ICLR

On Pre-trained Language Models for Antibody

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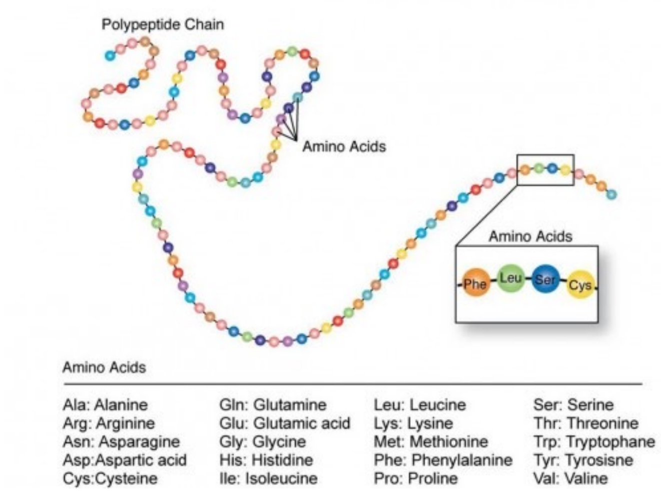
Protein & Antibody

❖ Protein

- Sequence composed of 20 amino acids



Amino Acids

Ala: Alanine
Arg: Arginine
Asn: Asparagine
Asp:Aspartic acid
Cys:Cysteine

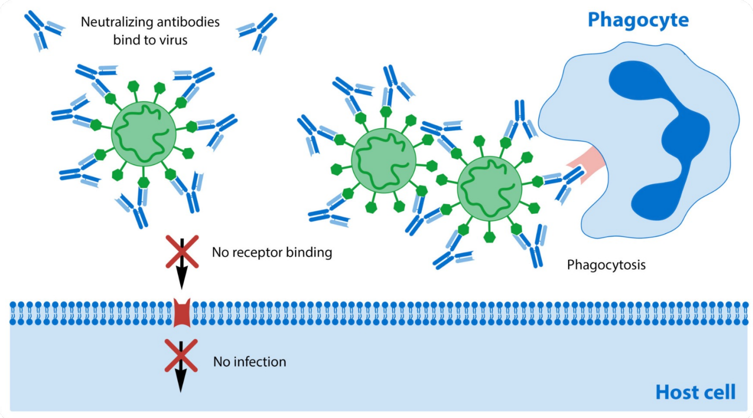
Gln: Glutamine
Glu: Glutamic acid
Gly: Glycine
His: Histidine
Ile: Isoleucine

Leu: Leucine
Lys: Lysine
Met: Methionine
Phe: Phenylalanine
Pro: Proline

Ser: Serine
Thr: Threonine
Trp: Tryptophane
Tyr: Tyrosisne
Val: Valine

❖ Antibody

- one type of therapeutic protein
- Y-shape to bind with virus



How to represent biological sequences?

Pretrained Language Models demonstrate remarkable achievements

- ❖ Pretrained Protein Language Models (PPLMs)
  - ➢ ESM (Rives et al., 2021)
  - ➢ MSA-Transformer (Rao et al., 2021)
  - ➢ ProtTrans (Elnaggar et al., 2021)
- ❖ Pretrained Antibody Language Models (PALMs)
  - ➢ Ablang (Olsen et al., 2022b)
  - ➢ AntiBERTy (Ruffolo et al., 2021)

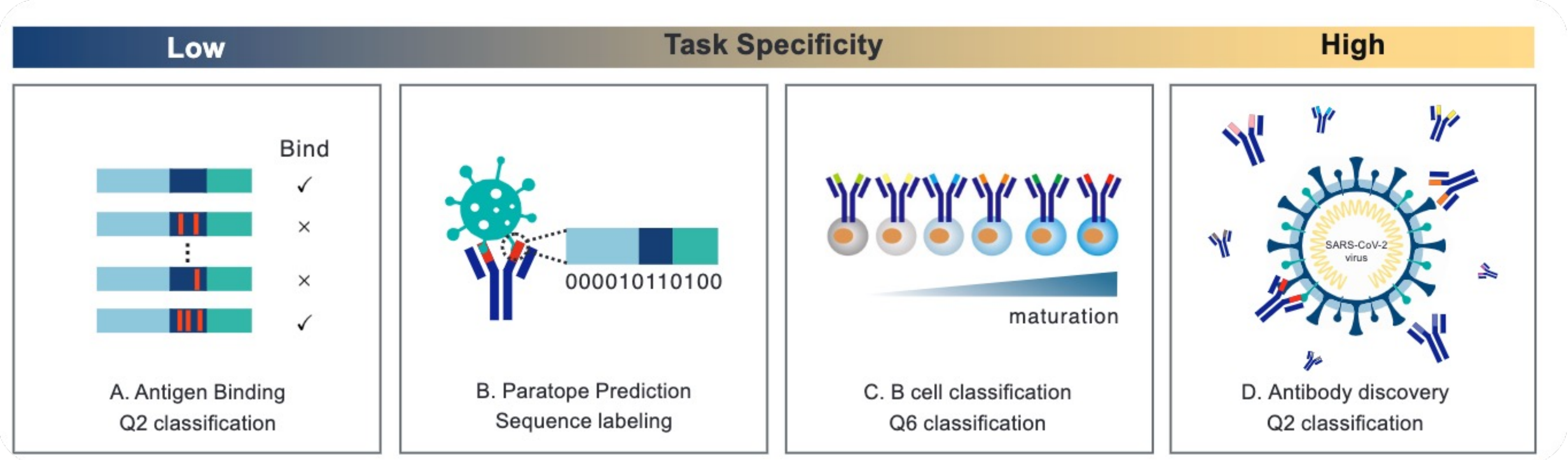
Q1: Can PPLMs directly be used for antibody tasks?

Q2: Are current PALMs highly related to real-world antibody discovery?

First, Real-world Antibody Discovery Tasks

=> a standard evaluation for antibody

- ❖ AnTibody Understanding Evaluation (ATUE)



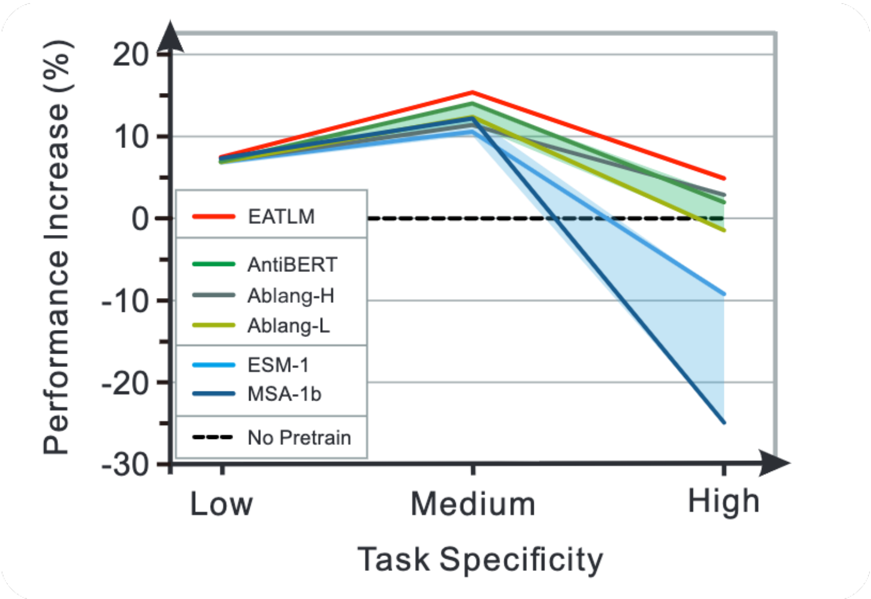
Key Observations on ATUE

- Low antibody-specificity
  - PPLMs perform similarly to PALMs
- Medium specificity
  - PALMs > PPLMs
- High specificity
  - PALMs are not enough

PPLMs can only solve low specificity tasks

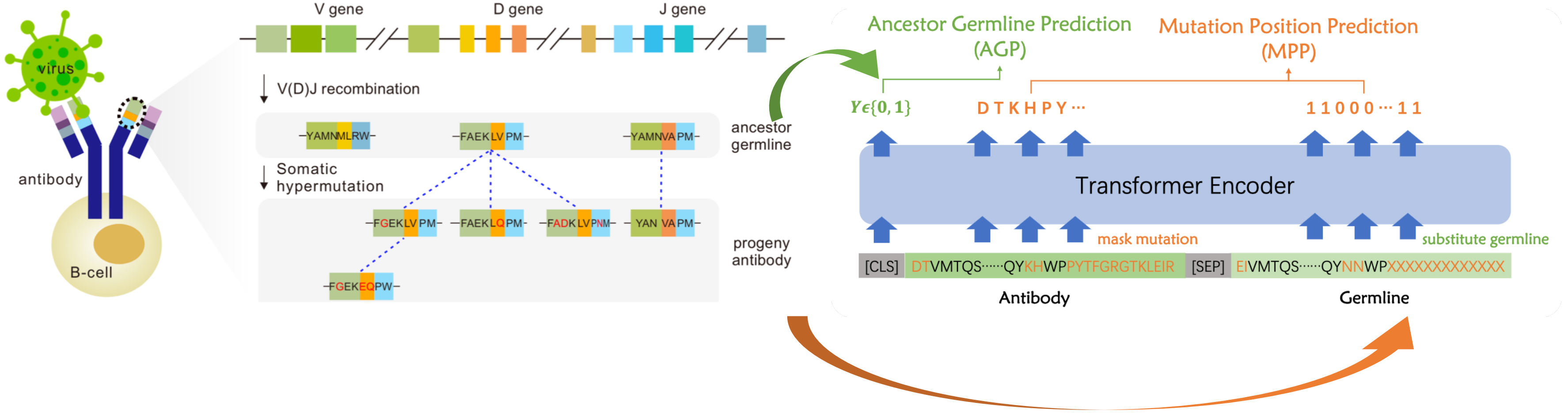
Current PALMs are not good antibody discovers

Opposite evolution mechanism



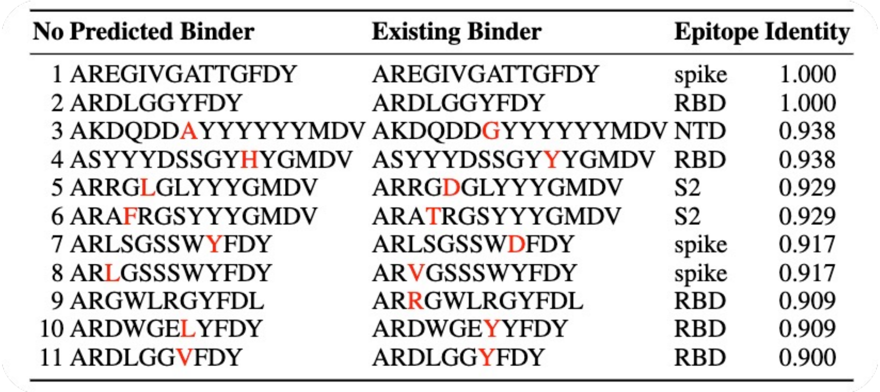
Secret of Antibody Evolution

- EvoluTion-aware AnTibody Language Model (EATLM)
  - Incorporate antibody evolution into pretraining

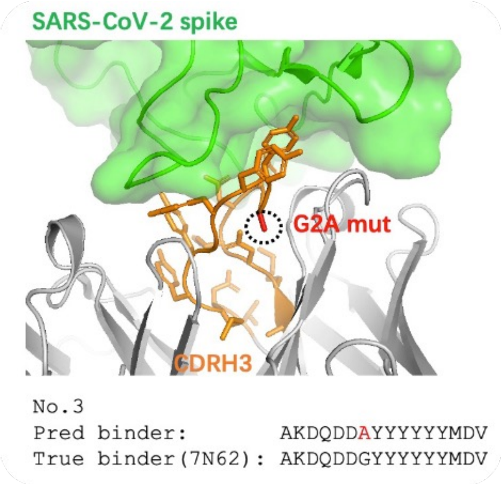


Accelerate Real-world Antibody Discovery

- Promising Antibody Binders for SARS-CoV-2



No	Predicted Binder	Existing Binder	Epitope	Identity
1	AREGIVGATTGFDY	AREGIVGATTGFDY	spike	1.000
2	ARDLGGYFDY	ARDLGGYFDY	RBD	1.000
3	AKDQDDAYYYYYYMDV	AKDQDDGYYYYYYMDV	NTD	0.938
4	ASYYYDSSGYHYGMDV	ASYYYDSSGYYYGMDV	RBD	0.938
5	ARRGLGLYYYGMDV	ARRGDGLYYYGMDV	S2	0.929
6	ARAFRGSYYYGMDV	ARATRGSYYYGMDV	S2	0.929
7	ARLSGSSWYFDY	ARLSGSSWDFDY	spike	0.917
8	ARLGSSSWYFDY	ARVGSSSWYFDY	spike	0.917
9	ARGWLRGYFDL	ARRGWLRGYFDL	RBD	0.909
10	ARDWGELYFDY	ARDWGEYYFDY	RBD	0.909
11	ARDLGGVFDY	ARDLGGYFDY	RBD	0.900



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No.3
Pred binder:          AKDQDDAYYYYYYMDV
True binder(7N62):    AKDQDDGYYYYYYMDV
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Take Away

- ❖ Present PPLMs struggle with antibody specificity tasks.
- ❖ By integrating the antibody evolution process, the pretraining can more accurately capture specificity.
- ❖ EATLM successfully identifies multiple promising SARS-Cov-2 binders.

Thanks for listening!

Code

Paper