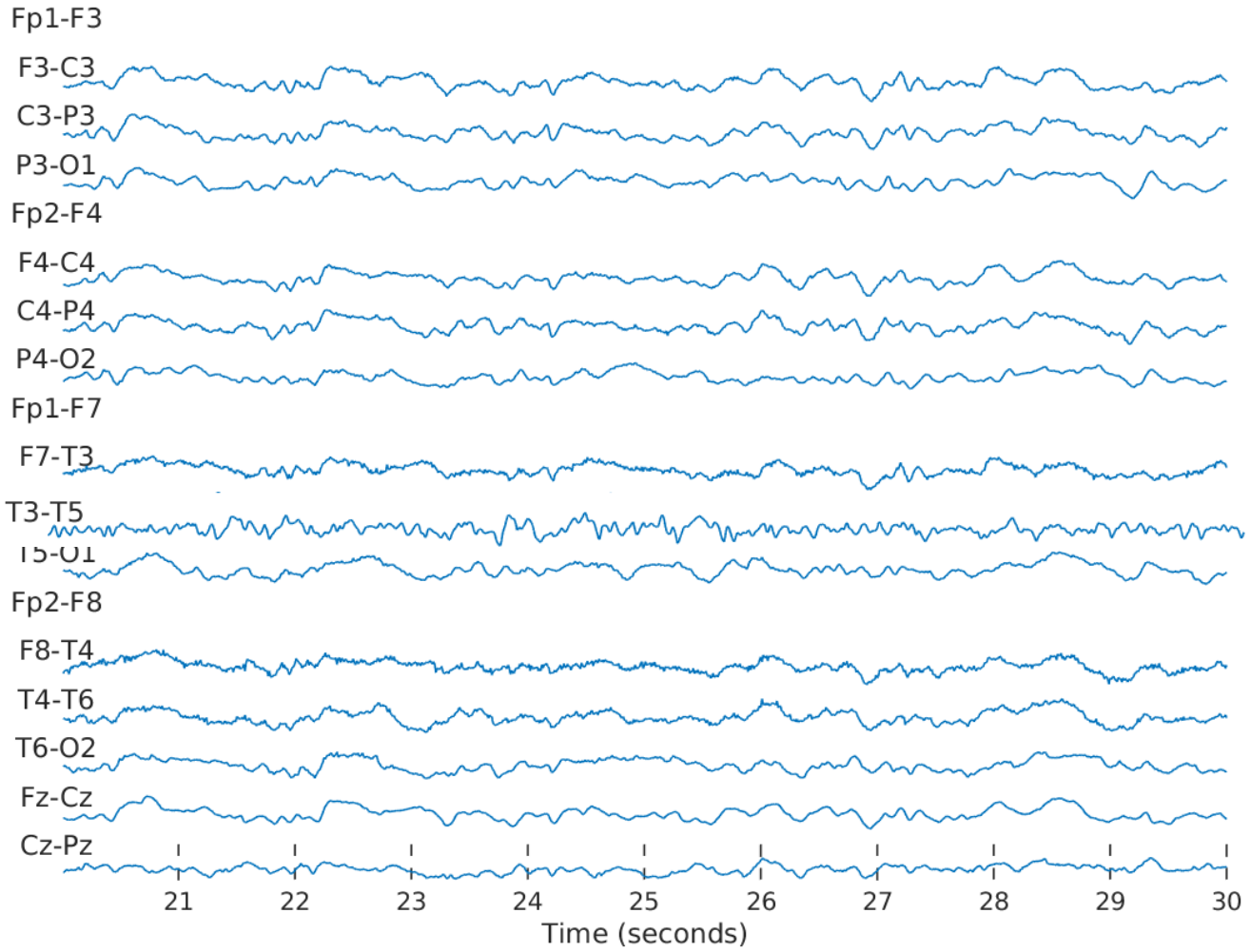

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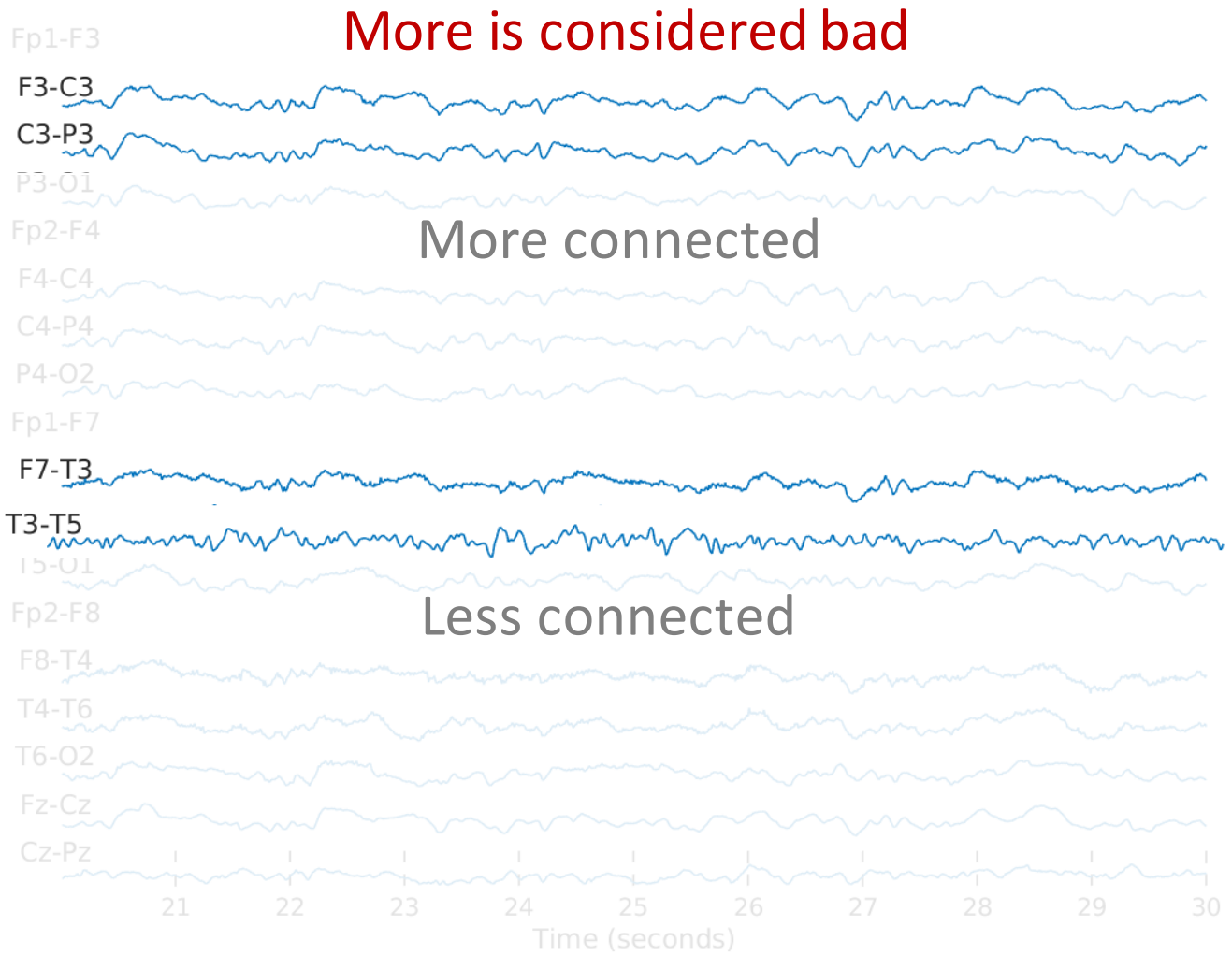
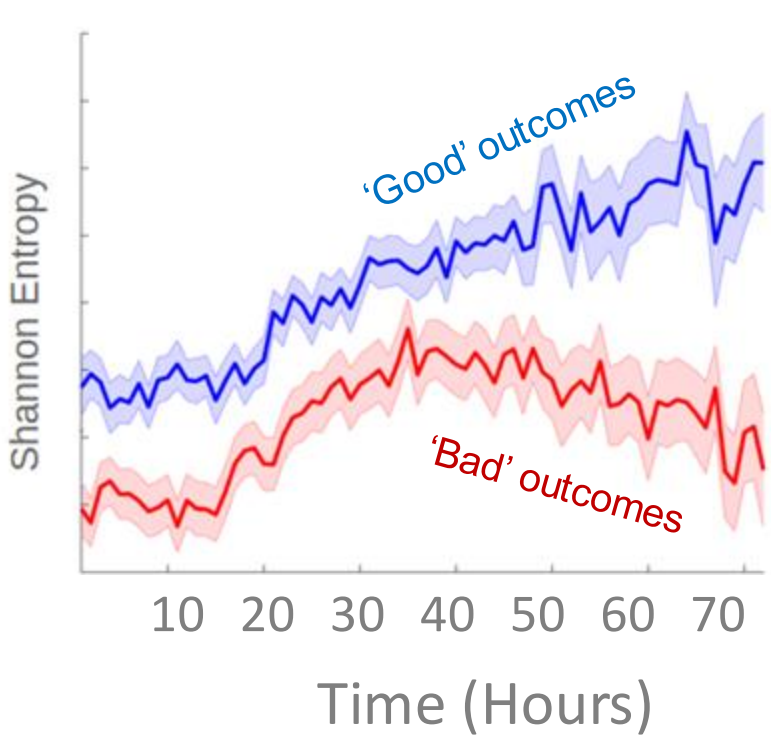
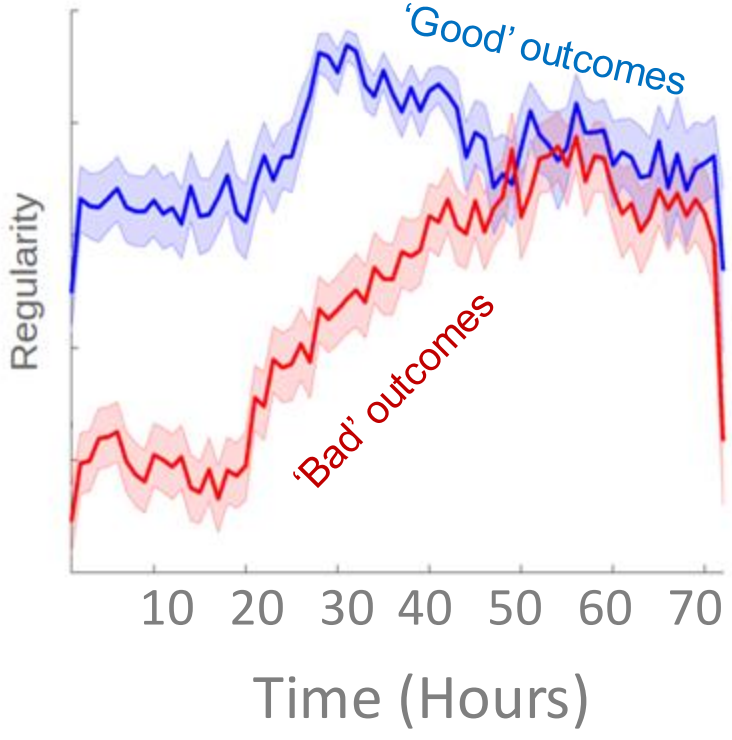
  e.g. cross correlation

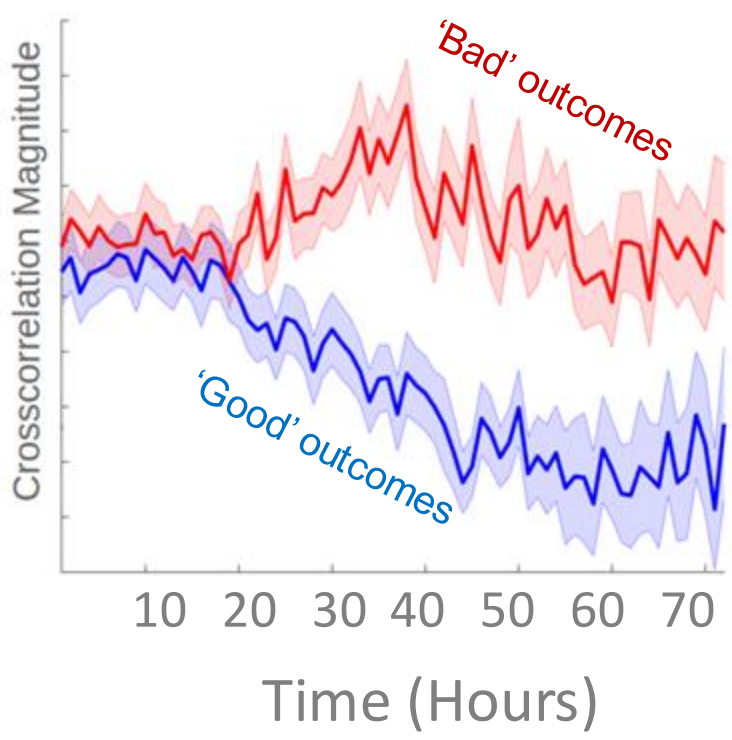


Feature-outcome relationship is time-dependent

The mean and standard error of three features for the study population, partitioned by outcome

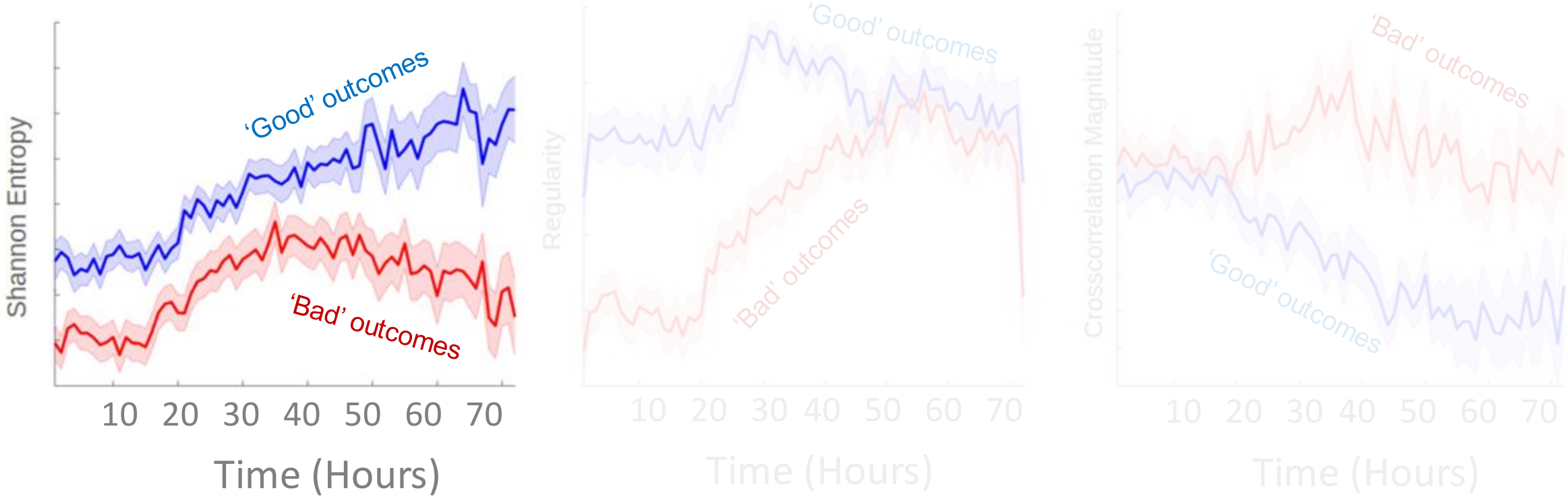






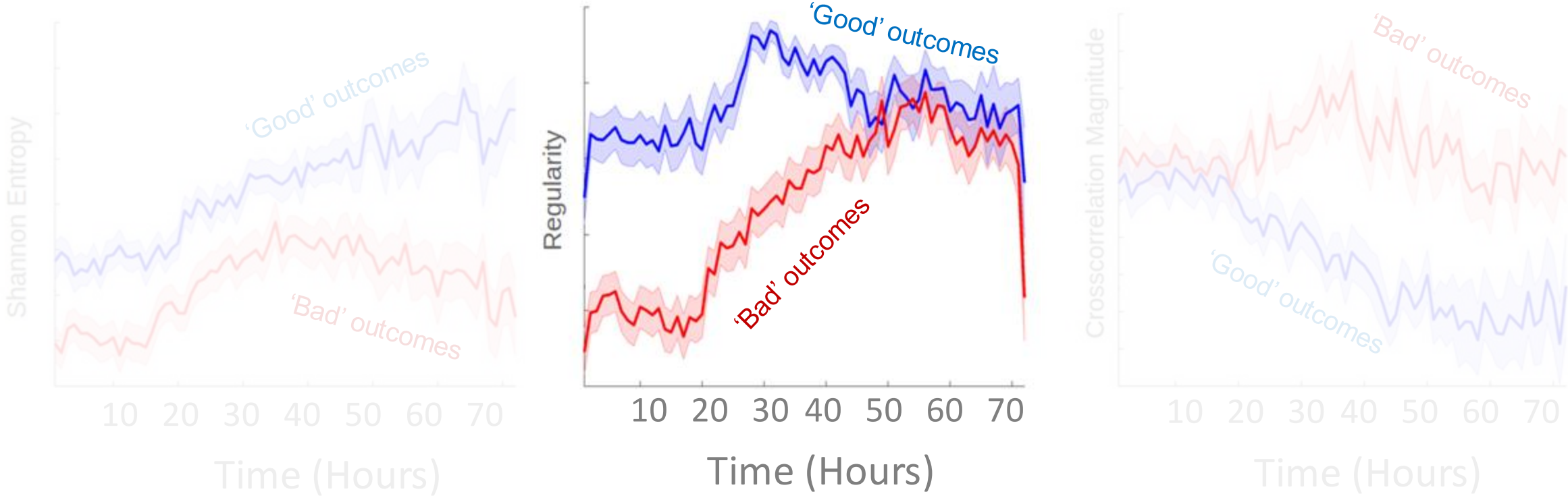
Feature-outcome relationship is time-dependent

Shannon Entropy (a measure of complexity) distinguishes ‘Good’ and ‘Bad’ consistently



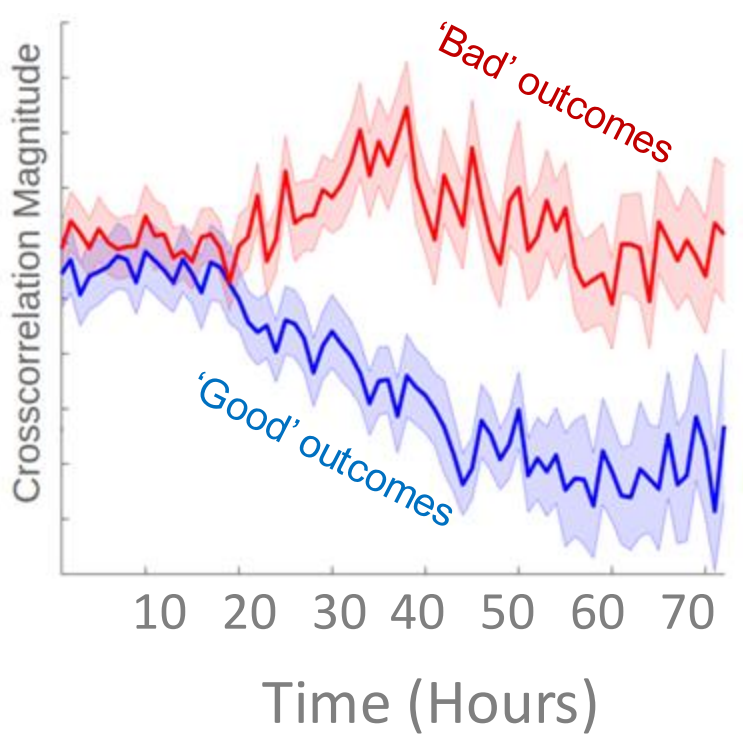
Feature-outcome relationship is time-dependent

Regularity (a measure of burst-suppression) distinguishes ‘Good’ and ‘Bad’ earlier



Feature-outcome relationship is time-dependent

Cross correlation (a measure of complexity) distinguishes ‘Good’ and ‘Bad’ later

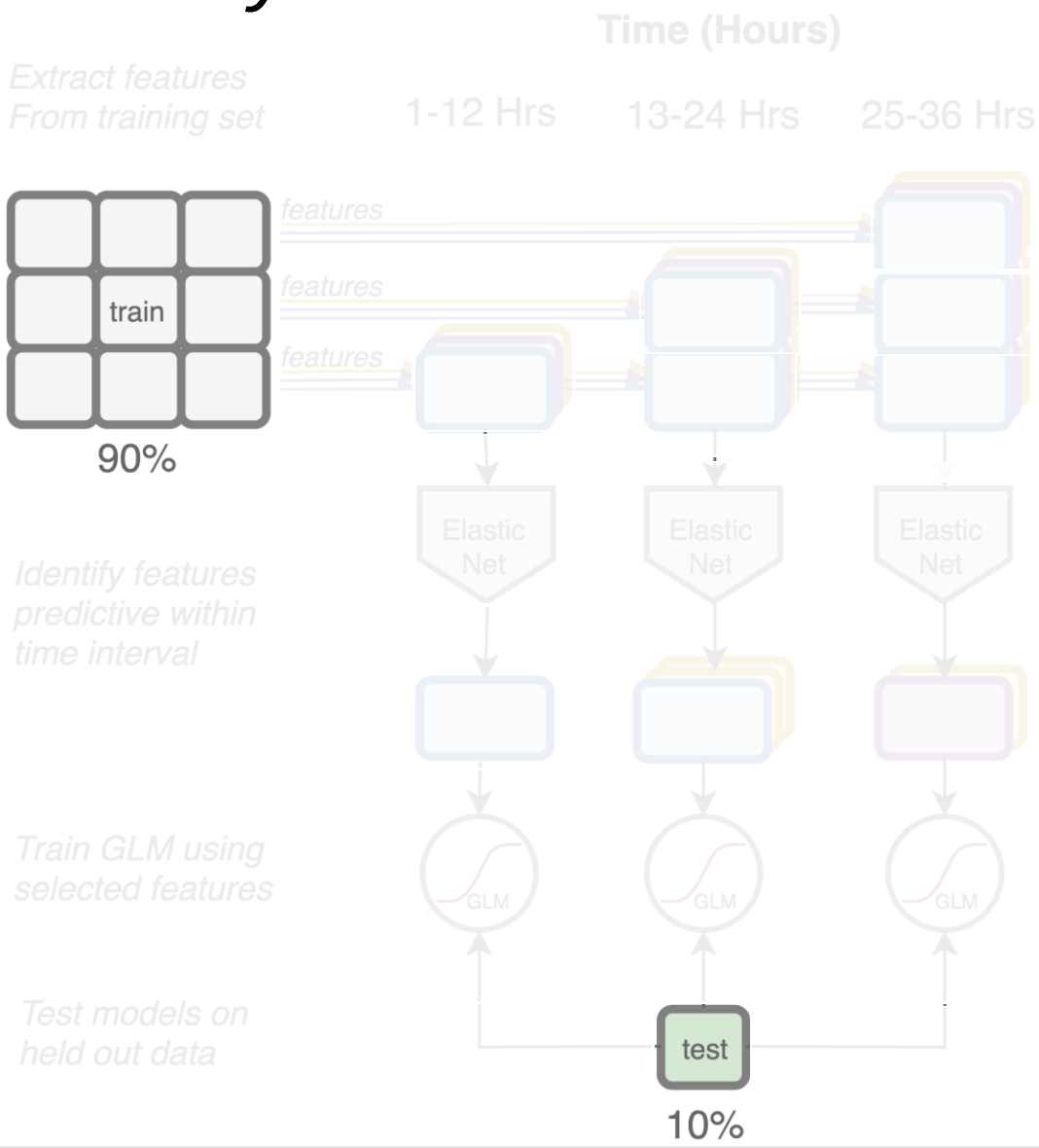


Conclusion

- The relationship between features and outcomes changes over time
- Suggests a modelling approach where coefficients evolve over time

Logistic Regression with *Elastic Memory*

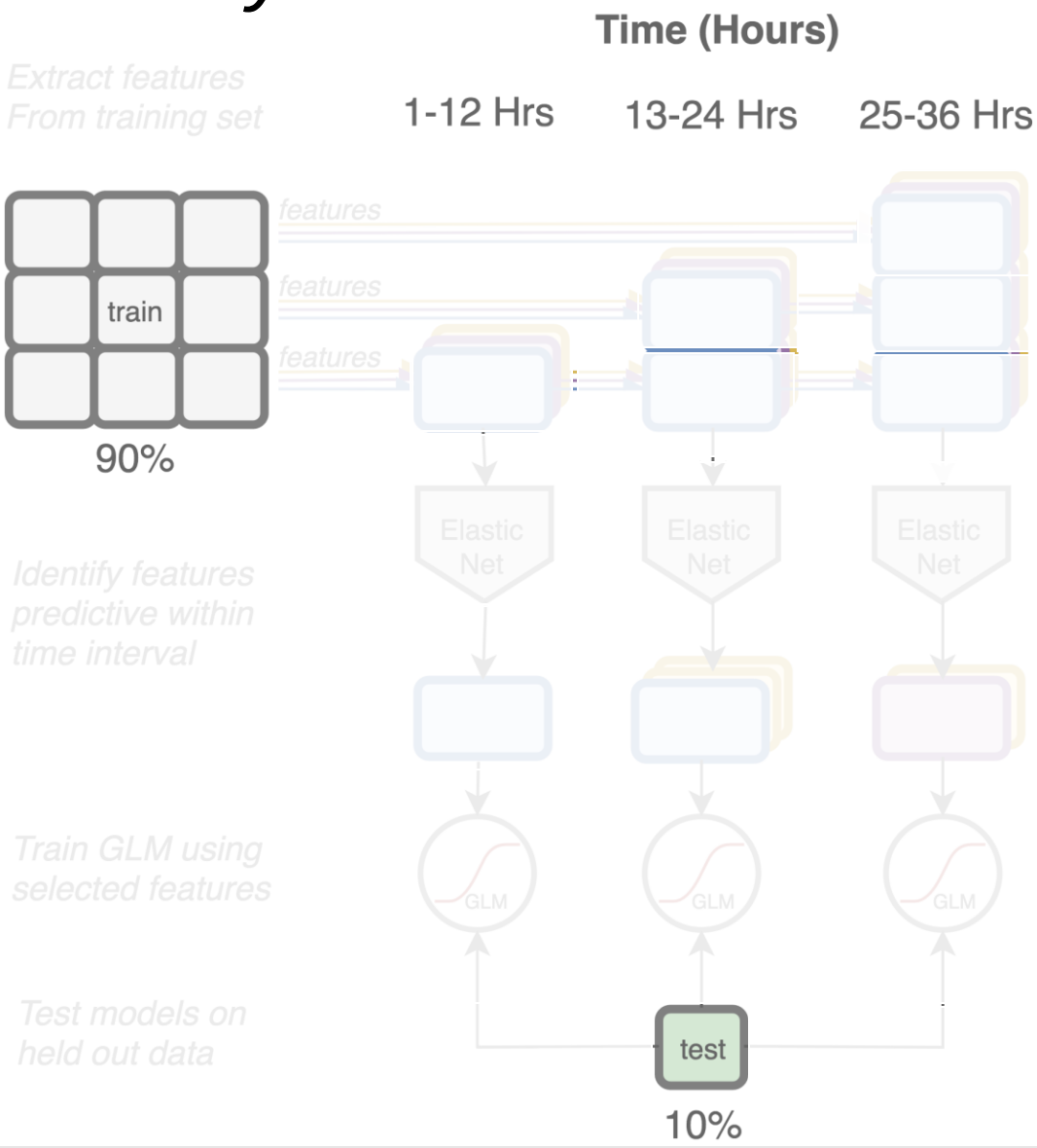
- Data is split into 10 training and testing folds.



Logistic Regression with *Elastic Memory*

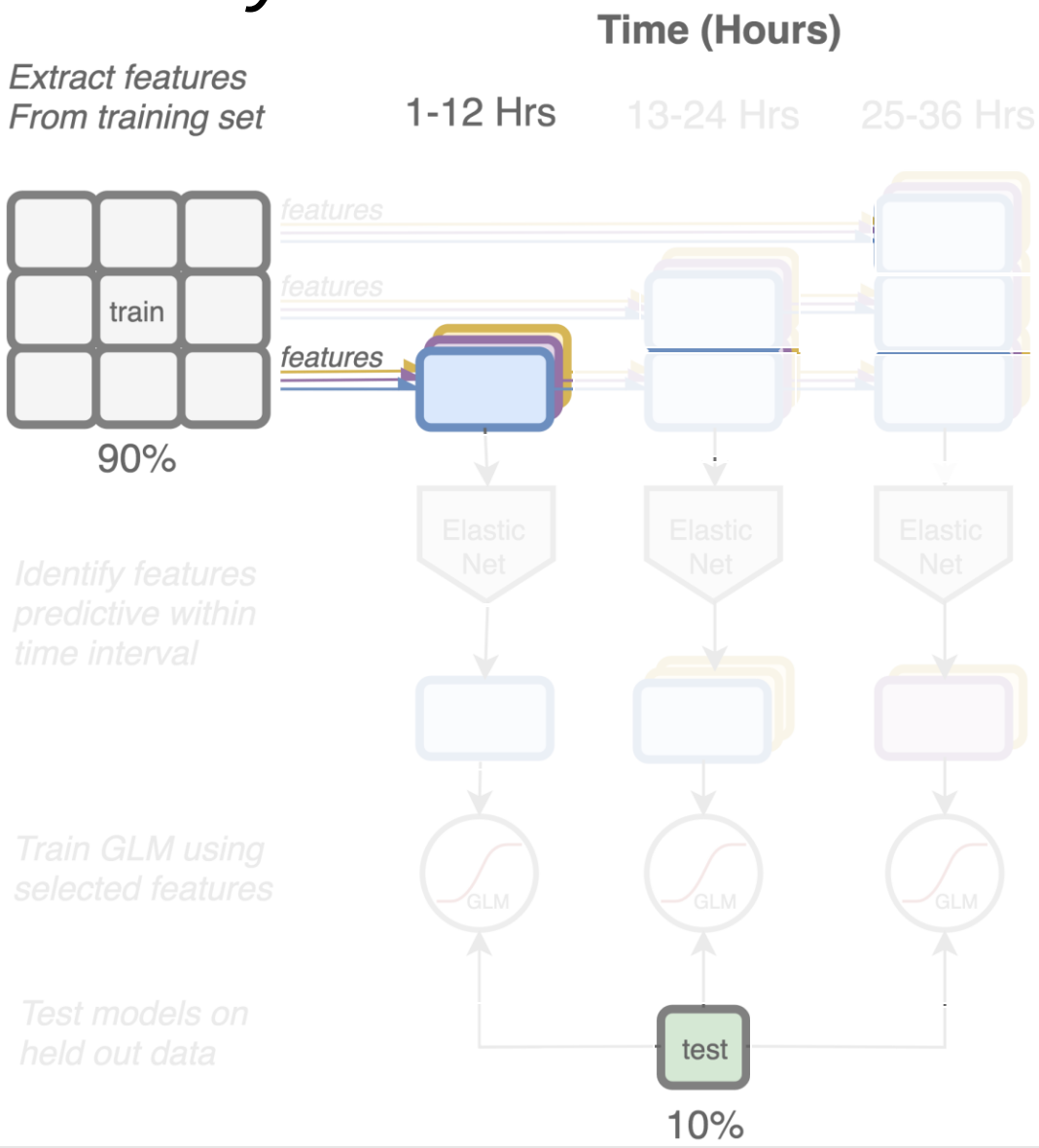
- We train a series of models that classify patient outcomes, in particular time intervals:

  1-12 hours
  13-24 hours
  25-36 hours etc.



Logistic Regression with *Elastic Memory*

- Features are extracted at particular time intervals
- 1-12 hours



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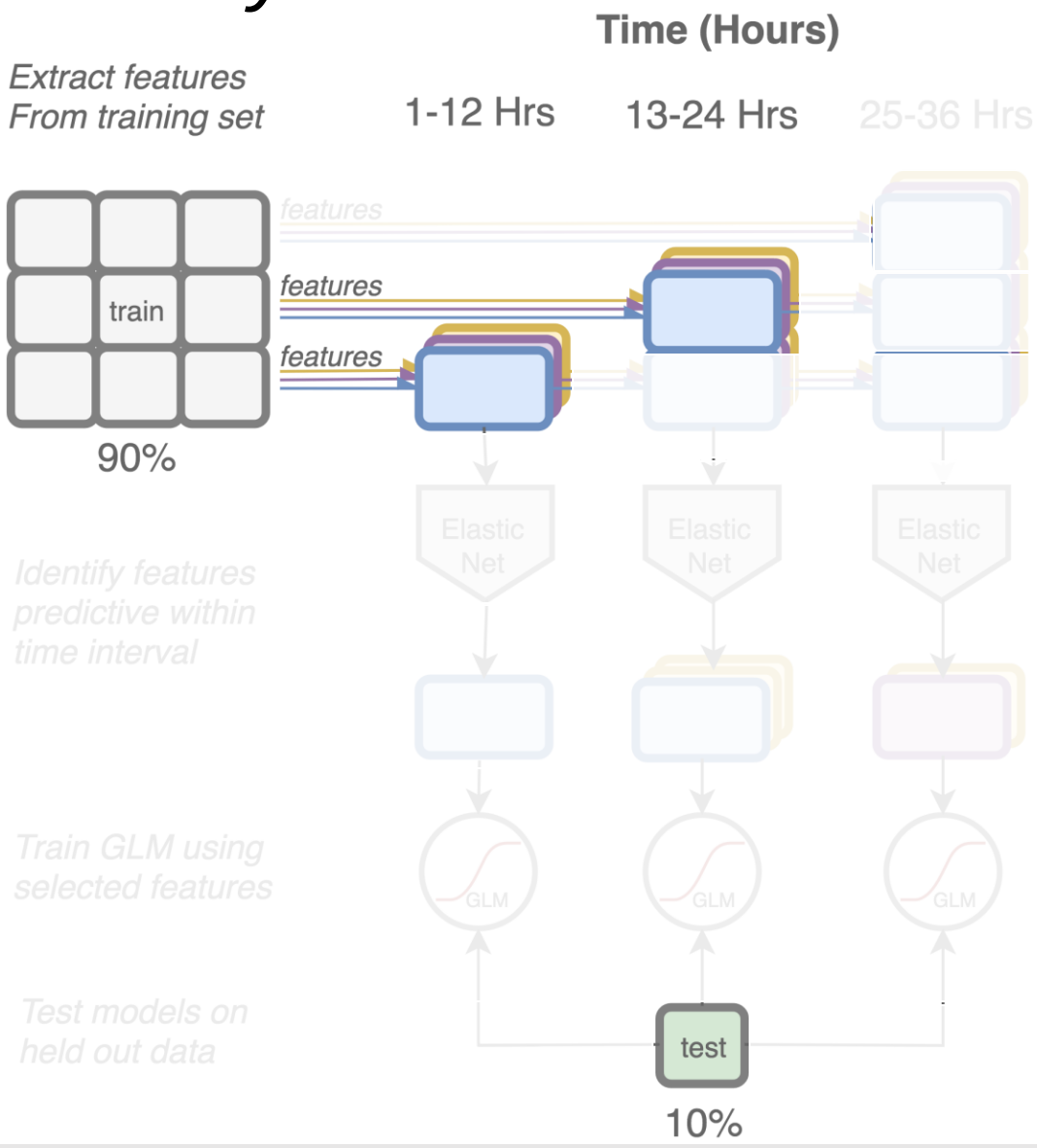
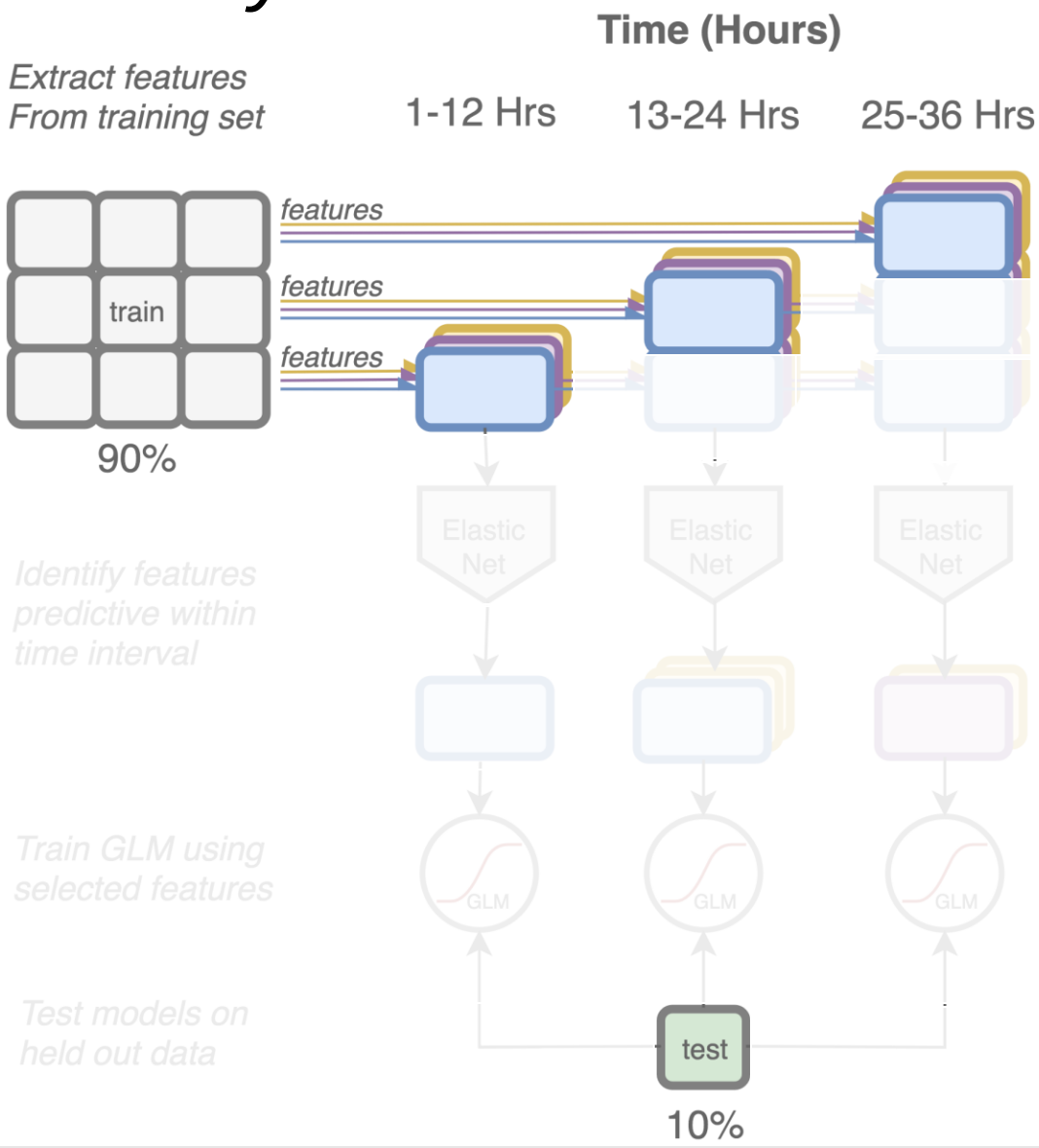


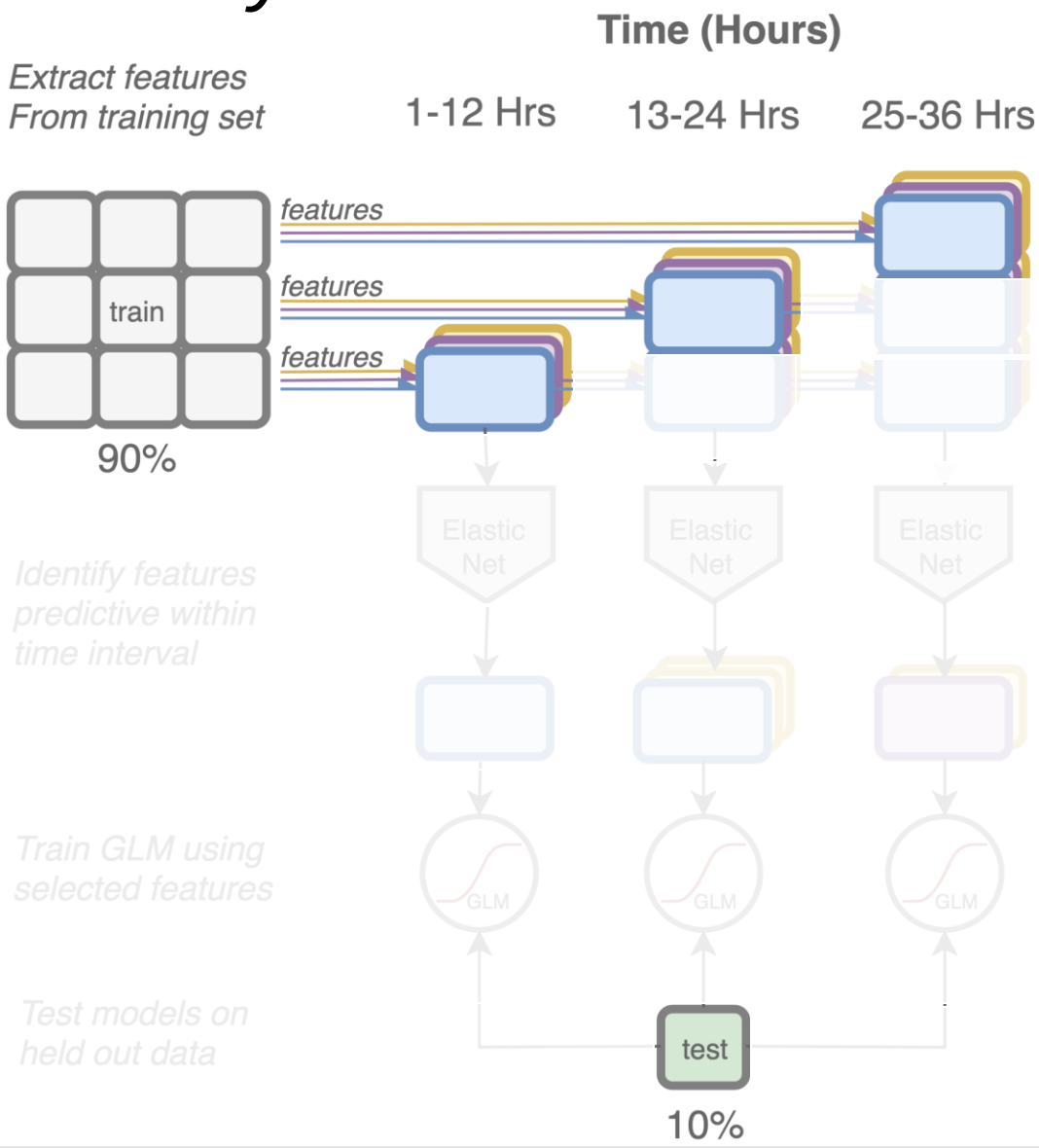
Logistic Regression with *Elastic Memory*

- Features are extracted at particular time intervals
- 25-36 hours, and so on…



Logistic Regression with *Elastic Memory*

- Features used by models in earlier time intervals are passed forward as ‘memories’ for models in future time intervals



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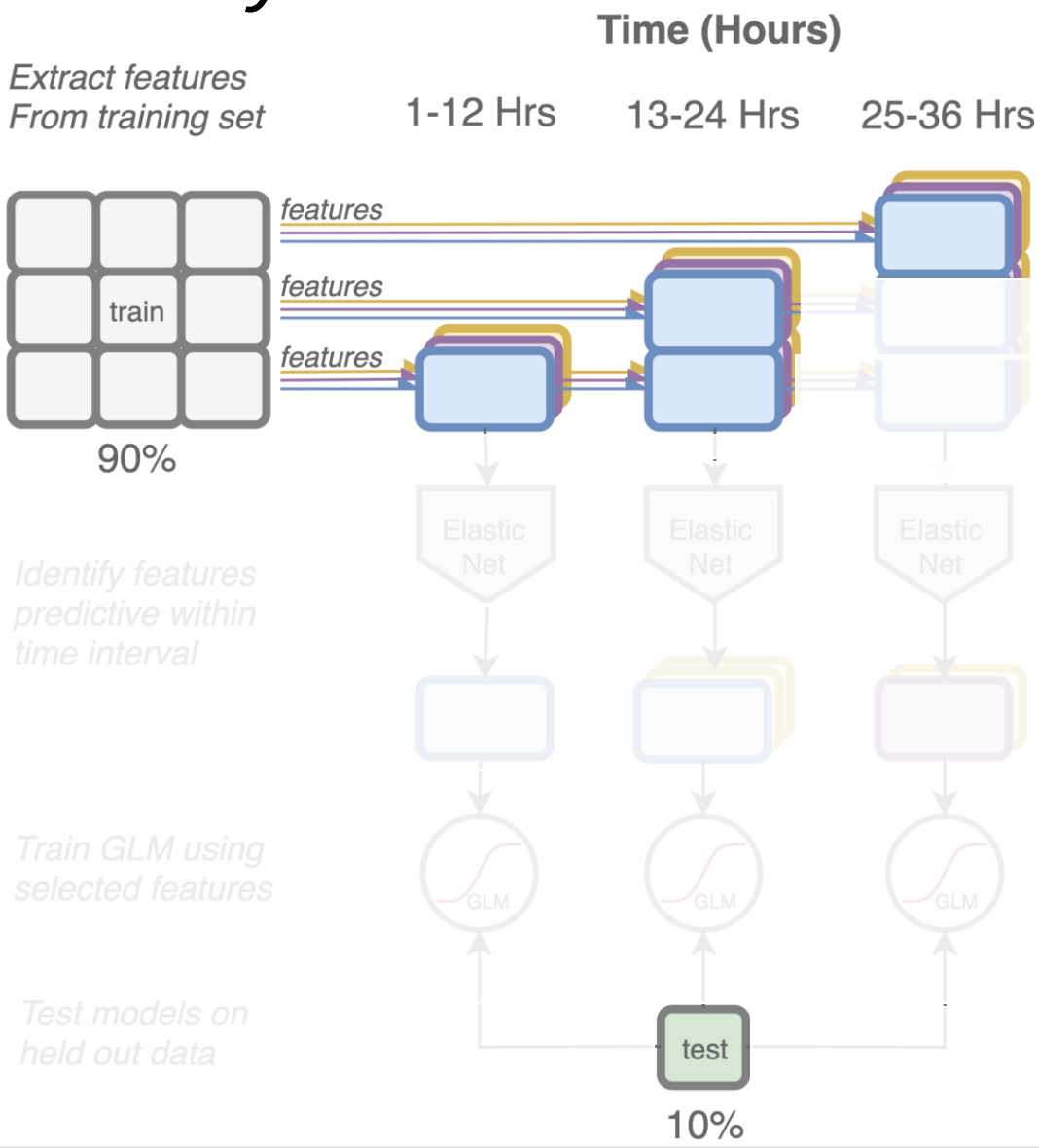
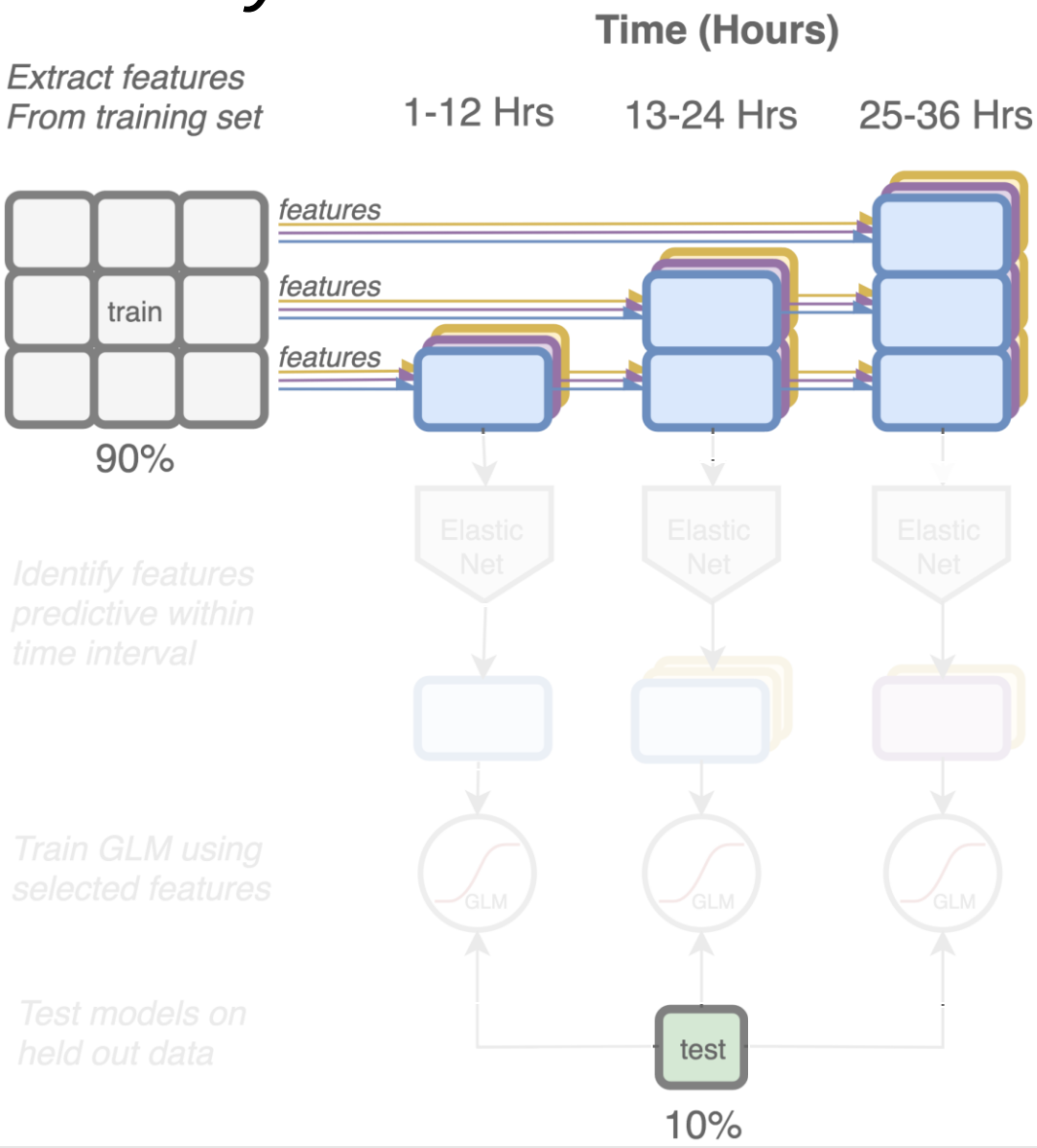


Logistic Regression with *Elastic Memory*

- Features used by models in earlier time intervals are passed forward as ‘memories’ for models in future time intervals

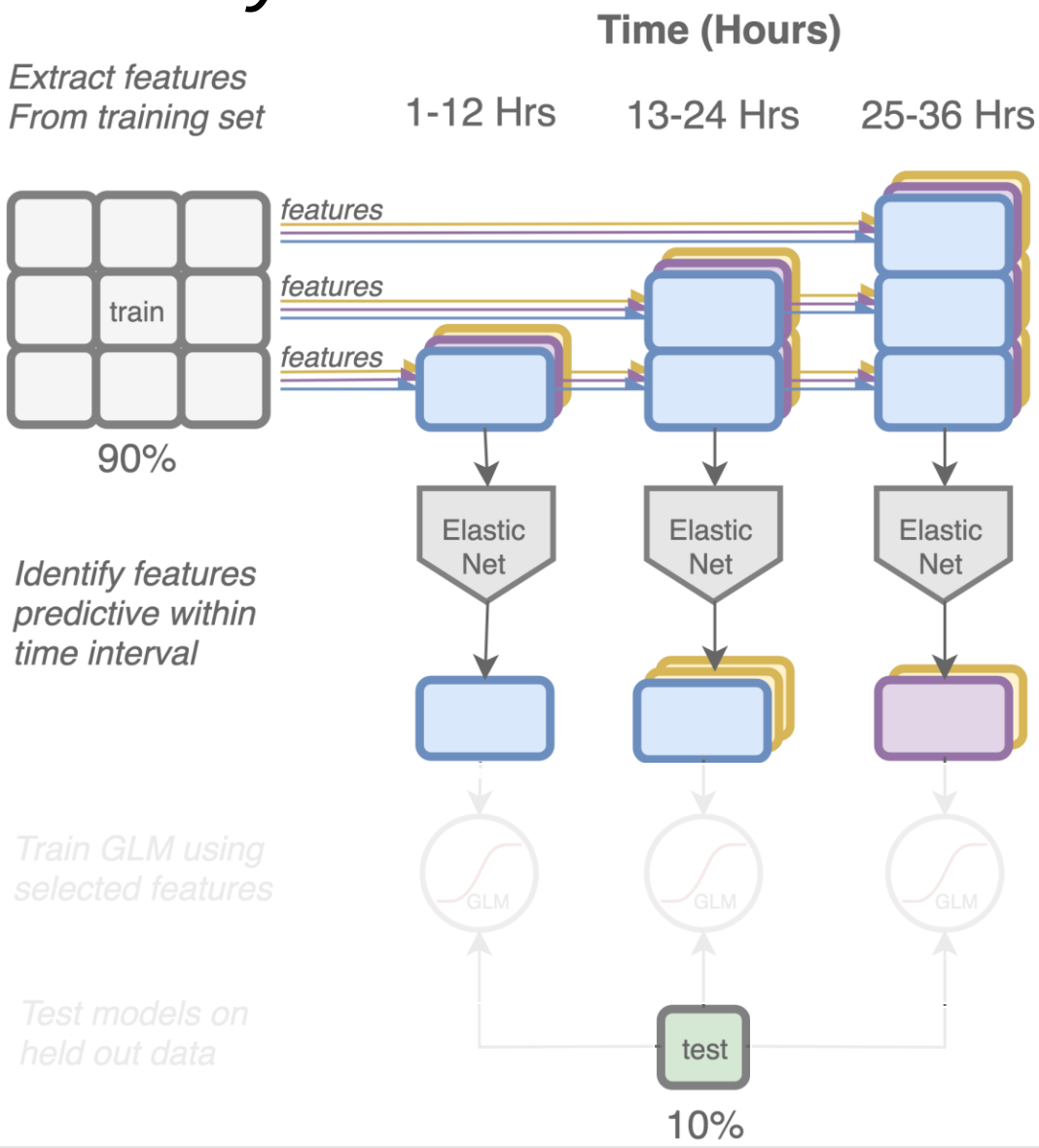


Logistic Regression with *Elastic Memory*

- We retain only the most important features using Elastic Net

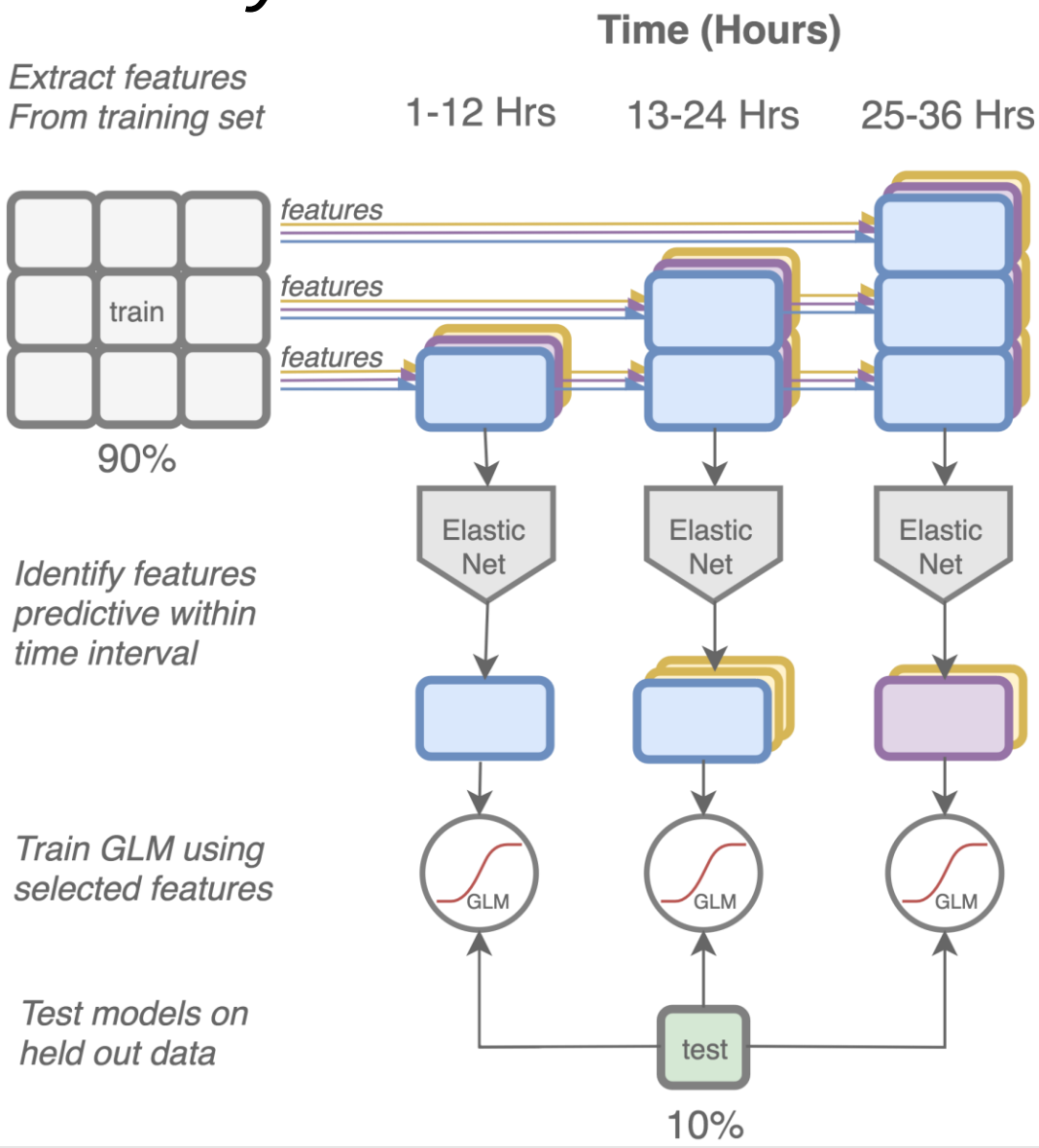
- Penalizes the size of the regression coefficients based on both their l^1 norm and their l^2 norm :

$$argmax_{\beta} \sum_{i} \log L(y_{i,}; \beta, x_i) - \lambda[\alpha||\beta||_1 + \frac{1}{2}(1-\alpha)||\beta||_2^2]$$



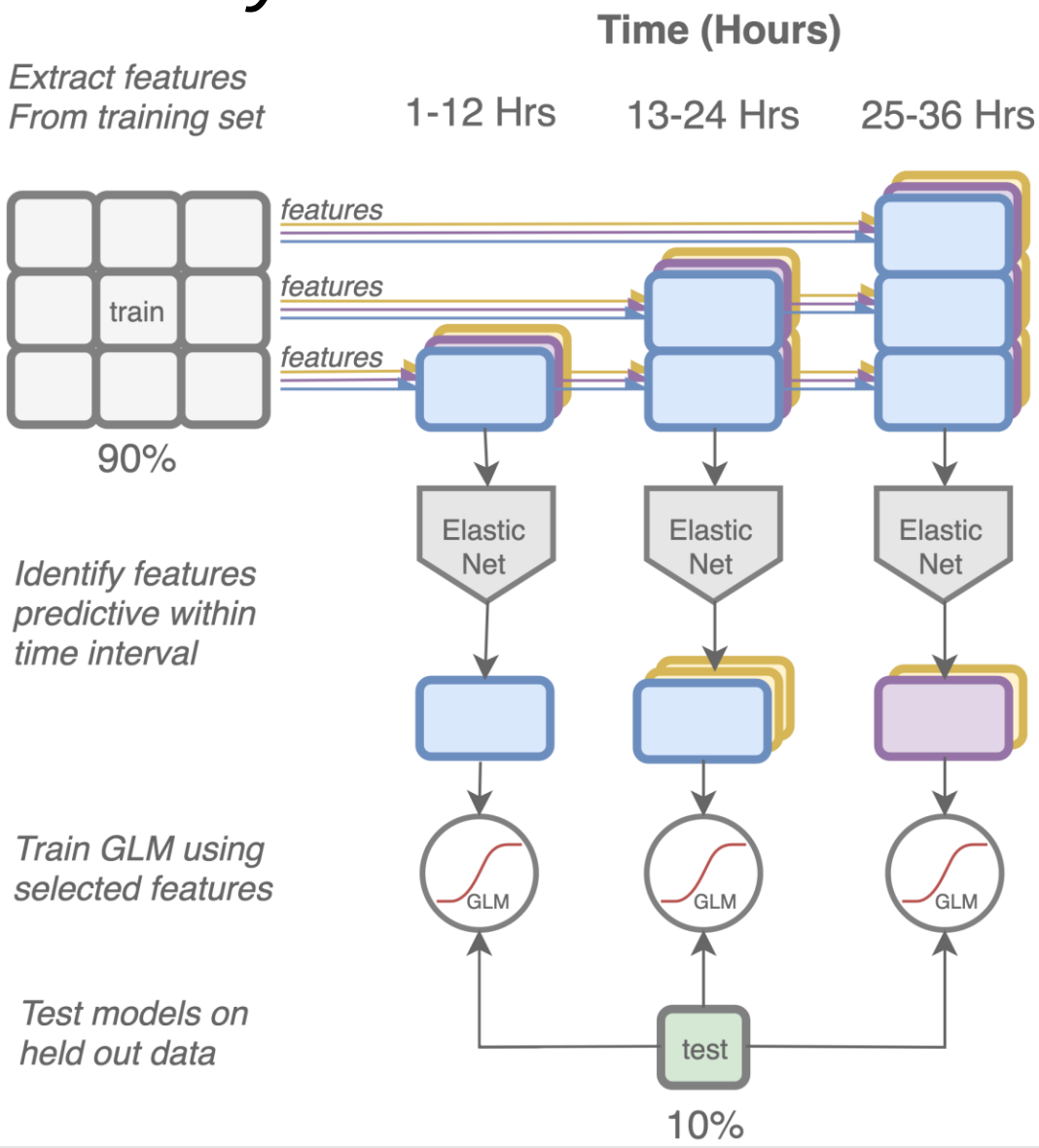
Logistic Regression with *Elastic Memory*

- A logistic regression model with the selected features is used to evaluate performance on the held out test-sets

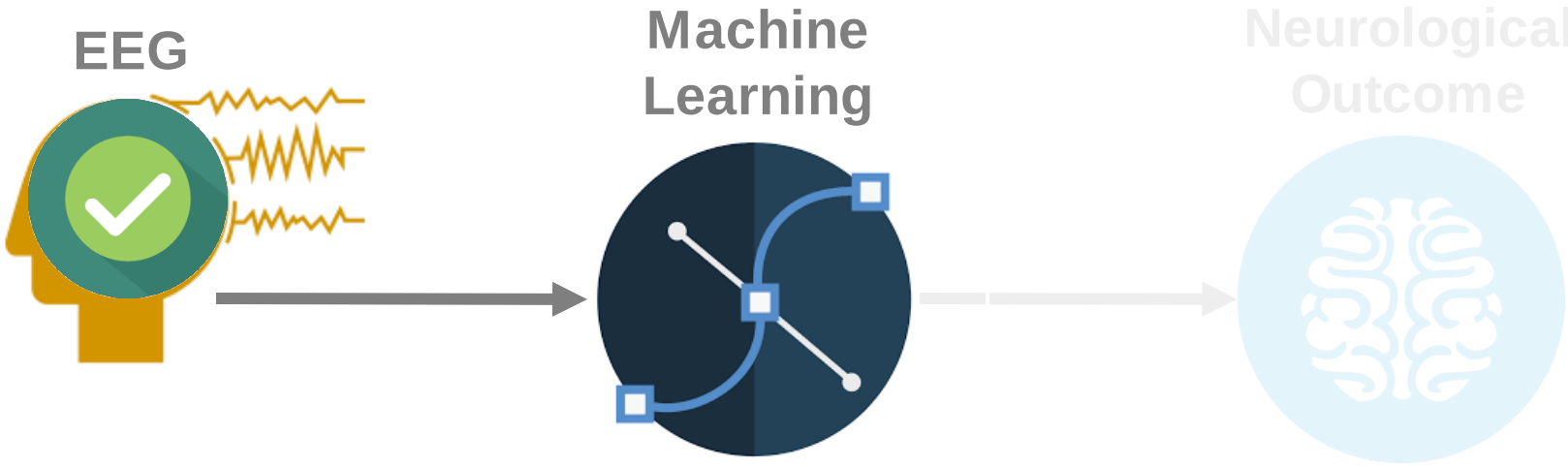


Logistic Regression with *Elastic Memory*

- A logistic regression model with the selected features is used to evaluate performance on the held out test-sets
- This process was designed to mimic how actual providers perform prognosis



Deploy *time-sensitive* modeling approaches

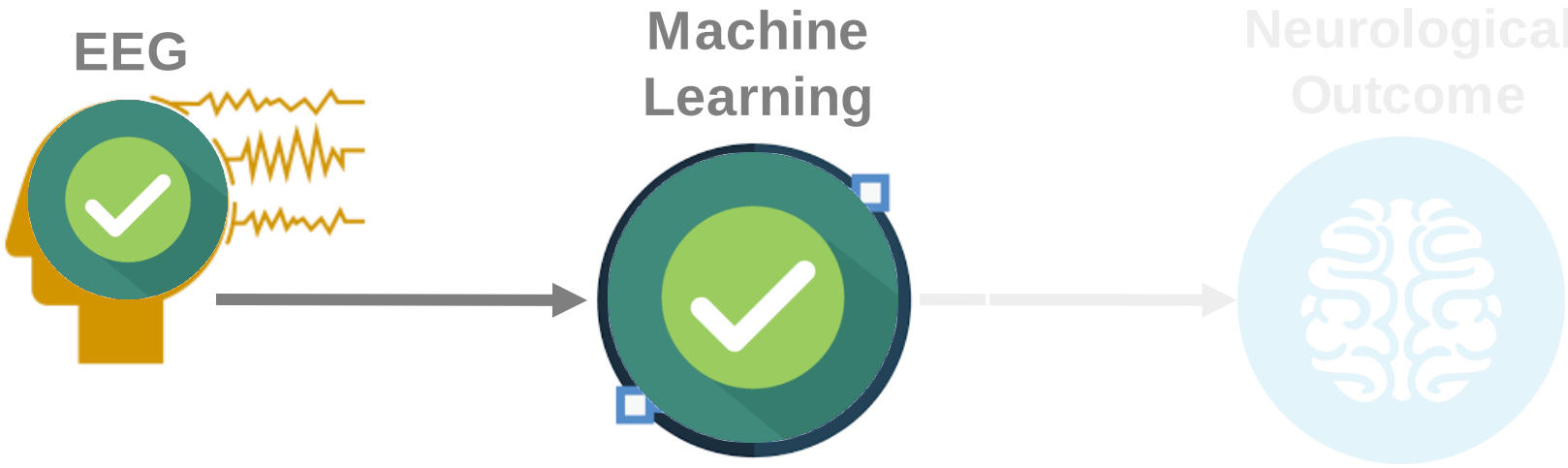


1. Collected an EEG archive 2x larger than largest set previously described in the literature

2. Time-sensitive

3. Models that assess risk

Deploy *time-sensitive* modeling approaches



1. Collected an EEG archive 2x larger than largest set previously described in the literature
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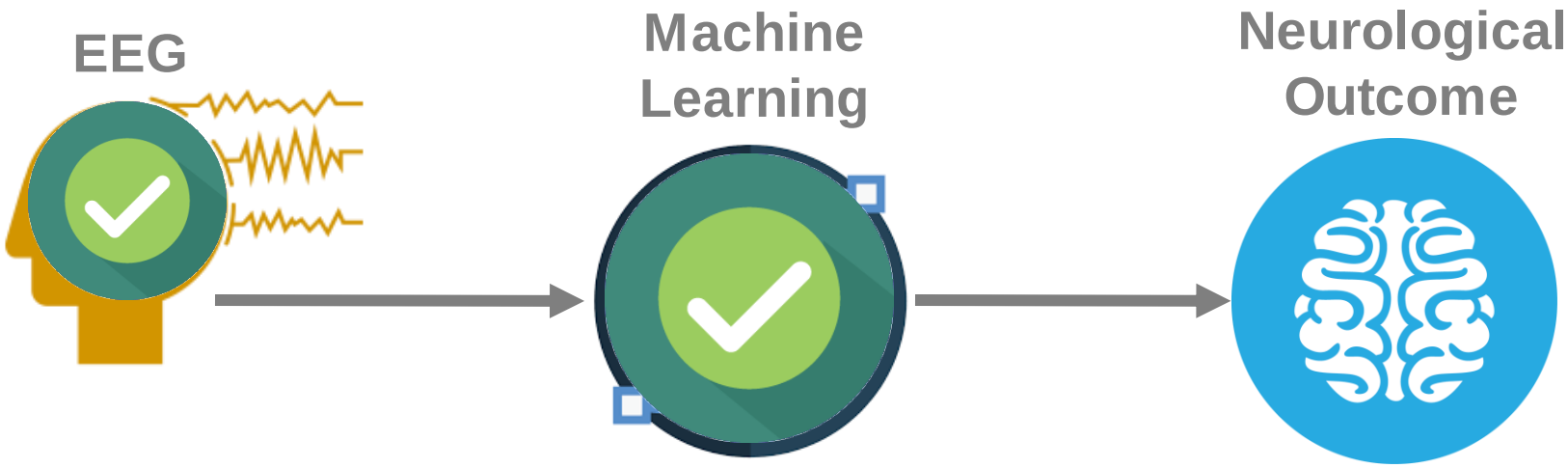
3. Models that assess risk

Assessing performance: classification and calibration



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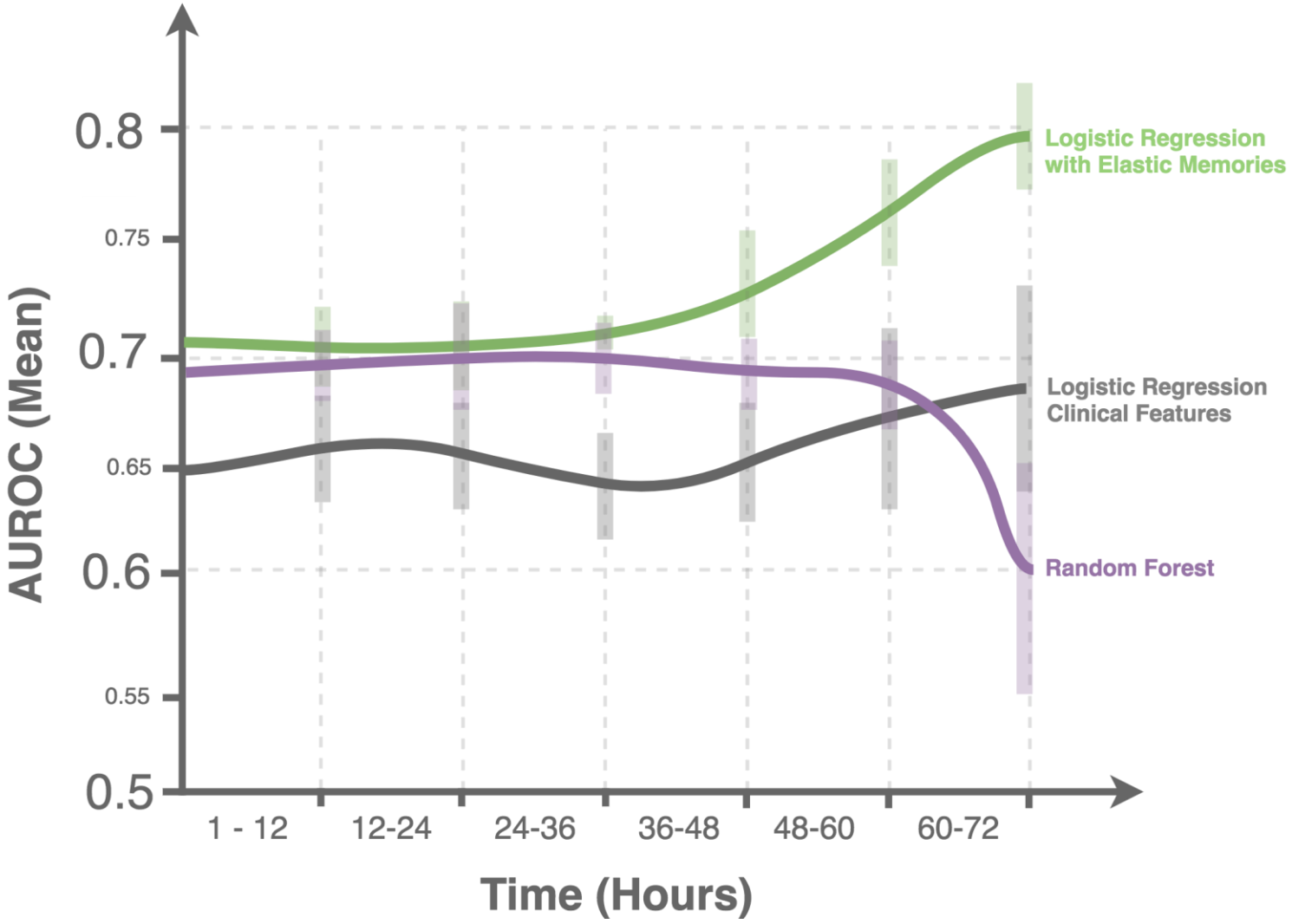
Classification

Classification

- Our approach exhibited enhanced classification performance compared to the literature baseline

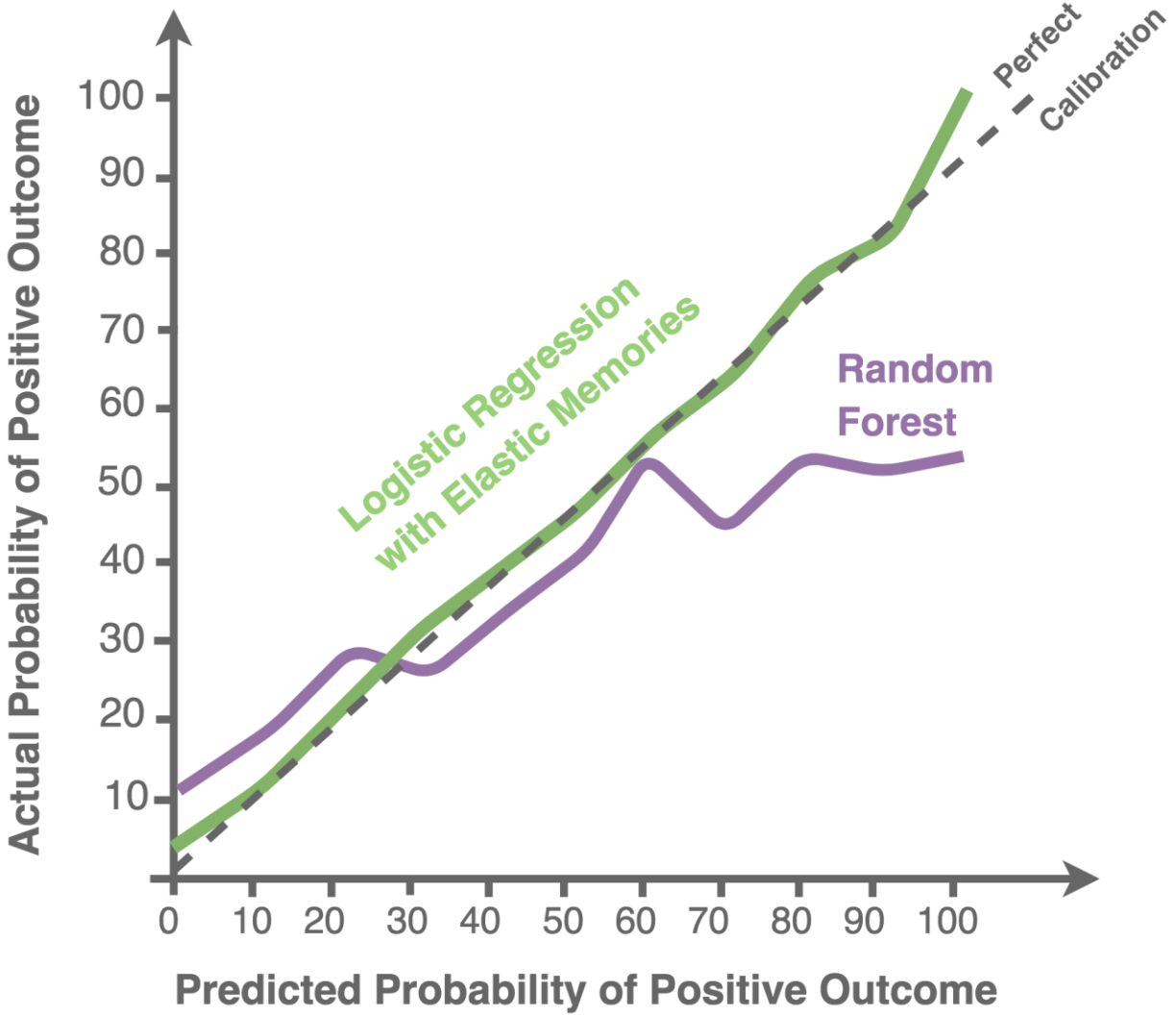
- Improvement was most pronounced at later time intervals



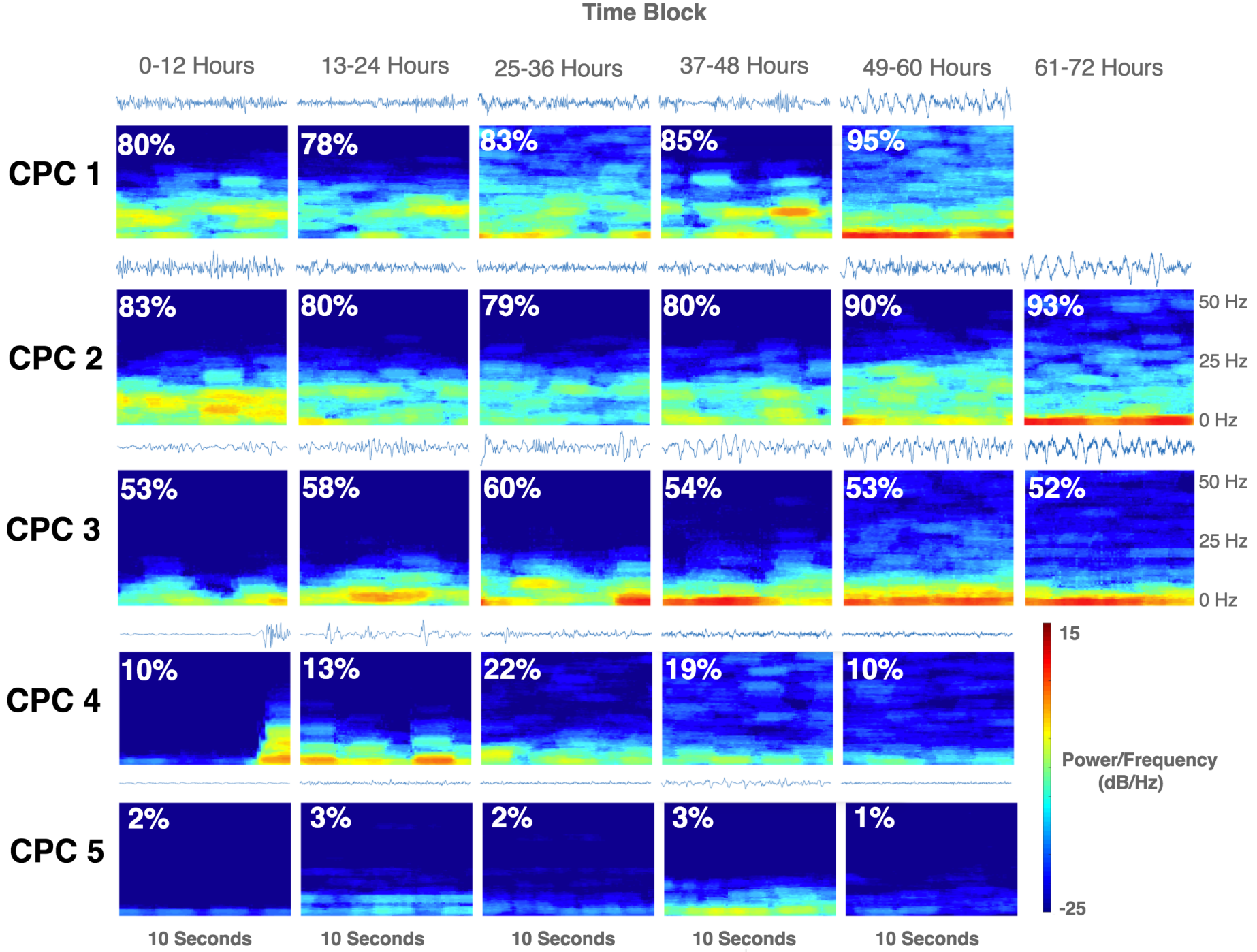
Calibration

- Our approach exhibited enhanced calibration compared to the literature baseline

- This allows for a more nuanced use of the model, compared to existing approaches



Exemplary Patients



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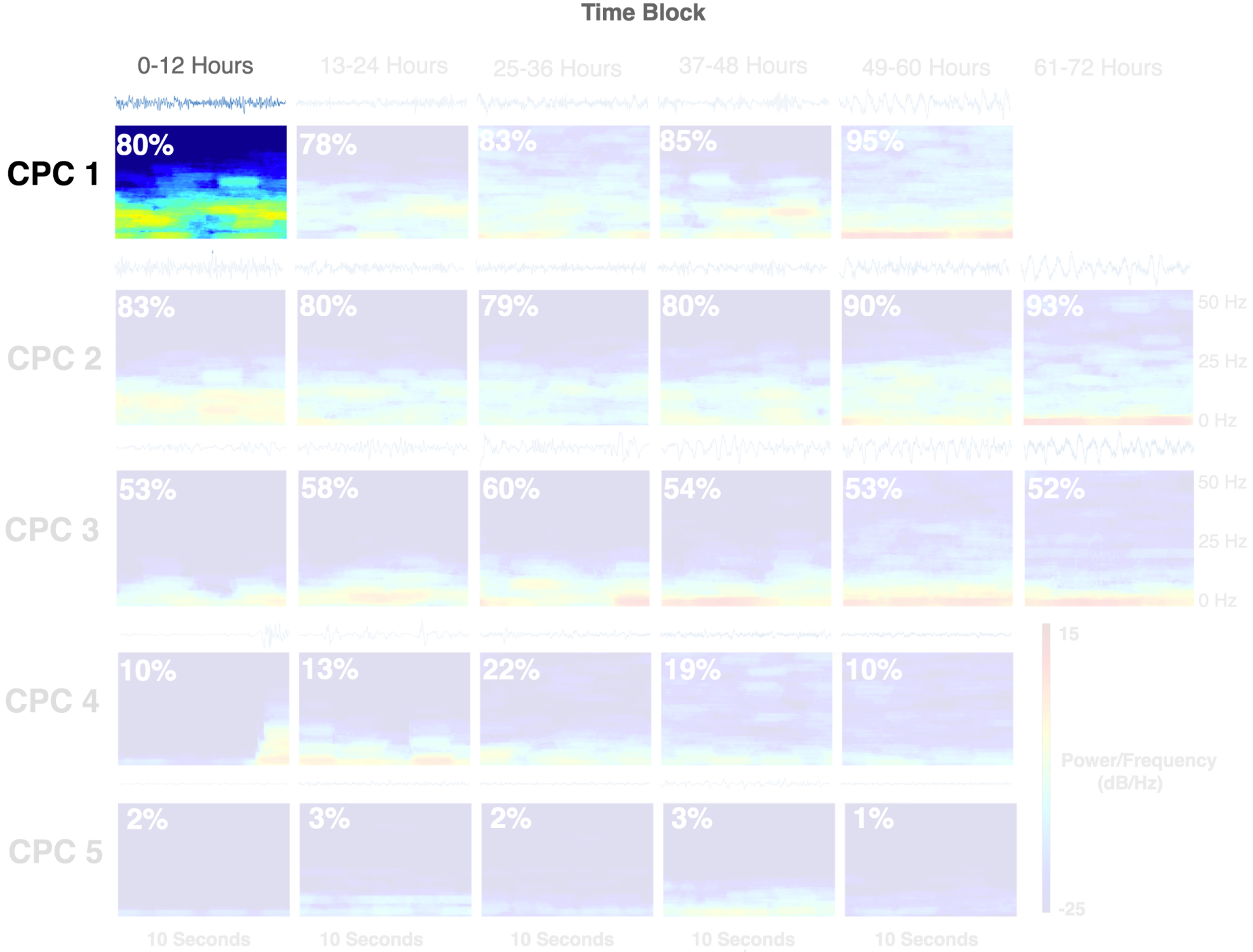

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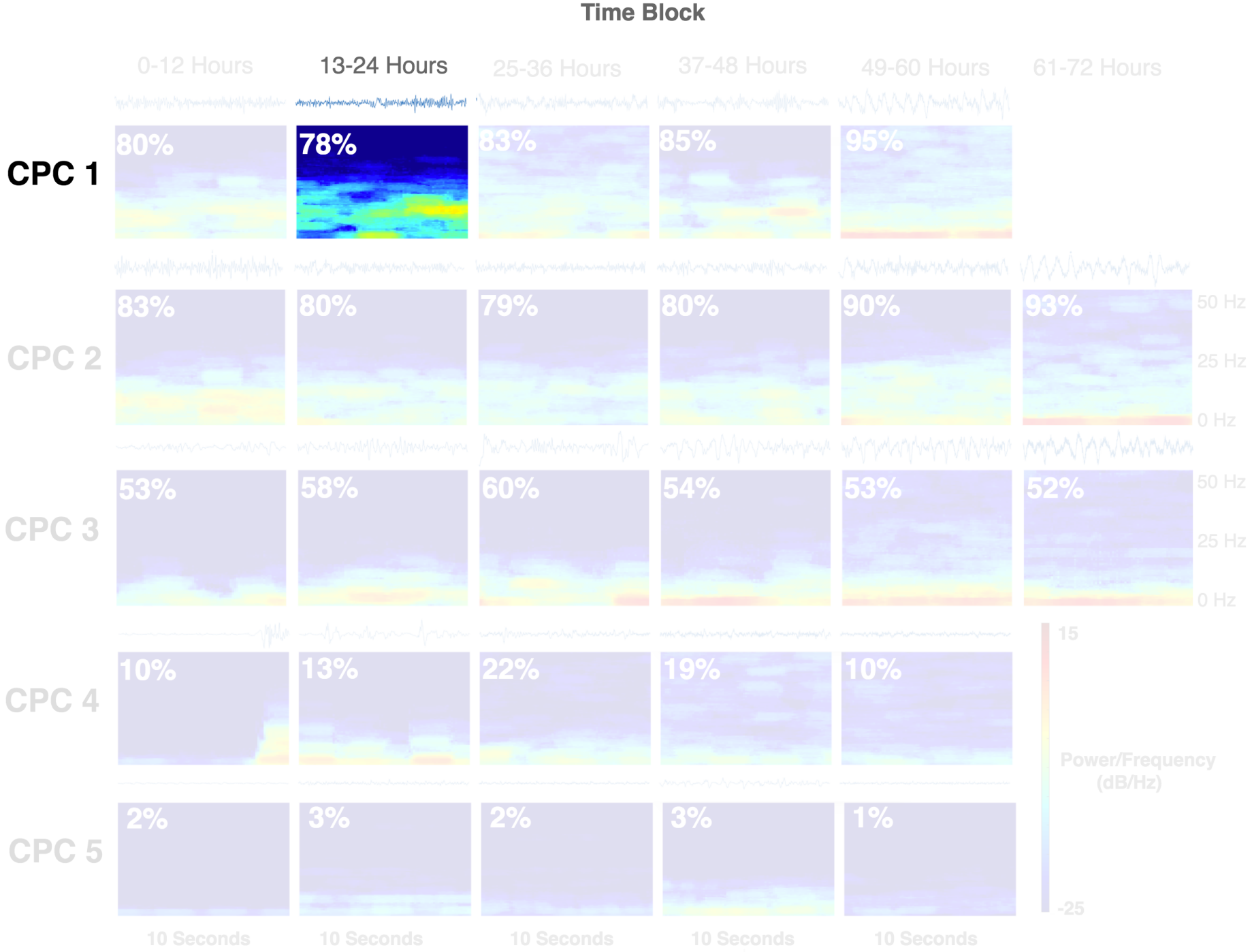

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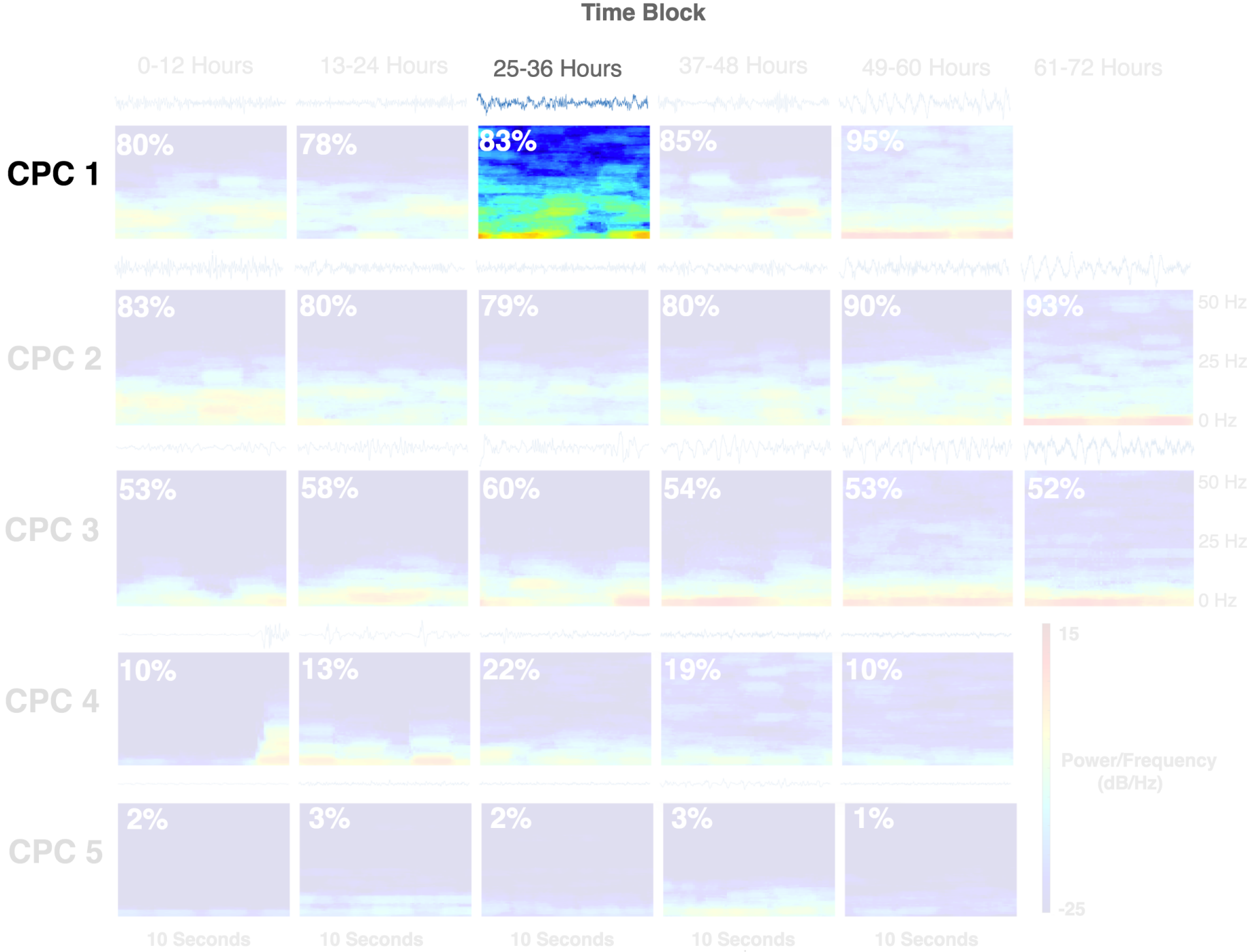

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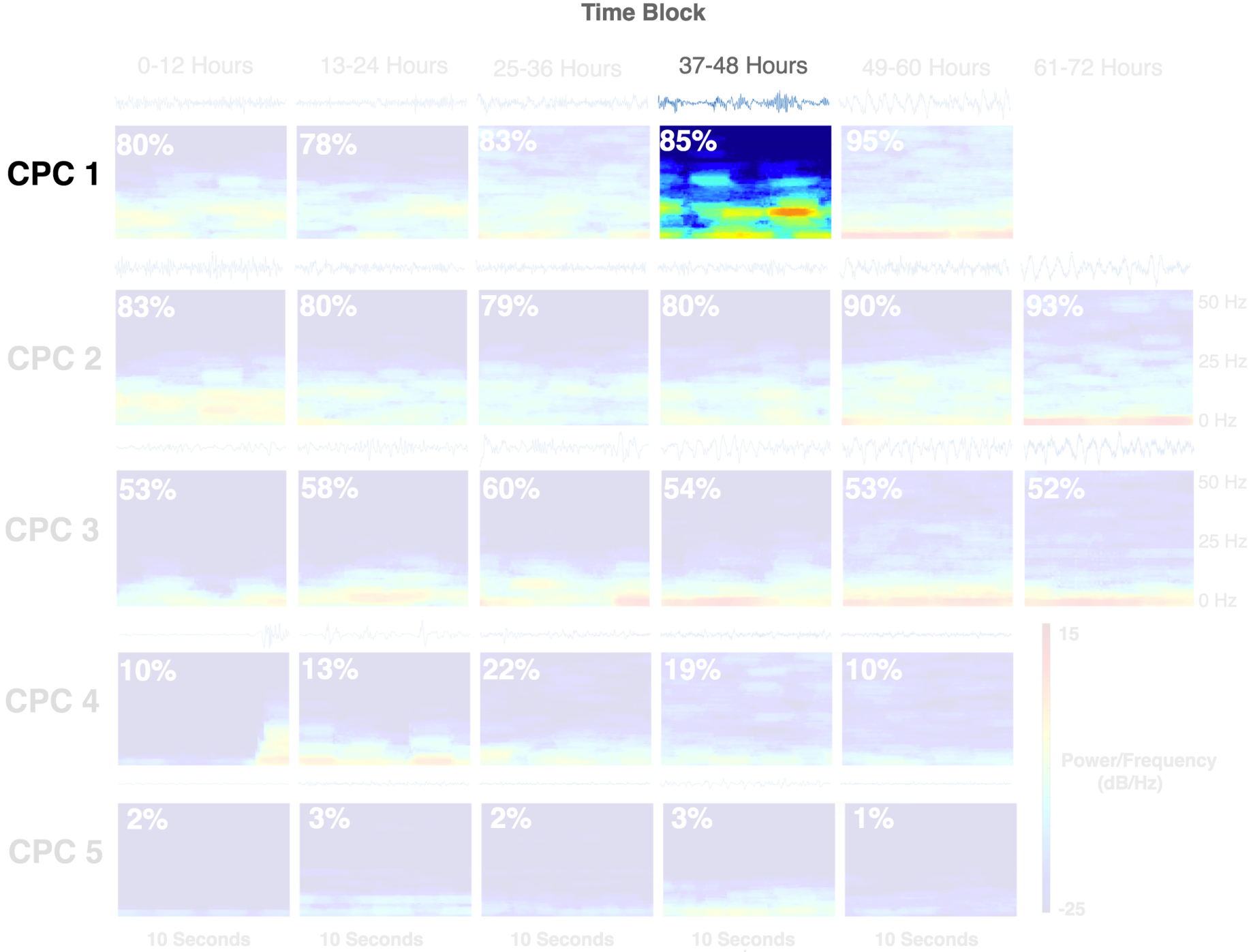

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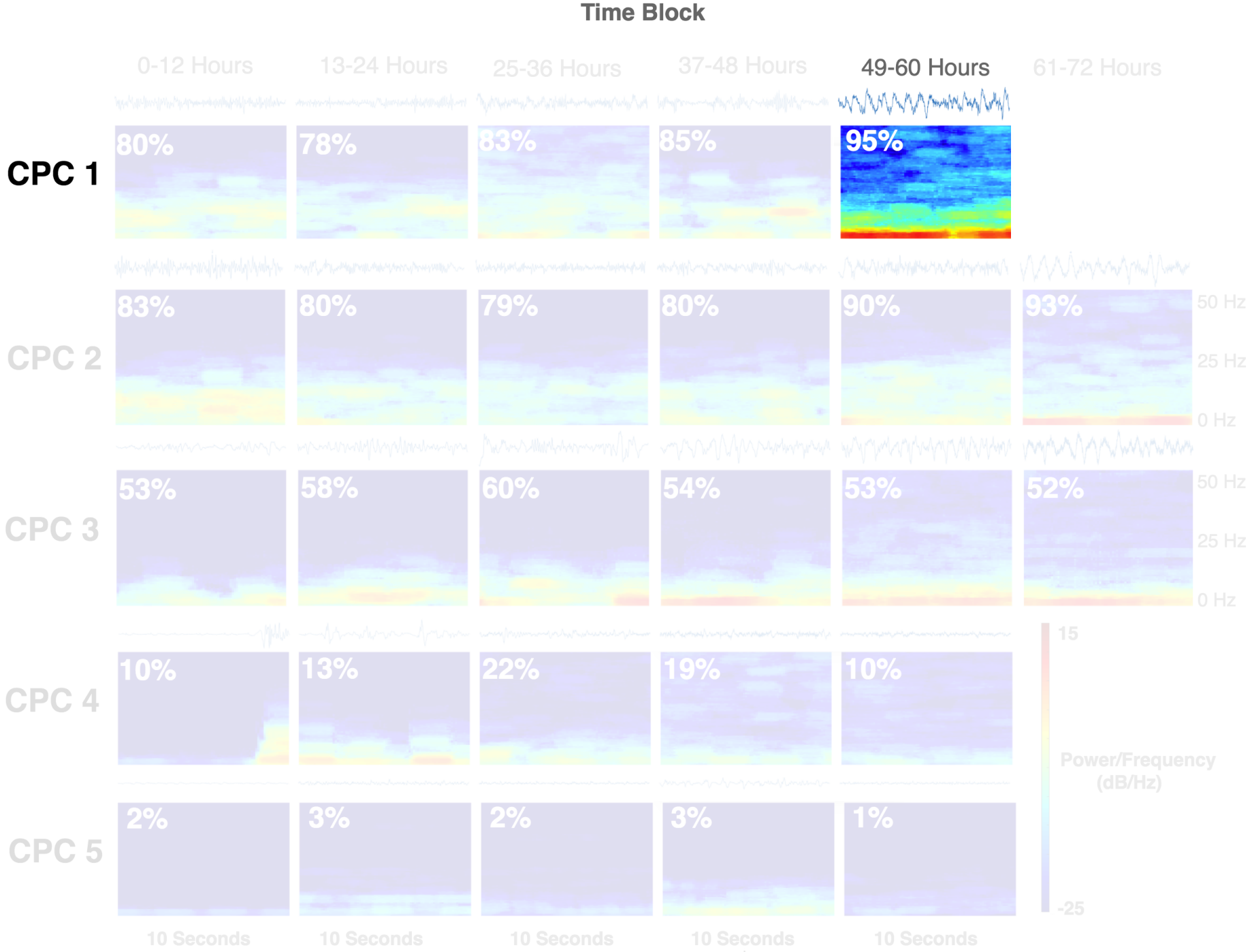

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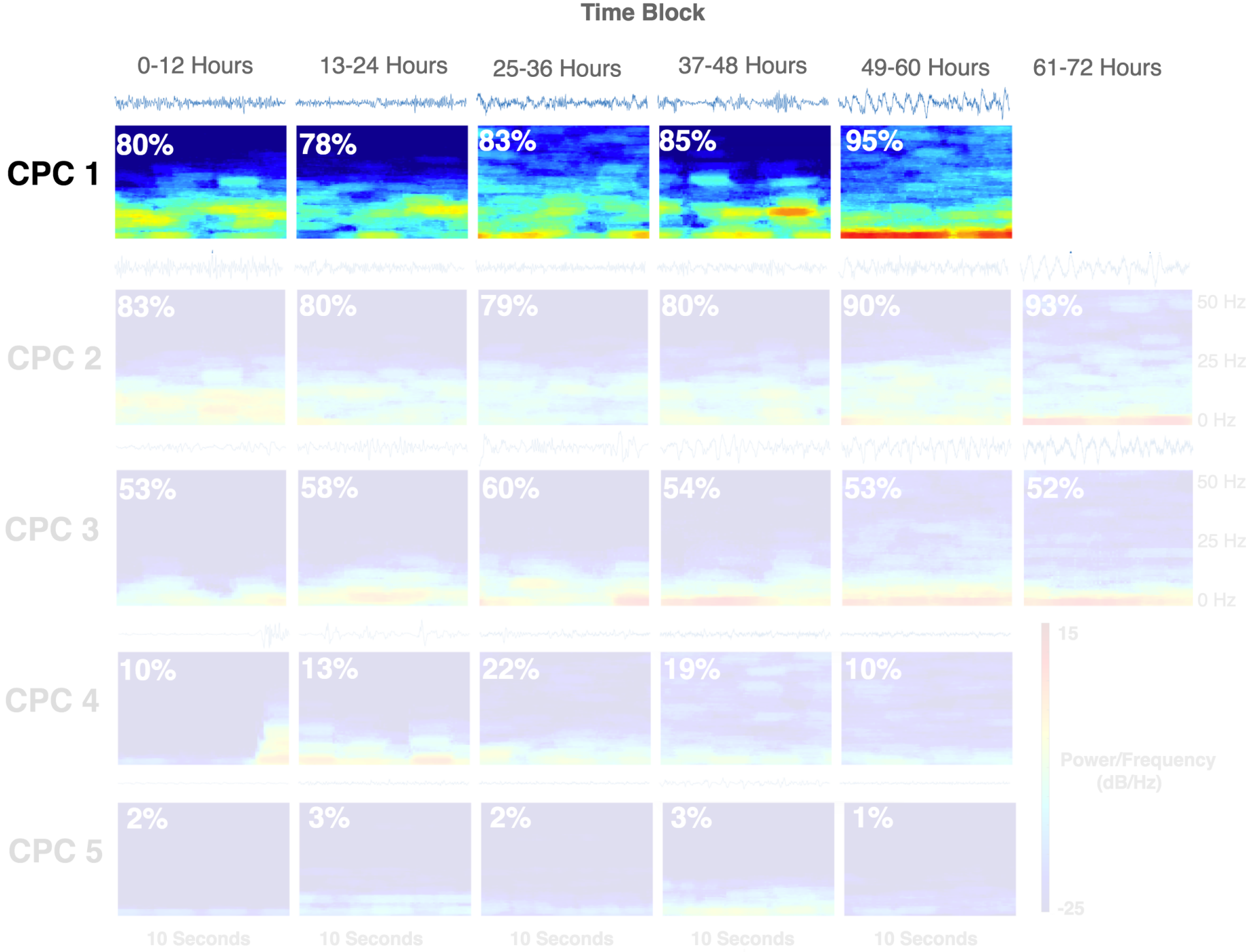

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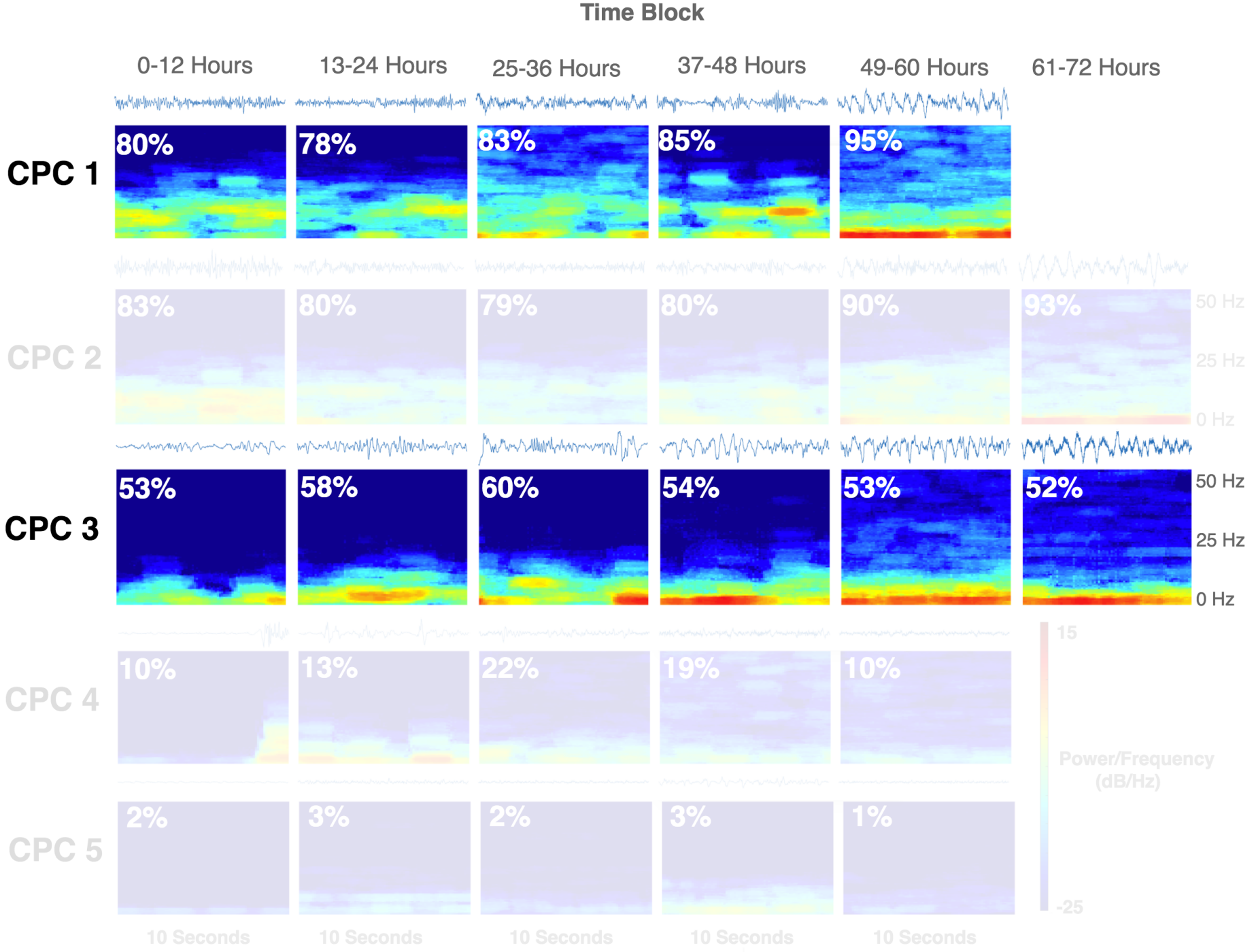

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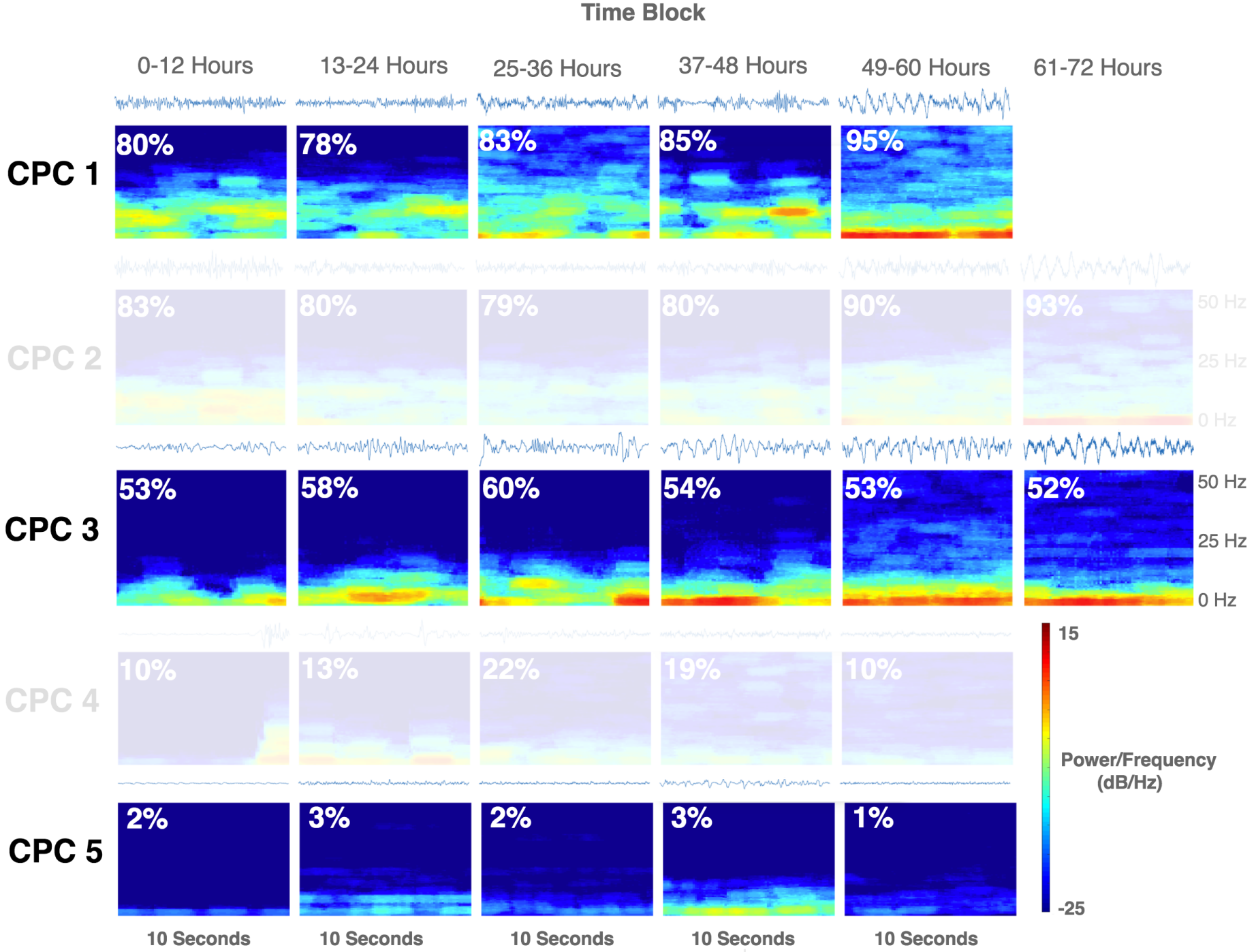

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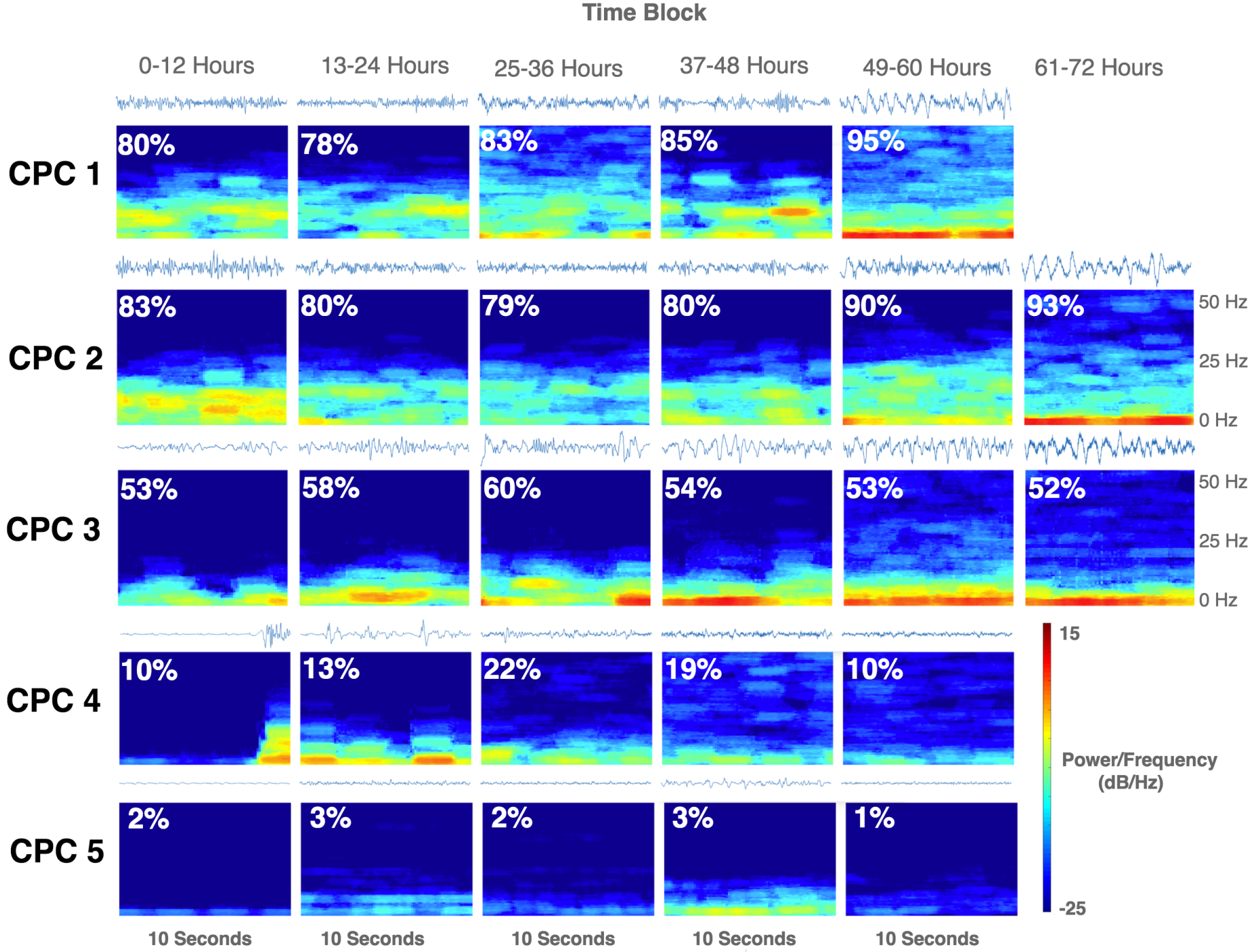
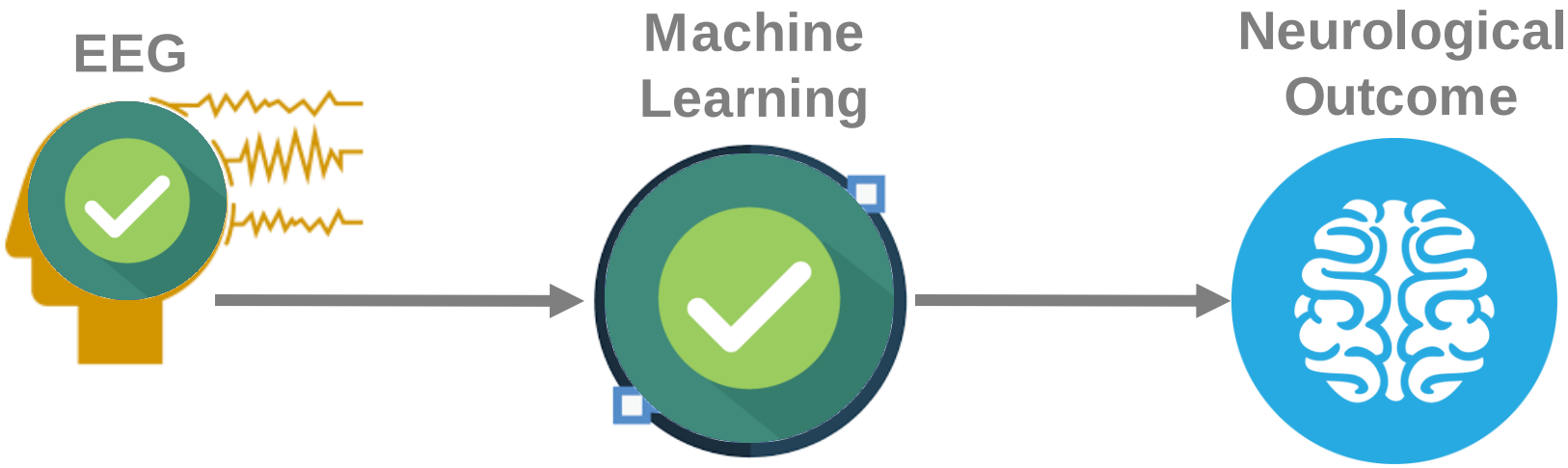


Assessing performance: classification and calibration



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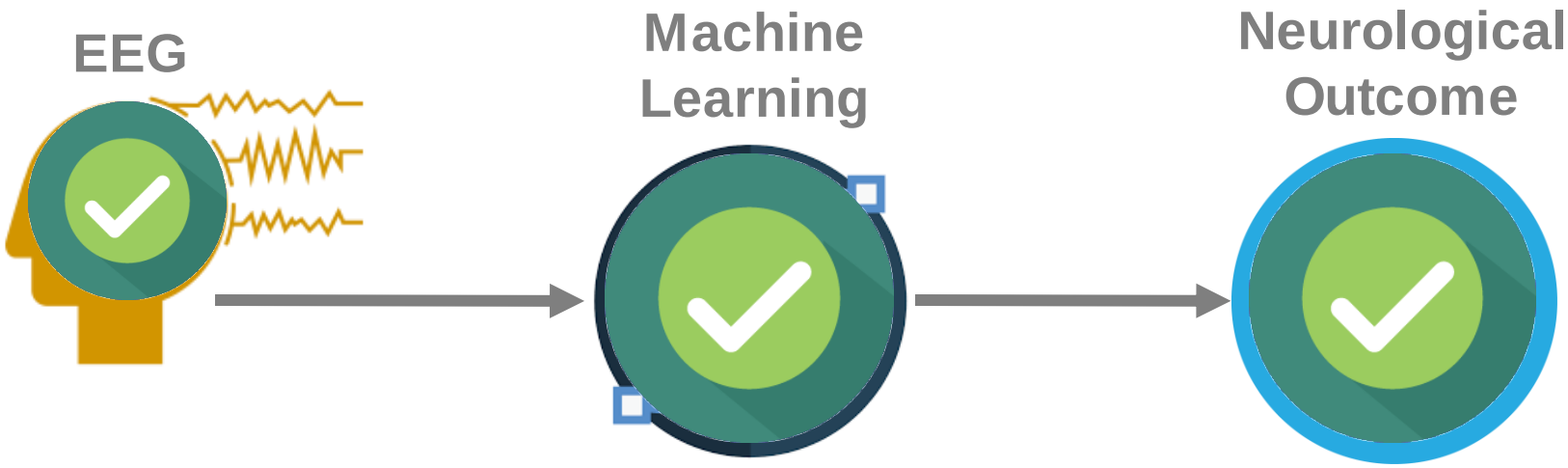

1. Collected an EEG archive 2x larger than largest set previously described in the literature

2. Logistic Regression with Elastic Memories and ~10x the features used in prior work

3. Our model had superior calibration and classification performance compared to state-of-the-art approaches

Conclusion

- A model that accounts for temporal fluctuations in feature values is better at prognosis, and better calibrated than models which do not

Acknowledgements and Thanks

Contributors:
Edilberto Amorim
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Siddharth Biswal
Valdery Moura Junior
Michael Donnino
Susan Herman

Prof. Roger G. Mark

Prof. Emery N. Brown

Dr. M. Brandon Westover

Prof. Thomas Heldt

Todays Talk:

~~**1. Data collection:**~~
~~Tool to translate paper data from hospital spreadsheets into digital form~~

~~**2. Decision support:**~~
~~Method to prognosticate coma outcomes after cardiac arrest~~

3. Optimal Control:
AI for passive monitoring of narrative mood during conversations

4. Moving Forward
Future directions, and opportunities for collaboration

Personalized Medication Dosing Using Volatile Data Streams

AAAI (2018)

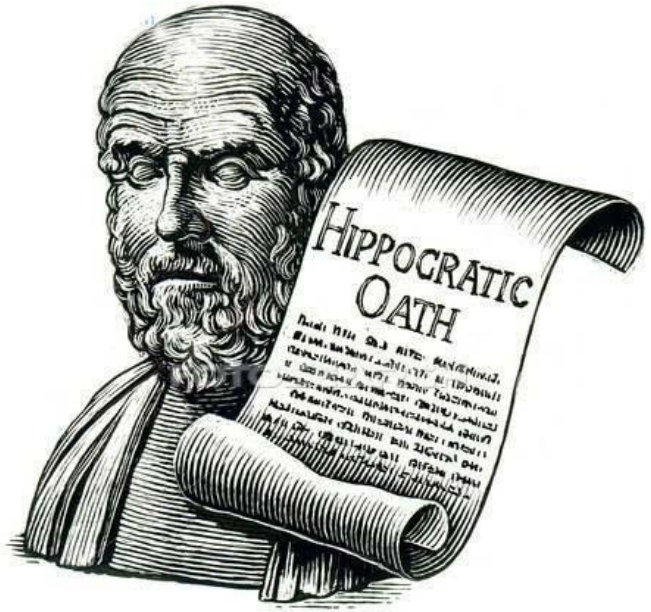
Personalized medicine: A brief history

- 460BC: Personalized medicine was envisioned by Hippocrates
- 1990-2003: A surge of interest in personalized medicine following the human genome project
- 2017: FDA approves record number of personalized medicines

Allen Frances, M.D., Contributor
Allen Frances MD is Professor Emeritus of Psychiatry and former Chair at Duke University

Patient-Centered Vs. Lab-Centered 'Personalized Medicine'

07/24/2017 01:12 pm ET | **Updated** Jul 24, 2017



"It is more important to know the patient who has the disease than the disease the patient has." — Hippocrates

Allen Frances, MD, Professor of Psychiatry, Duke University

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PMC PERSONALIZED MEDICINE COALITION

NEWS

FDA Approves Record Number of Personalized Medicines in 2017

But what is “personalization”

Personalized medicine:
Two approaches

- Static personalization is often performed at the level of demography
  (e.g. gender, weight)

- Dynamic personalization begins with demography, and becoming more patient-specific as better data and responses to treatment are collected
  (e.g. anesthesia control)

Drug Dosage Recommendations[1] (3)

Table. 4.4

Dose in mg/kg (maximum dosage in parentheses)							
Drug	Adults/Children[2]			Daily	1 time/week[3]	2 times/ week[3]	3 times/ week[3]
EMB[4]	Adults	Weight	40-55 kg	14.5-20 mg/kg (800 mg)		36.4-50 mg/kg (2000 mg)	21.8-30 mg/kg (1200 mg)
			56-75 kg	16-21.4 mg/kg (1200 mg)		37.3-50 mg/kg (2800 mg)	26.7-35.7 mg/kg (2000 mg)
			76-90 kg	17.8-21.1 mg/kg (1600 mg)		44.4-52.6 mg/kg (4000 mg)	26.7-31.6 mg/kg (2400 mg)
	Children			15-20 mg/kg (1000 mg)		50 mg/kg (2500 mg)	

Ethambutol Dosing Suggestions

Personalized medicine: Two approaches

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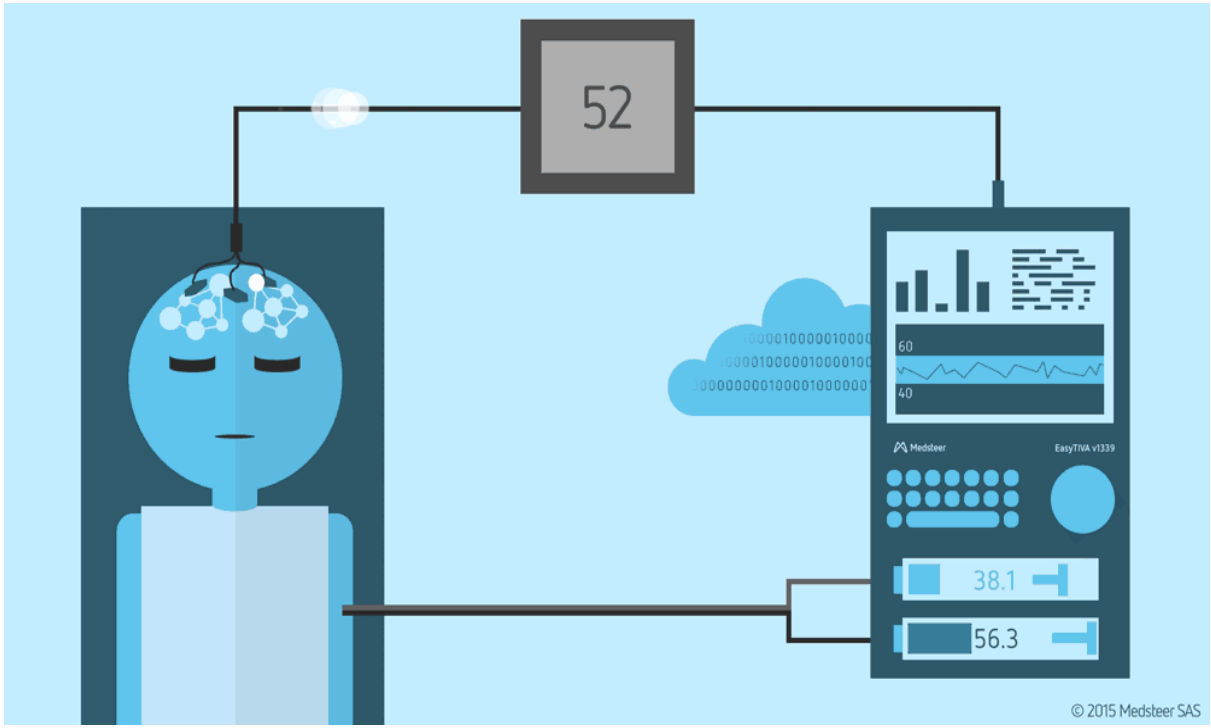
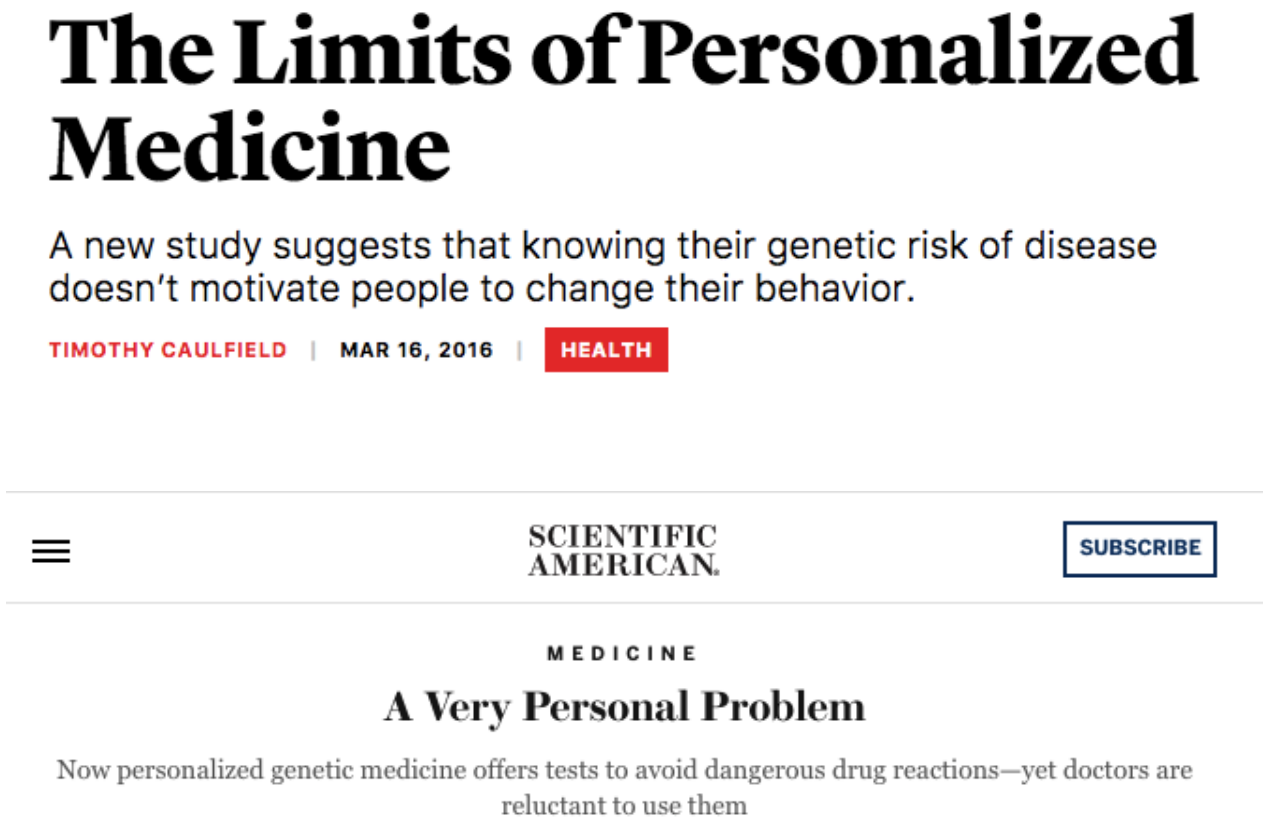
- Dynamic personalization begins with demography, and becoming more patient-specific as better data and responses to treatment are collected (e.g. anesthesia control)



Source: Medsteer, http://medsteer.com/

Personalized medicine:
Needs deployable approaches

- Patients and providers have been slow to adopt personalized medicines, or alter established behaviors
- Solutions must work under real-world, imperfect conditions
- Translational impact will require interpretable approaches that integrate with provider and patient workflows to address high-value problems



The Limits of Personalized Medicine

A new study suggests that knowing their genetic risk of disease doesn't motivate people to change their behavior.

TIMOTHY CAULFIELD | MAR 16, 2016 | HEALTH

SCIENTIFIC AMERICAN.

SUBSCRIBE

MEDICINE

A Very Personal Problem

Now personalized genetic medicine offers tests to avoid dangerous drug reactions—yet doctors are reluctant to use them

Personalized medicine:
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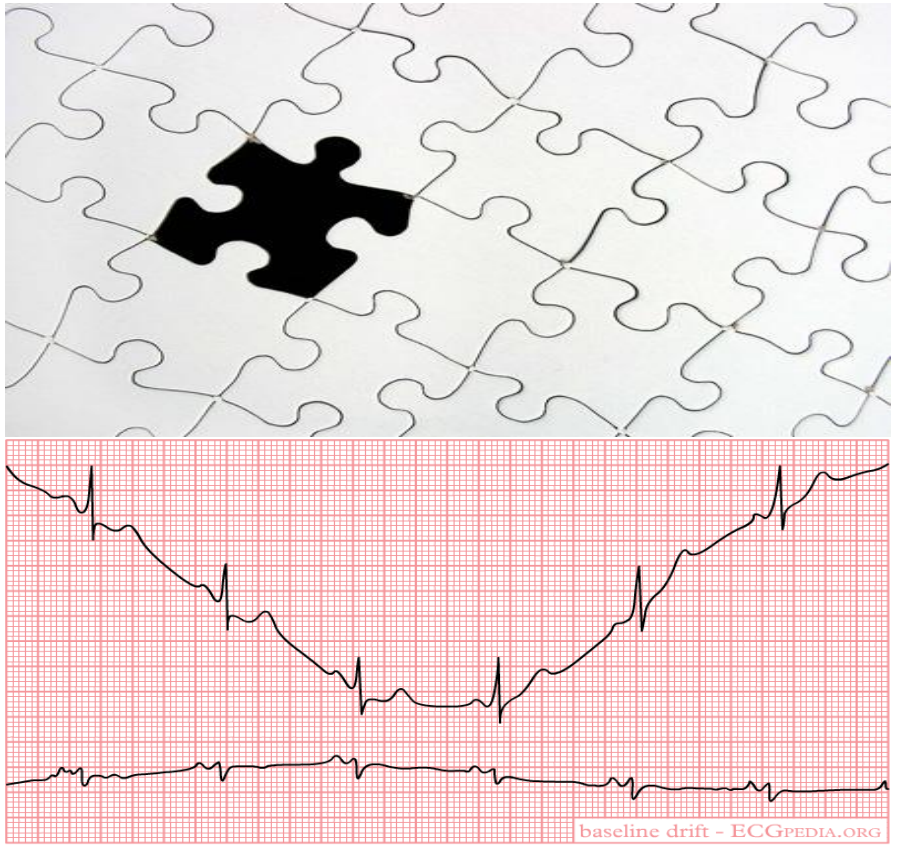
Missing Data



Artifacts

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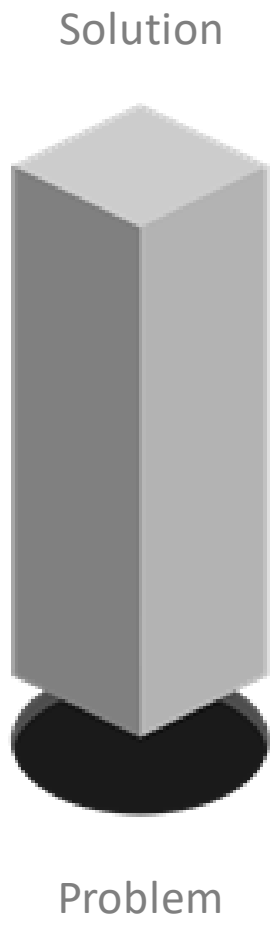

Personalized medicine:
High value problem

- Medication dosing

- Errors are responsible for ~400,000 preventable hospital deaths each year

- Over- or under- dosing can
  - Extended hospital stay,
  - Require follow-up interventions,
  - Incur additional morbidity.

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- A personalized medication dosing policy for a common anticoagulant, heparin

- Provide an **initial dose** based on static demographics

- Provide **subsequent doses** based on real-time, noisy data stream

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Methods

The data

- We extracted 4,470 patients from MIMIC who received intravenous UFH infusions during their ICU stay

- MIMIC is a de-identified, publicly available EMR archive of 40,000+ unique ICU admissions between 2001 - 2016.

If you use MIMIC data or code in your work, please cite the following publication:

MIMIC-III, a freely accessible critical care database. Johnson AEW, Pollard TJ, Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolovits P, Celi LA, and Mark RG. Scientific Data (2016). DOI: 10.1038/sdata.2016.35.
Available from: http://www.nature.com/articles/sdata201635

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The outcome

- Clinicians dose heparin, wait 6-12 hours, measure anticoagulation, then adjust dose as needed

- Goal is to obtain a therapeutic level of anticoagulation as quickly as possible, as indicated by aPTT

- aPTT may be categorized into one of three **states: therapeutic, sub-therapeutic, and supra-therapeutic**

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Clinical Features

- We extracted all features that are believed to confound the relationship between UFH and aPTT

Features (N= 9684)	Mean	Standard Deviation	Missing Data (%)
Static Features			
Age	68.01	14.91	0.00
Gender (%Male)	58	-	0.00
ICU Type (%Surgical)	35	-	0.00
Ethnicity (%White)	69	-	0.00
End Stage Renal Disease (%)	3	-	0.00
Pulmonary Embolism (%)	9	-	0.00
Continuously Measured Features			
Heparin Dose (units/kg)	11.79	4.11	6.88
White Blood Cell Count	12.26	6.35	6.23
Creatinine	1.58	1.48	5.18
Carbon Dioxide	24.61	4.67	5.69
Heart Rate (Mean)	84.81	17.12	0.01
Glasgow Coma Score	12.40	3.63	0.02
Hematocrit	31.50	4.65	4.27
Hemoglobin	10.63	1.66	6.45
Platelet Count	226.76	118.29	5.10
Urea	31.72	23.45	6.03
Temperature (F)	98.28	2.71	7.05
International Normalized Ratio	1.50	1.10	7.03
Prothrombin Time	15.22	3.99	0.12
Peripheral Capillary Oxygen Saturation	97.24	2.65	0.01

Clinical Features

- Static features are single measures that don't change over time

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- These features are routinely collected (no missing data)

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Pulmonary Embolism (%)	9	-	0.00
Continuously Measured Features			
Heparin Dose (units/kg)	11.79	4.11	6.88
White Blood Cell Count	12.26	6.35	6.23
Creatinine	1.58	1.48	5.18
Carbon Dioxide	24.61	4.67	5.69
Heart Rate (Mean)	84.81	17.12	0.01
Glasgow Coma Score	12.40	3.63	0.02
Hematocrit	31.50	4.65	4.27
Hemoglobin	10.63	1.66	6.45
Platelet Count	226.76	118.29	5.10
Urea	31.72	23.45	6.03
Temperature (F)	98.28	2.71	7.05
International Normalized Ratio	1.50	1.10	7.03
Prothrombin Time	15.22	3.99	0.12
Peripheral Capillary Oxygen Saturation	97.24	2.65	0.01

Clinical Features

- Continuously measured features change over time
- Heparin dose is one of these features

Features (N= 9684)	Mean	Standard Deviation	Missing Data (%)
Static Features			
Age	68.01	14.91	0.00
Gender (%Male)	58	-	0.00
ICU Type (%Surgical)	35	-	0.00
Ethnicity (%White)	69	-	0.00
End Stage Renal Disease (%)	3	-	0.00
Pulmonary Embolism (%)	9	-	0.00
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Heparin Dose (units/kg)	11.79	4.11	6.88
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Clinical Features

- Continuously measured features change over time
- Among several

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Clinical Features

- Continuously measured features change over time
- The value of these features are occasionally missing, or for some patients unmeasured

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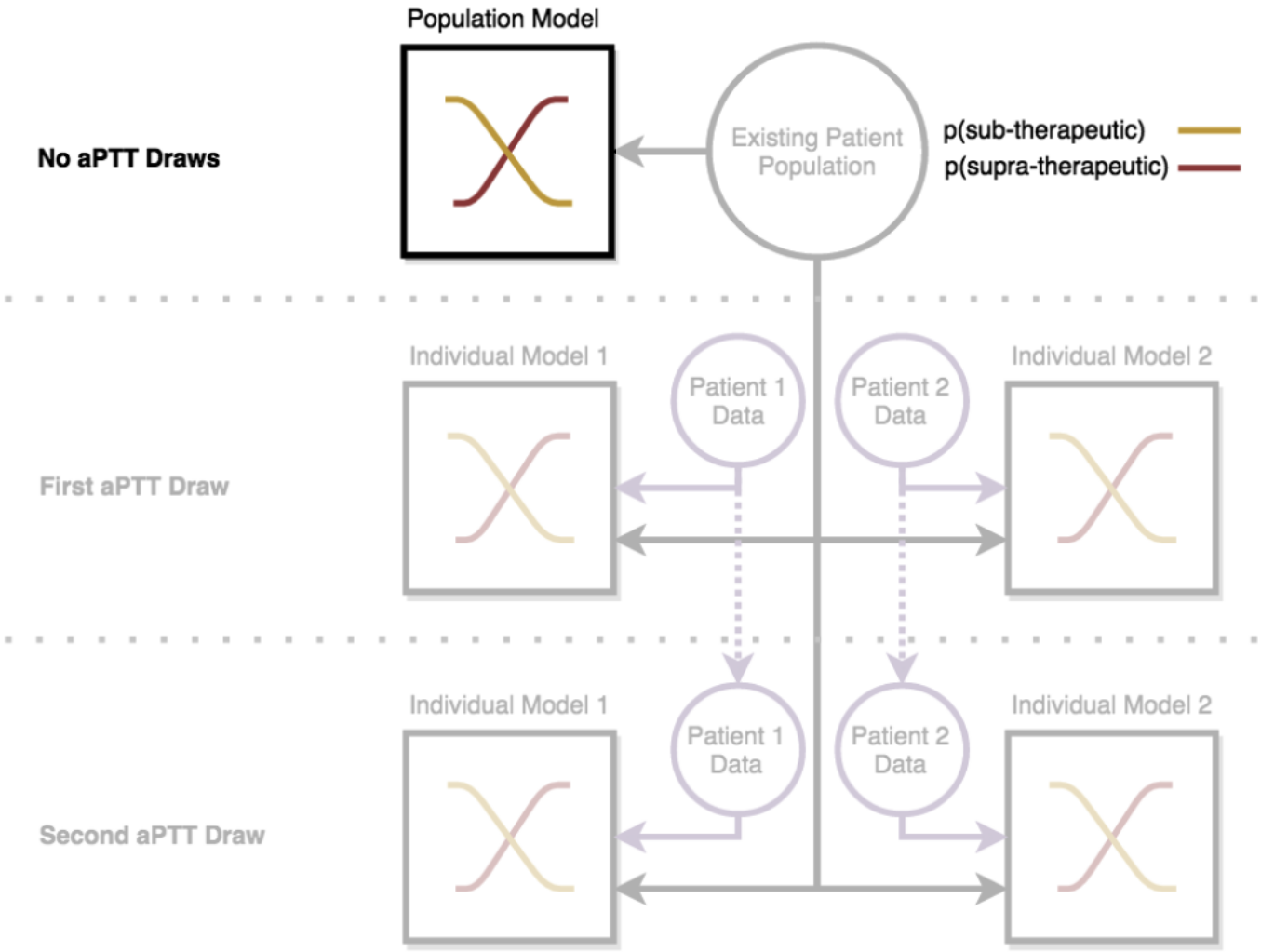
Proposed Approach

- Multinomial logistic regression (MNR) where model features and parameters are re-estimated for each patient, at each aPTT draw using a weighted combination of the data from
  - a population of existing patients, and
  - the individual patient's real-time data stream



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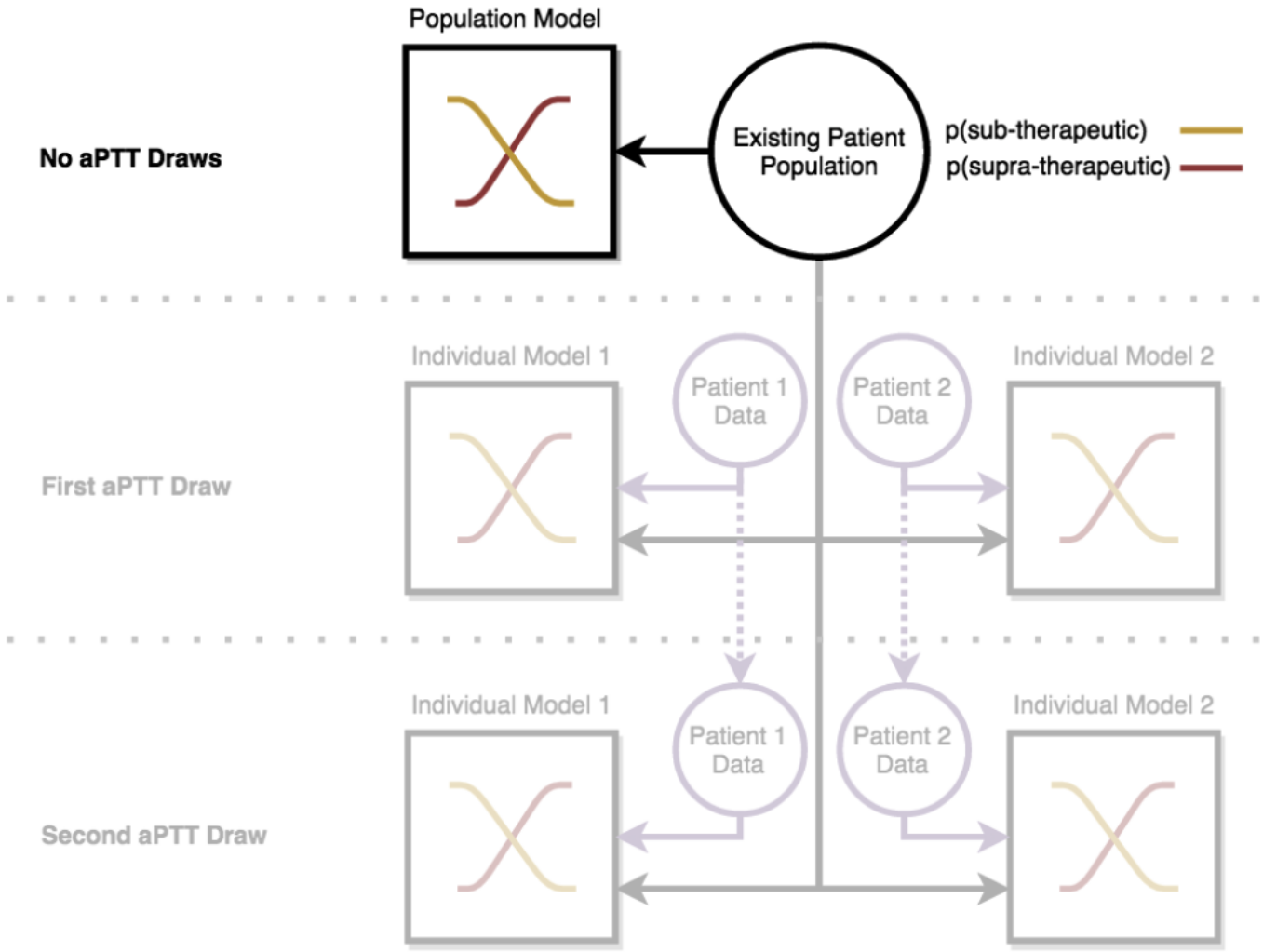

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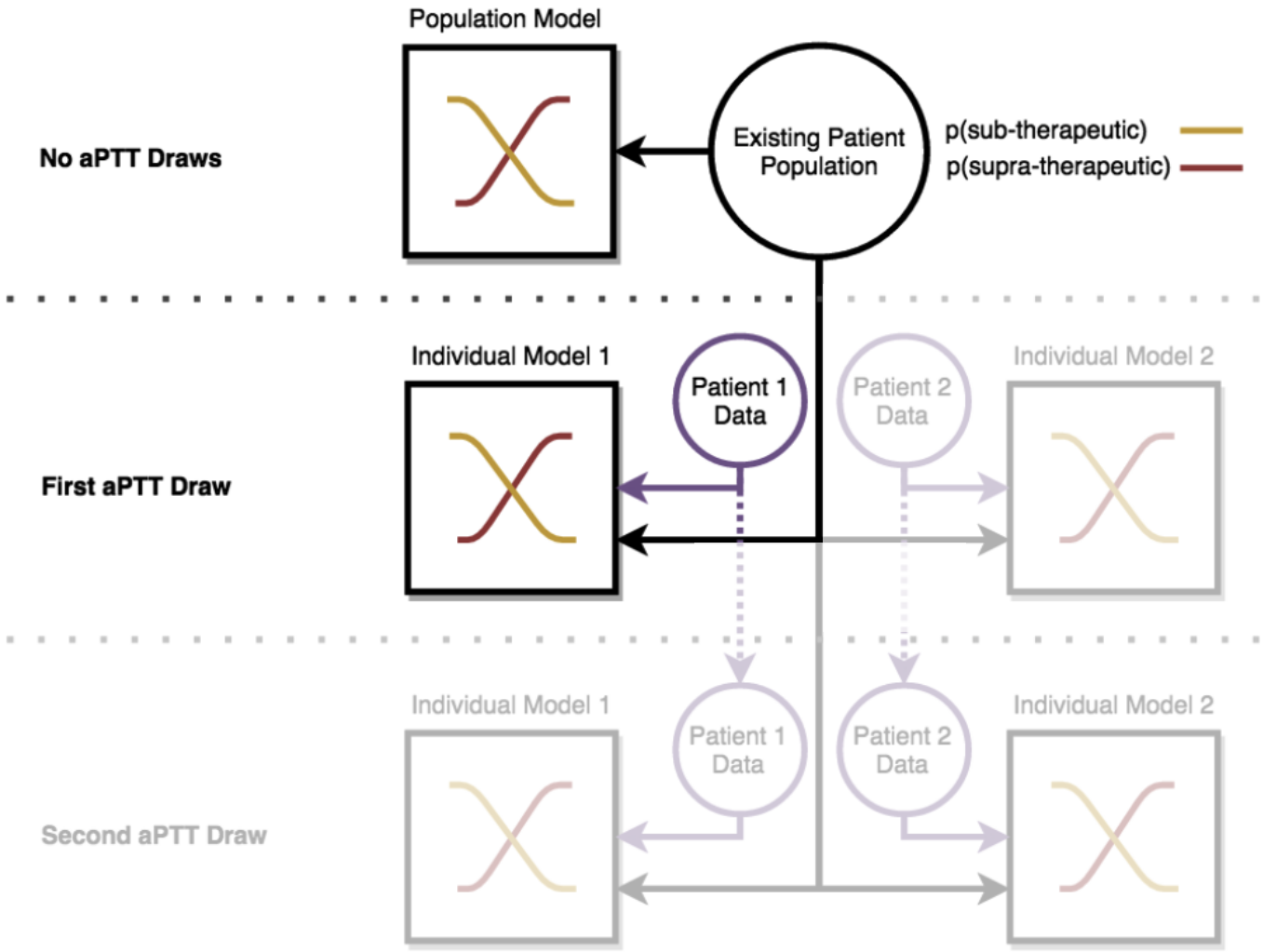

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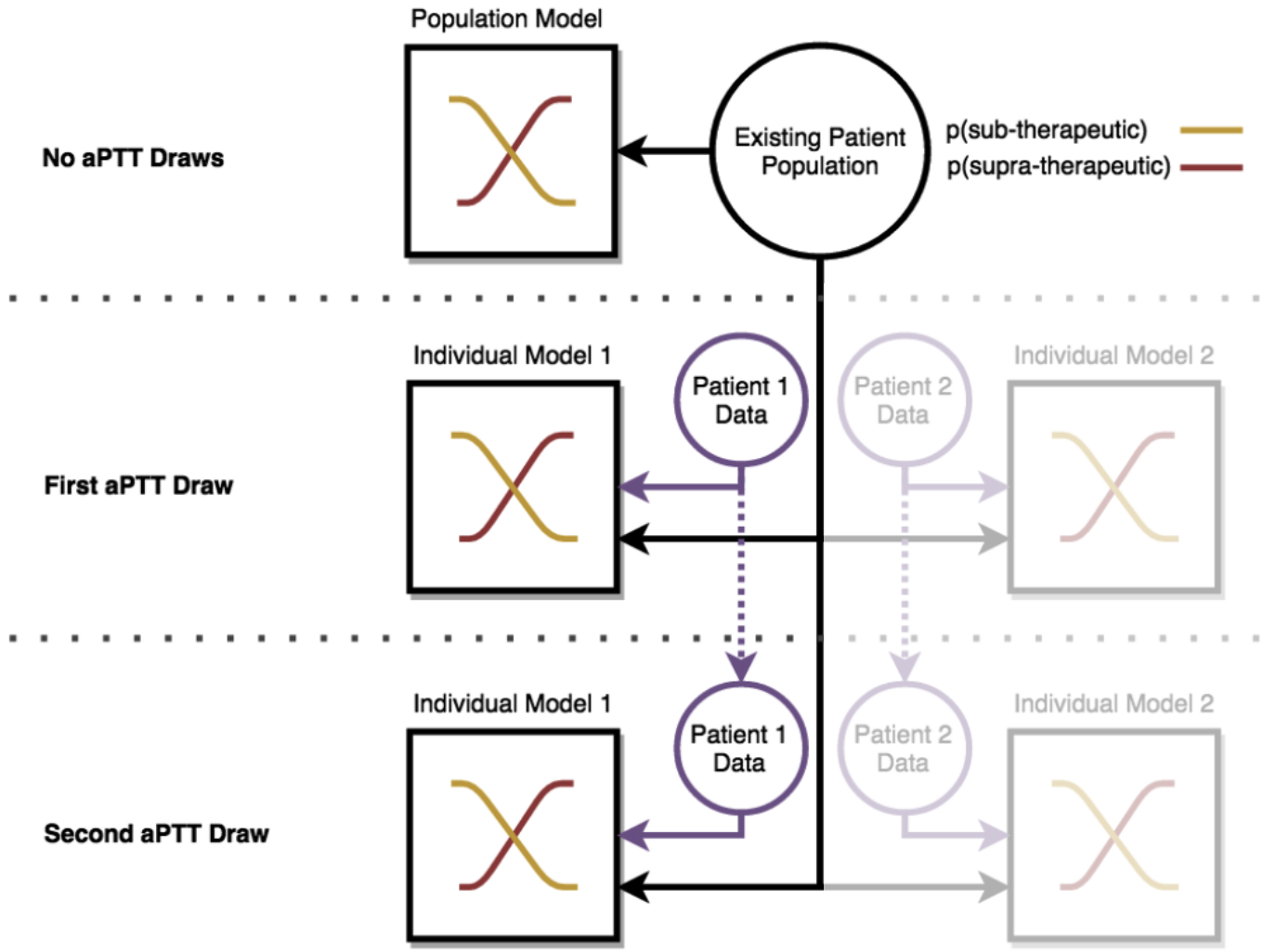

Method, formally:

State	Interval	Individual	Population
s	n	i	p

Data	Samples	Features	Outcome
X_i^n	r_i^n	c_i^n	$\mathbf{y}_i^n$
X_p^n	r_p^n	c_i^n	$\mathbf{y}_p^n$

Parameters	Data row (p)	Data row (i)
$\theta_{i,s}^n$	$\mathbf{x}_p^{(k)} y_p^{(k)}$	$\mathbf{x}_i^{(j)} y_i^{(j)}$

α γ	weighting hyper-parameters

Multinomial Logistic Regression, at each interval

$$p(y_i^n = s|\mathbf{x}_i^n, \theta_i^n) = \frac{e^{\mathbf{x_i}^\mathsf{T}\theta_{i,s}^n}}{\sum_{k=1}^{3} e^{\mathbf{x_i}^\mathsf{T}\theta_{i,k}^n}}$$

Where likelihood is a weighted combination of *p* and *i* data

$$\mathcal{L}(\theta_i^n) = \prod_{j=1}^{r_i^n} p(y_i^{(j)}|\mathbf{x}_i^{(j)}, \theta_i^n)^{\phi(n)} \times \prod_{k=1}^{r_p} p(y_p^{(k)}|\mathbf{x}_p^{(k)}, \theta_i^n)$$

Population versus individual data weight is time-dependent

$$\phi(n) = \frac{\alpha}{1 + e^{-(\gamma_0 + \gamma_1 * n)}}$$

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P(supra) increases wrt dose; P(sub) decreases wrt dose; P(ther) is maximum when:

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Yielding: $$d_i^n = \frac{\kappa_{i,u}^{n} - \kappa_{i,o}^{n}}{\beta_{i,o}^{n} - \beta_{i,u}^{n}}$$

Where:

	Heparin parameter	Non-heparin feature impact
over	$\beta_{i,o}^{n}$	$\kappa_{i,o}^{n}$
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Non-personalized baseline methods

- **Baseline 1: Multinomial logistic regression using static features**, without personalization
- **Baseline 2: Multinomial logistic regression using all features**, without personalization and excluding subjects with missing data (23.6%) of all patients
- **Baseline 3: Multilayer neural network.** Densely connected, feed-forward, two hidden layers, softmax output, ReLU activation, Xavier initialization, scaled conjugate gradient descent optimization, grid search topology selection.
- **Baseline 4: Reinforcement learning via deterministic policy network**. We defined the state, action, and rewards as follows: (1) State: aPTT and laboratory measures (2) Actions: maintain dose, increase dose, decrease dose. (4) Rewards: proportional to the aPTT error.

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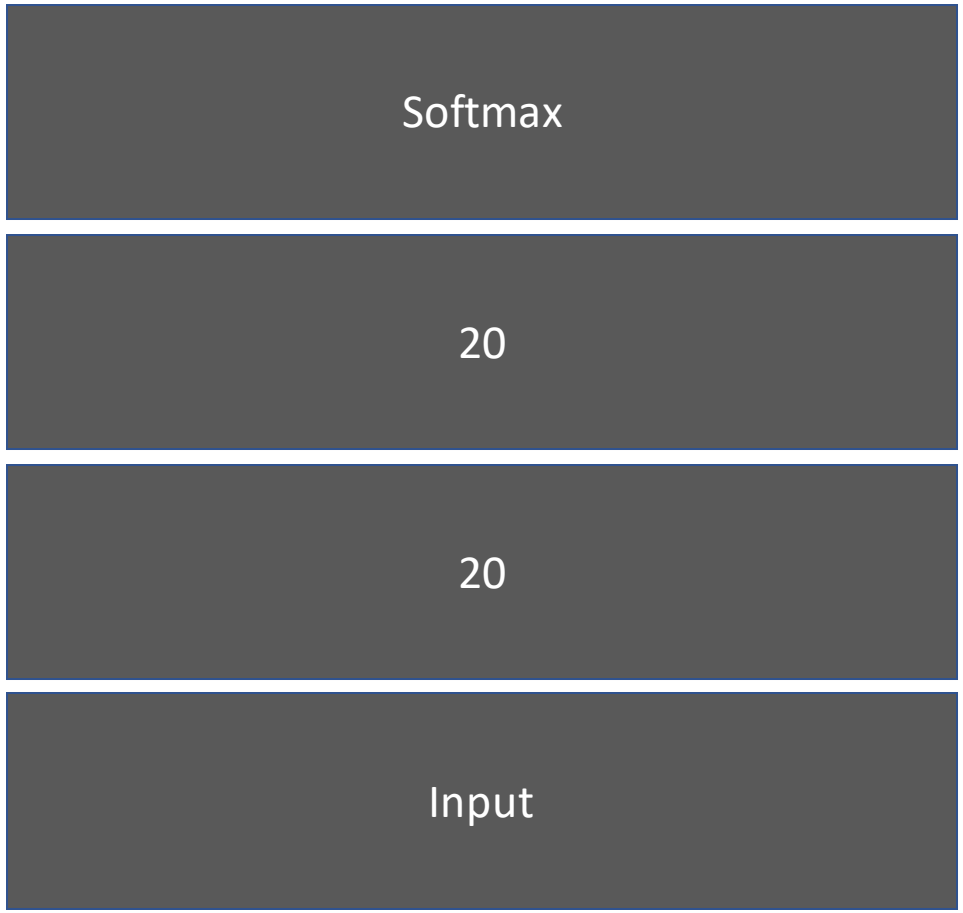

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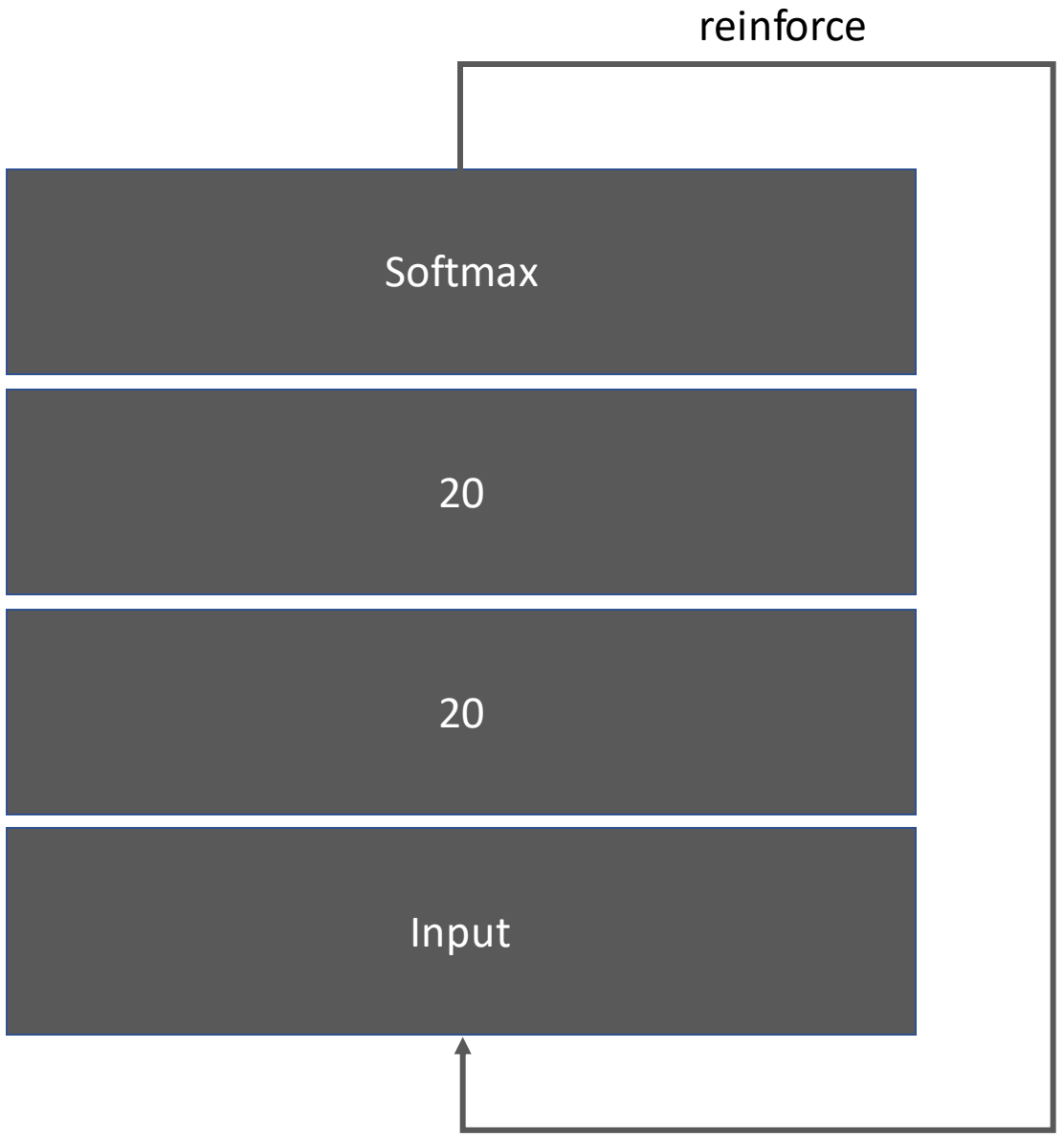
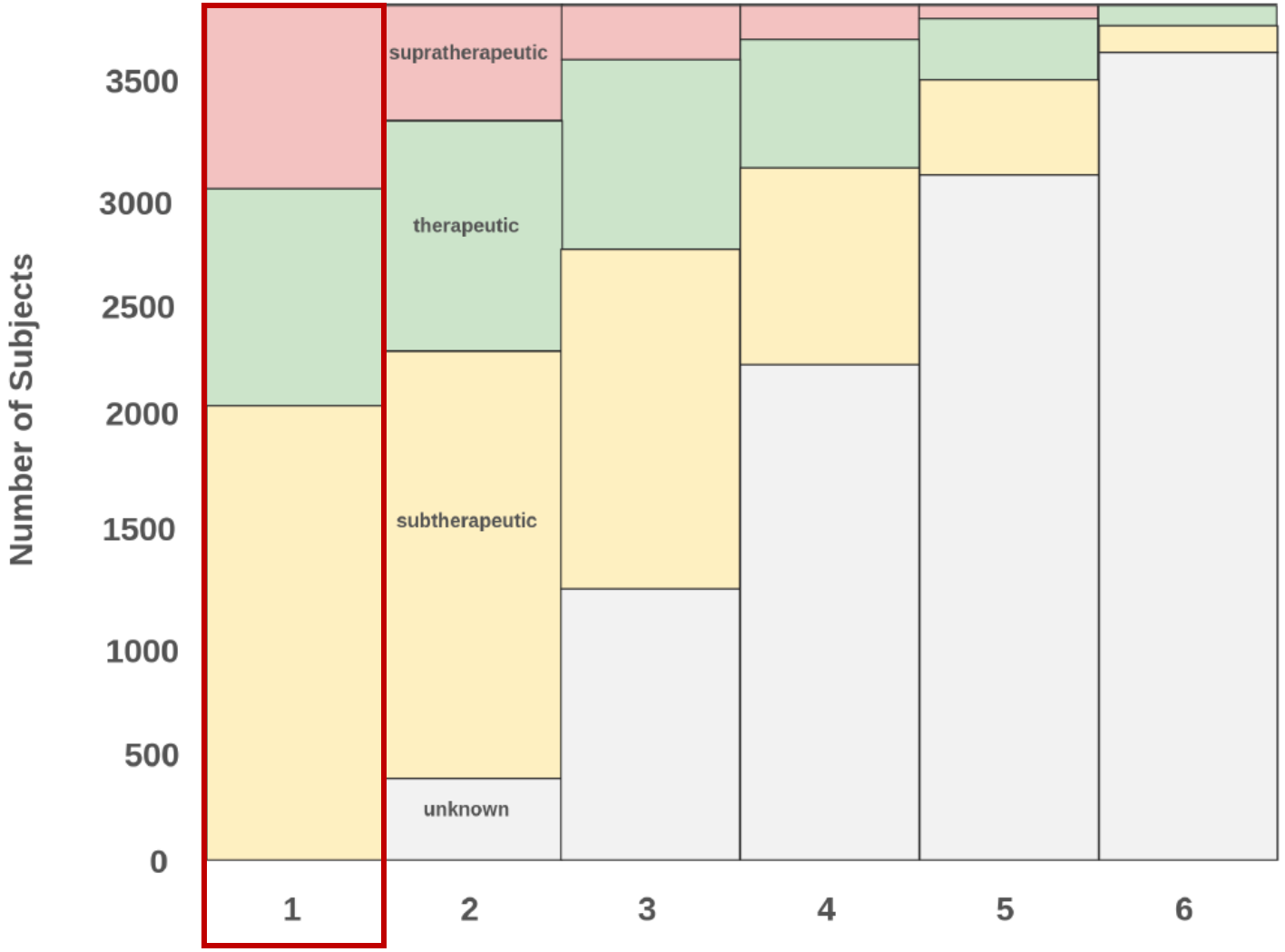


Results

Data characteristics

- UFH misdoing is consistently error-prone even after multiple aPTT draws (and consequent opportunities for dose adjustment).
- 80% of our sample stopped receiving aPTT draws after their fifth adjustment
- 5% of the 3,883 patient with recorded aPTT values had a sixth dose adjustment.



2/3 of patients mis-dosed

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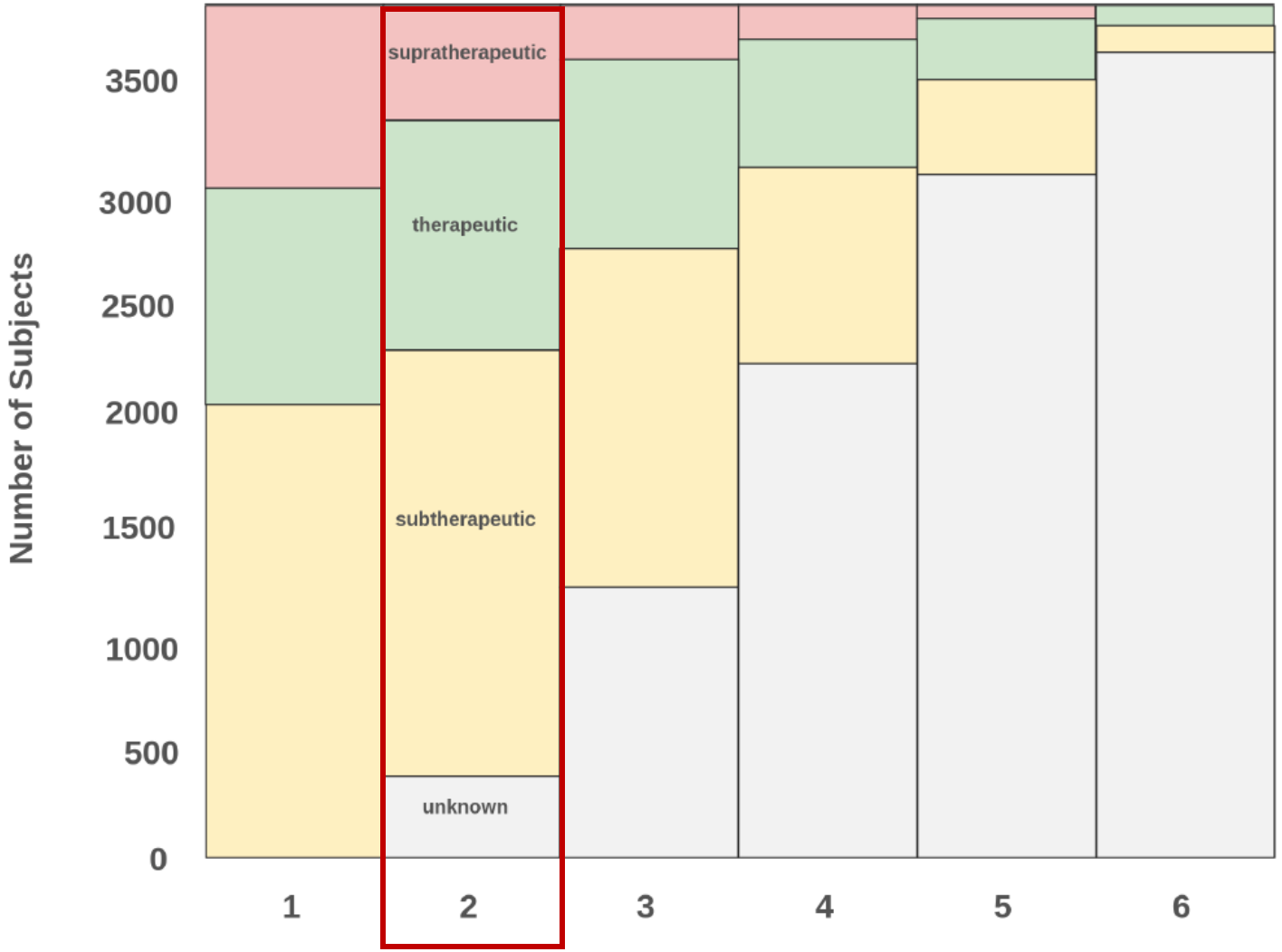

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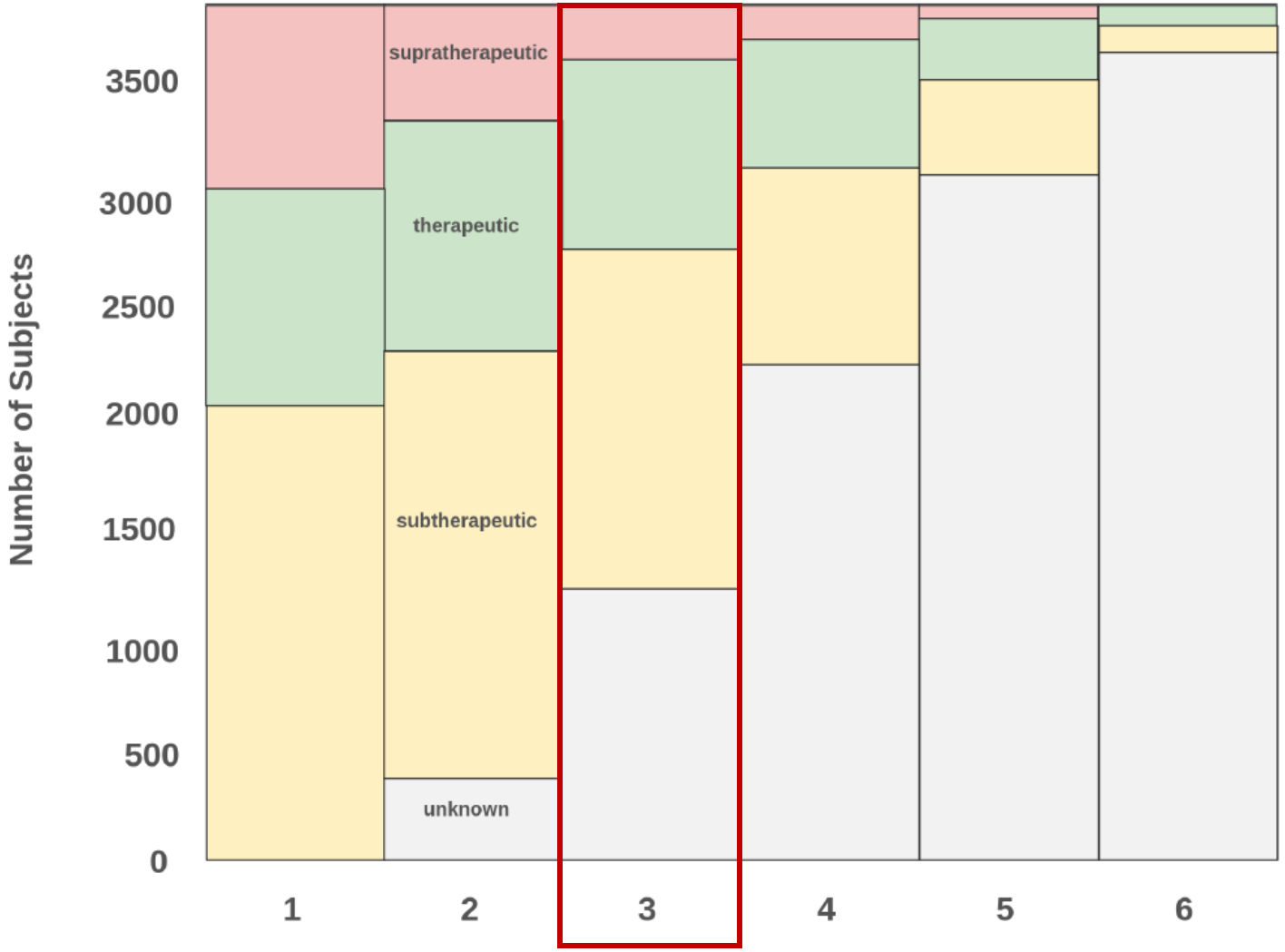

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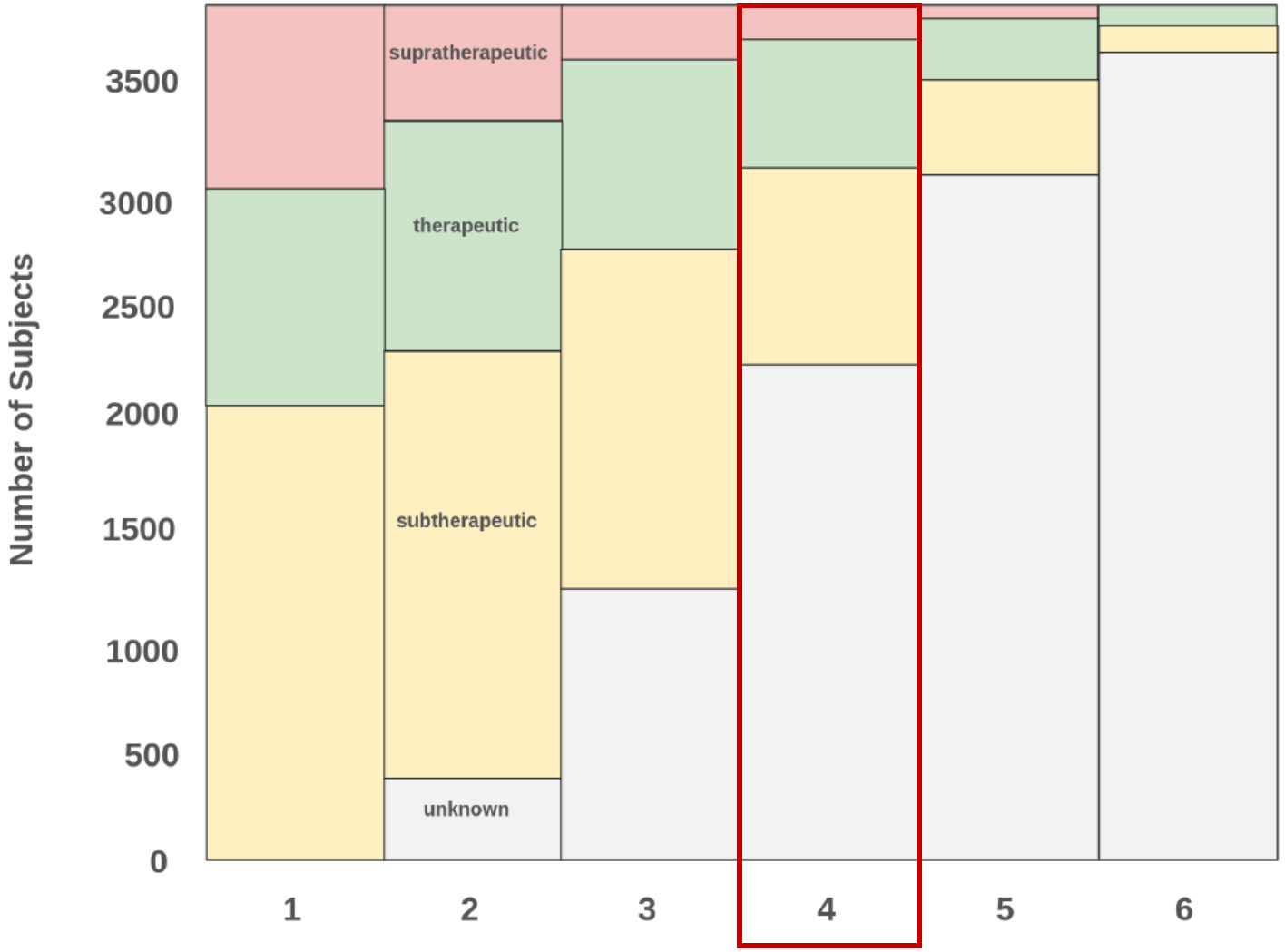

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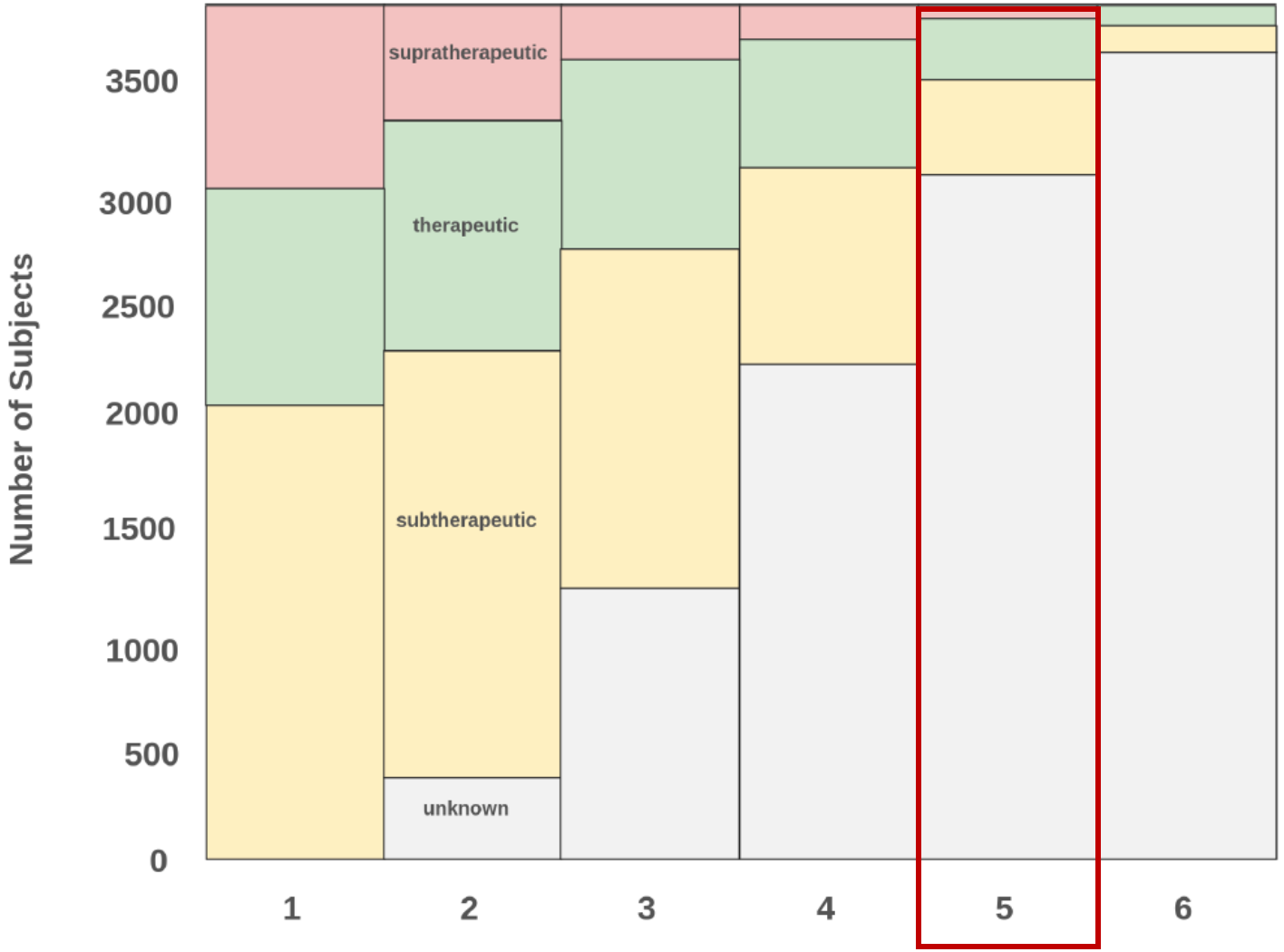

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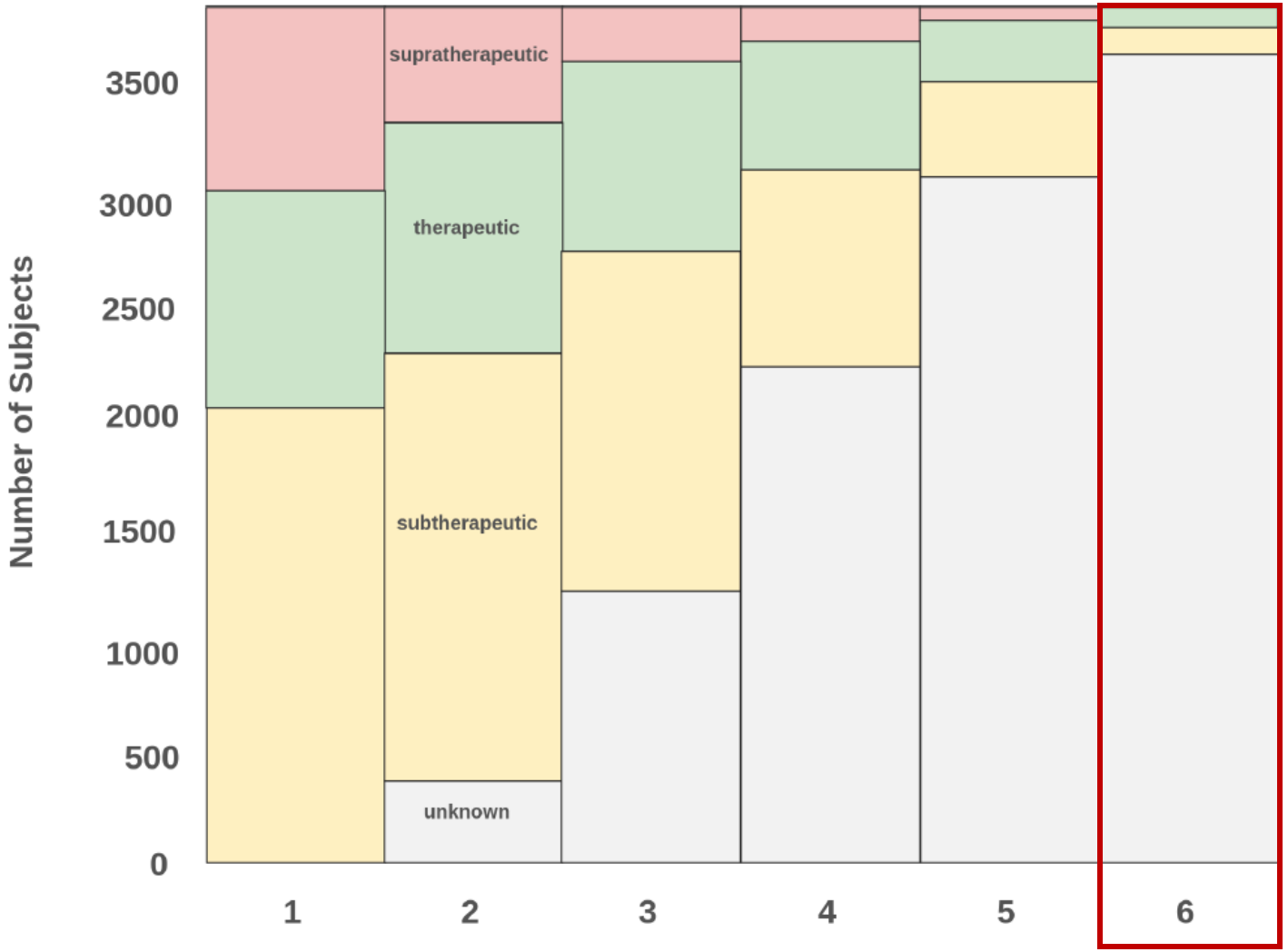

Overall performance of personalized approach

- Highest overall accuracy (60%)
- Highest overall VUS (0.46), a 0.02 improvement over the RL approach
- 7.3% more likely to detect supra-therapeutic doses than the population model that didn’t exclude patients

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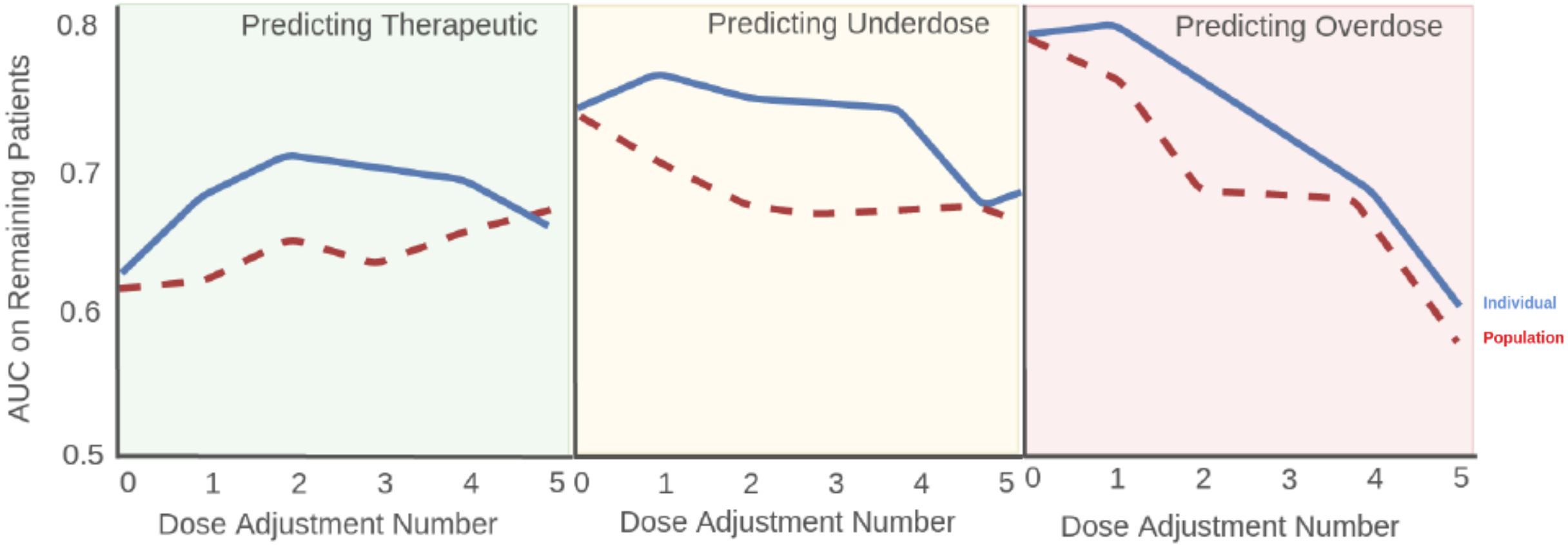
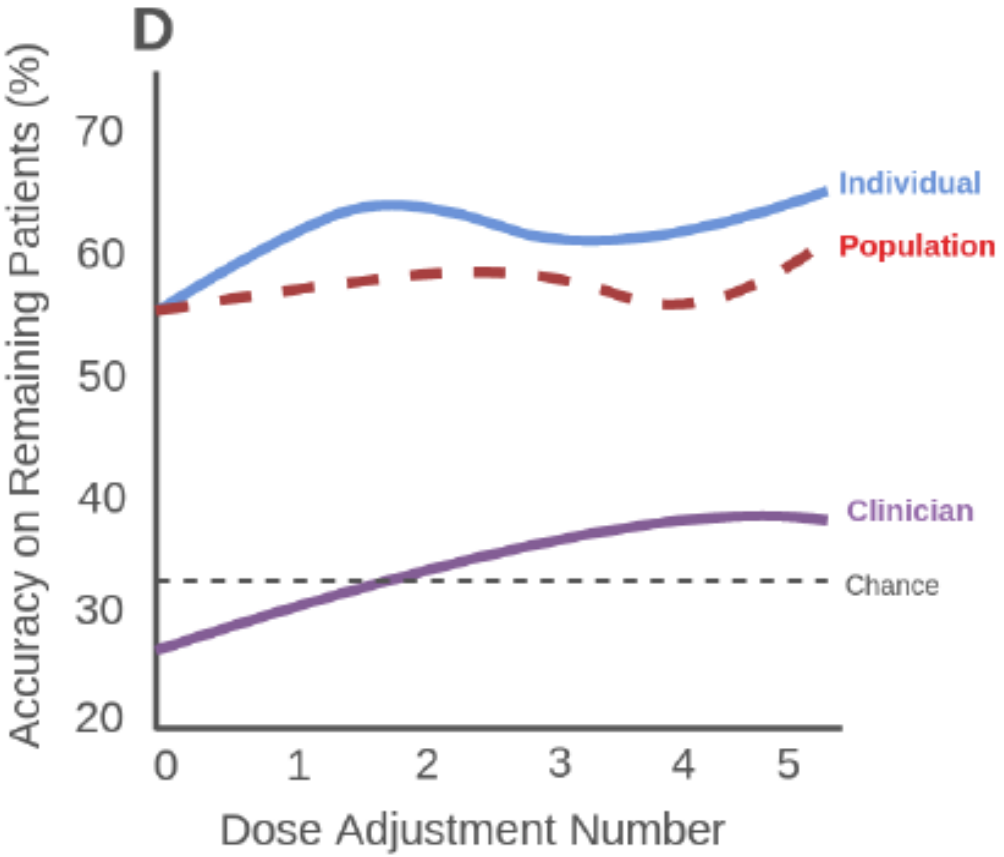
Temporal performance of personalized approach

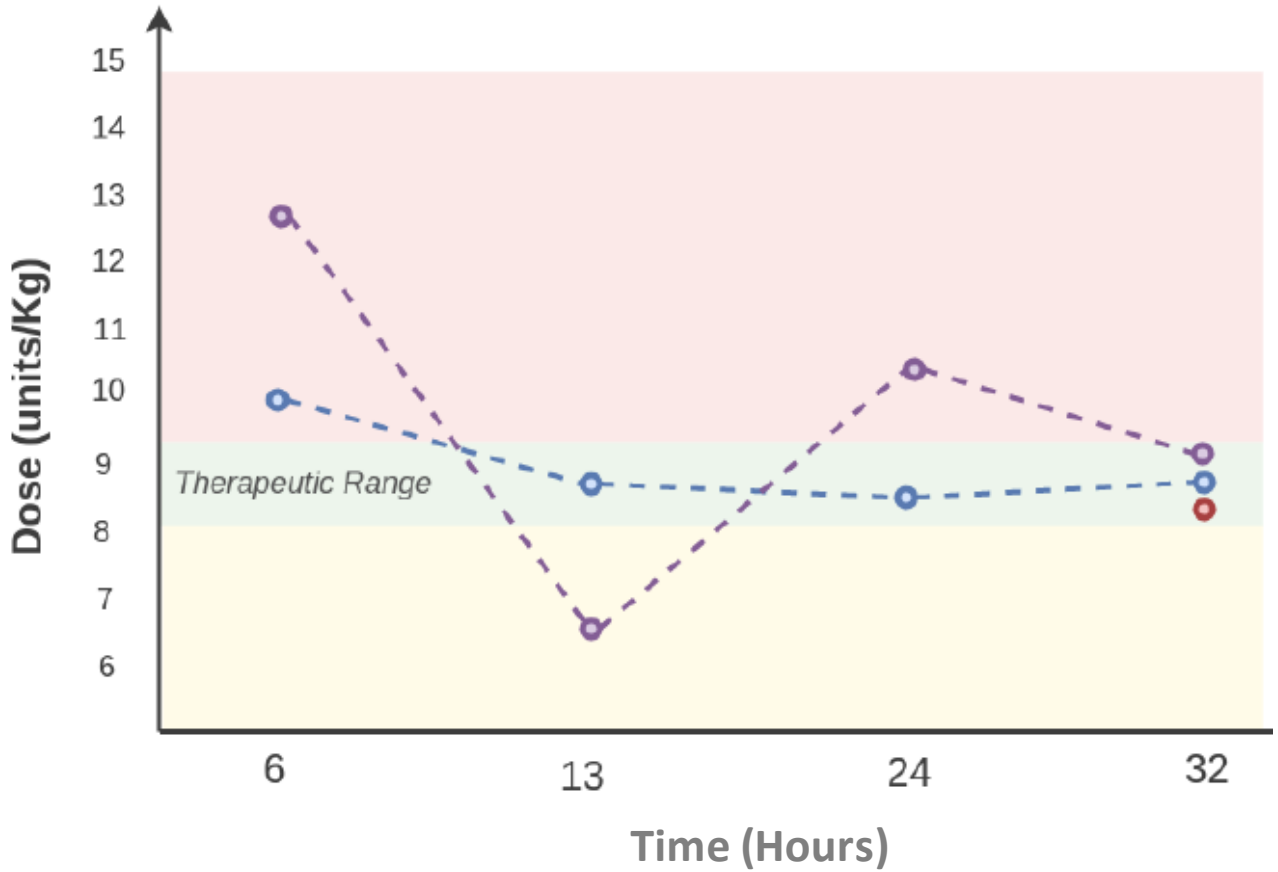
Our approach consistently outperformed the best comparable baseline across time



Temporal performance of personalized approach

Our approach might reduce errors, and bring patients to therapeutic aPTT, faster.





Conclusion and Future Direction

- Heparin dosing guidelines are based on population models
- Patient-specific modeling has the potential to improve performance
- We are working to deploy this algorithm within the BIDMC for real-world impact

Questions and Collaborations:

http://ghassemi.xyz

Todays Talk:

~~**1. Data collection:**~~
~~Tool to translate paper data from hospital spreadsheets into digital form~~

~~**2. Decision support:**~~
~~Method to prognosticate coma outcomes after cardiac arrest~~

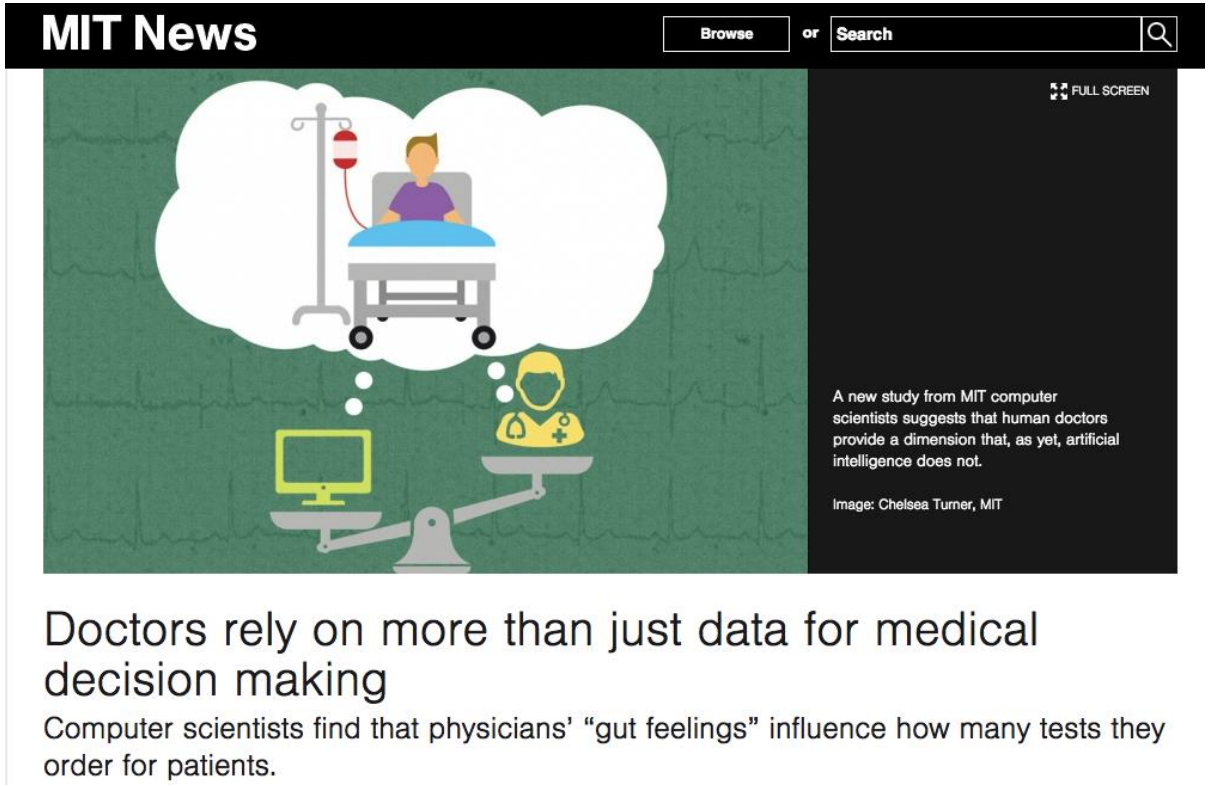
~~**3. Optimal Control:**~~
~~AI for passive monitoring of narrative mood during conversations~~

4. Moving Forward
Future directions, and opportunities for collaboration

Future Directions

- Building a more complete health profile using on-hospital and out-of-hospital data

- This should include the input of clincial experts, directly.



Predicting Latent Narrative Mood using Audio and Physiologic Data

As presented at AAAI-17

Experiment: Tell us a story

 or 

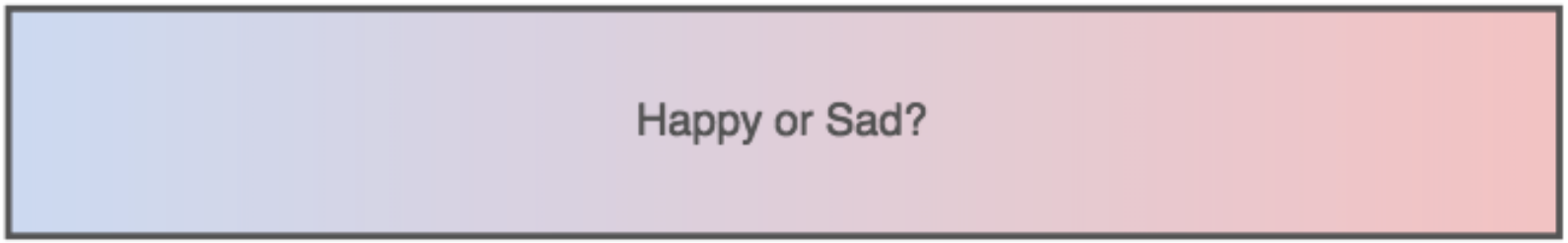
Participants

x6

x4

Modalities

Conversation score



Data

- Physiologic

  Accelerometer, Bio-impedance, ECG, GSR, PPG, Skin Temperature, Gyroscope

- Audio

  RMS Energy, MFCC, Pitch, Zero Crossing Rate, Voicing Probability

- Text

  Positive/Negative Sentiment

Data + Features

- Physiologic - 222

  Accelerometer, Bio-impedance, ECG, GSR, PPG, Skin Temperature, Gyroscope

  {mean, median, variance}

- Audio - 386

  RMS Energy, MFCC, Pitch, Zero Crossing Rate, Voicing Probability

  {mean, max, min, std, skew, kurtosis, range, absolute pos., linear regression offset/slope/mse}

- Text - 2

  Positive/Negative Sentiment

  {mean}

Data + Features

- Physiologic - 222

  Accelerometer, Bio-impedance, ECG, GSR, PPG, Skin Temperature, Gyroscope

  {mean, median, variance}

- Audio - 386

  RMS Energy, MFCC, Pitch, Zero Crossing Rate, Voicing Probability

  {mean, max, min, std, skew, kurtosis, range, absolute pos., linear regression offset/slope/mse}

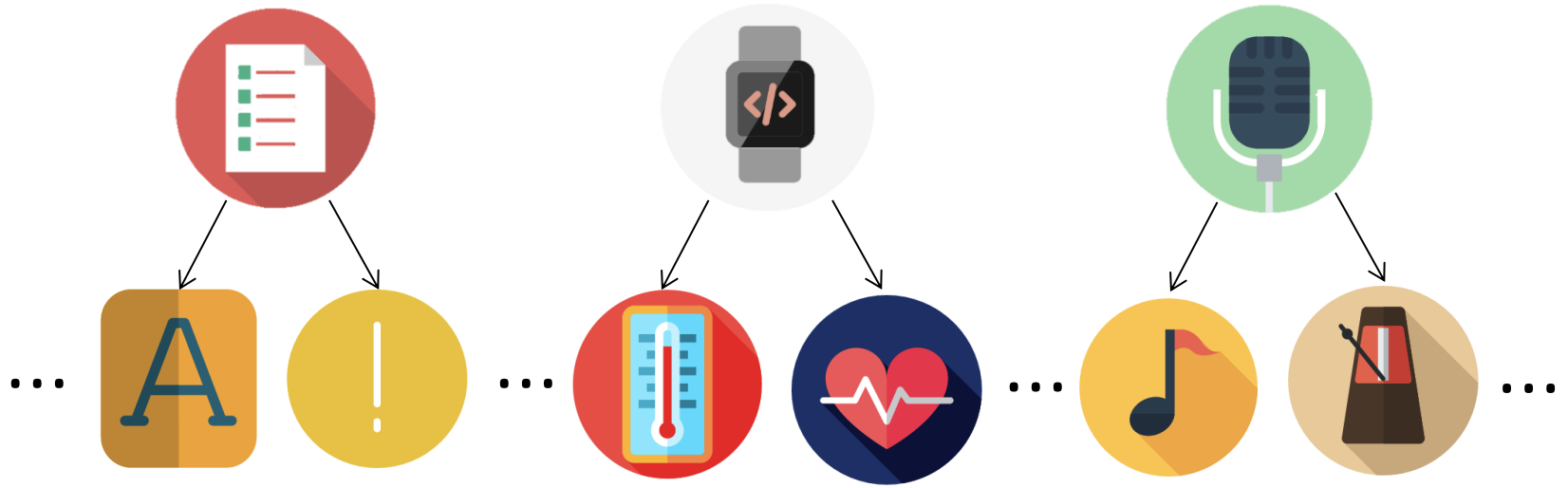
- Text - 2

  Positive/Negative Sentiment

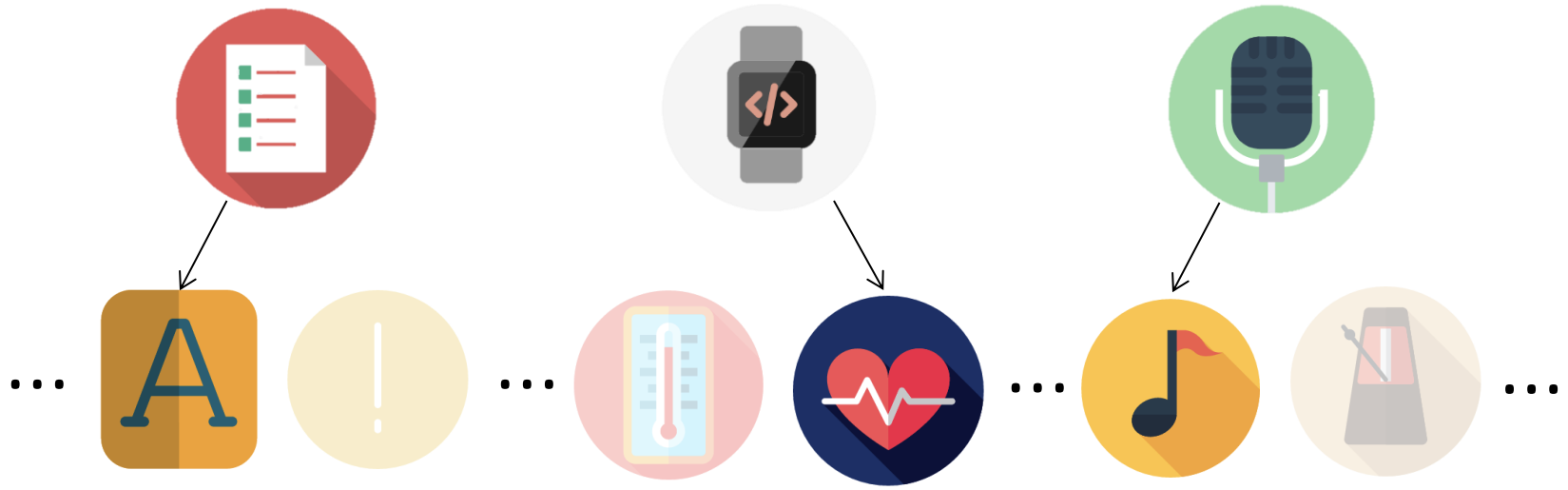
  {mean}

500+ Features

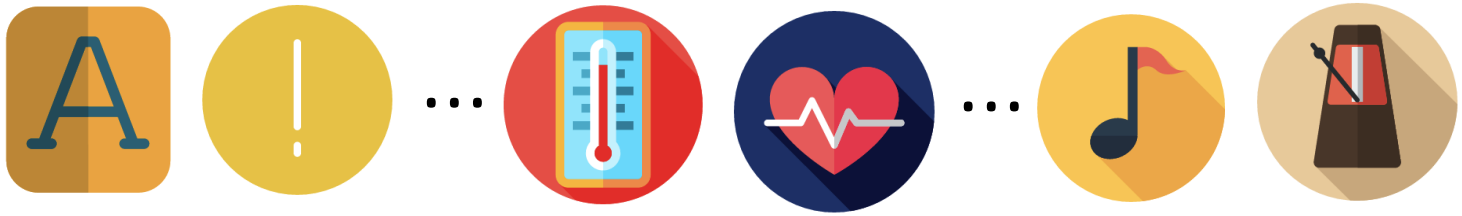
There are many things we can look at



Want to use the most important



Forward Feature Selection



N = 536

Logistic Regression Model

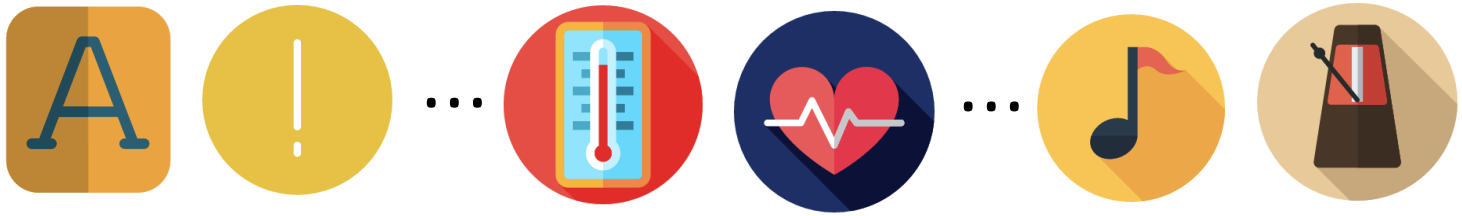
or

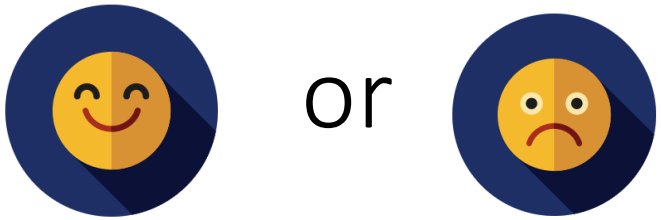
Conversation Mood

70%

or

70%



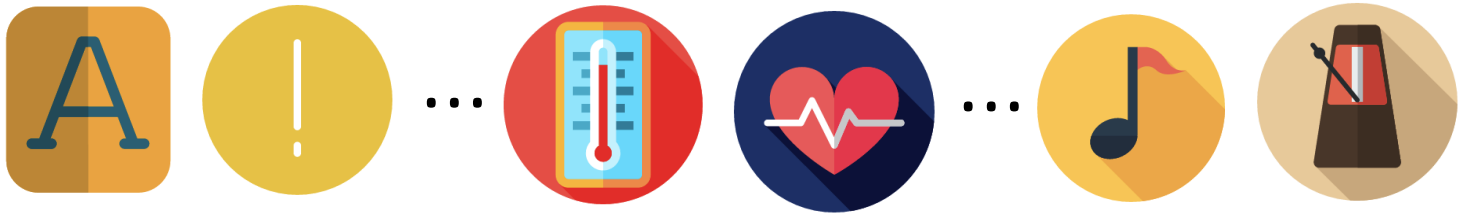


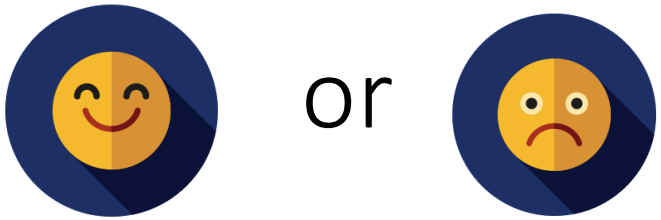
70%

60%

or

70% 60%





70%

60%

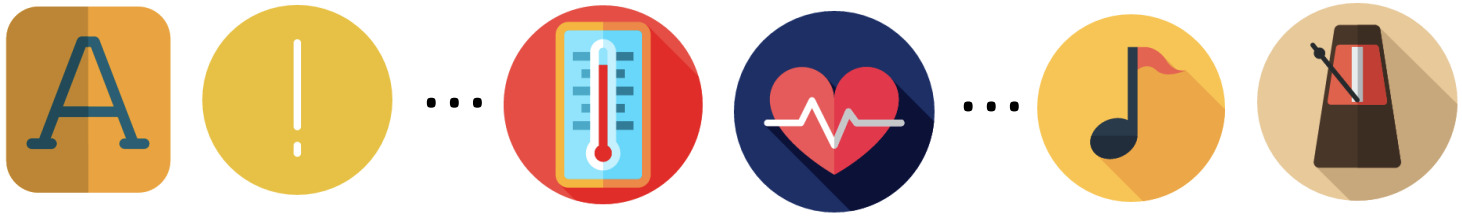
...

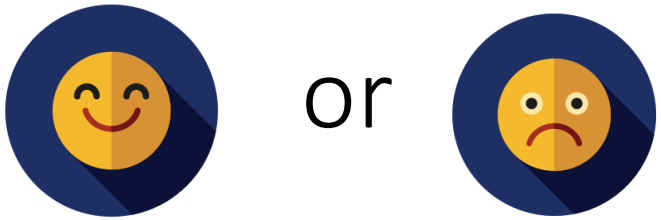
...

90%

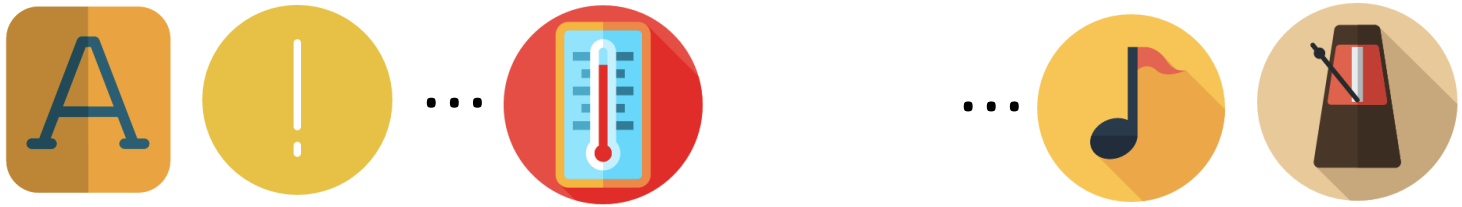
or

70% 60% 90%





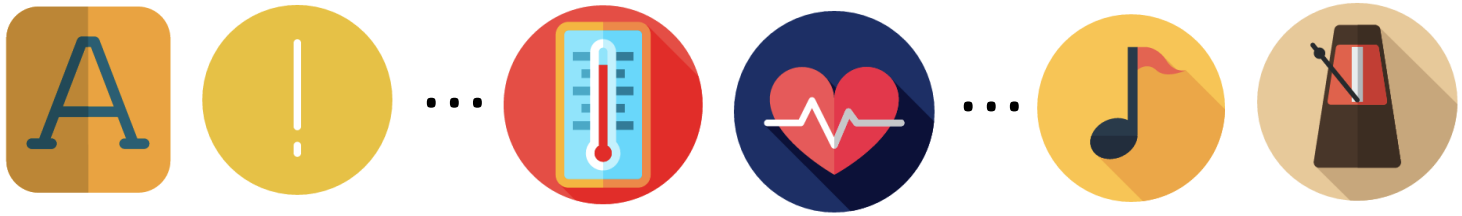
70% 60% 90%

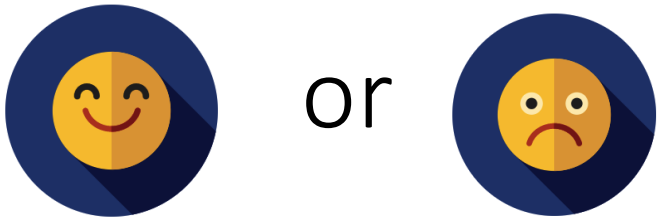


80%

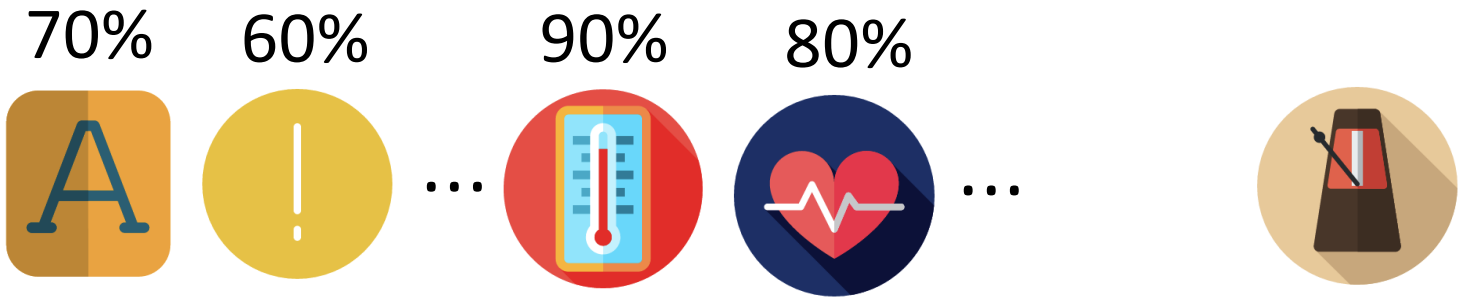
or

70% 60% 90% 80%

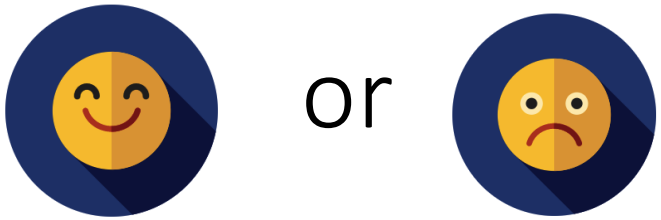




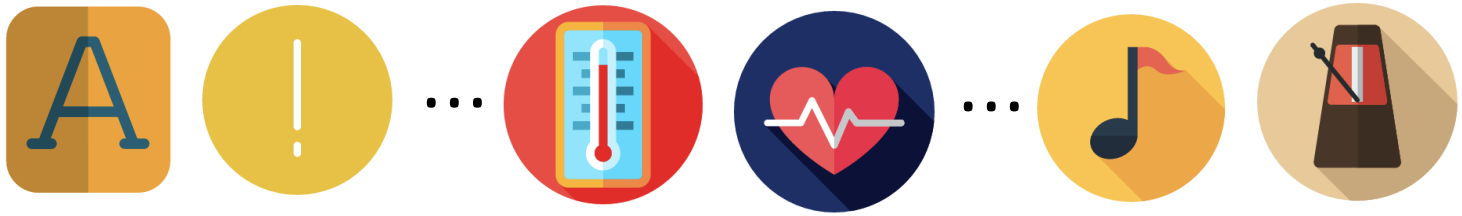
or

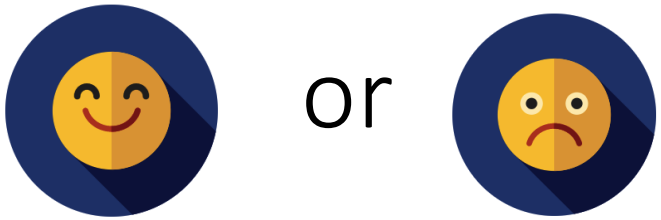


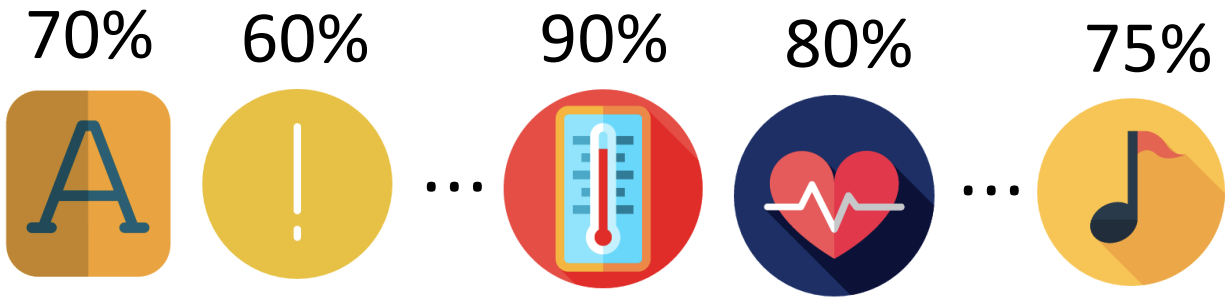
75%



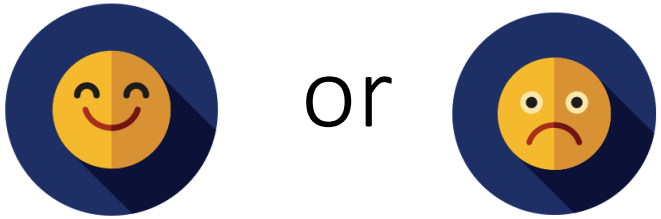
70% 60% 90% 80% 75%



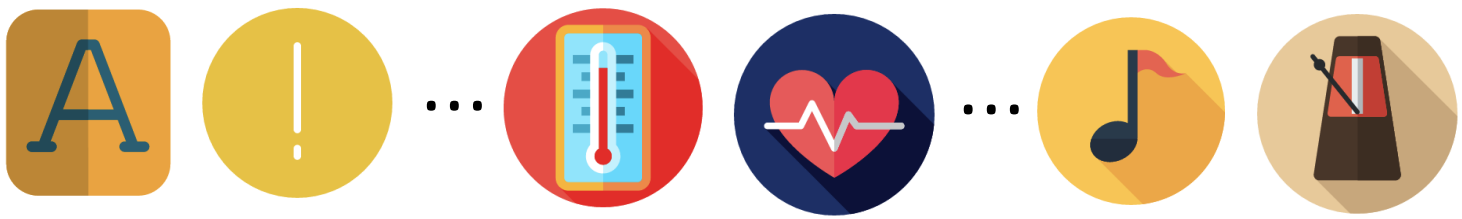


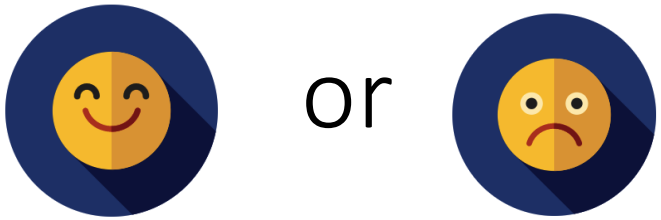


65%



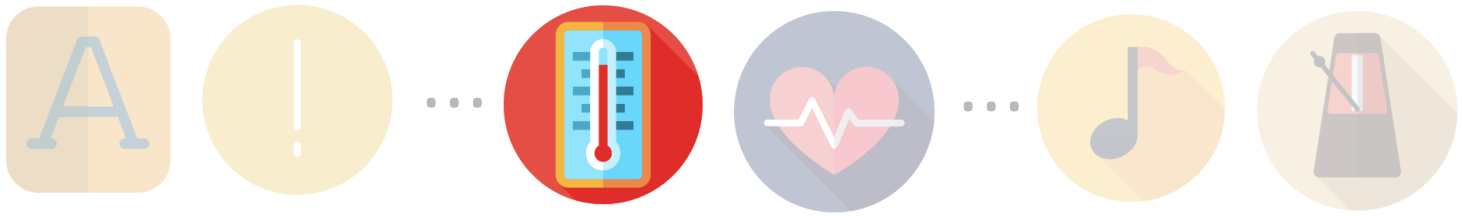
70% 60% 90% 80% 75% 65%

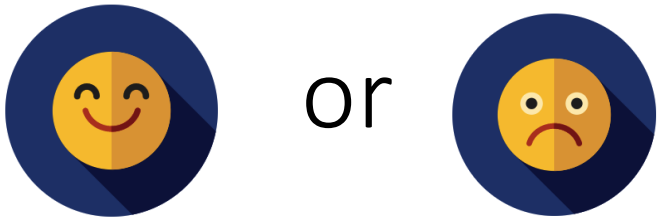


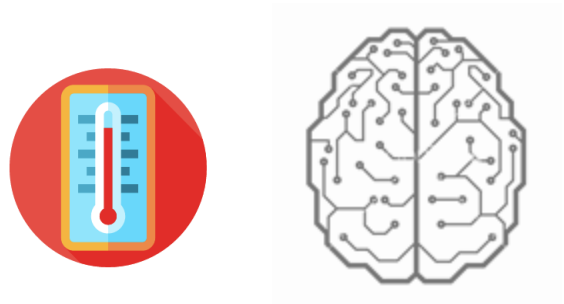


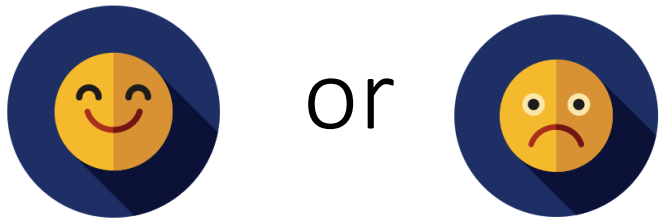
or

70% 60% 90% 80% 75% 65%








or

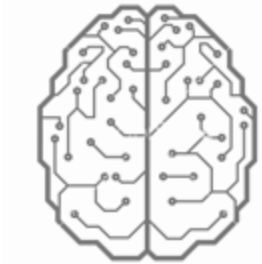
92%

or

92%

or

92%



91%

or

92% 91%

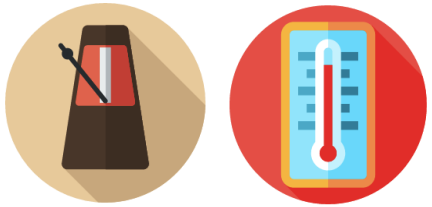
or

92% 91% 90% 94% 95%

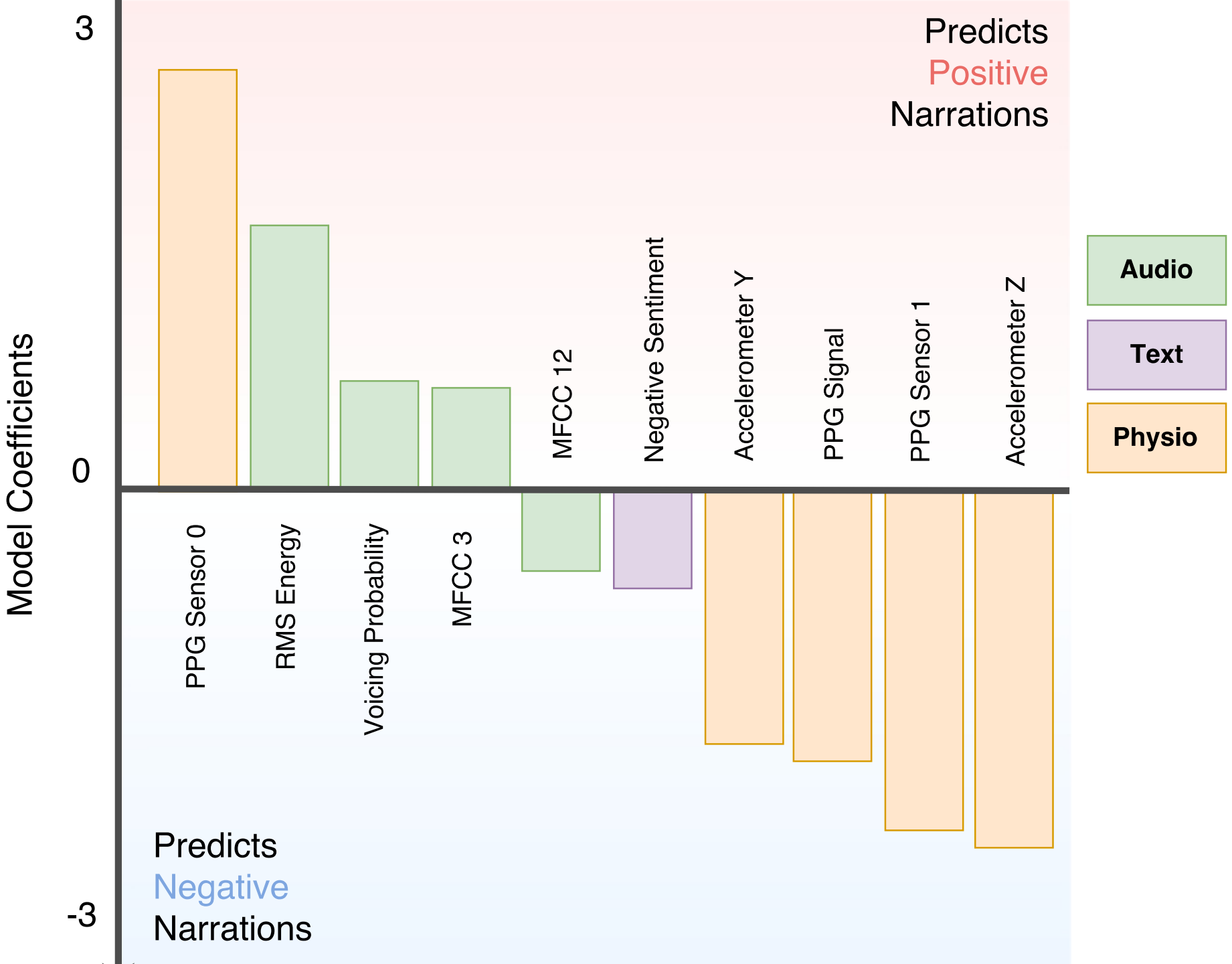
or

92% 91% 90% 94% 95%

or



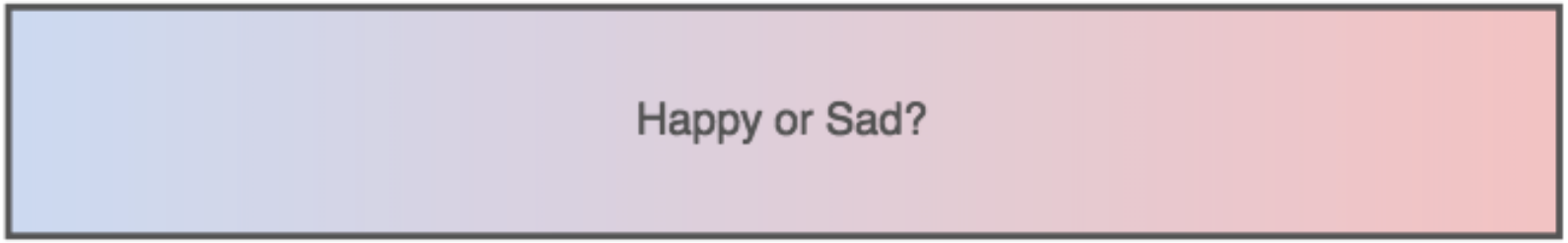
or


Model Coefficients
3
0
-3
Predicts
Positive
Narrations
Predicts
Negative
Narrations
PPG Sensor 0
RMS Energy
Voicing Probability
MFCC 3
MFCC 12
Negative Sentiment
Accelerometer Y
PPG Signal
PPG Sensor 1
Accelerometer Z
Audio
Text
Physio

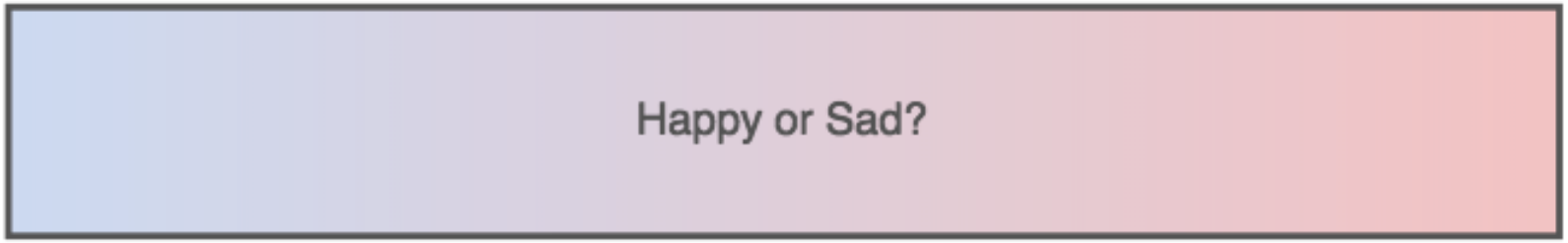
Narrative-Level Classification

Model	**AUC** (μ)	**AUC** (σ)	**Percentile** [25th 75th]
Weighted KNN	0.74	0.14	[0.68 0.85]
Medium KNN	0.74	0.14	[0.68 0.84]
Cubic KNN	0.76	0.10	[0.69 0.84]
Quadratic SVM	0.77	0.16	[0.64 0.90]
Coarse KNN	0.82	0.07	[0.77 0.89]
Quadratic Disc.	0.83	0.06	[0.79 0.89]
Gaussian SVM	0.86	0.07	[0.80 0.93]
Linear Disc.	0.90	0.07	[0.83 0.95]
Subspace Disc. Ens.	0.90	0.06	[0.85 0.95]
Logistic Regression	**0.92**	**0.05**	**[0.88 0.95]**

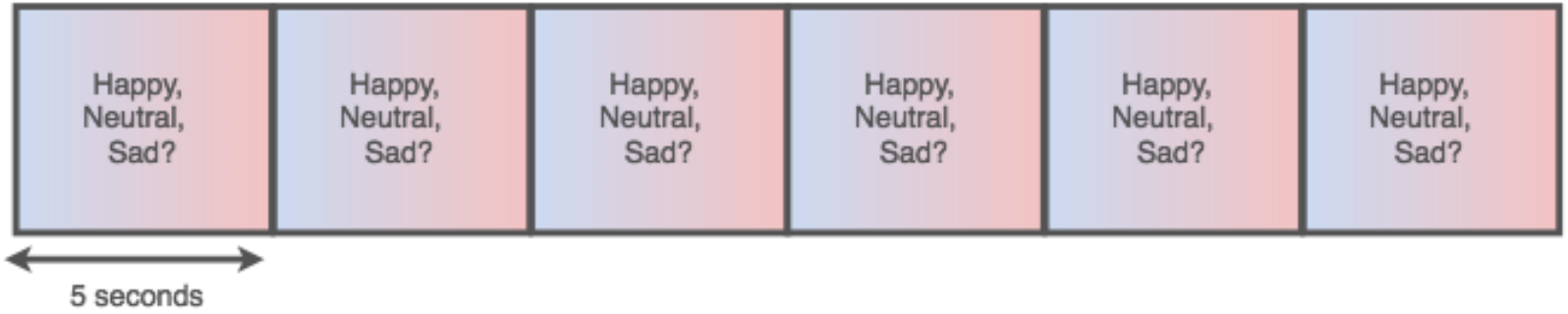
Conversation score

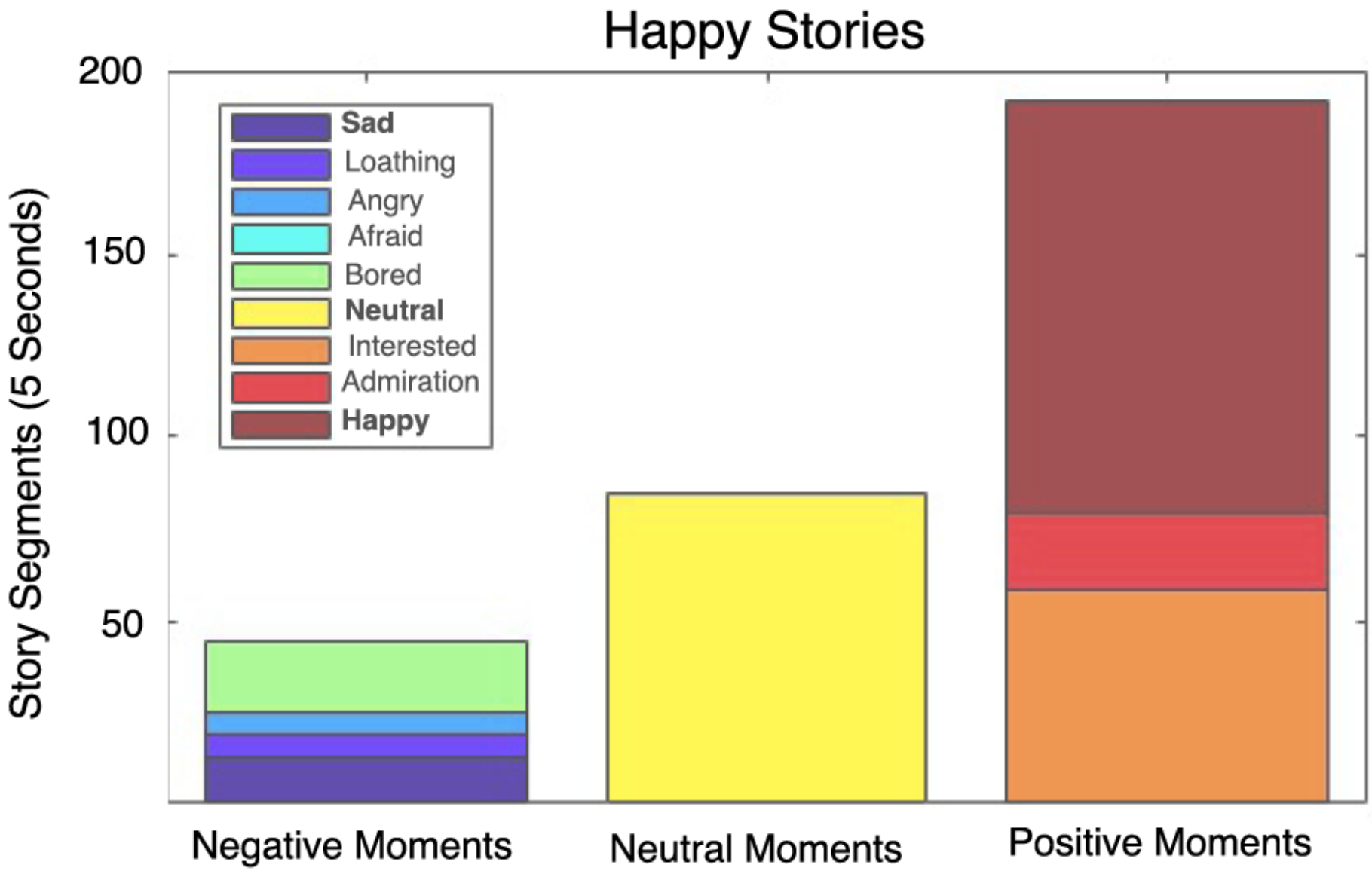


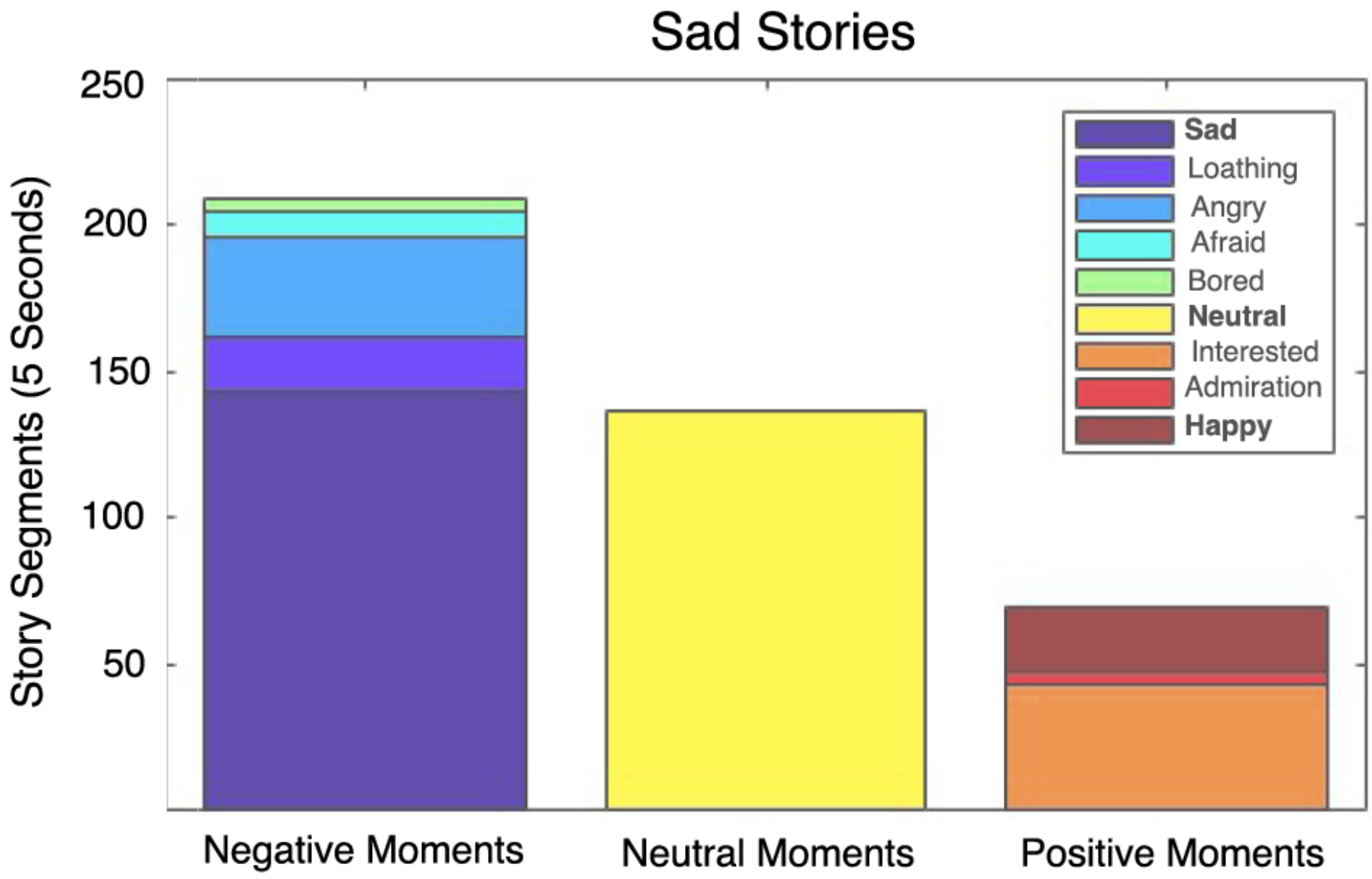
Conversation score



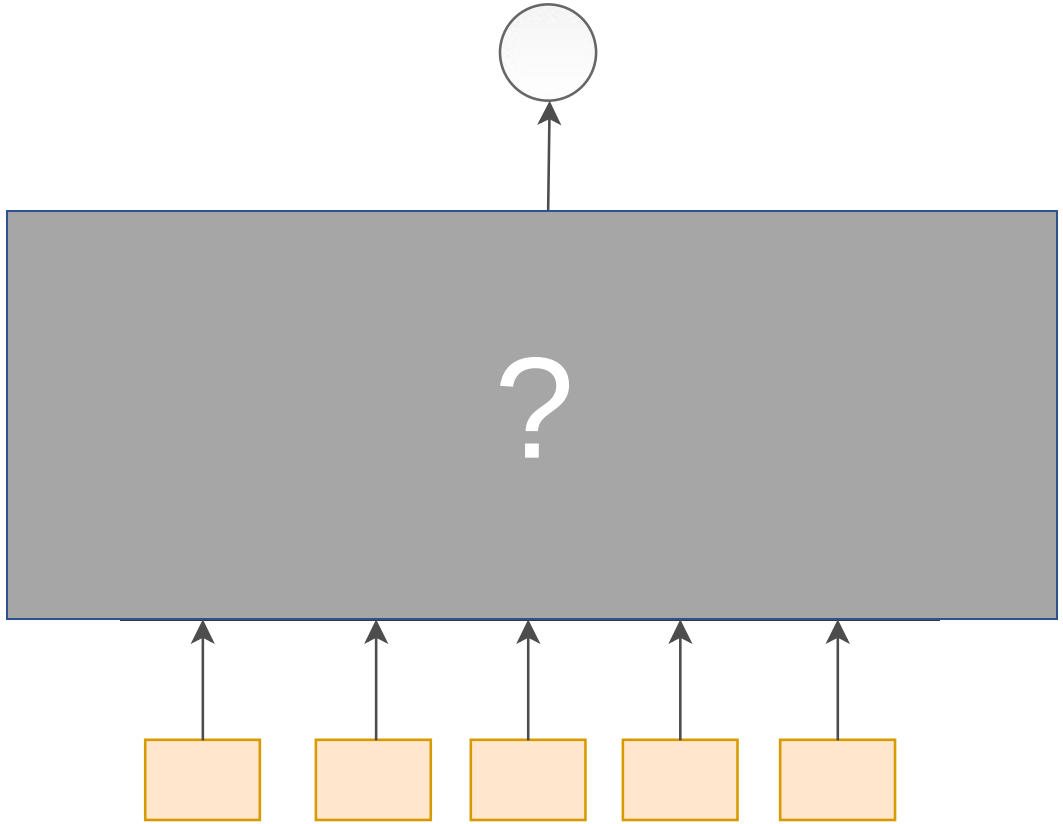
Segment score




Happy Stories
Story Segments (5 Seconds)
200
150
100
50
Sad
Loathing
Angry
Afraid
Bored
Neutral
Interested
Admiration
Happy
Negative Moments
Neutral Moments
Positive Moments


Sad Stories
Story Segments (5 Seconds)
250
200
150
100
50
Sad
Loathing
Angry
Afraid
Bored
Neutral
Interested
Admiration
Happy
Negative Moments
Neutral Moments
Positive Moments

Neural networks are a powerful solution

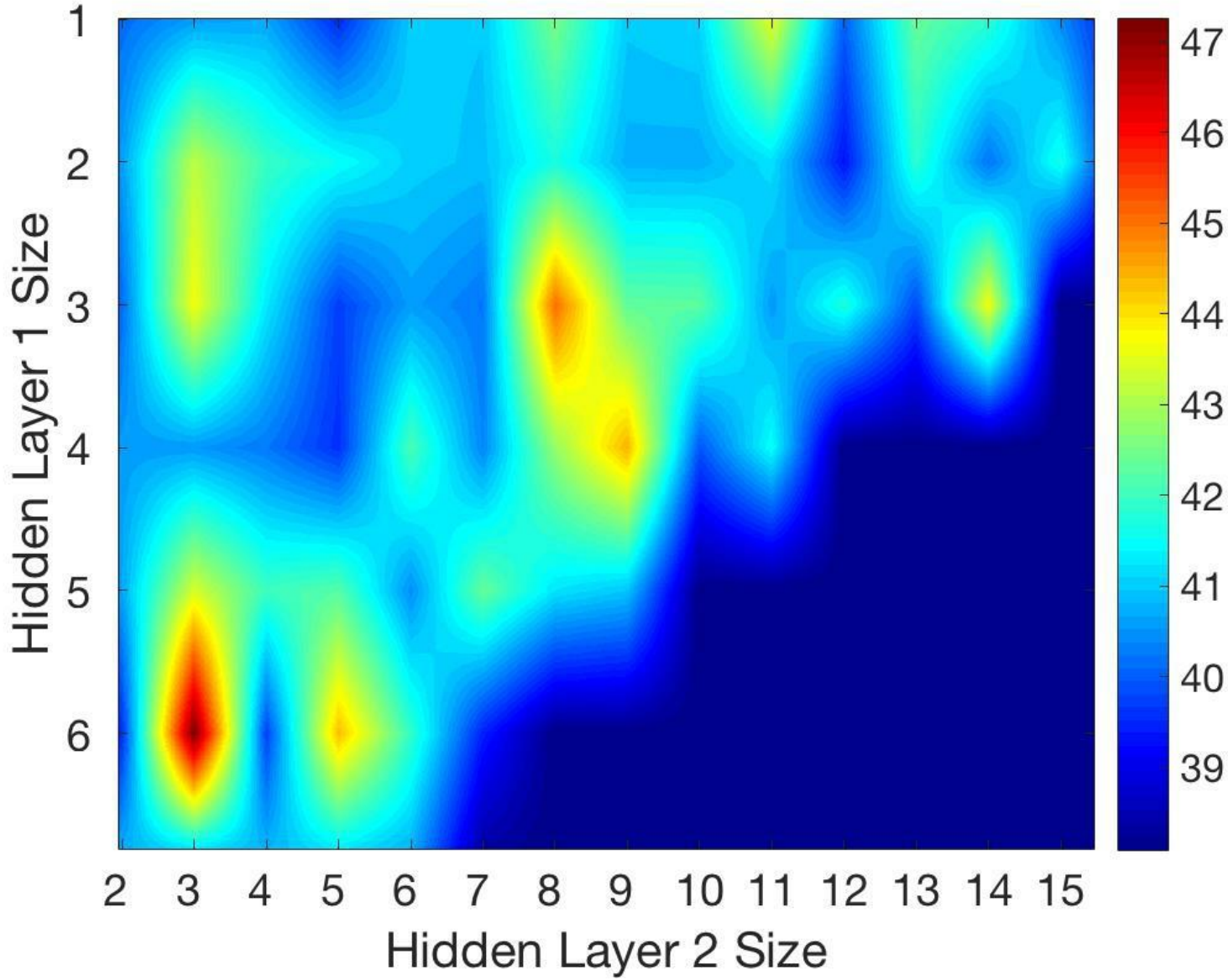


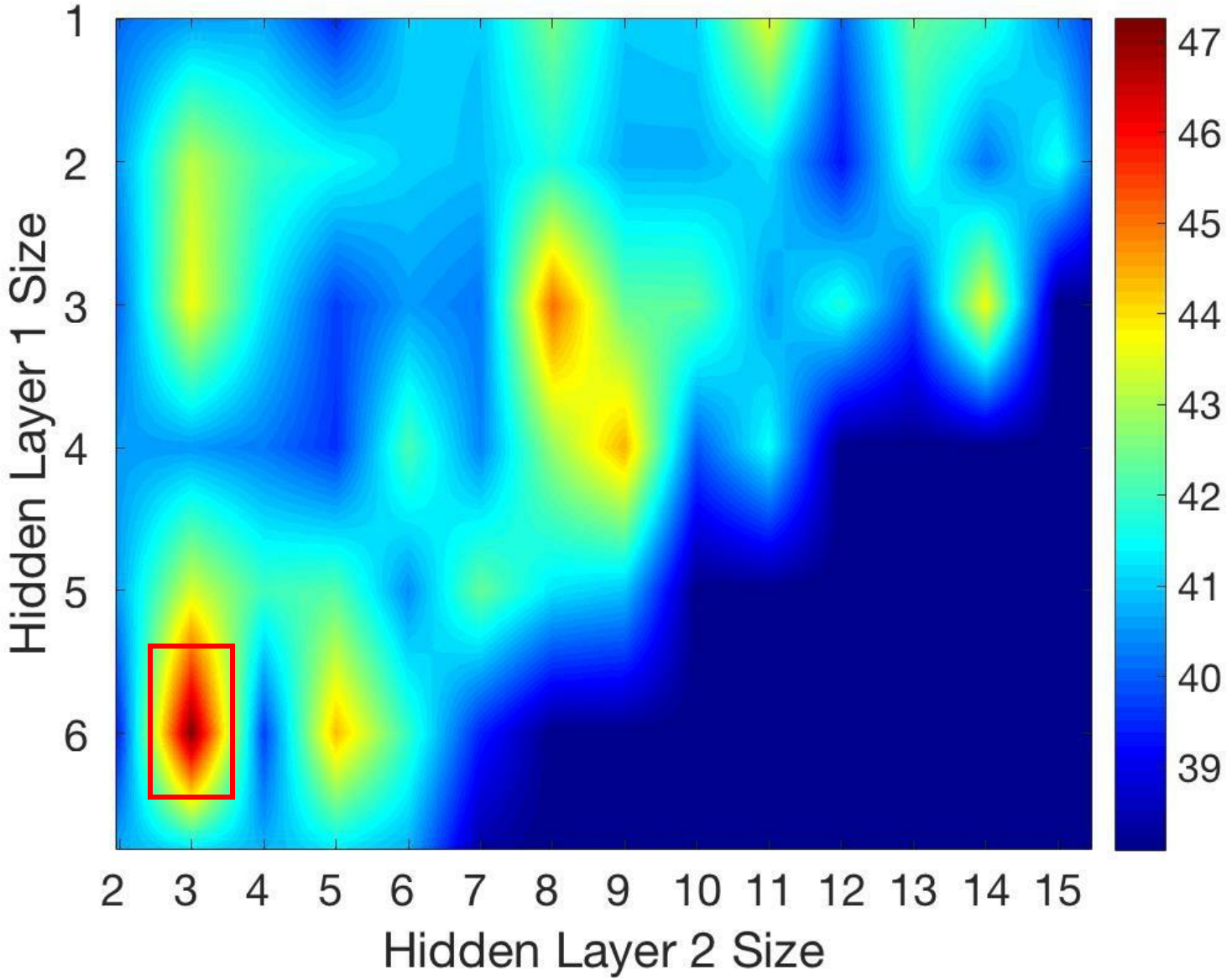
Optimize NN size

Number of Layers : {0,1,2}

Number of Nodes in each Layer : [1-15]

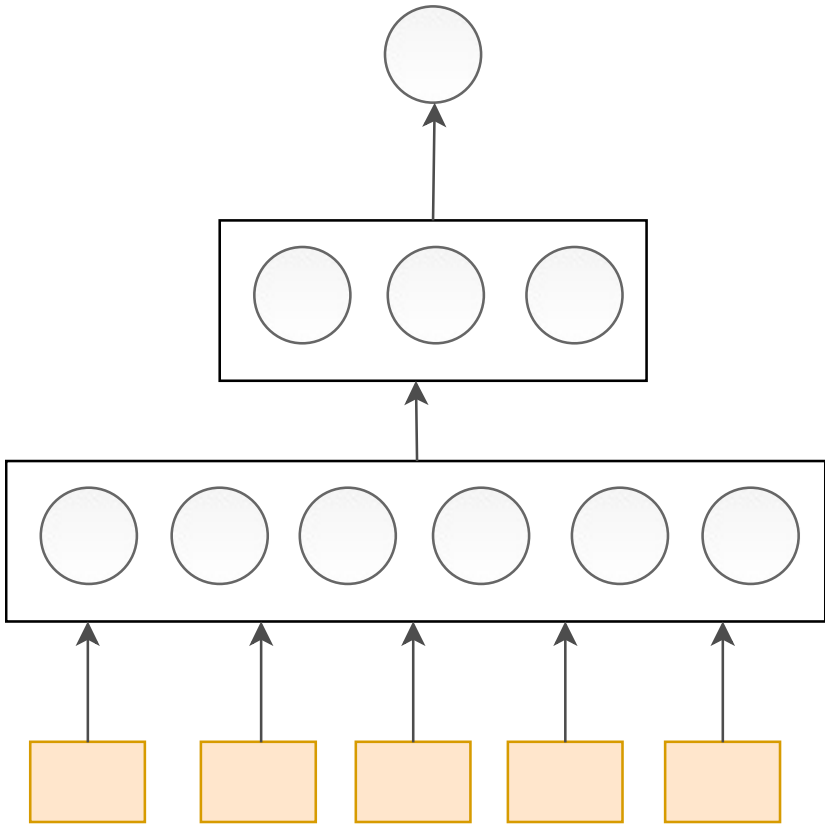
Num. of Examples / Num. of Features > 10


Hidden Layer 1 Size
1
2
3
4
5
6
Hidden Layer 2 Size
2 3 4 5 6 7 8 9 10 11 12 13 14 15
47
46
45
44
43
42
41
40
39

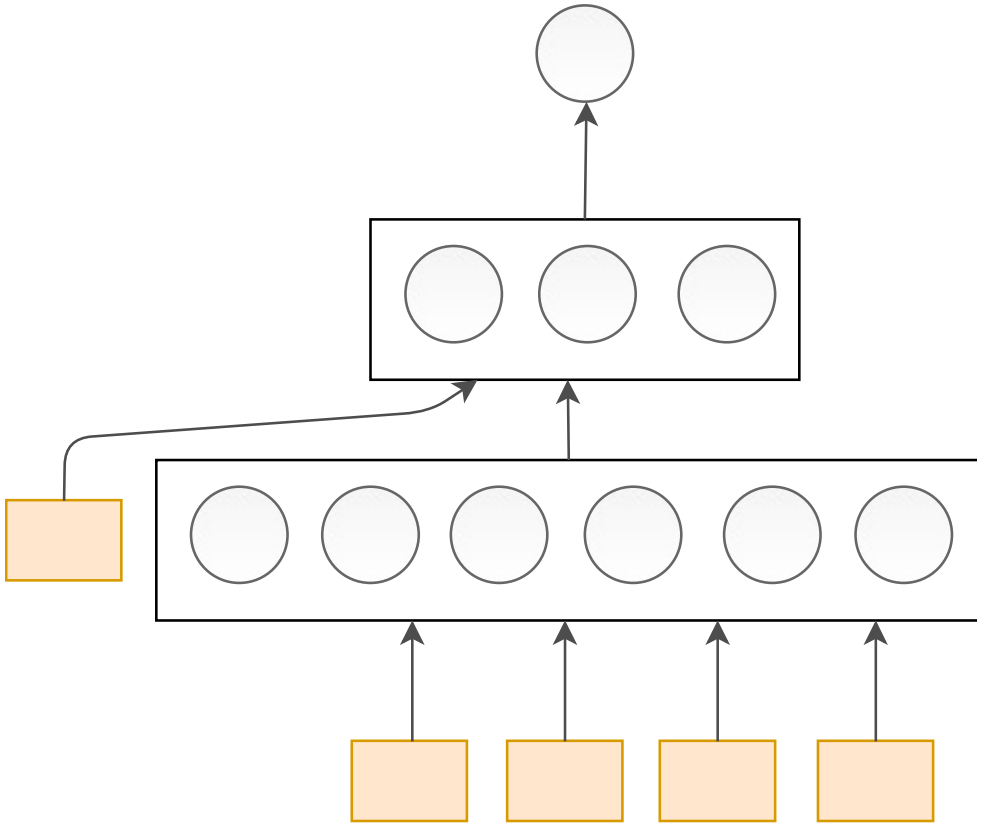

Hidden Layer 1 Size
1
2
3
4
5
6
Hidden Layer 2 Size
2 3 4 5 6 7 8 9 10 11 12 13 14 15
47
46
45
44
43
42
41
40
39

But there is yet more optimization

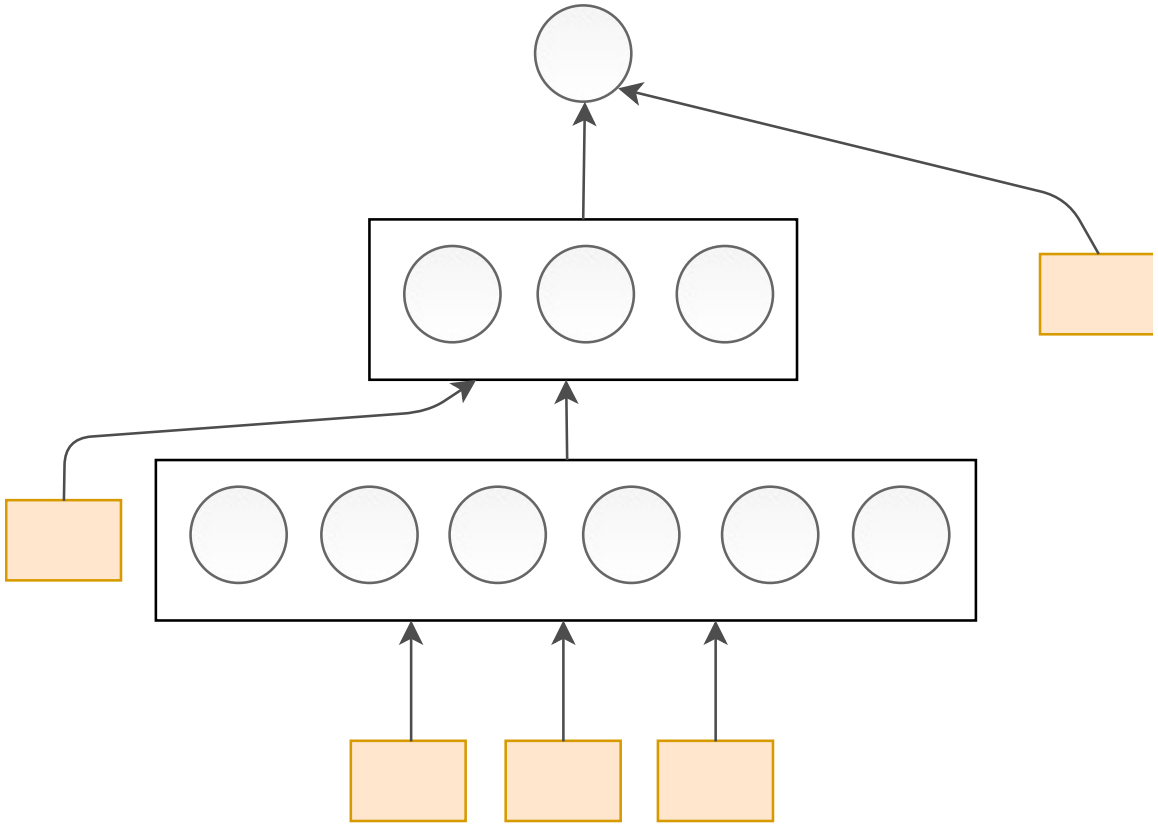
Feature Insertion



Feature Insertion

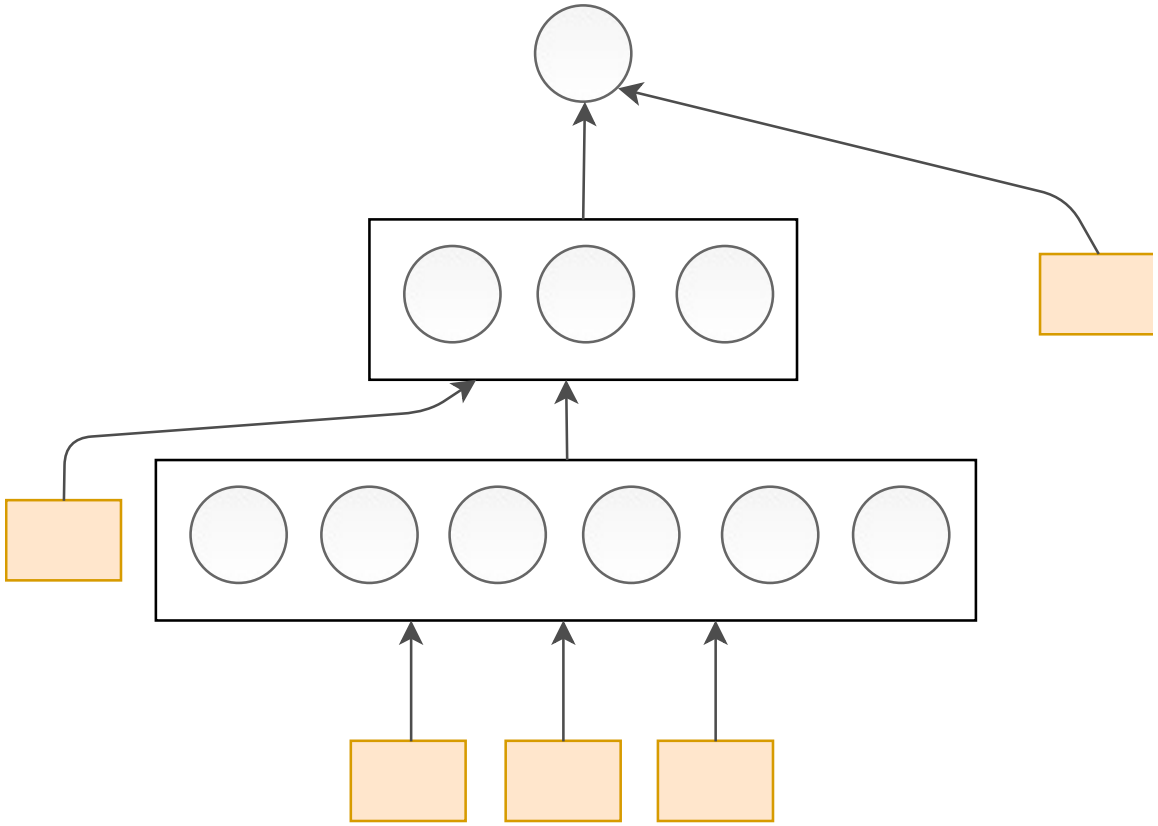


Feature Insertion

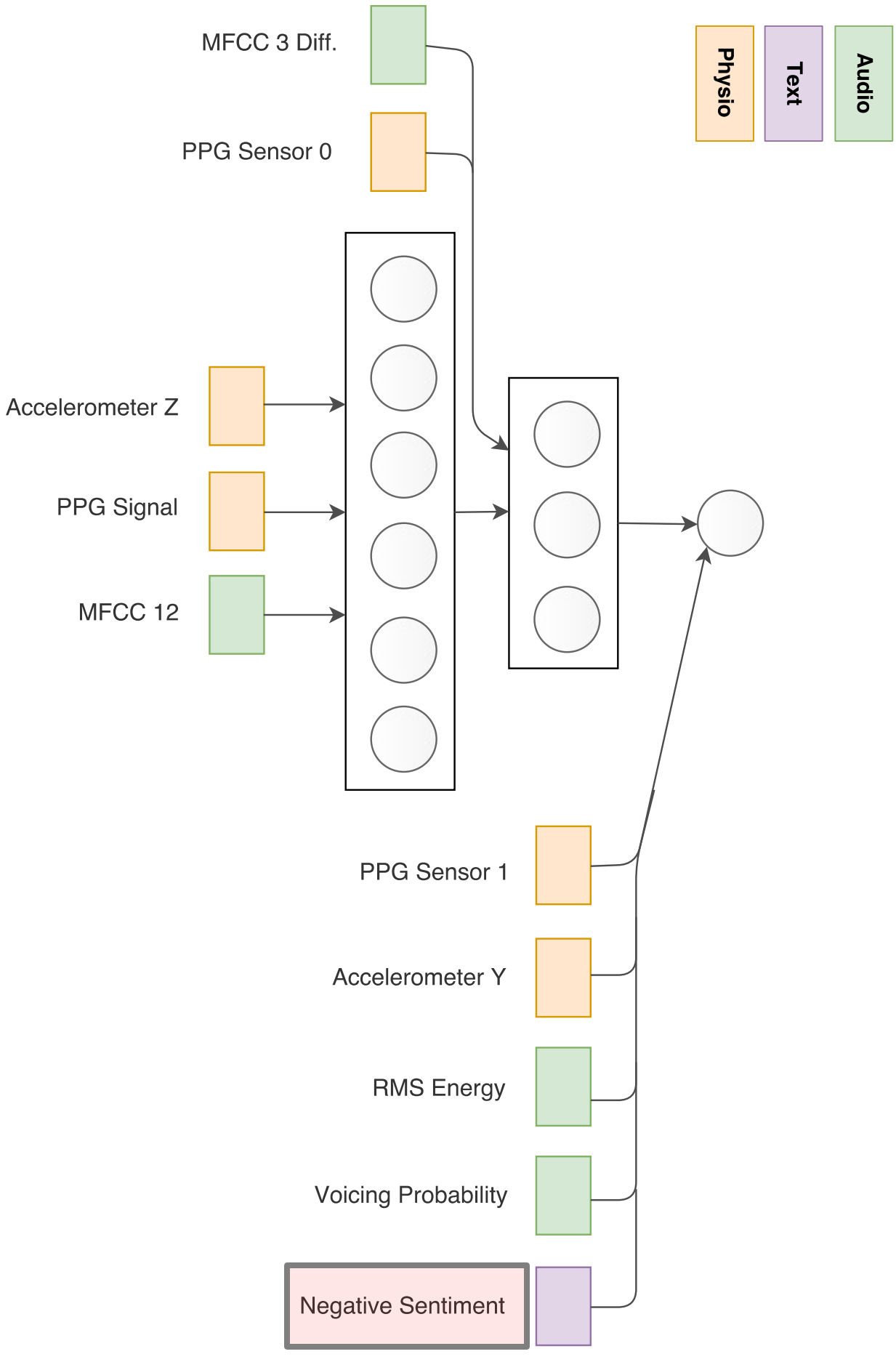


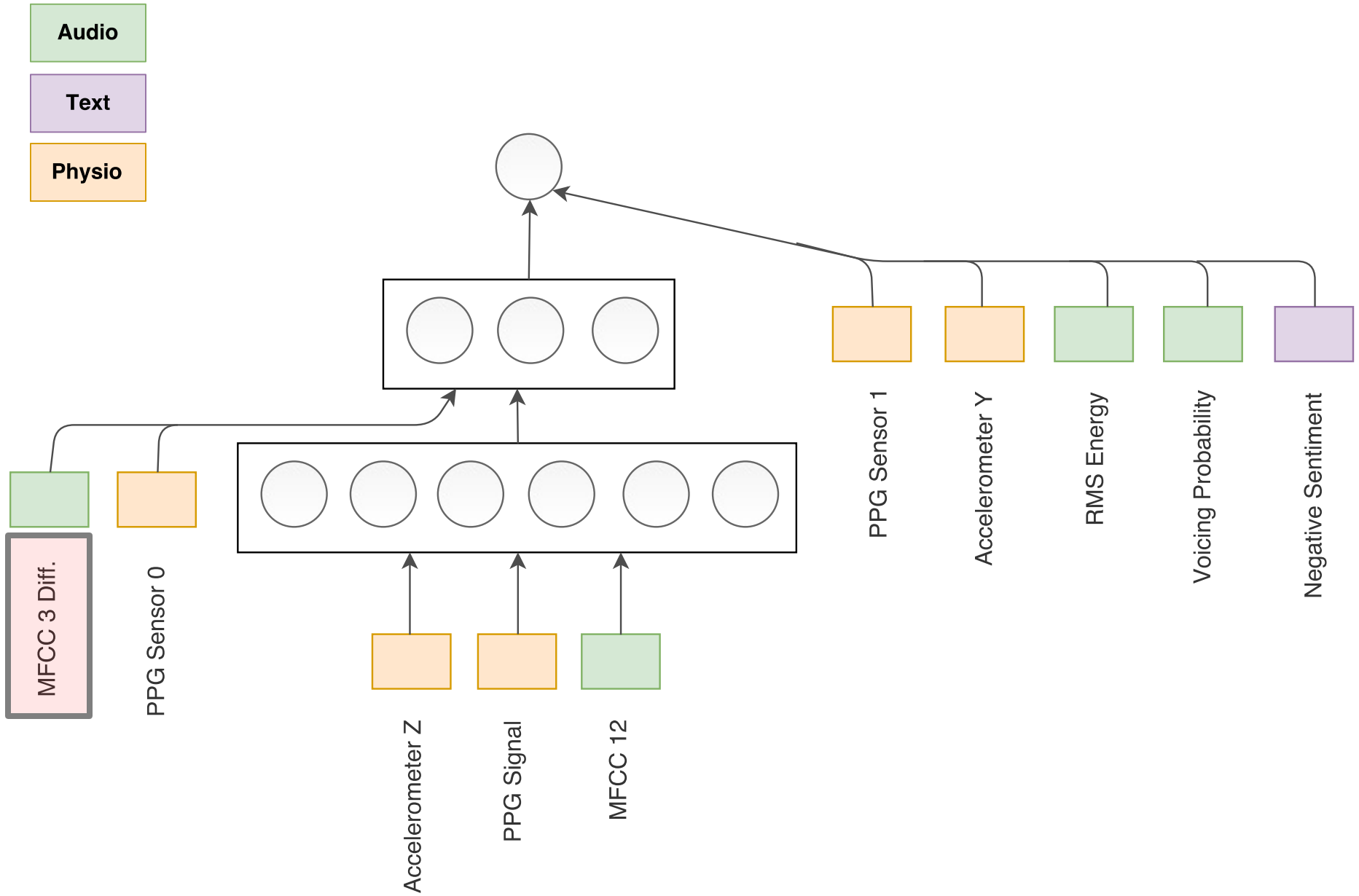
Feature Insertion

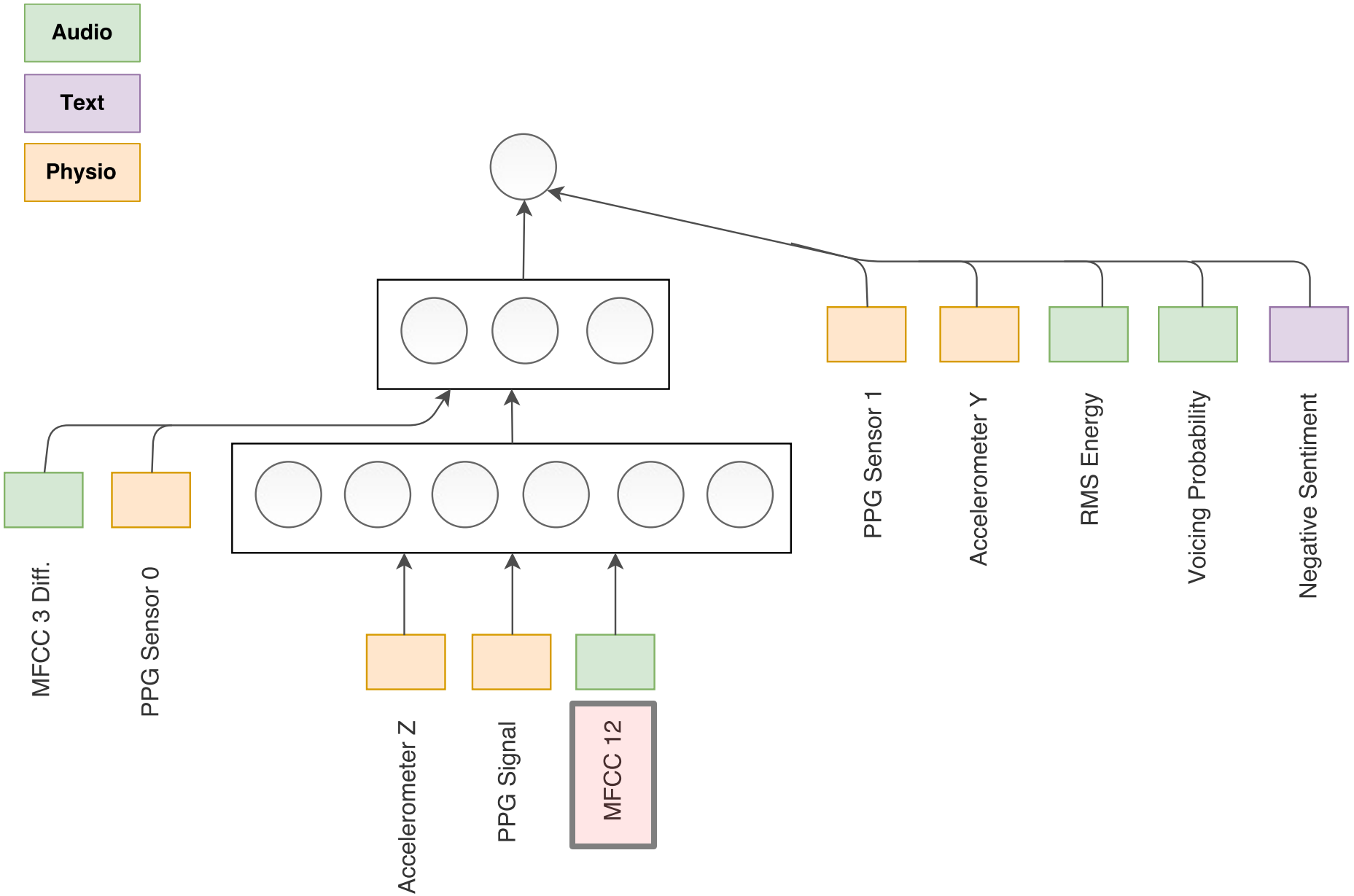
- 3^{10} possible configurations
- Explored random 10% the space



Audio
Text
Physio
MFCC 3 Diff.
PPG Sensor 0
Accelerometer Z
PPG Signal
MFCC 12
PPG Sensor 1
Accelerometer Y
RMS Energy
Voicing Probability
Negative Sentiment

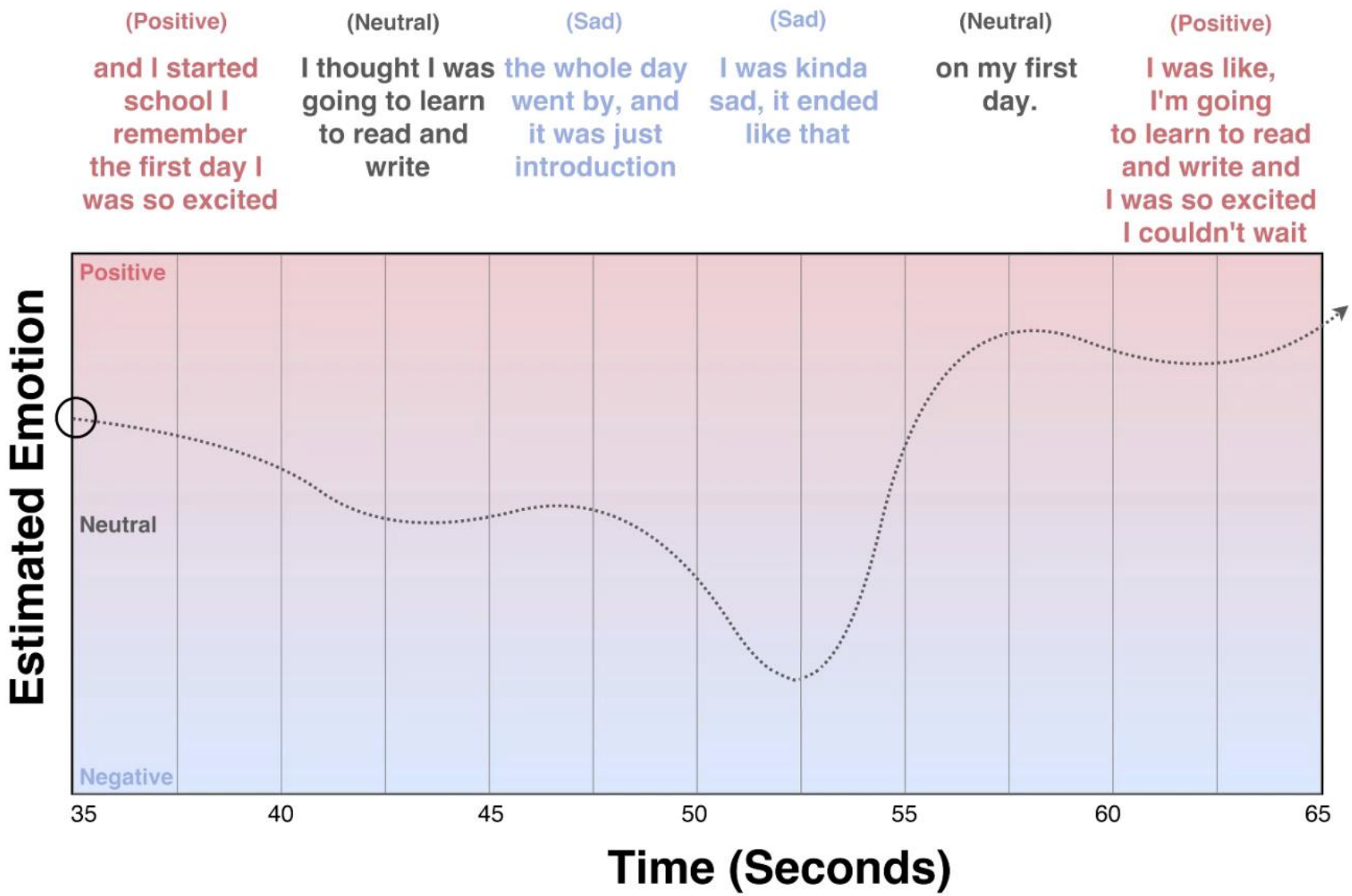

Physio
Text
Audio
MFCC 3 Diff.
PPG Sensor 0
Accelerometer Z
PPG Signal
MFCC 12
PPG Sensor 1
Accelerometer Y
RMS Energy
Voicing Probability
Negative Sentiment

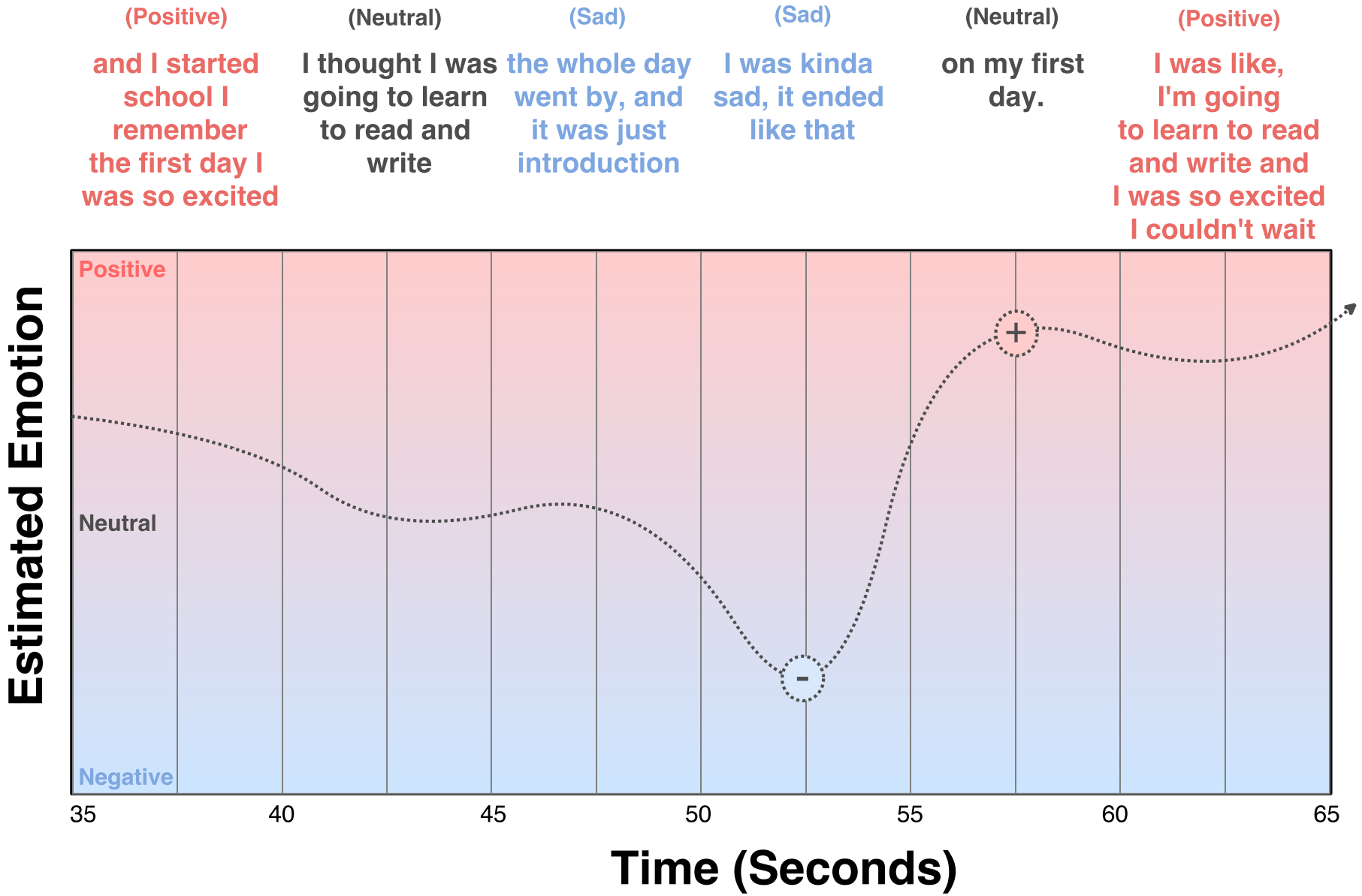

Audio
Text
Physio
MFCC 3 Diff.
PPG Sensor 0
Accelerometer Z
PPG Signal
MFCC 12
PPG Sensor 1
Accelerometer Y
RMS Energy
Voicing Probability
Negative Sentiment


Audio
Text
Physio
MFCC 3 Diff.
PPG Sensor 0
Accelerometer Z
PPG Signal
MFCC 12
PPG Sensor 1
Accelerometer Y
RMS Energy
Voicing Probability
Negative Sentiment

Segment-Level Classification

Model	**Accuracy** (%) (μ)	**Accuracy** (%) (σ)	**Percentile** [25th 75th]
Random	33.3	-	-
Multinomial Logistic Reg.	40.8	7.36	[34.1 46.0]
NN (2L-6x3N)	45.3	8.10	[38.5 49.0]
+ Feature Optimization	**47.3**	**8.72**	**[39.9 55.1]**


(Positive)
and I started school I remember the first day I was so excited
(Neutral)
I thought I was going to learn to read and write
(Sad)
the whole day went by, and it was just introduction
(Sad)
I was kinda sad, it ended like that
(Neutral)
on my first day.
(Positive)
I was like, I'm going to learn to read and write and I was so excited I couldn't wait
Positive
Neutral
Negative
Estimated Emotion
35
40
45
50
55
60
65
Time (Seconds)


(Positive)
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the whole day went by, and it was just introduction
(Sad)
I was kinda sad, it ended like that
(Neutral)
on my first day.
(Positive)
I was like, I'm going to learn to read and write and I was so excited I couldn't wait
Positive
Neutral
Negative
+
-
Estimated Emotion
35
40
45
50
55
60
65
Time (Seconds)

Learn More

http://ghassemi.xyz