## **Transparente KI Methoden** in der Medizin **Carsten Eickhoff**

EBERHARD KARLS UNIVERSITÄT TÜBINGEN







## Overview

- **1. Background, Research Interests, Lab**
- 2. Some Teasers
- 3. Zero-shot [Text Classification | Diagnostic Decision Support]
- 4. Discussion

# About me

- Hannover
- University of Edinburgh
- TU Delft
- Microsoft
- ETH Zurich
- Harvard University
- Brown University
- University of Tübingen



- **Dense Retrieval**
- XIR
- Uncertainty Aware Models
- Grounded Language Modeling
- Manifold Learning for Neural LMs
- **Clinical Decision Support**

## Interests

## ACL NAACL **ICLR EMNLP**

**KDD** IR WWW **WSDM** 

SIGIR

JAMIA

Health

**Nature - Digital Medicine** 

Lancet - Respiratory Medicine





ADEEL ABBASI ASSISTANT PROFESSOR



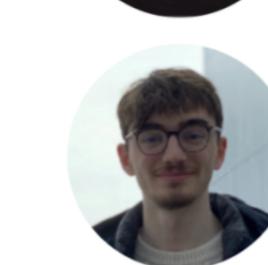


ALI BAHRAINIAN POSTDOC

AMINA ABDULLAHI

PHD STUDENT





JACK MERULLO PHD STUDENT



CARSTEN EICKHOFF PROFESSOR, DIRECTOR





CATHERINE CHEN PHD STUDENT



## Team

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MICHAL GOLOVANEVSKY PHD STUDENT



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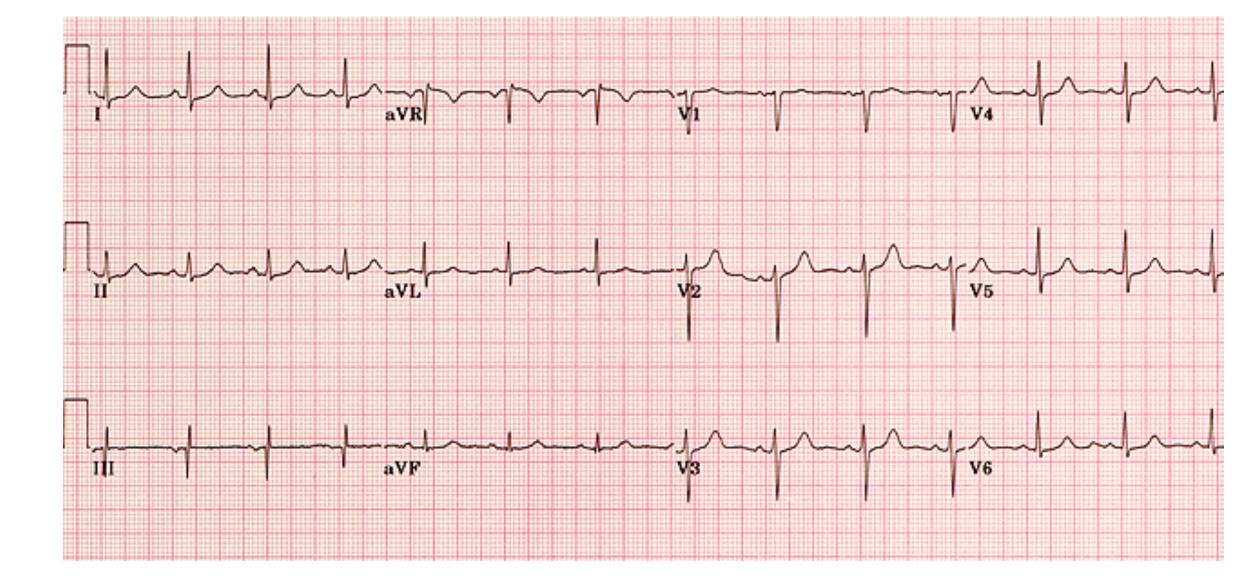


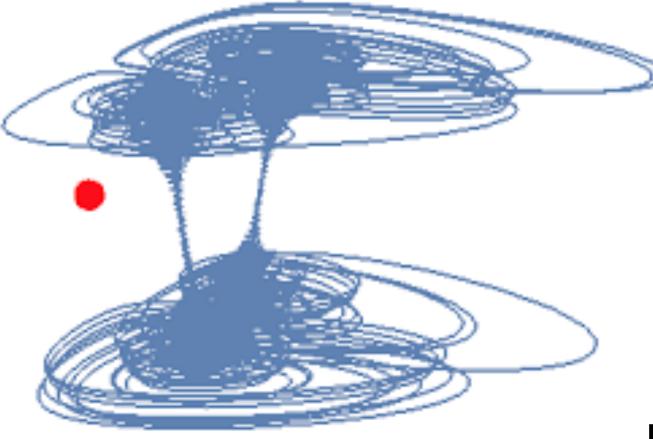
SHAKILA MOSTAAN SCIENTIFIC GRANT WRITER



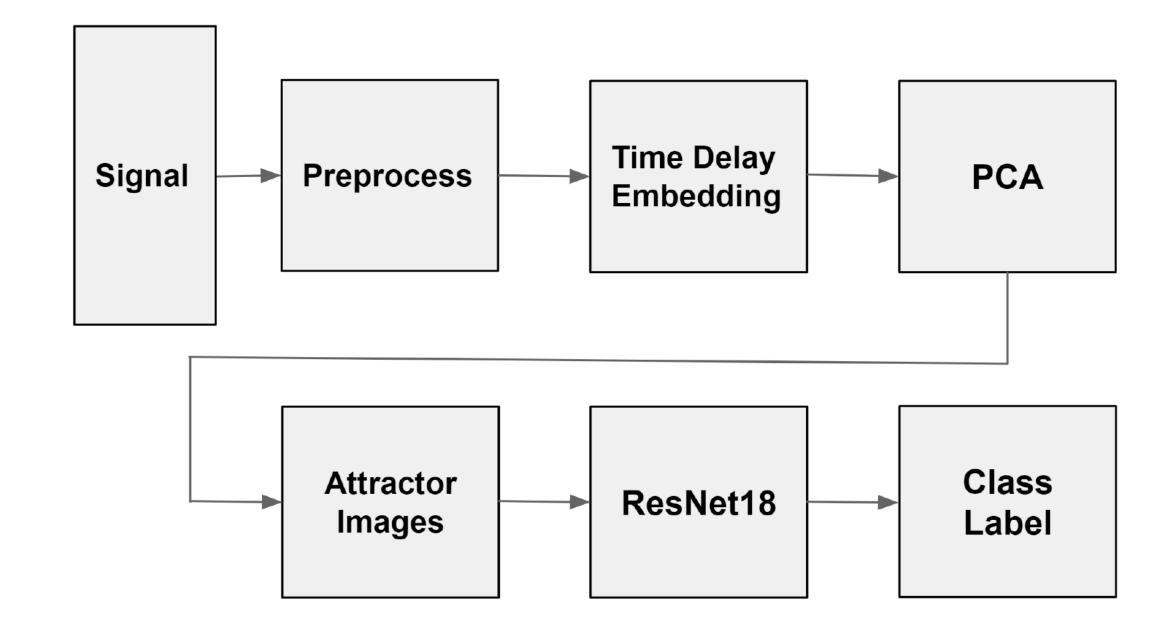
WILLIAM RUDMAN PHD STUDENT

# Cardiac Arrhythmia Localization via ECG Attractor Imaging





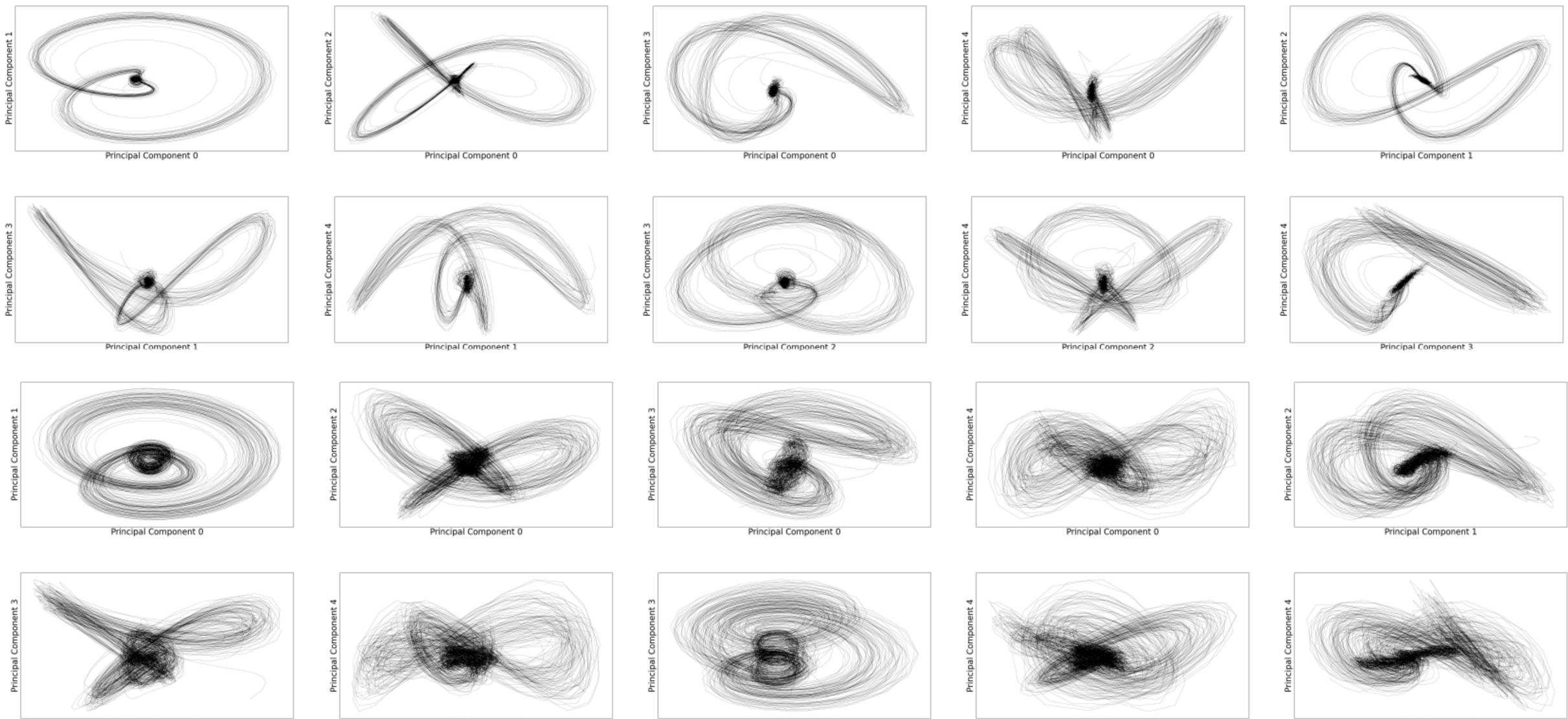
Rudman et al. CinC 2022: ACQuA: Arrhythmia Classification with Quasi-Attractors



	Normal	AFib	Other	Noise	Avg. Scor
Zabihi et. al. [33]	90.49	79.43	75.64	61.11	81.85
Datta et. al. [9]	91.00	79.00	77.00	—	_
Hong et. al. [15]	92.04	86.92	80.68	81.56	85.30
Spectrogram	76.78	43.08	44.71	54.55	54.78
Signal	94.84	96.77	91.93	90.41	93.49
Naïve Attractor	93.93	85.71	94.40	94.87	92.23
01 PCA Attractor	99.66	98.95	98.46	100	99.27



# Some Examples

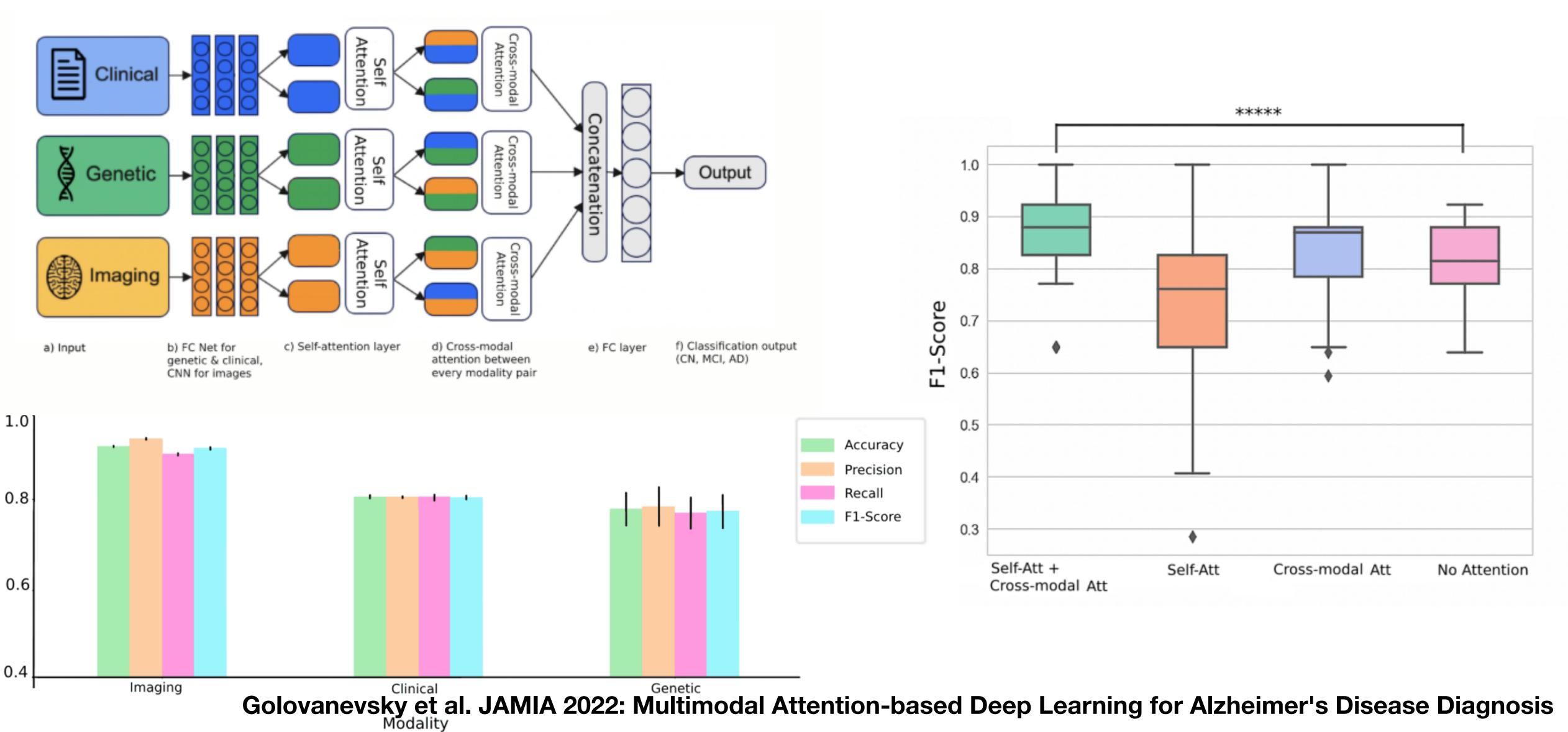


Principal Component 1

Principal Component 1

Principal Component 2

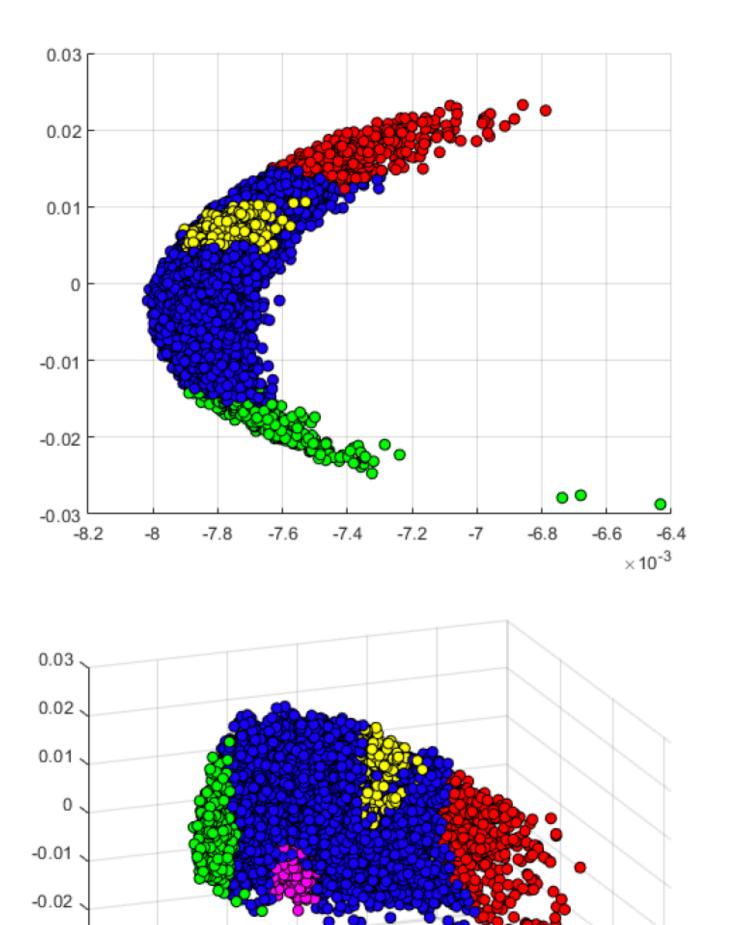
Principal Component 2



# Multimodal Classification



## Health Outcome Disparities on the EHR



-0.03 -0.02 -0.01

-0.03 -8

×10<sup>-3</sup>

-7.5

-6.5

## Self Attention ٠ Contextual Embeddings

the patient reported that he had been feeling well without chest pain, shortness of breath, or dyspnea on exertion. The patient underwent a cardiac catheterization on the morning of arrival with pci to the native rca and stents and brachytherapy to the vein graft. the patient tolerated the procedure well and approximately hours later developed a chest pain noted as out of substernal radiating to his throat and back without shortness of breath, diaphoresis, nausea or vomiting. ekg at that time revealed st elevation in ii, iii, and avf

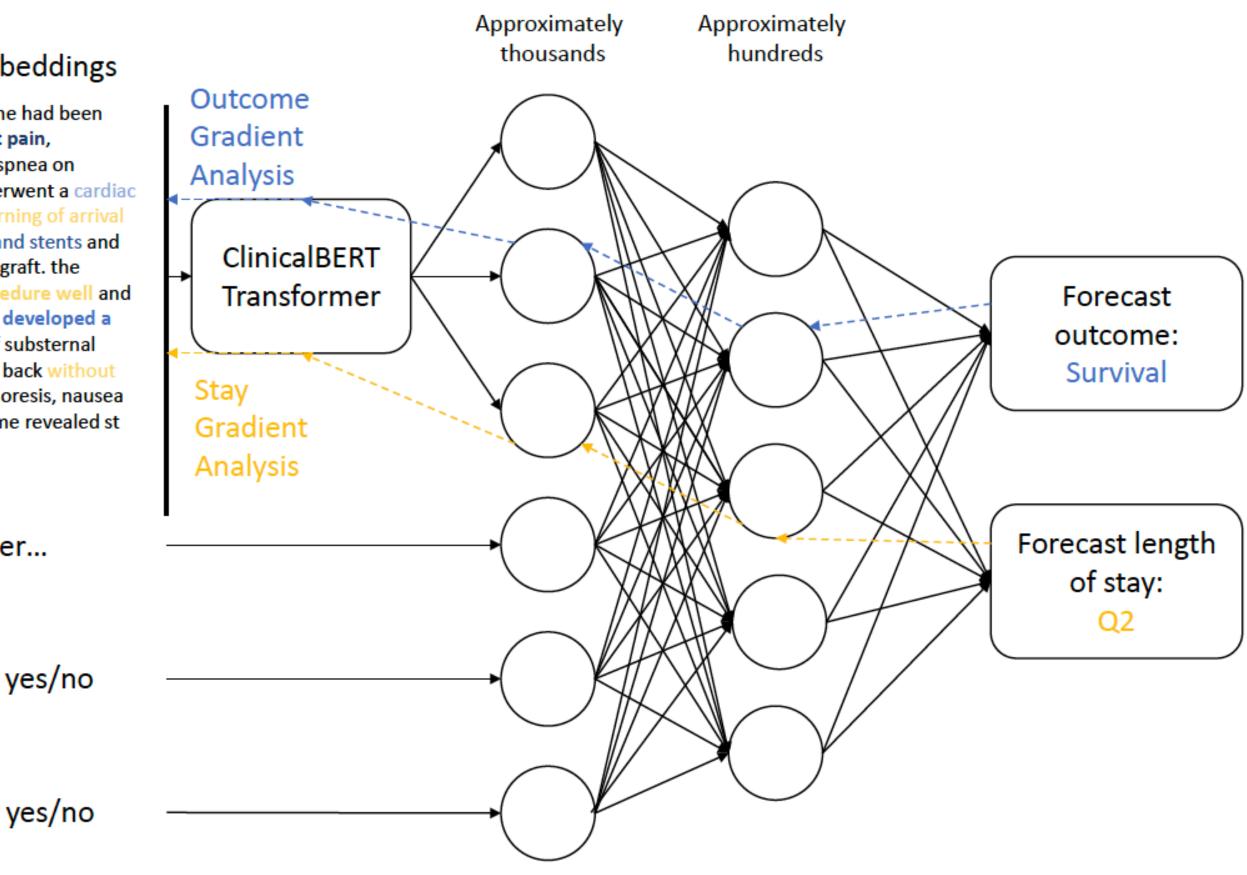
- Age, sex, insurer... •
- Comorbidity 1 yes/no ٠
- Comorbidity n yes/no •

...

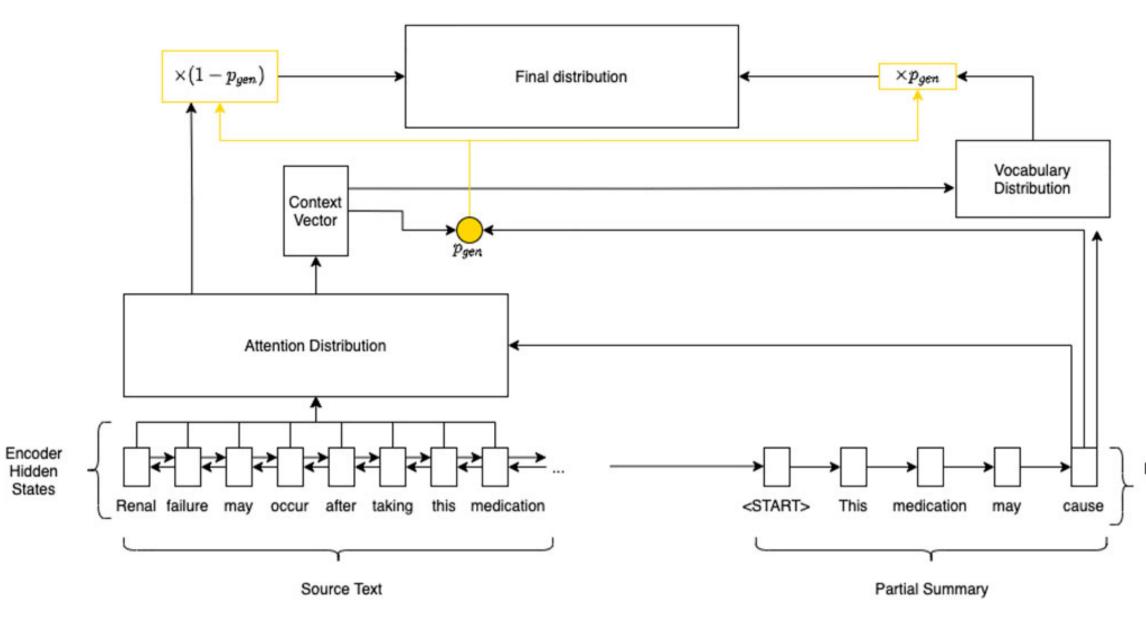
0.02 0.03

0.01

0



Garcia-Agundez et al. AMIA 2022: When BERT Fails - The Limits of EHR Classification



## Meyer et al. Frontiers in Pharmacology 2023: Neural text Generation in Regulatory Medical Writing

## Generating Drug Leaflets

## Raw Text

WARNINGS Reduced effectiveness due to impaired CYP2C19 function: The inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19. This metabolism can b impaired by genetic variations in CYP2C19 and by concomitant medications that interfere with it. Avoid use of Plavix in patients with impaired CYP2C19 function. Genetic variations: Patients with genetically reduced CYP2C19 function have diminished antiplatele sponses and generally exhibit higher cardiovascular event rate following myocardial infarction than do patients with normal CYP2C19 function. Co-administration of Plavix with omeprazole, proton pump inhibitor that is an inhibitor of CYP2C19, reduces the pharmacological activity of Plavix if given concomitantly or if given 1 hours apart. There is no evidence that other drugs that reduce stomach acid, such as most H2 blockers (except cimetidine) antacids interfere with the antiplatelet activity of clopidogre Thrombotic thrombocytopenic purpura (TTP): TTP has been reporte rarely following use of Plavix, sometimes after a short exposure (< weeks). TTP is a serious condition that can be fatal and requires urgent treatment including plasmapheresis. It is characterized b hrombocytopenia, microangiopathic hemolytic anemia, neurological findings, renal dysfunction, and fever.

## Aligned Text

## VARNINGS Reduced effectiveness due to impaired CYP2C19 unction: The inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19. This metabolism can be impaired by genetic variations in CYP2C19 and by concomitant medications that interfere with it. Avoid use of Plavix in patients with impaired CYP2C19 function. Genetic variations: Patients with genetically reduced CYP2C19 function have diminished antiplatelet sponses and generally exhibit higher cardiovascular event rates ollowing myocardial infarction than do patients with normal CYP2C19 function. Co-administration of Plavix with omeprazole, a proton pump inhibitor that is an inhibitor of CYP2C19, reduces the harmacological activity of Plavix if given concomitantly or if given 12 ours apart. There is no evidence that other drugs that reduce tomach acid, such as most H2 blockers (except cimetidine) o intacids interfere with the antiplatelet activity of clopidogrel. hrombotic thrombocytopenic purpura (TTP): TTP has been reported rarely following use of Plavix, sometimes after a short exposure (< weeks). TTP is a serious condition that can be fatal and requires urgent treatment including plasmapheresis. It is characterized by rombocytopenia, microangiopathic hemolytic anemia, neurological findings, renal dysfunction, and fever

Aligned Text

Co-administration

Plavix with omeprazole,

a proton pump inhibitor

that is an inhibitor of

CYP2C19, reduces the

pharmacological activity

of Plavix if given

concomitantly or if given

12 hours apart.



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요 안 요 안 집 놀

Assess Destaure

CHORDRONOVO-

tions into

## Warnings

Use Plavix exactly as directed on the label, or as prescribed.

Co-administration Plavix with omeprazole might reduce the pharmacological activity of Plavix if given concomitantly or 12 hours apart.



## Raw Text

WARNINGS Reduced effectiveness due to impaired CYP2C19 function: The inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19. This metabolism can be impaired by genetic variations in CYP2C19 and by concomitant nedications that interfere with it. Avoid use of Plavix in patients with impaired CYP2C19 function. Genetic variations: Patients with genetically reduced CYP2C19 function have diminished antiplatelet responses and generally exhibit higher cardiovascular event rates following myocardial infarction than do patients with normal CYP2C19 function. Co-administration of Plavix with omeprazole, a proton pump inhibitor that is an inhibitor of CYP2C19, reduces the harmacological activity of Plavix if given concomitantly or if given 12 hours apart. There is no evidence that other drugs that reduc stomach acid, such as most H2 blockers (except cimetidine) of antacids interfere with the antiplatelet activity of clopidogre hrombotic thrombocytopenic purpura (TTP): TTP has been reported rarely following use of Plavix, sometimes after a short exposure (<2 weeks). TTP is a serious condition that can be fatal and requires urgent treatment including plasmapheresis. It is characterized by hrombocytopenia, microangiopathic hemolytic anemia, neurological indings, renal dysfunction, and fever.

Use Plavix exactly as directed on the label, or as prescribed.

Warnings

Co-administration Plavix with omeprazole might reduce the pharmacological activity of Plavix if given concomitantly or 12 hours apart.

Decoder Hidden States



WARNINGS Reduced effectiveness due to impaired CYP2C19 function: The inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. Clopidogrel is metabolized to this active metabolite in part by CYP2C19. This metabolism can be impaired by genetic variations in CYP2C19 and by concomitant medications that interfere with it. Avoid use of Plavix in patients with impaired CYP2C19 function. Genetic variations: Patients with genetically reduced CYP2C19 function have diminished antiplatelet responses and generally exhibit higher cardiovascular event rate CYP2C19 function. Co-administration of Plavix with omeprazole, a proton pump inhibitor that is an inhibitor of CYP2C19, reduces the pharmacological activity of Plavix if given concomitantly or if given 12 hours apart. There is no evidence that other drugs that reduce stomach acid, such as most H2 blockers (except cimetidine) or antacids interfere with the antiplatelet activity of clopidogre Thrombotic thrombocytopenic purpura (TTP): TTP has been reporte rarely following use of Plavix, sometimes after a short exposure (< weeks). TTP is a serious condition that can be fatal and require urgent treatment including plasmapheresis. It is characterized b hrombocytopenia, microangiopathic hemolytic anemia, neurologica indings, renal dysfunction, and fever.

## Aligned Text



Co-administration of

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a proton pump inhibitor

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12 hours apart.

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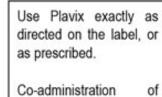
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Tetra Service

PGN





 Plavix with omeprazole might reduce the pharmacological activity of Plavix if given concomitantly or 12 hours apart.

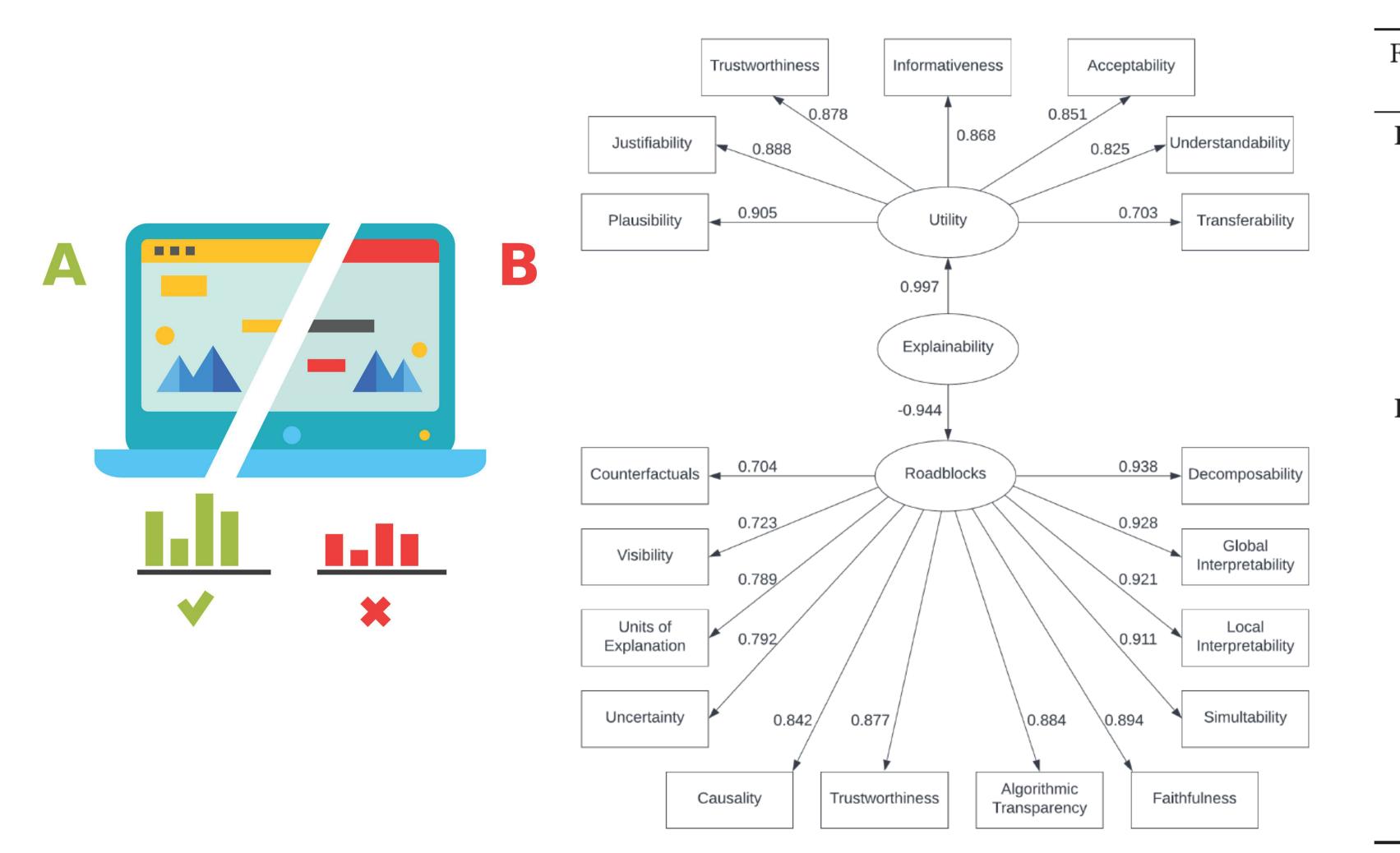






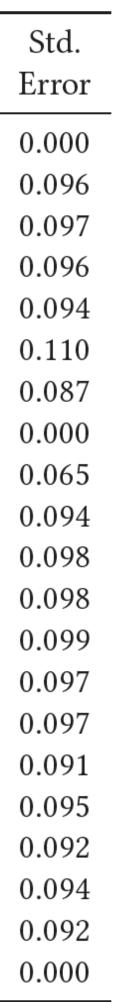


# Measuring System Explainability

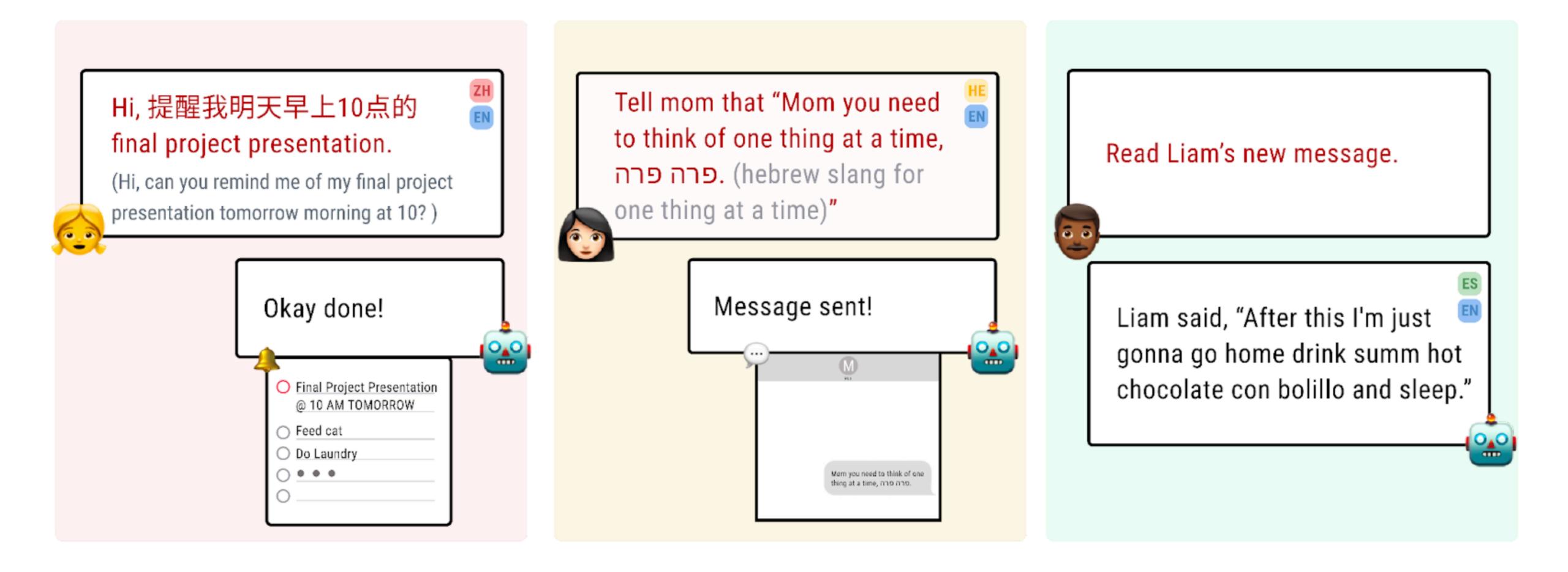


## Chen et al. under review: Evaluating Search Explainability with Psychometrics and Crowdsourcing

Factors & Items	Original Factor Label	Std. Loading
Factor 1		0.997
41	Plausibility	0.905
49	Justifiability	0.888
47	Trustworthiness	0.878
21	Informativeness	0.868
37	Acceptability	0.851
19	Understandability	0.825
15	Transferability	0.703
Factor 2		-0.944
2	Decomposability	0.938
22	Global Interpretability	0.928
24	Local Interpretability	0.921
0	Simultability	0.911
38	Faithfulness	0.894
4	Algorithmic Transparency	0.884
46	Trustworthiness	0.877
6	Causaility	0.842
8	Uncertainty	0.792
34	Units of Explanation	0.789
12	Visibility	0.723
26	Counterfactuals	0.704



## Language Generation in a Code-switched World



Zhang et al. under review: CroCoSum A Benchmark Dataset for Cross-Lingual Code-Switched Summarization

# Are Language Models World Models?



A frozen image encoder encodes an image as a feature map

💥 Image Encoder 💥



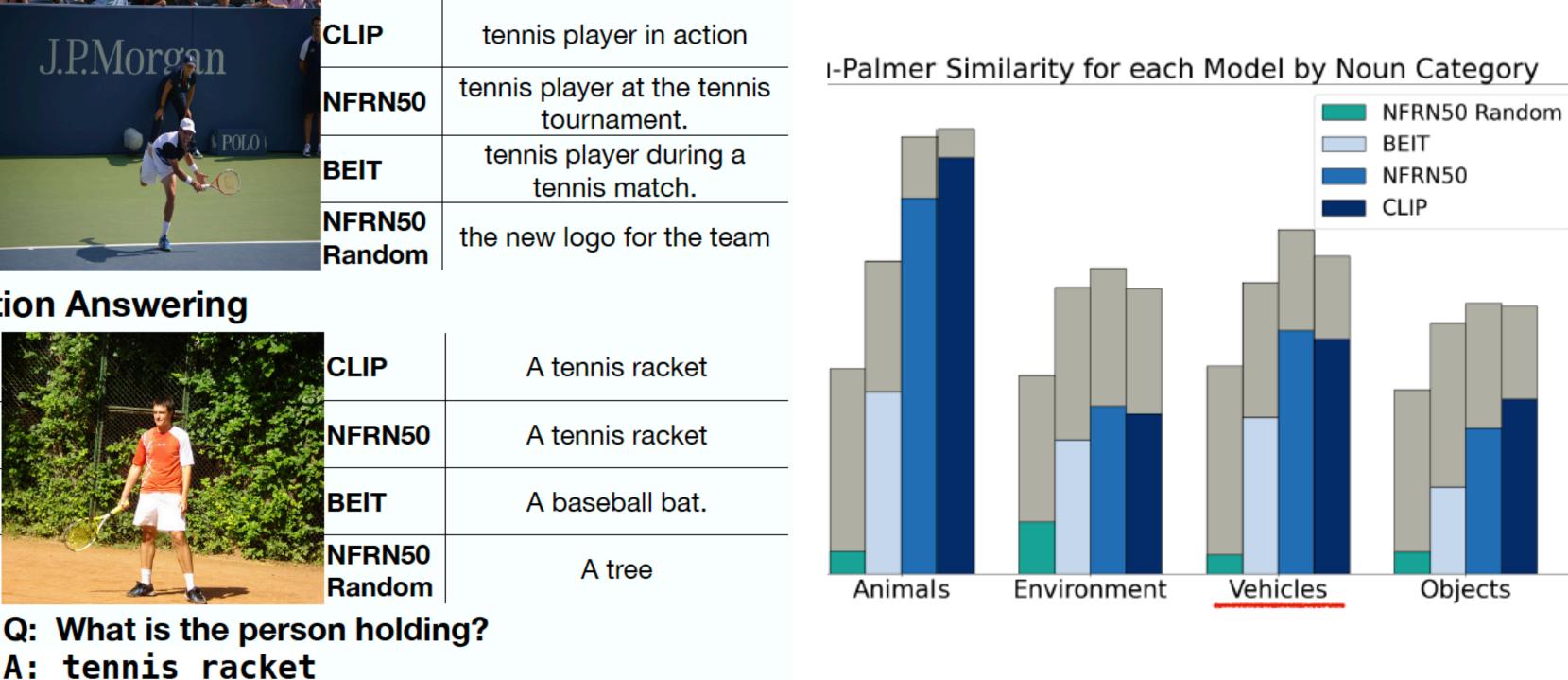


CLIP	a giraffe in the lobby of the building	J.P.Morgan
NFRN50	the giraffe in the zoo.	
BEIT	a peacock in the garden	POLO
NFRN50 Random	a man and a woman in a field of flowers	

## **Visual Question Answering**



LIP	He is surfing a wave.
FRN50	He is surfing the waves.
EIT	He is jumping into the water.
FRN50 andom	He is swimming in the pool.

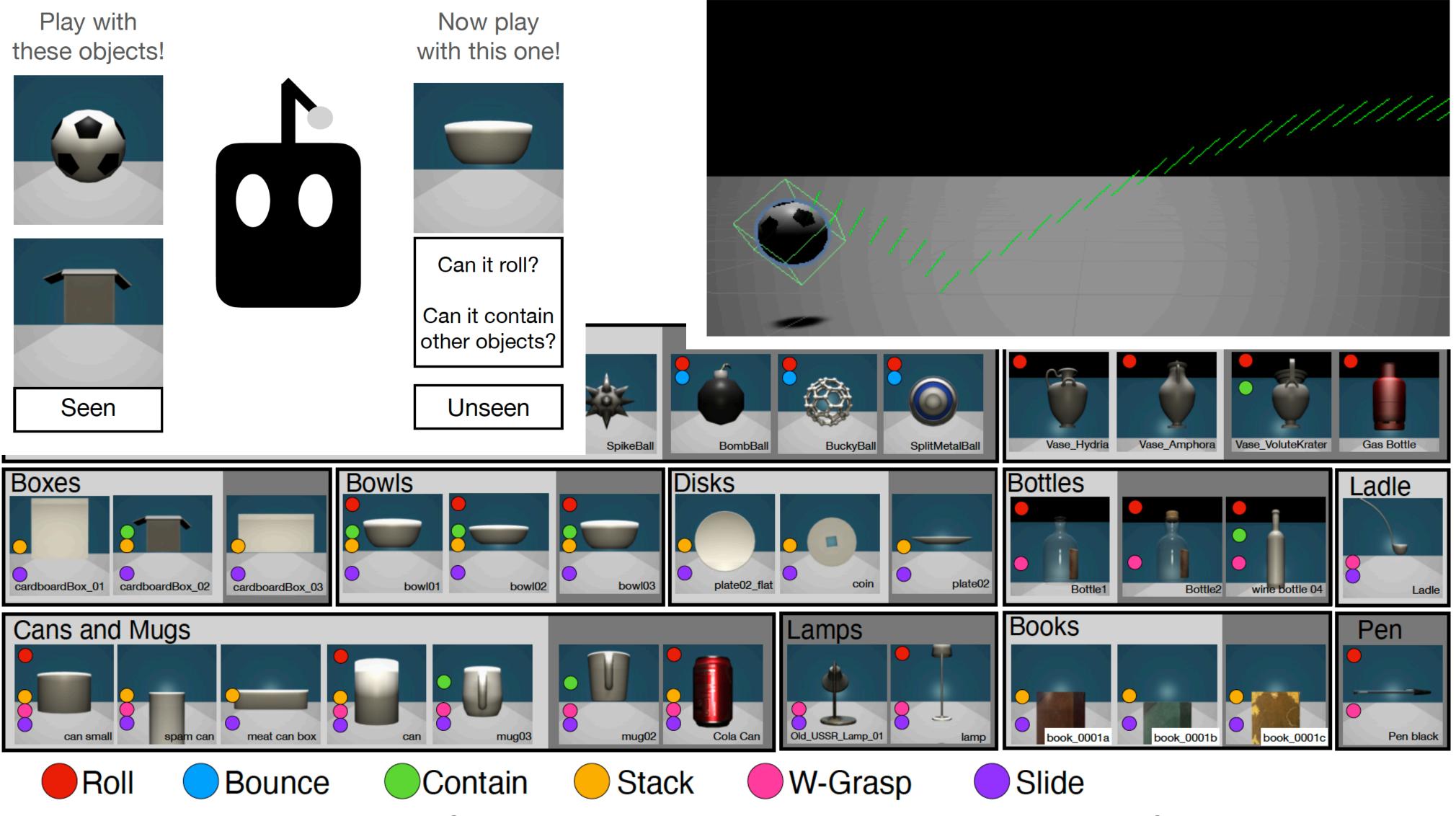


What is the person doing? A: surfing

Merullo et al. ICLR 2023: Linearly Mapping from Image to Text Space



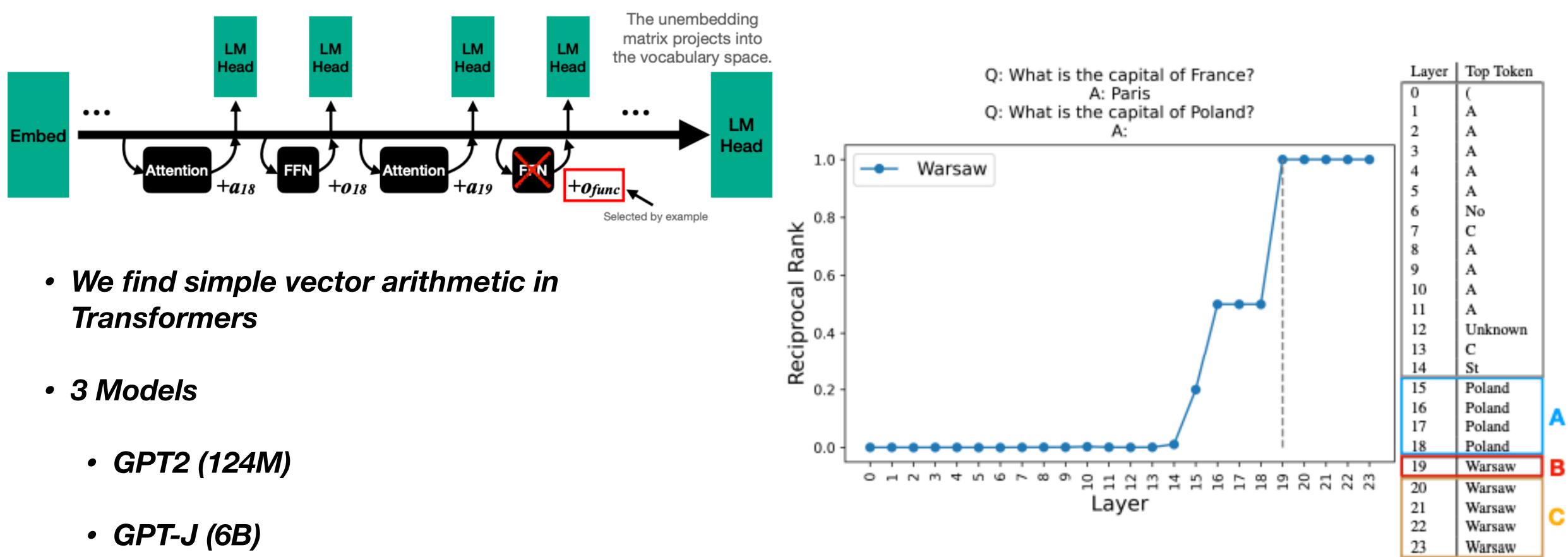
## Grounding Language Models in Physics



Merullo et al. \*SEM 2022: Pretraining on Interactions for Learning Grounded Affordance Representations



# **LLM Vector Arithmetics**



- - Bloom (176B)

Merullo et al. *under review*: Language Models Implement Simple Word2Vec-style Vector Arithmetic

# ZERO-SHOT DIAGNOSTIC DECISION SUPPORT

DANGER HIGH VOLTAGE



Surgical & Medication Errors

0 of outpatient office visits

> of hospital inpatient deaths

In the second a diagnostic error in their lifetime "

## Diagnostic Errors-

..... 😢 1 of hospital adverse events

# $\mathbf{8}$ 18 MILLON

diagnostic **ERRORS** each year





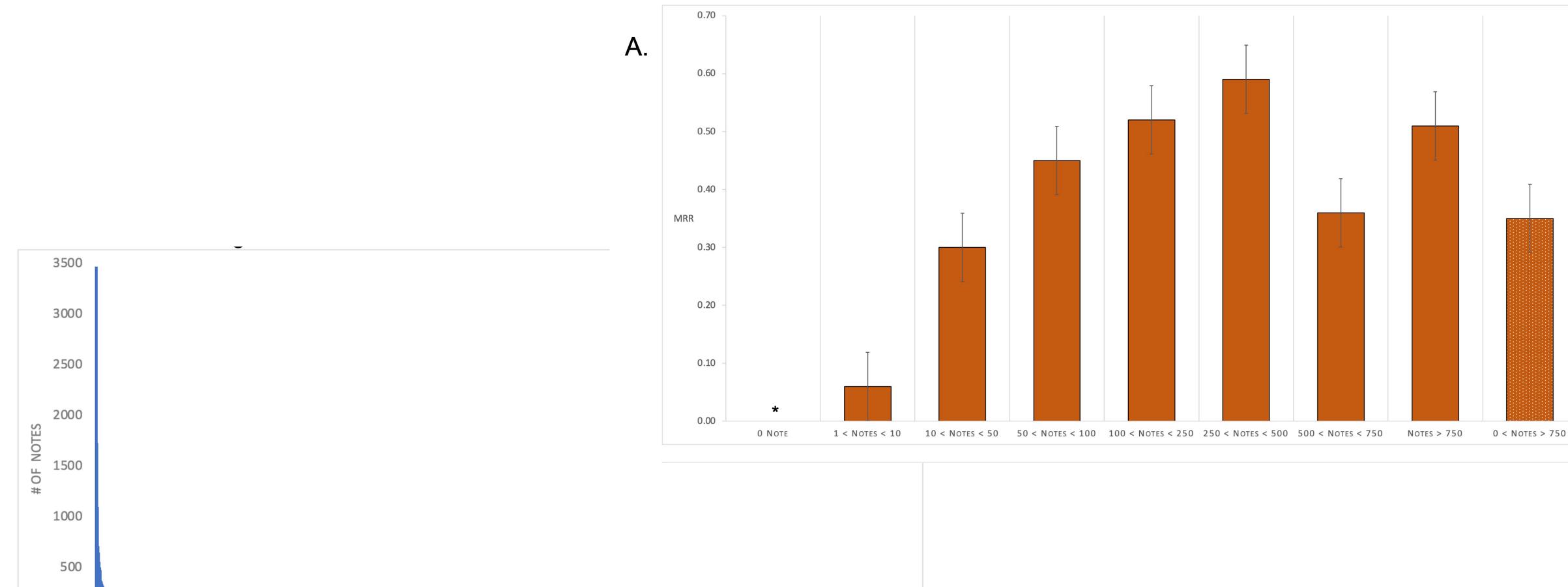
# ML to the Rescue

- Golovanevsky et al. 2022: Alzheimers (92.28%)
- Delahanty et al. 2018: Sepsis (97%)
- Gulshan et al. 2016: Diabetic Retinopathy (99.1%)
- Rudman et al. 2022: Cardiac Arrhythmias (99.27%)
- •

# ML to the Rescue

- Golovanevsky et al. 2022: Alzheimers (92.28%) [n= 2,384]
- Delahanty et al. 2018: Sepsis (97%) [n= 2,759,529]
- Gulshan et al. 2016: Diabetic Retinopathy (99.1%) [n= 128,175]
- Rudman et al. 2022: Cardiac Arrhythmias (99.27%) [n= 8,528]
- •

# But only if you have the Data!



Diagnoses ranks according to note frequency

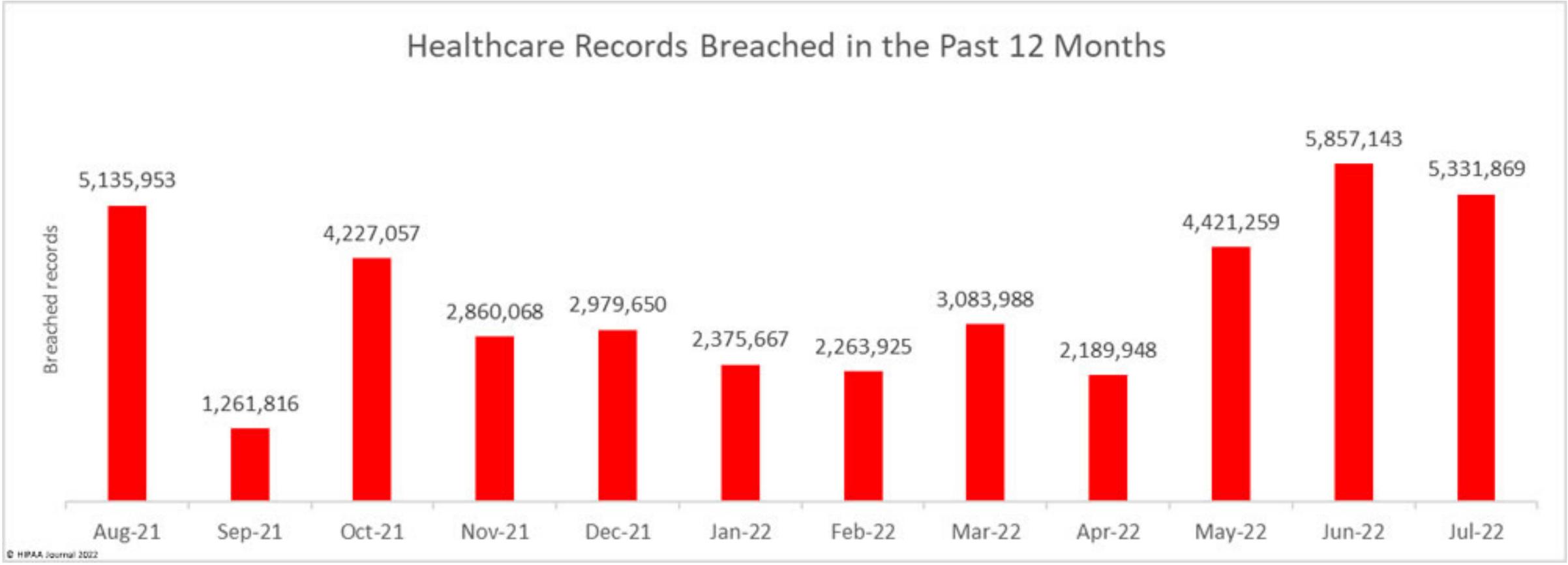
165<sup>1</sup>

 $\searrow$ 

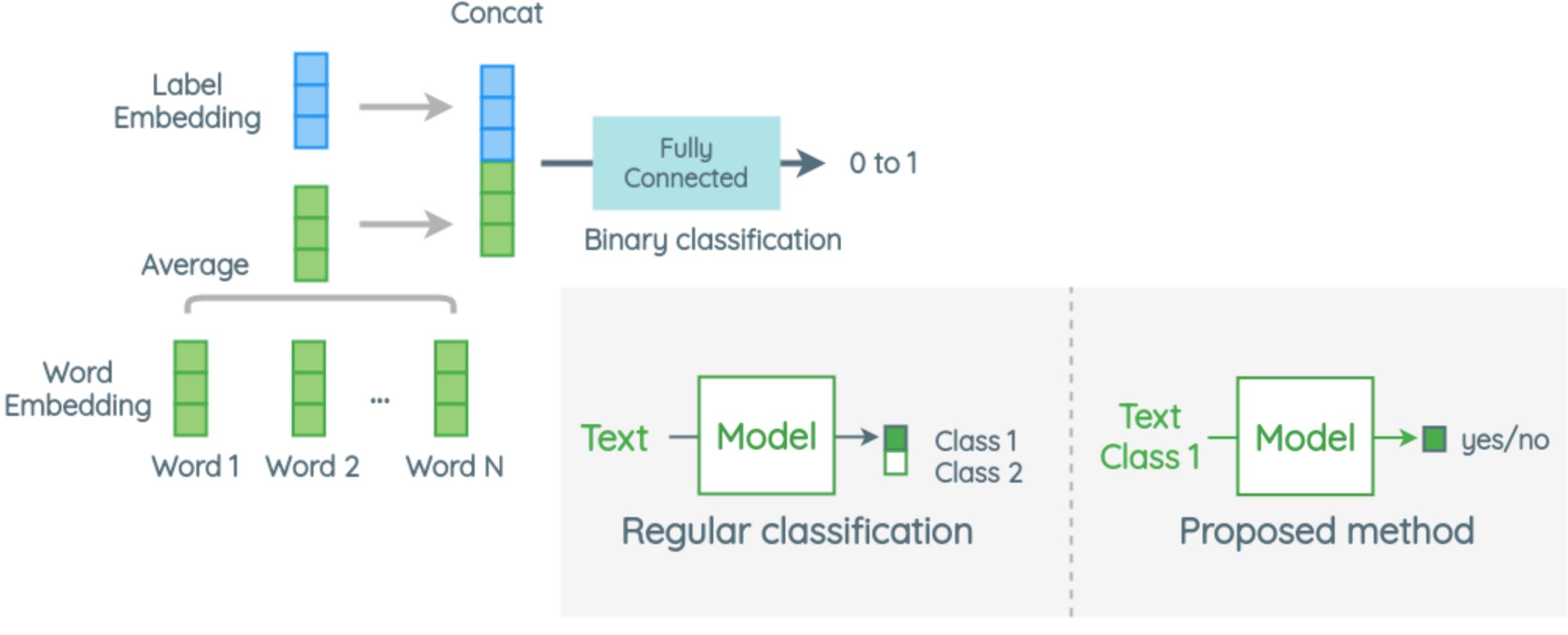




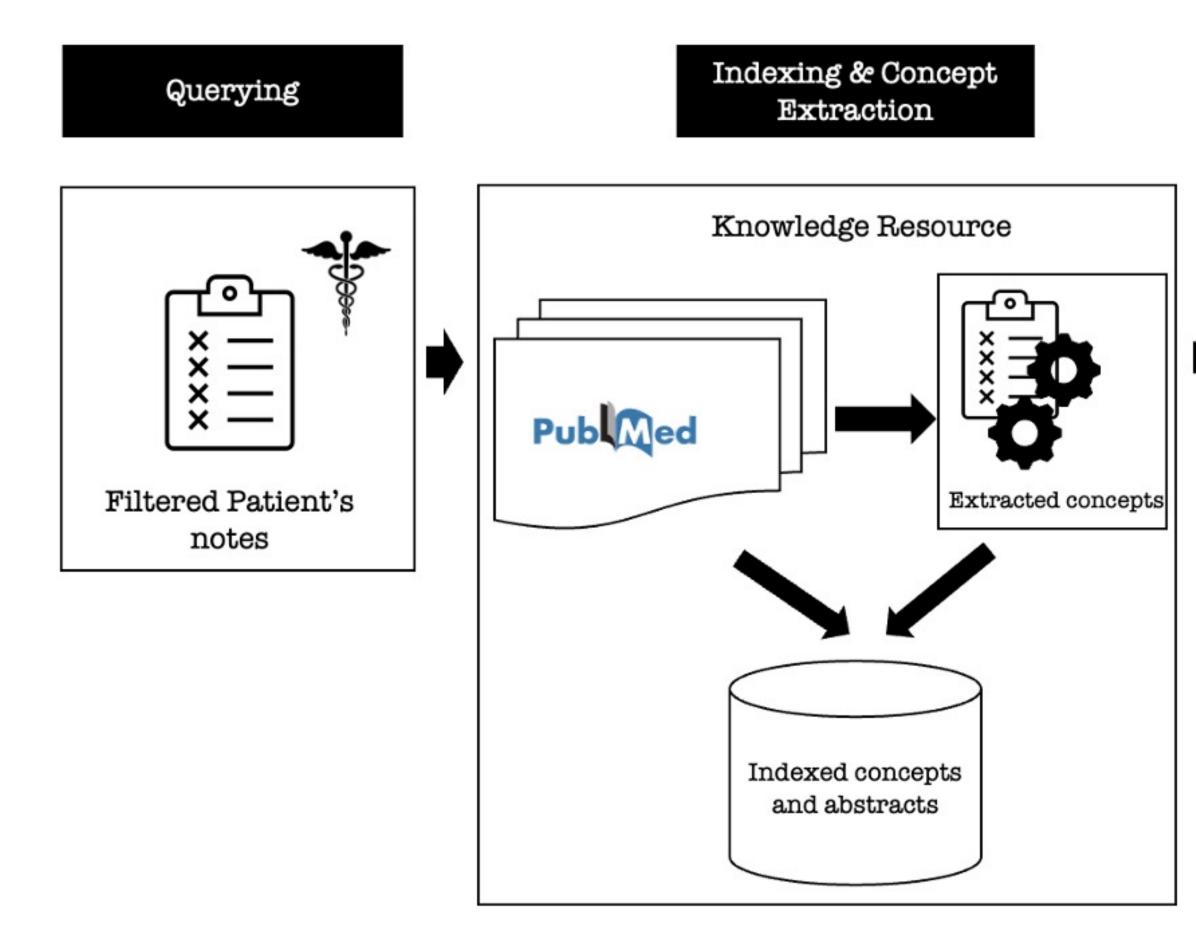
# Sharing is ...



# Zero-shot Text Classification



# Via Retrieval



## Retrieval

Label Generation & Ranking

Retrieved information: 1.PMID: 231, {mitral valve regurgitation, mitral stenosis}

2.PMID: 240, {mitral valve regurgitation, mitral stenosis}

3.PMID: 249,{ mitral stenosis, aortic valve replacement} ⇒

Rank list of diagnoses:

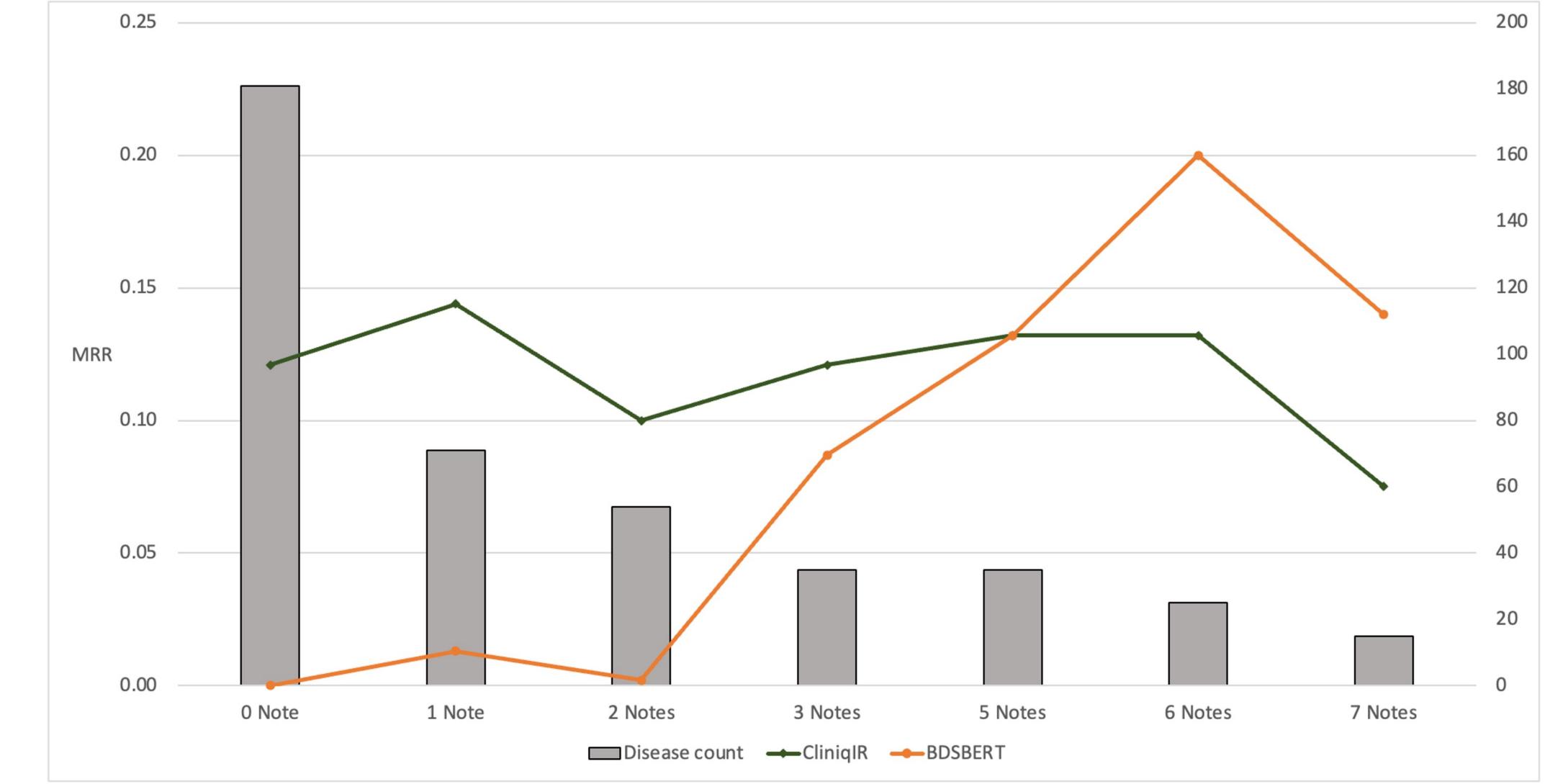
- 1. mitral stenosis
- 2. mitral valve regurgitation
- 3. aortic valve replacement



## Datasets

- PubMed
  - 33M abstracts
- MIMIC III
  - 50,000 ICU encounters
  - 2643 unique diagnoses
  - 902 of them occur exactly once
- DC3
  - 31 (difficult) case reports

# Results I



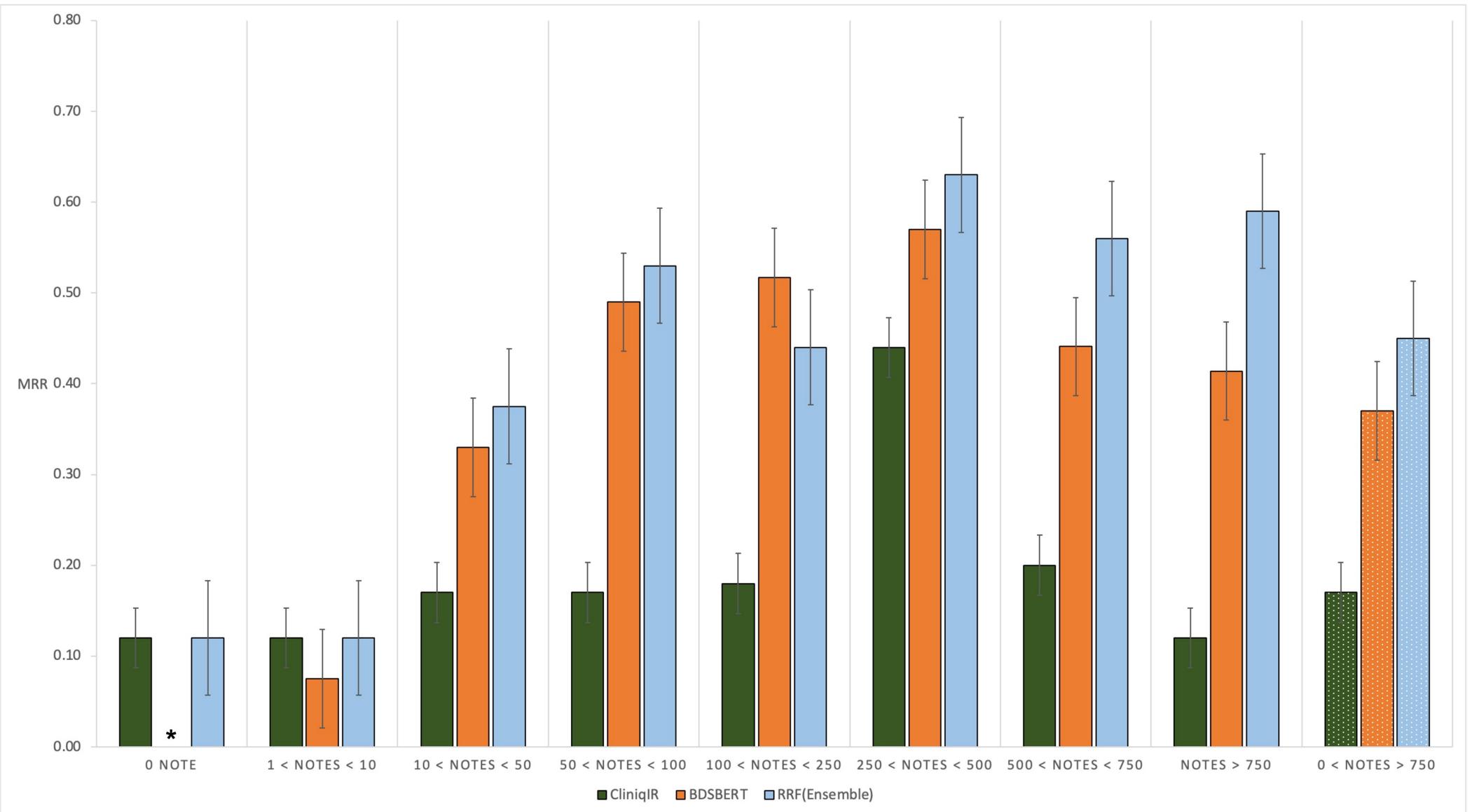
Α.

- d: diagnosis
- e: encounter
- $\mu$ : Dirichlet prior, median # of training examples per diagnosis
- |d|: # of training examples for diagnosis d

Ensembling  $P'(d, e) = \frac{P_s(d, e) + \mu P_u(d, e)}{|d| + \mu}$ 

# **Results** II

Β. 0.70 0.60



## Reasons to Care

- The world is Zipfian
- Effective zero-shot approaches rely on structured information (KB triples)
- Unstructured data is abundantly available and growing fast
- Using unstructured collections for unsupervised learning unlocks considerable resources
- Next stop: Going beyond diagnostics

# DISCUSSION

