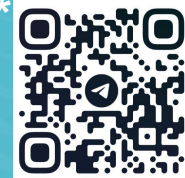


# Calculating of SARS-CoV-2 RBD and antibody complex energy by metadynamics in MARTINI 3

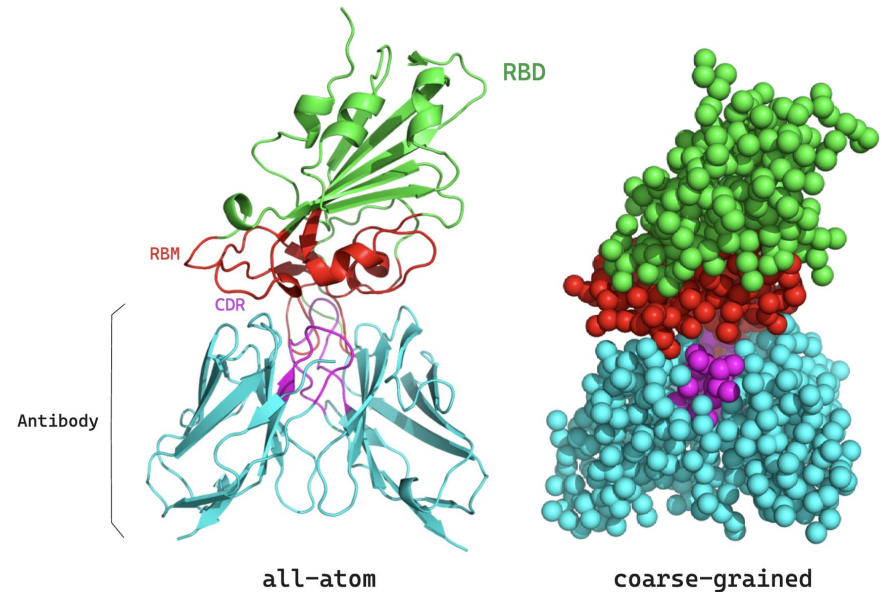
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## THE OBJECTIVE

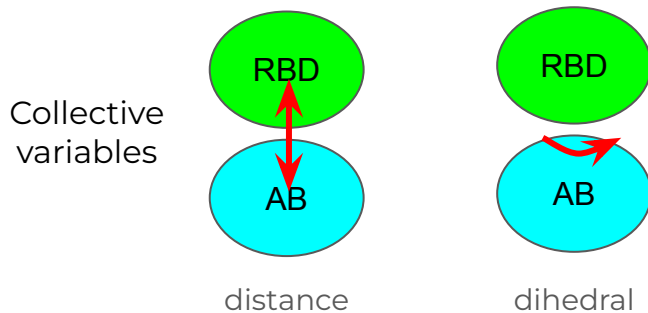
- ! Neutralising antibodies are effective in treating viral and autoimmune diseases. For SARS-CoV-2, rapid antibody design is urgently needed to address emerging variants and maintain efficacy.
- ? Generative ML models for protein design are currently gaining popularity. However, there is a need to develop a rapid method for evaluating and ranging new structures.
- ✓ The use of metadynamics in coarse-grained force fields to obtain the free energy surface allows us to evaluate the efficiency of antibody-antigen complex formation.



# ANTIBODY DESIGN PIPELINE

## Metadynamics in MARTINI 3

validation of the method on known complexes



## Making the average antibody structure

"average antibody structure" — a starting point for the generation of new antibody CDRs

**Method:** MODELLER

**Materials:** structures and CDRs sequences from the CoVAbDab

## Redesign of antibody CDRs

(based on "average antibody" complex states)

**Methods:**

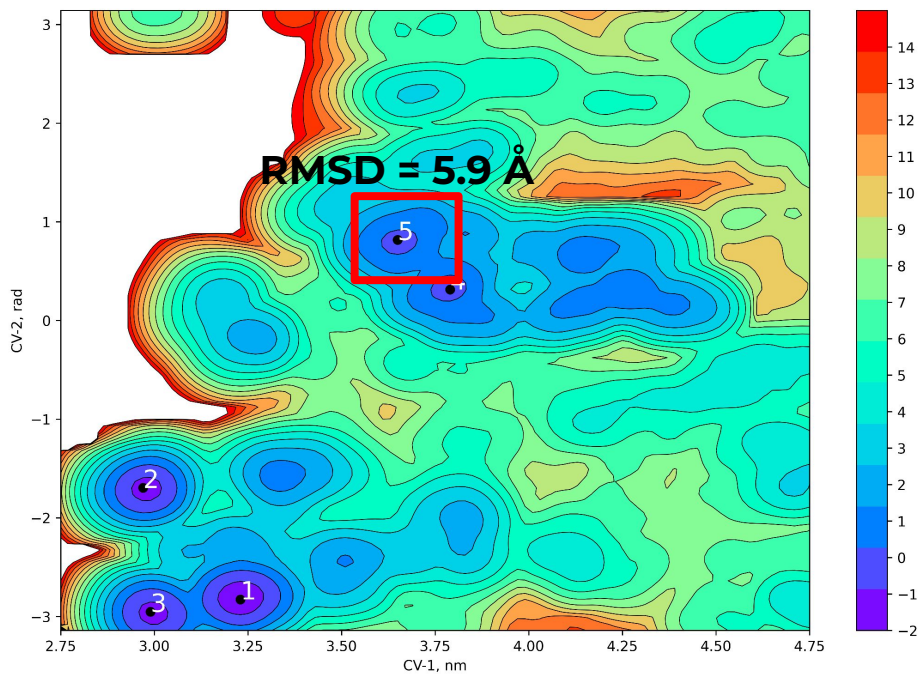
RFDiffusion+ProteinMPNN

## Ranging obtained structures

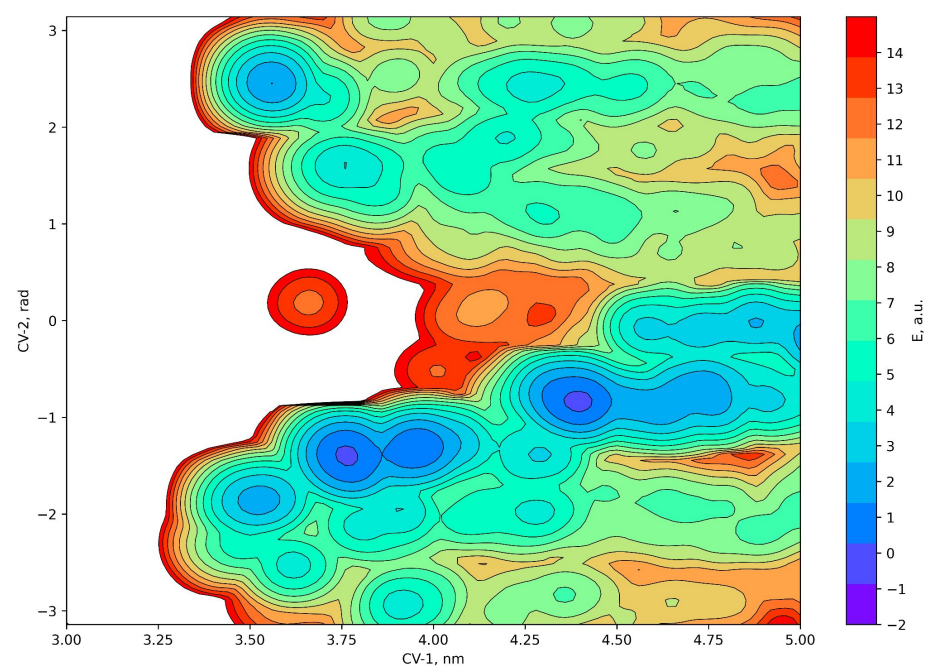
by metadynamics in MARTINI 3

# RESULTS: validation of the method

Antibody C102 (PDB ID: 7K8M)



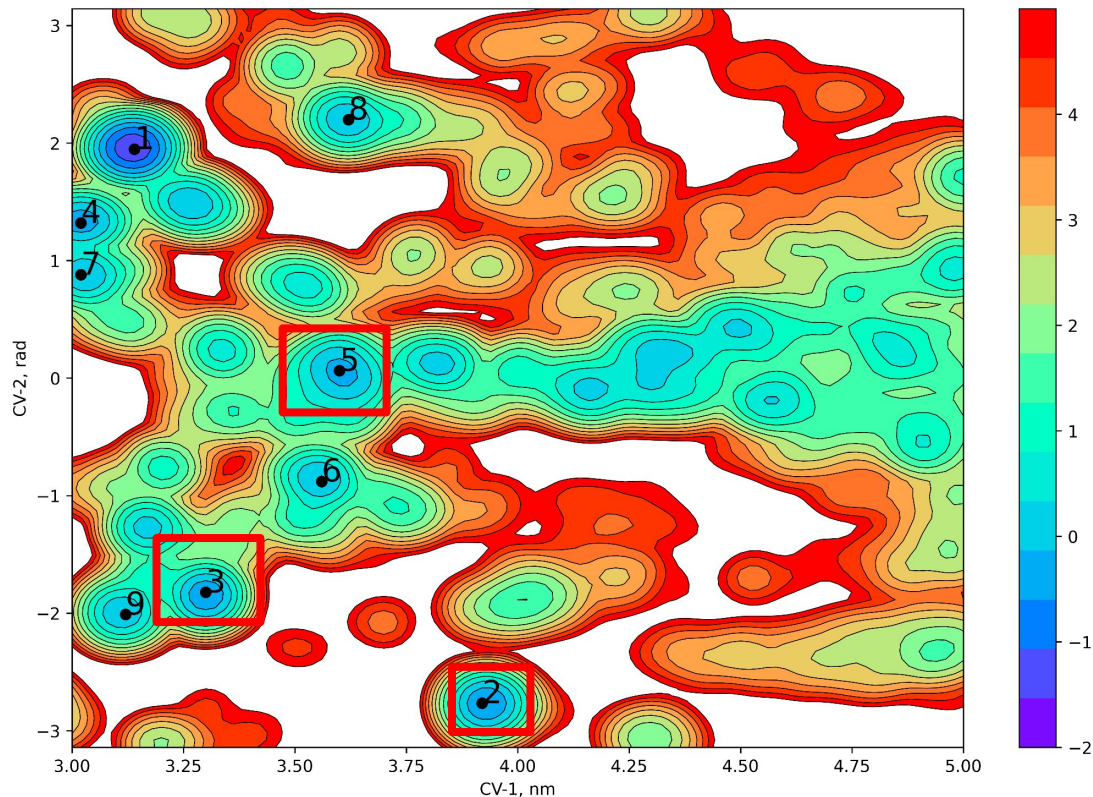
Negative test: antibody to HIV-1



Free energy surface plots.

CV-1 — distance between COMs, CV-2 — dihedral angle.

# RESULTS: averaged antibody structure



The **highlighted** minima were closest in RMSD value to the natural RBD-antibody complexes. They will be the starting point for further design of new antibodies.

## Free energy surface plot

CV-1 — distance between COMs, CV-2 — dihedral angle.

# CONCLUSIONS

- MARTINI 3 force-field metadynamics is applicable to reproduce antibody-antigen binding states from X-Ray data.
- MARTINI 3 force field metadynamics allows for efficient ranking of antibodies for binding to the RBD domain of the virus.

## Further steps:

- method optimization: using data-driven (mlcolvar) collective variables.
- more accurate antibody ranging, comparison with known data.
- design of a variety of new antibodies to the RBD of SARS-CoV-2 and their evaluation by the described method.

## References:

1. Ray D., Parrinello M. Kinetics from Metadynamics: Principles, Applications, and Outlook // J. Chem. Theory Comput. 2023. Vol. 19, N° 17. P. 5649–5670.
2. Lamprakis C. et al. Evaluating the Efficiency of the Martini Force Field to Study Protein Dimerization in Aqueous and Membrane Environments // J. Chem. Theory Comput. 2021. Vol. 17, N° 5. P. 3088–3102.
3. Raybould M.I.J. et al. CoV-AbDab: the coronavirus antibody database // Bioinformatics. 2021. Vol. 37, N° 5. P. 734–735.