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ABSTRACT

Over the past decades **nanopore technology** has emerged as a **cheap, fast, single-molecule, label-free alternative** to standard analysis techniques of biological samples. This technique was already successfully employed for DNA sequencing [1]. The further development of nanopore based fluidic devices for molecular characterization would have relevant consequences in biosciences and energy applications [2]. A first mandatory requirement for an effective nanopore based sequencing system is that the single residues have to be associated to different current levels [3].

In our recent works, using **all-atom molecular dynamics simulations**, we investigated the theoretical blockage of small homopeptides and other chemicals (related to sulfur-based batteries) in α -Hemolysin nanopore. In the first we estimated the hindrance associated to different **homopeptides**, one for each standard amino acid [4], showing that current blockage is affected by **amino acid volume, hydrophobicity and net charge**. In the second we demonstrate that supramolecular polysulfide/cyclodextrin complexes only **differing by one sulfur** can be discriminated at the single molecule level [5].

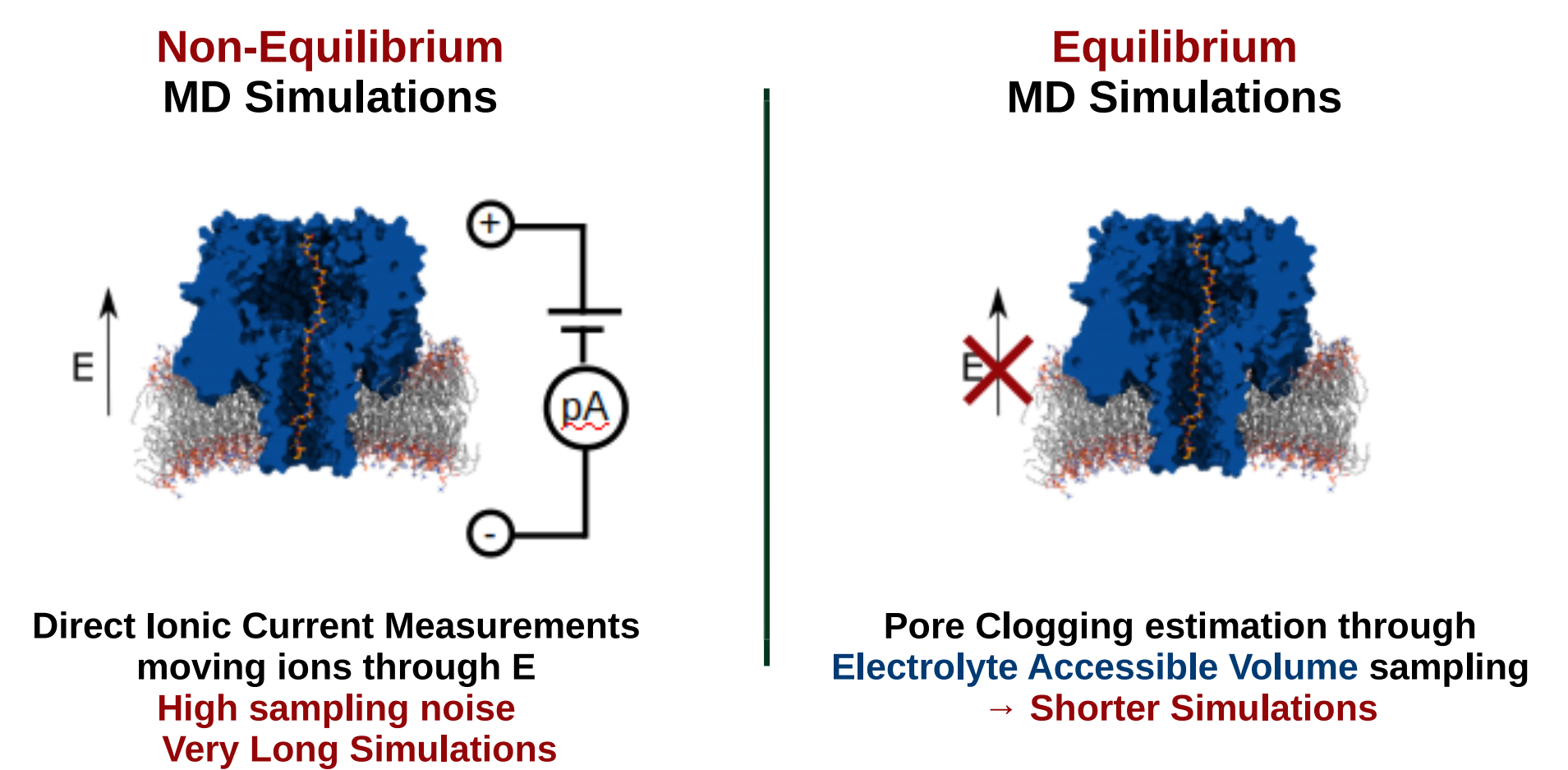
Our findings offer molecular insights into **protein sequencing**, and innovative perspectives to use nanopores as electrolyte sensors for designing **new generation lithium-sulfur batteries**.

Nanopore Sensing

Fundamental Requirements

- Capture and Translocation
- Distinguishability (this poster)

All-atom Molecular Dynamics



PORE HINDRANCE ESTIMATOR [4]

In a quasi-1D continuum description, the pore resistance can be expressed as

$$R = \int_0^L \frac{\rho(z)}{A(z)} dz,$$

We assumed that ρ is constant along the pore. The $A(z)$ profile is estimated computing a 3D map of the **electrolyte occupancy** inside the pore, using the VMD Volmap plug-in [6].

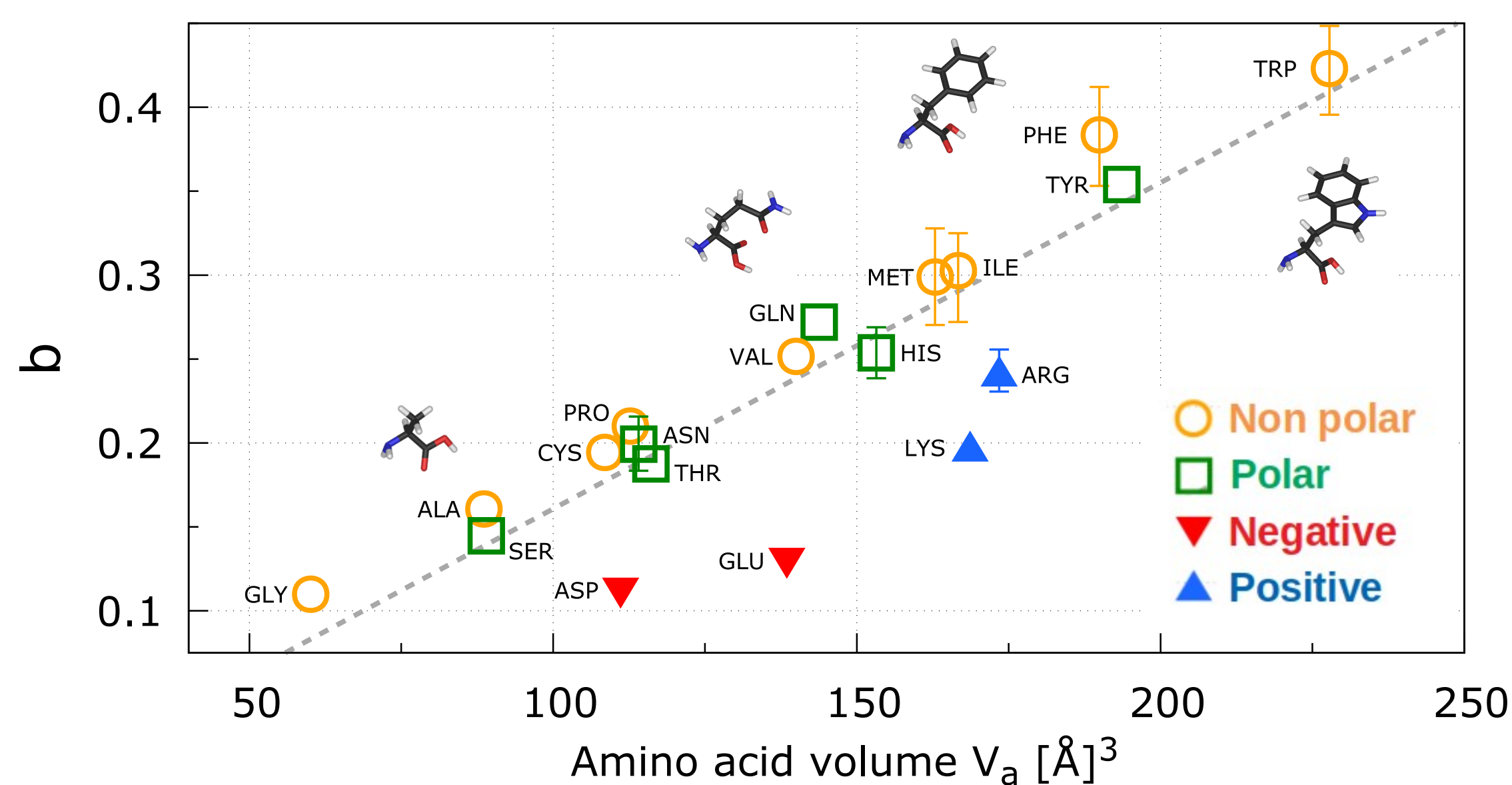
We defined the **pore hindrance estimator** as

$$b = \frac{\Delta I}{I_0} = 1 - \frac{R_0}{R}.$$

- L pore length and z -axis corresponding to the pore axis;
- $\rho(z)$ electrical resistivity of the electrolyte;
- $A(z)$ area of the pore section available to the electrolyte.

PROTEIN SEQUENCING [4]

Homopeptides distinguishability in α -Hemolysin nanopore.



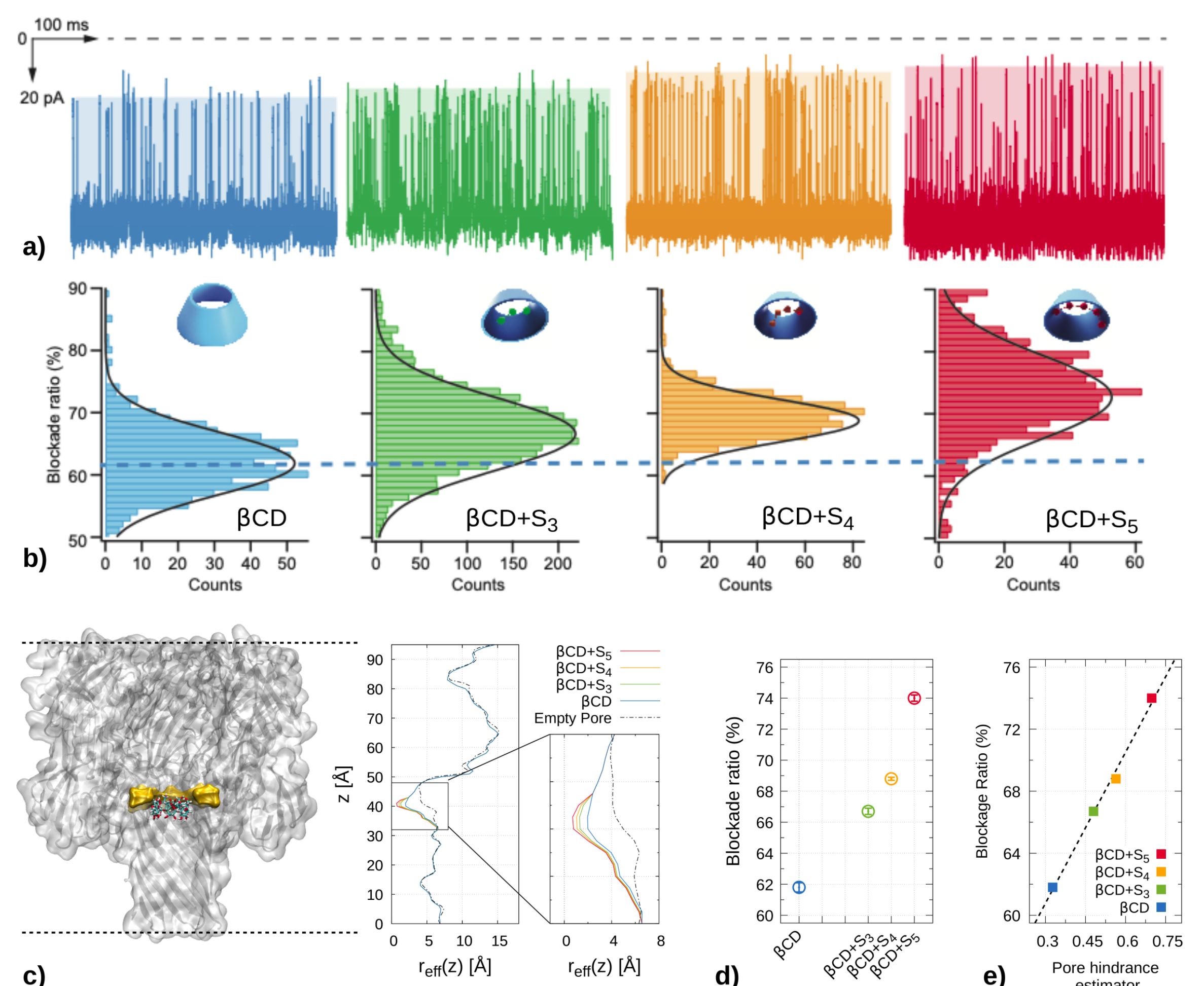
○ Non polar
Amino acid **nominal volume** rules the pore blockage
→ **linear dependence**

□ Polar
Higher hydrophilicity brings more electrolyte in the pore
→ **slight lower blockage**

▼ Negative ▲ Positive
Charged residues bring more ions in the pore
→ **significant lower blockage**

POLYSULFIDES DETECTION IN BATTERIES [5]

Supramolecular polysulfide/cyclodextrin complexes discrimination at single-sulfur atom level in α HL nanopore.



a) Experimental current traces of an α -HL pore in the presence of 1 mM β -CD (blue), Na2S3/ β -CD (green), Na2S4/ β -CD (orange), Na2S5/ β -CD (red). b) Histograms of blockade ratio for β -CD (blue), Na2S3/ β -CD (green), Na2S4/ β -CD (orange), Na2S5/ β -CD (red). c) Accessible volume estimation from Molecular Dynamics simulations. α -HL constriction is highlighted in yellow, while β -CD atoms are represented as balls-and-sticks. The plot reports the radius of the effective pore section available for ion passage. The effective pore section in the presence of β -CD and Na2Sx/ β -cyclodextrin are represented using the same color code of the other panels. d) Experimental current blockades. e) Nanopore hindrance estimator calculated from atomistic model. Panel (c) was made using the VMD software.

REFERENCES

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