AI in Medicine Lab

Boltzmann Semantic Score: A Semantic Metric to Evaluate Large Vision Models using Large Language Models

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The University of British Columbia

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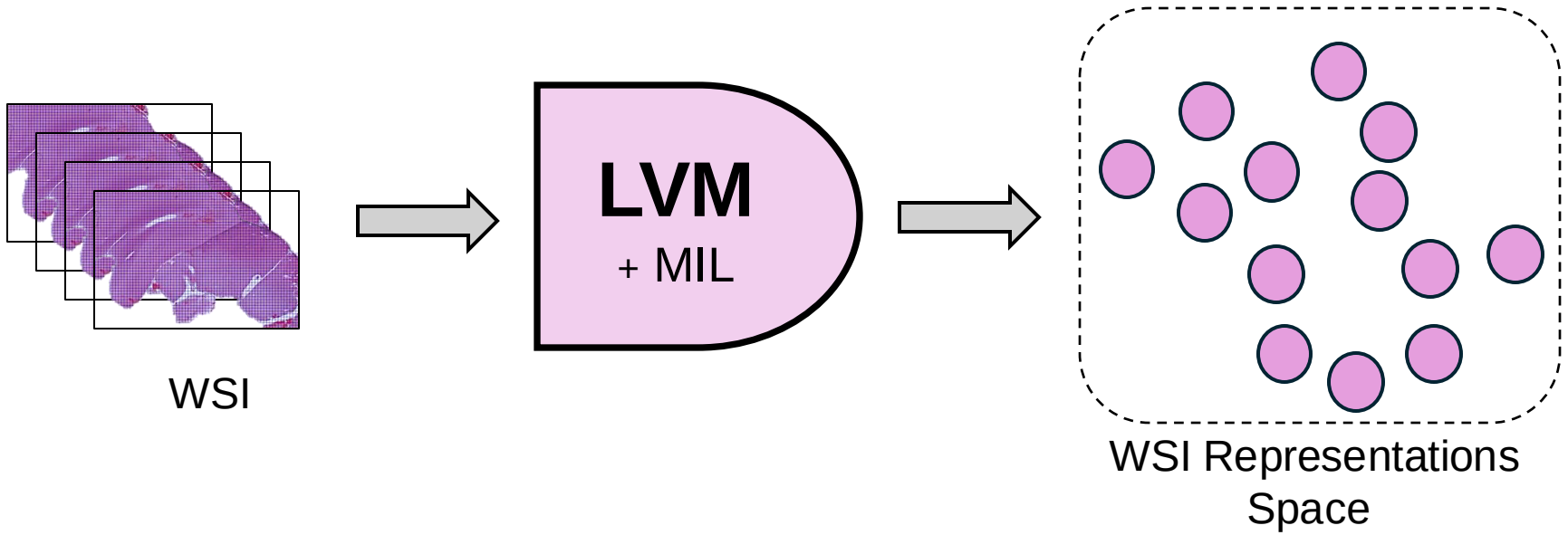
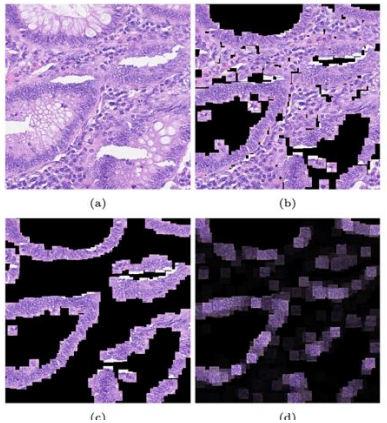
Question:



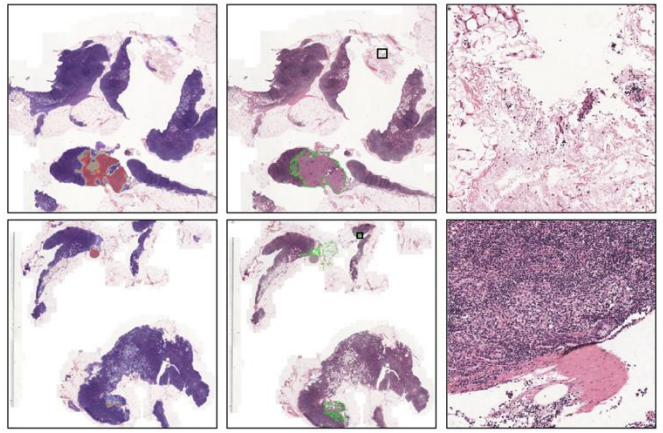
Do Large Vision Models (LVMs) extract **semantically relevant** features similar to those identified by human experts?

What people do now:

- Gradient Visualization or Attention Score Visualization:
  - ➢ Comparison with Expert Annotations
  - ➢ Expert Evaluations of the Heatmaps



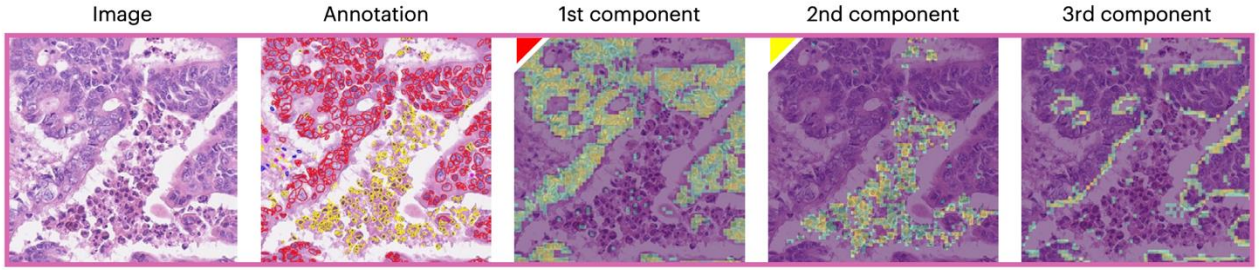
Instance Attention Score Visualization[1]



Attention Heatmaps and Comparison with Expert Annotations[2]

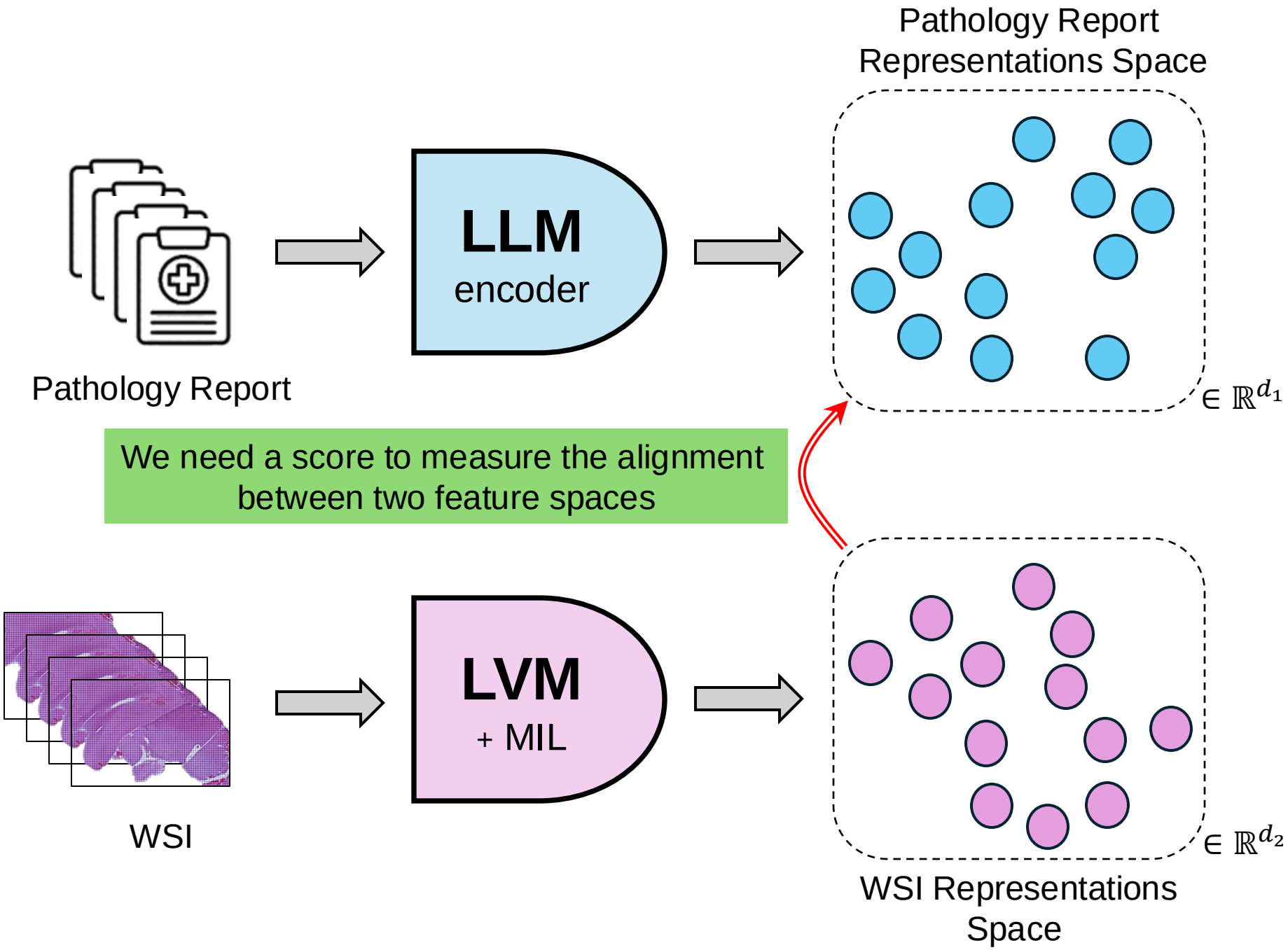
Problems with this approach:

- **Subjective**
- **Subject to Variability**
- **Small Sample Size**
- **Limited to Certain Cancers**



PCA on Tile Features and Compare with Annotations[3]

Solution:


Pathology Report
Representations Space
LLM
encoder
Pathology Report
$\in \mathbb{R}^{d_1}$
We need a score to measure the alignment between two feature spaces
LVM
+ MIL
WSI
$\in \mathbb{R}^{d_2}$
WSI Representations Space

Challenges & Questions:

Q1: Can LLMs encode Pathology Reports properly?

Q2: How to measure the structural similarity of two spaces with non-identical dimensions?

Zero-shot LLM representation in Pathology:

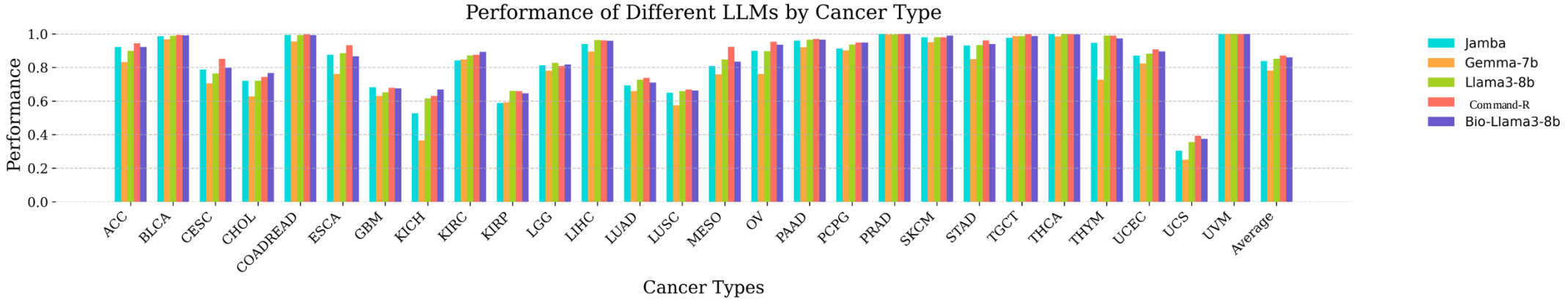
- 5 Tasks with 5 LLMs:
  - Information Retrieval in Organ-Independent and Organ-Specific settings with original and perturbed texts
  - Survival prediction

Command-R UMAP plot of TCGA: ~9,500 pathology reports

The C-index of RSF for Survival Prediction

LLM	BRCA	GBM	KIRC	KIRP	LGG	LUAD	LUSC	UCEC
Command-R	$0.622_{\pm 0.02}$	$0.537_{\pm 0.03}$	$0.722_{\pm 0.04}$	$0.743_{\pm 0.10}$	$0.643_{\pm 0.05}$	$0.611_{\pm 0.04}$	$0.547_{\pm 0.03}$	$0.602_{\pm 0.08}$
Gemma-7b	$0.603_{\pm 0.04}$	$0.512_{\pm 0.03}$	$0.707_{\pm 0.02}$	$0.634_{\pm 0.11}$	$0.611_{\pm 0.08}$	$0.570_{\pm 0.03}$	$0.543_{\pm 0.04}$	$0.600_{\pm 0.04}$
Jamba	$0.625_{\pm 0.05}$	$0.501_{\pm 0.02}$	$0.689_{\pm 0.06}$	$0.745_{\pm 0.09}$	$0.639_{\pm 0.06}$	$0.595_{\pm 0.06}$	$0.545_{\pm 0.01}$	$0.617_{\pm 0.07}$
Llama3-8b	$0.629_{\pm 0.05}$	$0.521_{\pm 0.04}$	$0.713_{\pm 0.03}$	$0.759_{\pm 0.07}$	$0.607_{\pm 0.07}$	$0.585_{\pm 0.07}$	$0.520_{\pm 0.06}$	$0.580_{\pm 0.08}$
Bio-Llama3-8b	$0.627_{\pm 0.07}$	$0.537_{\pm 0.03}$	$0.709_{\pm 0.05}$	$0.726_{\pm 0.08}$	$0.587_{\pm 0.07}$	$0.583_{\pm 0.03}$	$0.548_{\pm 0.04}$	$0.621_{\pm 0.04}$
Average	$0.621_{\pm 0.01}$	$0.522_{\pm 0.02}$	$0.708_{\pm 0.01}$	$0.721_{\pm 0.05}$	$0.617_{\pm 0.02}$	$0.589_{\pm 0.02}$	$0.541_{\pm 0.01}$	$0.604_{\pm 0.02}$

LLMs' top-1 accuracy in organ-specific setting with original text



Zero-shot LLM representation in Pathology:

- 5 Tasks with 5 LLMs:
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Command-R UMAP plot of TCGA: ~9,500 pathology reports

The C-index of RSF for Survival Prediction

LLM	[illegible]	GBM	KIRC	KIRP	LGG	LUAD	LUSC	UCEC
Command-R	[illegible]	$0.537_{\pm[illegible]}$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Gemma-7b	[illegible]	$0.512_{\pm0.03}$	$0.707_{\pm0.02}$	$0.634_{\pm0.11}$	$0.611_{\pm0.08}$	$0.570_{\pm0.03}$	$0.543_{\pm0.04}$	$0.600_{\pm0.04}$
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Llama3-8b	$0.629_{\pm0.05}$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
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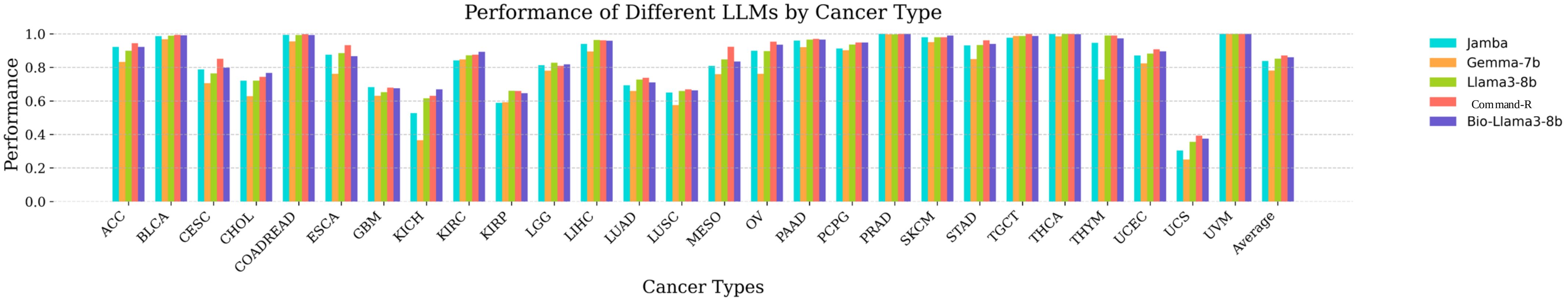
Q1: Can LLMs encode Pathology Reports properly?
Answer: **Yes, their performance is promising!**

LLMs' top-1 accuracy in organ-specific setting with original text

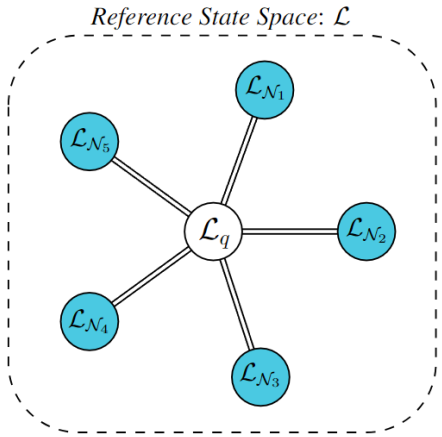


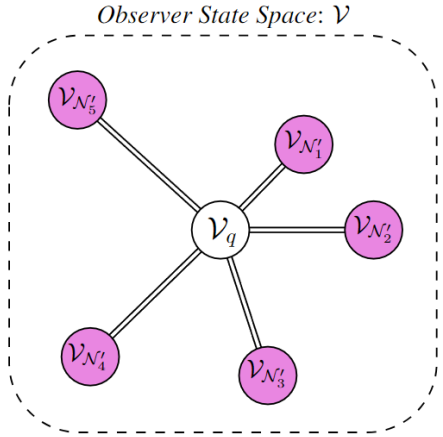
Challenges & Questions:

Q1: Can LLMs encode Pathology Reports properly?

Q2: How to measure the structural similarity of two spaces with non-identical dimensions?

Boltzmann Semantic Score: Theory



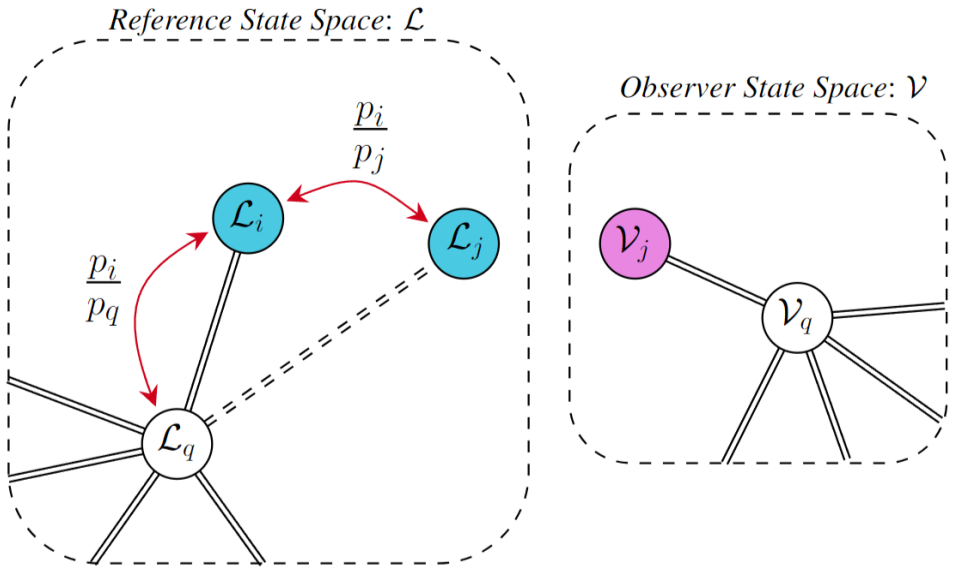


$\mathcal{L}_{\mathcal{N}_i}$: $\mathcal{N}_i$–th neighboring state of q

$\mathcal{L}_q$: the central state q

$\mathcal{V}_{\mathcal{N}'_i}$: $\mathcal{N}'_i$–th neighboring state of q

$\mathcal{V}_q$: the central state q



$\mathcal{L}_i$: the reference matching state

$\mathcal{L}_j$: the corresponding non-matching estimated state by Φ in $\mathcal{L}$

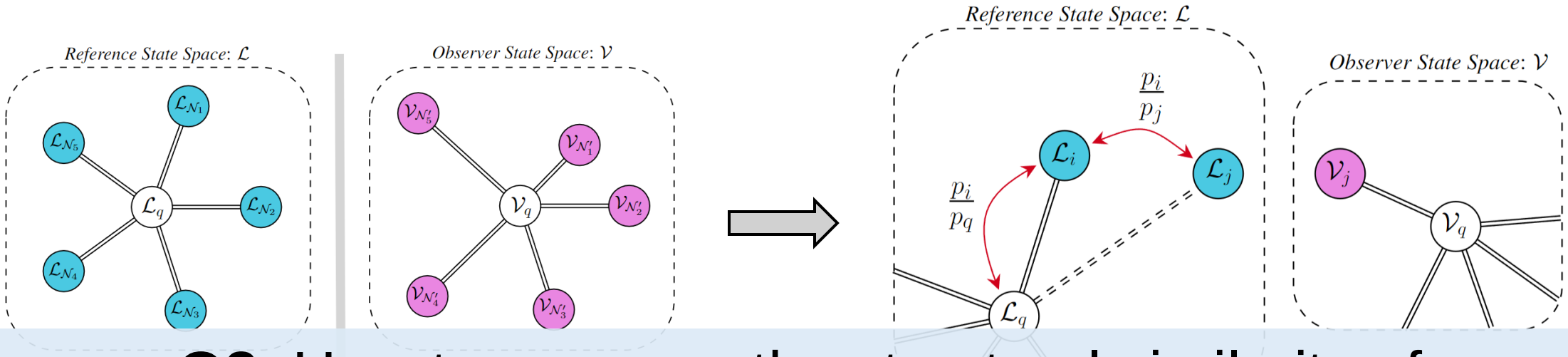
$\mathcal{V}_j$: the estimated state j by Φ in $G_{\mathcal{V},q}$

Boltzmann Factor: $$\frac{p_i}{p_q} = \exp\left(-\frac{\Delta\mathcal{E}}{kT}\right) = \exp\left(-\frac{\|\mathcal{L}_i - \mathcal{L}_q\|_2}{\sqrt{d_1}}\right)$$

Second-order Boltzmann Factor: $$b_{i;j|q} := \frac{p_i}{p_j} \cdot \frac{p_i}{p_q}$$

$$\mathcal{B}_q = \frac{\sum_{(i,j)\in\mathbb{A}} b_{i;j|q}}{\sum_{(i,j)\in\mathbb{A}\cup\mathbb{D}} b_{i;j|q}} = \frac{\sum_{(i,j)\in\mathbb{A}\cup\mathbb{D}} b_{i;j|q} - \sum_{(i,j)\in\mathbb{D}} b_{i;j|q}}{\sum_{(i,j)\in\mathbb{A}\cup\mathbb{D}} b_{i;j|q}} = 1 - \frac{\sum_{(i,j)\in\mathbb{D}} b_{i;j|q}}{\sum_{(i,j)\in\mathbb{A}\cup\mathbb{D}} b_{i;j|q}}$$

Boltzmann Semantic Score: Theory



Q2: How to measure the structural similarity of two spaces with non-identical dimensions?

Answer: **Boltzmann Semantic Score!**

Boltzmann Factor: $$\frac{p_i}{p_q} = \exp\left(-\frac{\Delta\mathcal{E}}{kT}\right) = \exp\left(-\frac{\|\mathcal{L}_i - \mathcal{L}_q\|_2}{\sqrt{d_1}}\right)$$

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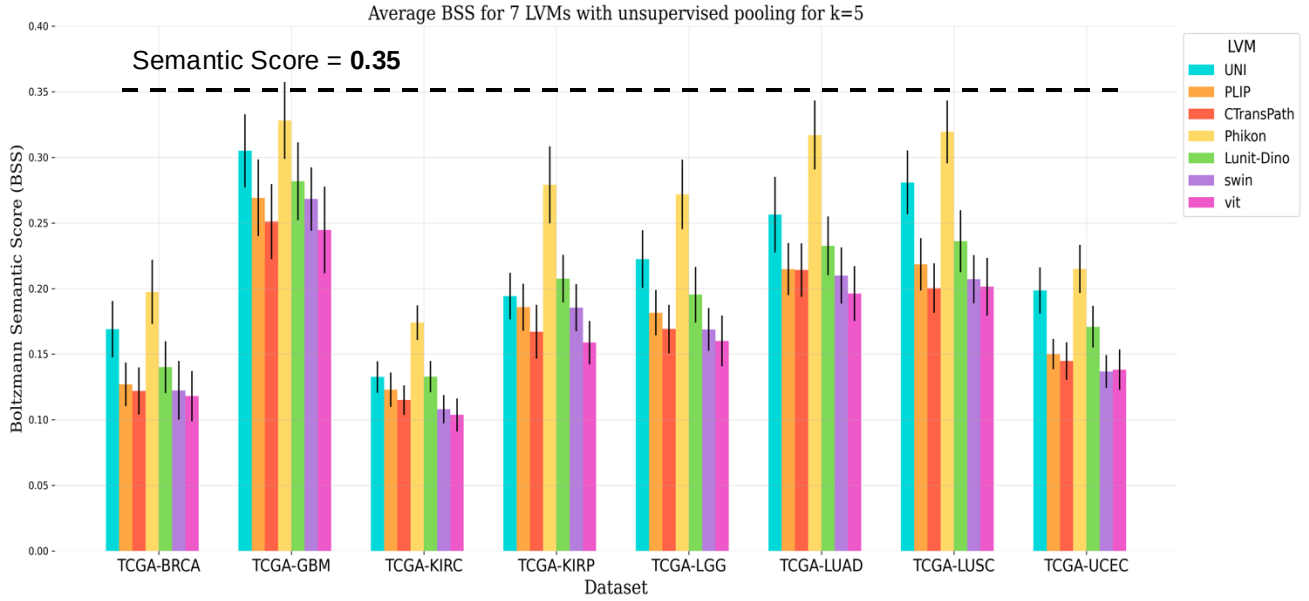
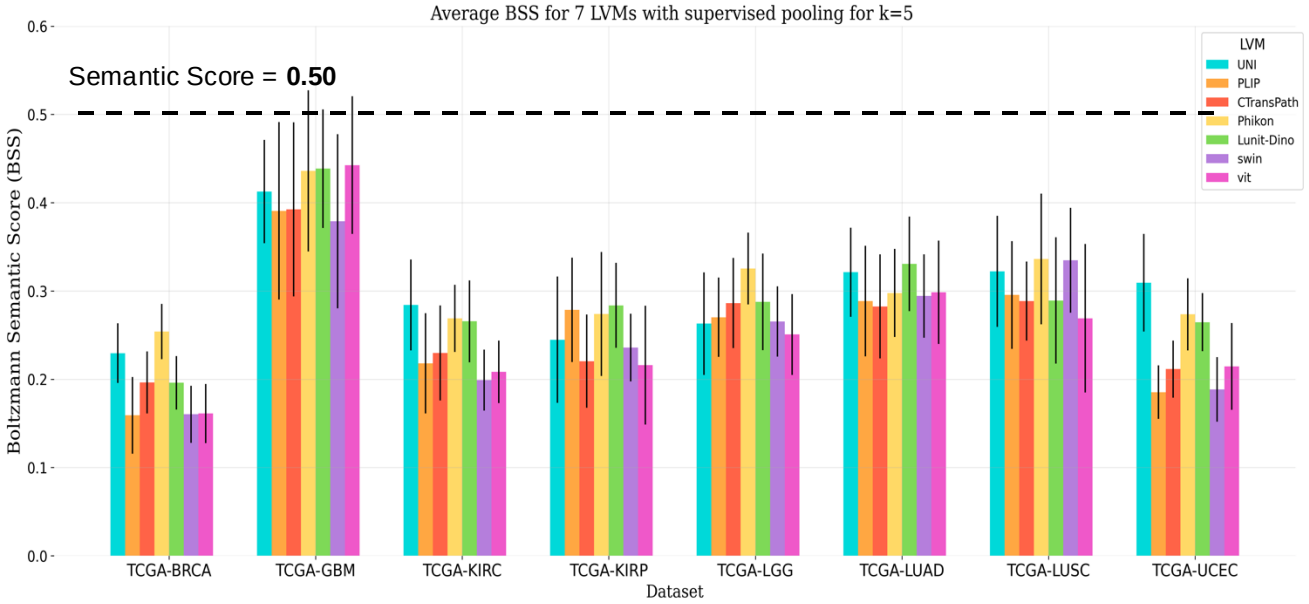
Boltzmann Semantic Score: Benchmark

- 7 LVMs were benchmarked using BSS
  - UNI
  - Phikon
  - PLIP
  - CTransPath
  - Lunit-Dino
  - SwinT
  - ViT
- Two setting for instance aggregation:
  - Supervised Pooling with AbMIL
  - Unsupervised Pooling with Mean-pooling
- The BSS reported here is average on 5 LLMs as the references





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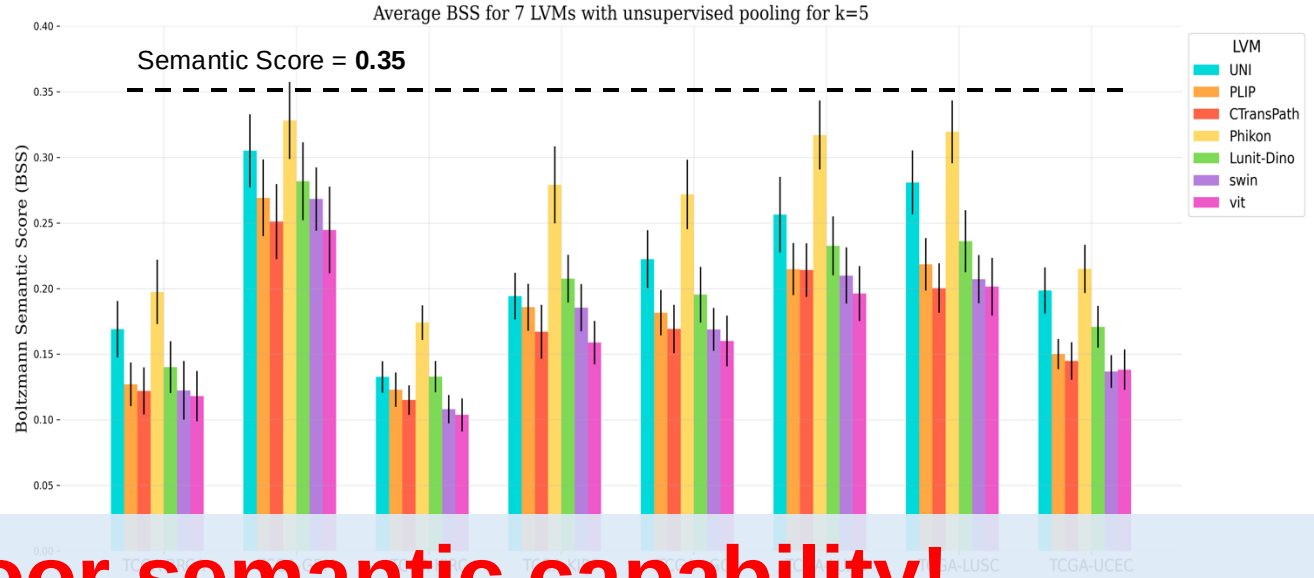

LVMs suffer from poor semantic capability!

- Two setting for instance aggregation:
  - Supervised Pooling with AbMIL
  - Unsupervised Pooling with Mean-pooling

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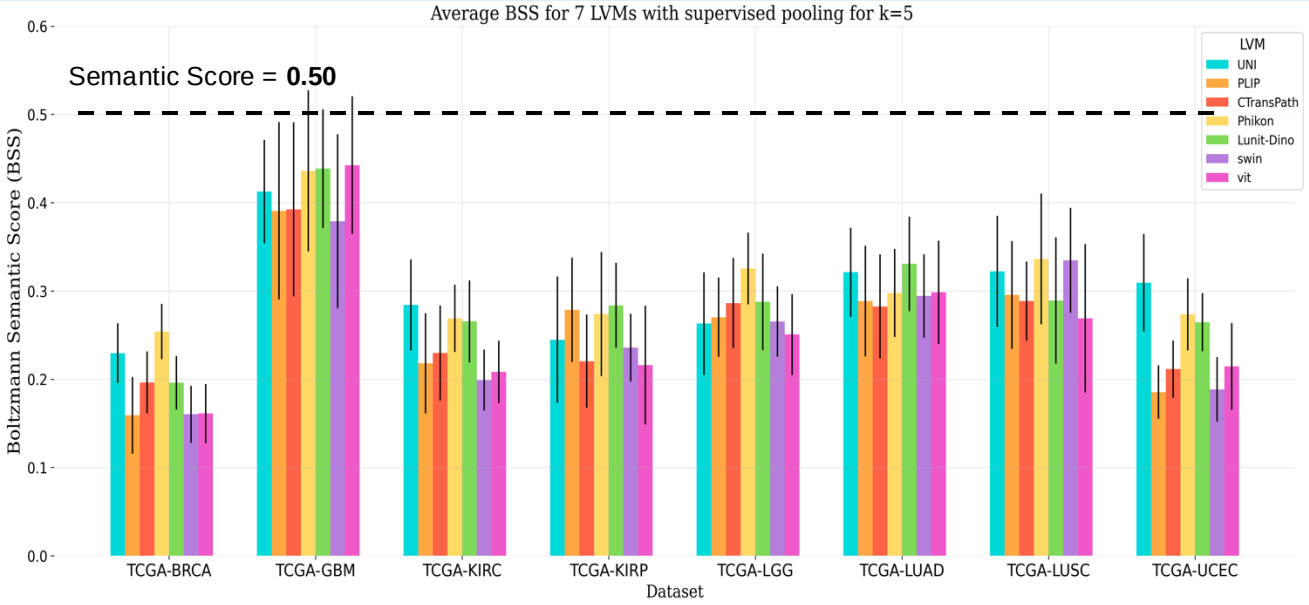
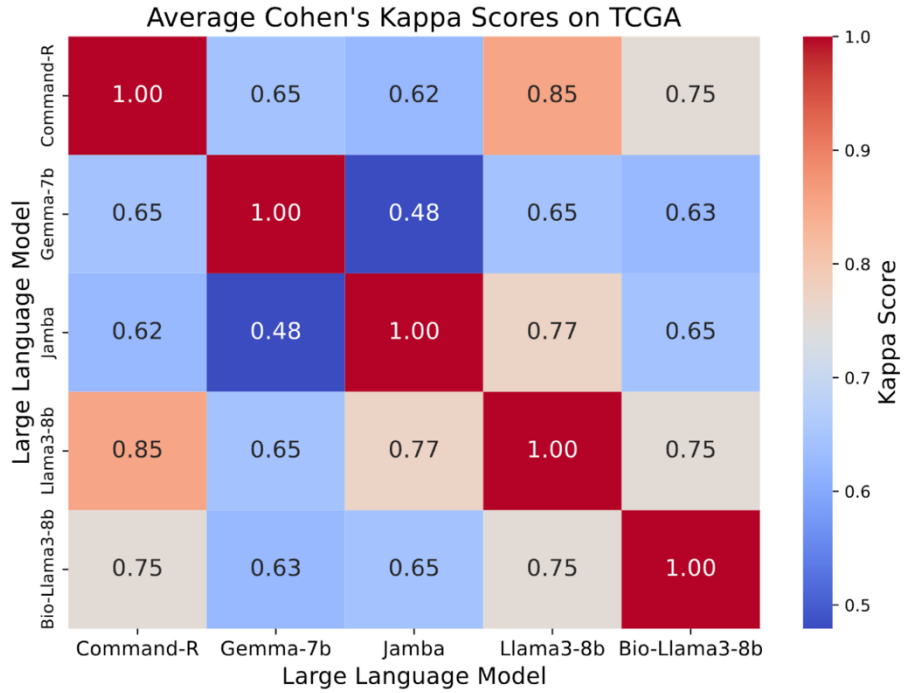


Boltzmann Semantic Score: Reliability

- Two Experiments:
  - ➢ LLMs' consensus in ranking LVMs using Cohen's Kappa
  - ➢ Downstream task metric predictability



(a) Correlation between BSS and top-1 Accuracy in Information Retrieval

LLM	GBM		KIRC		KIRP		LGG		LUAD		LUSC	
	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
Command-R	0.335	$4.6e^{-03}$	0.605	$2.9e^{-08}$	0.267	$2.5e^{-02}$	0.274	$2.2e^{-02}$	0.830	$6.4e^{-19}$	0.557	$5.4e^{-07}$
Gemma-7b	0.386	$9.6e^{-04}$	0.483	$2.3e^{-05}$	0.475	$3.3e^{-05}$	0.309	$9.2e^{-03}$	0.879	$1.4e^{-23}$	0.459	$6.4e^{-05}$
Jamba	0.302	$1.1e^{-02}$	0.583	$1.2e^{-07}$	0.247	$4.0e^{-02}$	0.259	$3.0e^{-02}$	0.838	$1.5e^{-19}$	0.517	$4.6e^{-06}$
Llama3-8b	0.293	$1.4e^{-02}$	0.550	$8.2e^{-07}$	0.326	$5.9e^{-03}$	0.227	$5.9e^{-02}$	0.807	$3.3e^{-17}$	0.540	$1.4e^{-06}$
Bio-Llama3-8b	0.355	$2.6e^{-03}$	0.572	$2.4e^{-07}$	0.323	$6.5e^{-03}$	0.231	$5.5e^{-02}$	0.834	$2.9e^{-19}$	0.575	$1.9e^{-07}$

(b) Correlation between BSS and C–index in Survival Prediction

LLM	BRCA		GBM		KIRC		KIRP		LGG		LUAD		LUSC		UCEC	
	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value	r	p-value
Command-R	0.344	$1.9e^{-11}$	−0.093	$9.6e^{-01}$	0.273	$1.1e^{-07}$	0.150	$2.4e^{-03}$	−0.027	$6.9e^{-01}$	0.233	$5.4e^{-06}$	0.099	$3.2e^{-02}$	0.367	$6.6e^{-13}$
Gemma-7b	0.307	$2.3e^{-09}$	−0.030	$7.1e^{-01}$	0.245	$1.8e^{-06}$	0.202	$7.1e^{-05}$	−0.017	$6.2e^{-01}$	0.223	$1.3e^{-05}$	0.081	$6.6e^{-02}$	0.352	$6.4e^{-12}$
Jamba	0.344	$2.0e^{-11}$	−0.080	$9.3e^{-01}$	0.257	$5.7e^{-07}$	0.144	$3.4e^{-03}$	−0.031	$7.2e^{-01}$	0.209	$3.9e^{-05}$	0.089	$4.8e^{-02}$	0.352	$5.7e^{-12}$
Llama3-8b	0.350	$7.8e^{-12}$	−0.085	$9.4e^{-01}$	0.272	$1.1e^{-07}$	0.151	$2.4e^{-03}$	−0.036	$7.5e^{-01}$	0.218	$1.9e^{-05}$	0.096	$3.6e^{-02}$	0.370	$4.4e^{-13}$
Bio-Llama3-8b	0.347	$1.2e^{-11}$	−0.087	$9.5e^{-01}$	0.287	$2.3e^{-08}$	0.131	$7.1e^{-03}$	−0.034	$7.4e^{-01}$	0.224	$1.1e^{-05}$	0.112	$1.8e^{-02}$	0.373	$2.9e^{-13}$

Conclusion:

Do Large Vision Models (LVMs) extract **semantically relevant** features similar to those identified by human experts?
Answer: LVMs suffer from poor semantic capability!

Q1: Can LLMs encode Pathology Reports properly?
Answer: **Yes, zero-shot LLMs are promising!**

Q2: How to measure the structural similarity of two spaces with non-identical dimensions?
Answer: **Yes, Boltzmann Semantic Score!**