

SSAGES-Qbox coupling: Applications to liquids and molecules

Cunzhi Zhang¹, Federico Giberti¹, Hythem Sidky², Emre Sevgen¹, Viktor Rozsa¹, Jonathan K. Whithmer²,

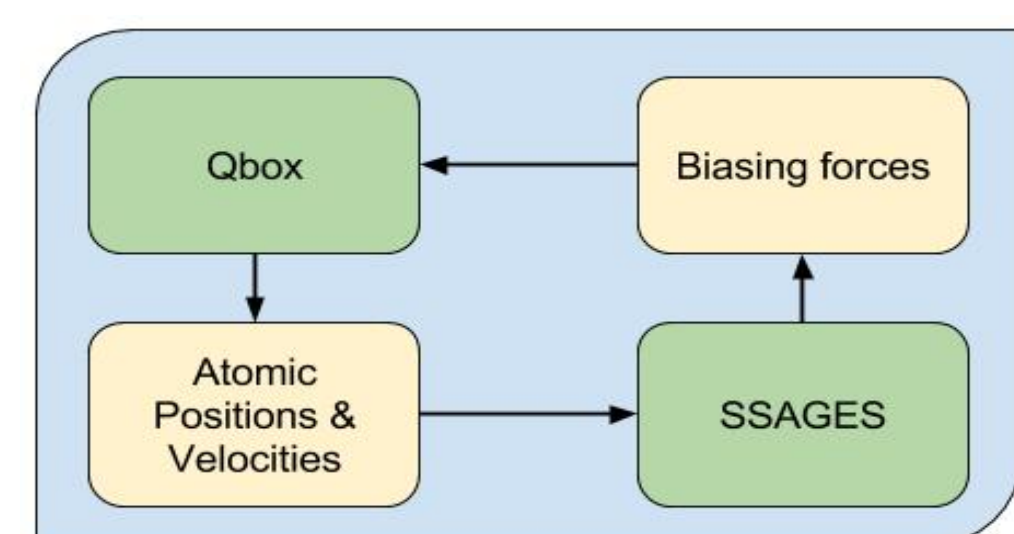
Francois Gygi⁴, Juan de Pablo^{1,3}, and Giulia Galli^{1,3}

¹University of Chicago, Chicago, IL 60637, ²Department of Chemical and Biomolecular Engineering, University of Notre Dame, Notre Dame, IN 46556, ³Materials Science Division, Argonne National Laboratory, Lemont, IL 60439, ⁴Department of Computer Science, University of California Davis, Davis, CA 95616

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Introduction



Q Qbox
First-Principles Molecular Dynamics

Many interesting physical processes are often “rare events”, where the characteristic time scale for a given transition is **inaccessible for standard molecular dynamics** due to large free energy barriers separating local minima in the free energy landscape. Therefore, a wide range of **advanced sampling methods have been developed to enhance the crossing of free energy barriers**.

Here, we coupled **Qbox**, a first principles MD engine, with **SSAGES** [1], a software suite for enhanced sampling simulations, to enable free energy calculations at different levels of theory within **DFT**. The **atomic interactions are calculated on the fly from first principles**, overcoming the transferability issues of classical potentials, and expanding the range of physical processes that can be studied.

Using this framework, we studied:

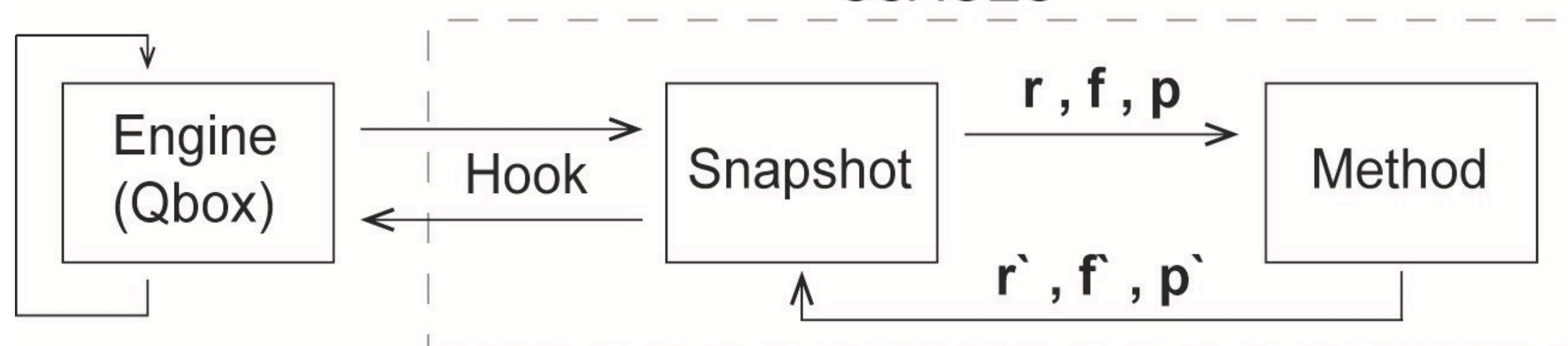
- NaCl Dissociation under High Pressure and Temperature
- Alanine Dipeptide Isomerization

Coupling details

The coupling is achieved using QBox's **client-server mode functionality**:

- **Qbox** performs the **DFT calculations** and the **Verlet integration** and transfers the system information ($r, v, F, T \dots$ etc) to **SSAGES**.
- **SSAGES** passes the information to the “**Method**” that we are using, which operates on the properties of the system ($r', v', F', T' \dots$ etc) and returns them to **SSAGES**.
- **SSAGES** saves the information of the bias, and then **returns** the information back to **Qbox**.

SSAGES

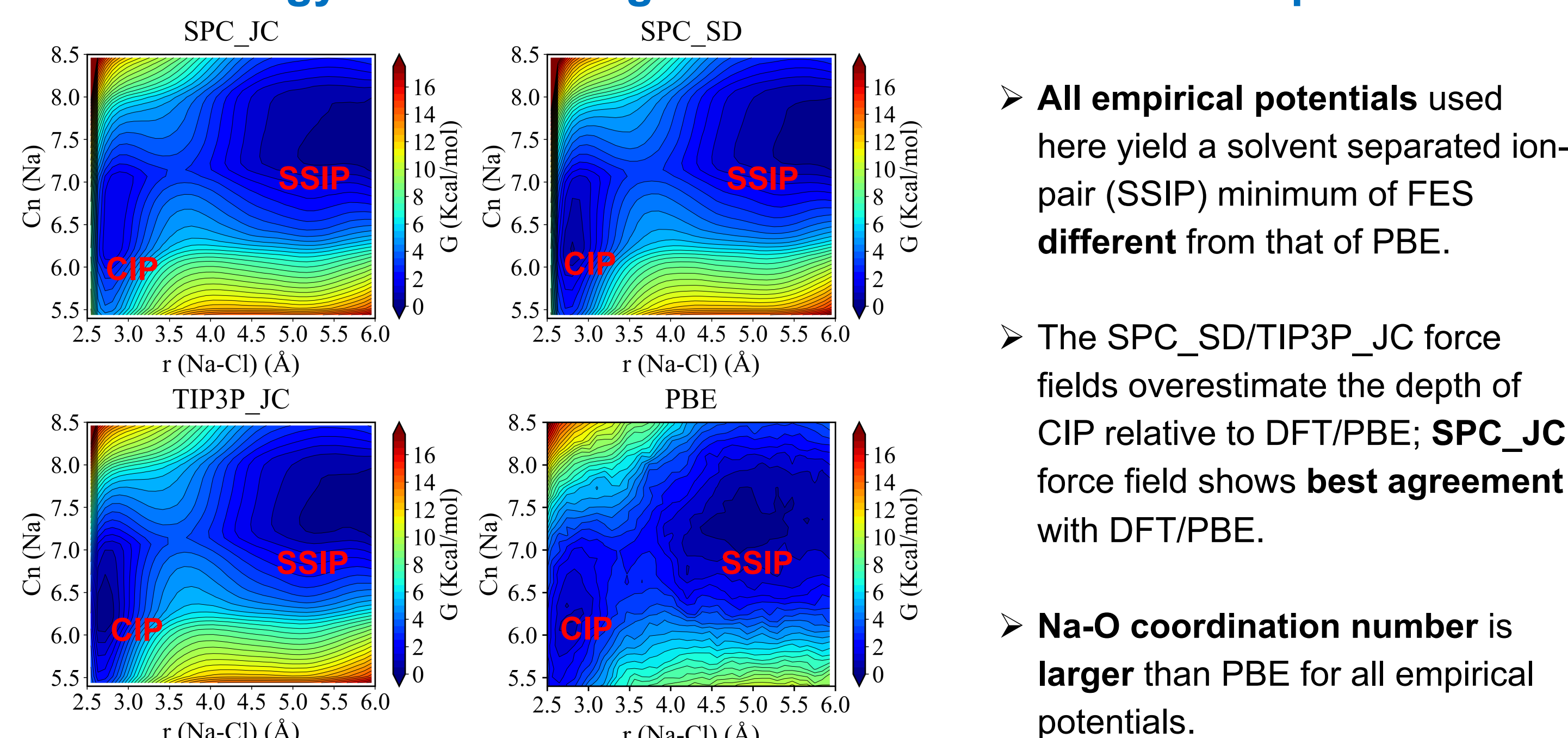


- **Qbox and SSAGES are compiled independently (no patches required) --> ease of development.**
- It is straightforward to create **multiple instances** of Qbox or SSAGES, e.g. to speed up the calculation using **multiple walkers**, or **Hamiltonian Replica Exchange**.
- The coupled SSAGES-Qbox framework permits a **hierarchical coupling: High level of theory (hybrid-functional) calculations can be restarted from previously converged lower level of theory (GGA) calculations.**

NaCl dissociation under high pressure and temperature (11 GPa, 1000 K)

In high P/T water, dissociation of water molecules and formation of complex ionic species are expected to influence the dissociation of salts and the solvation of cations and anions. We used FPMD and the adiabatic biasing force (ABF) method to study the free energy surface of NaCl dissociation in water under extreme conditions.

2D Free energy surface at high P/T obtained with different potentials



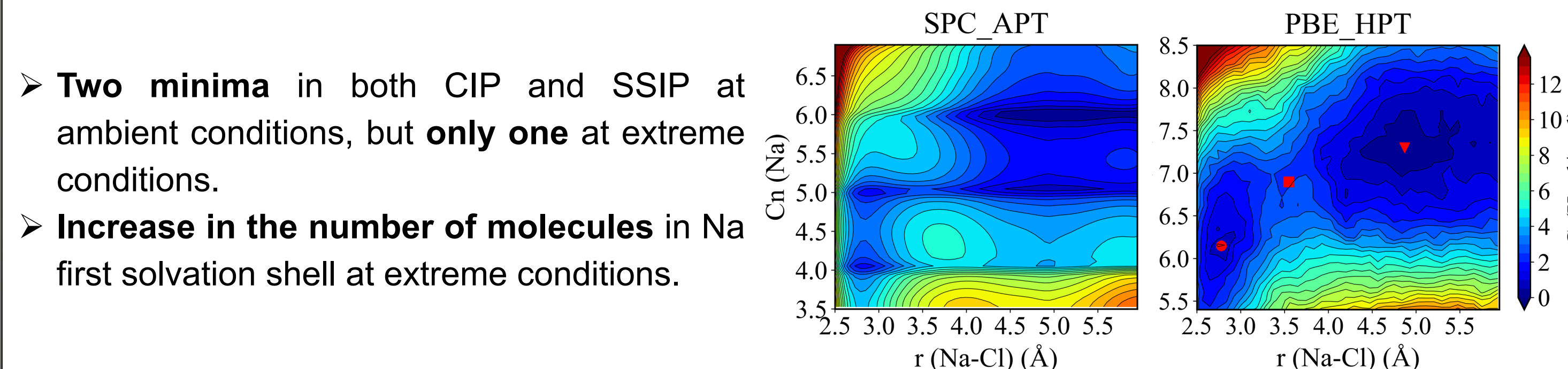
CIP: Contact Ion-Pair; **SSIP**: Solvent Shared Ion-Pair
Empirical potential: SPC_JC/TIP3P_JC [2] and SPC_SD [3]

➤ All empirical potentials used here yield a solvent separated ion-pair (SSIP) minimum of FES different from that of PBE.

➤ The SPC_SD/TIP3P_JC force fields overestimate the depth of CIP relative to DFT/PBE; **SPC_JC** force field shows **best agreement** with DFT/PBE.

➤ **Na-O coordination number is larger** than PBE for all empirical potentials.

2D Free Energy Surface obtained with DFT/PBE at high P/T and with SPC_JC at ambient P/T

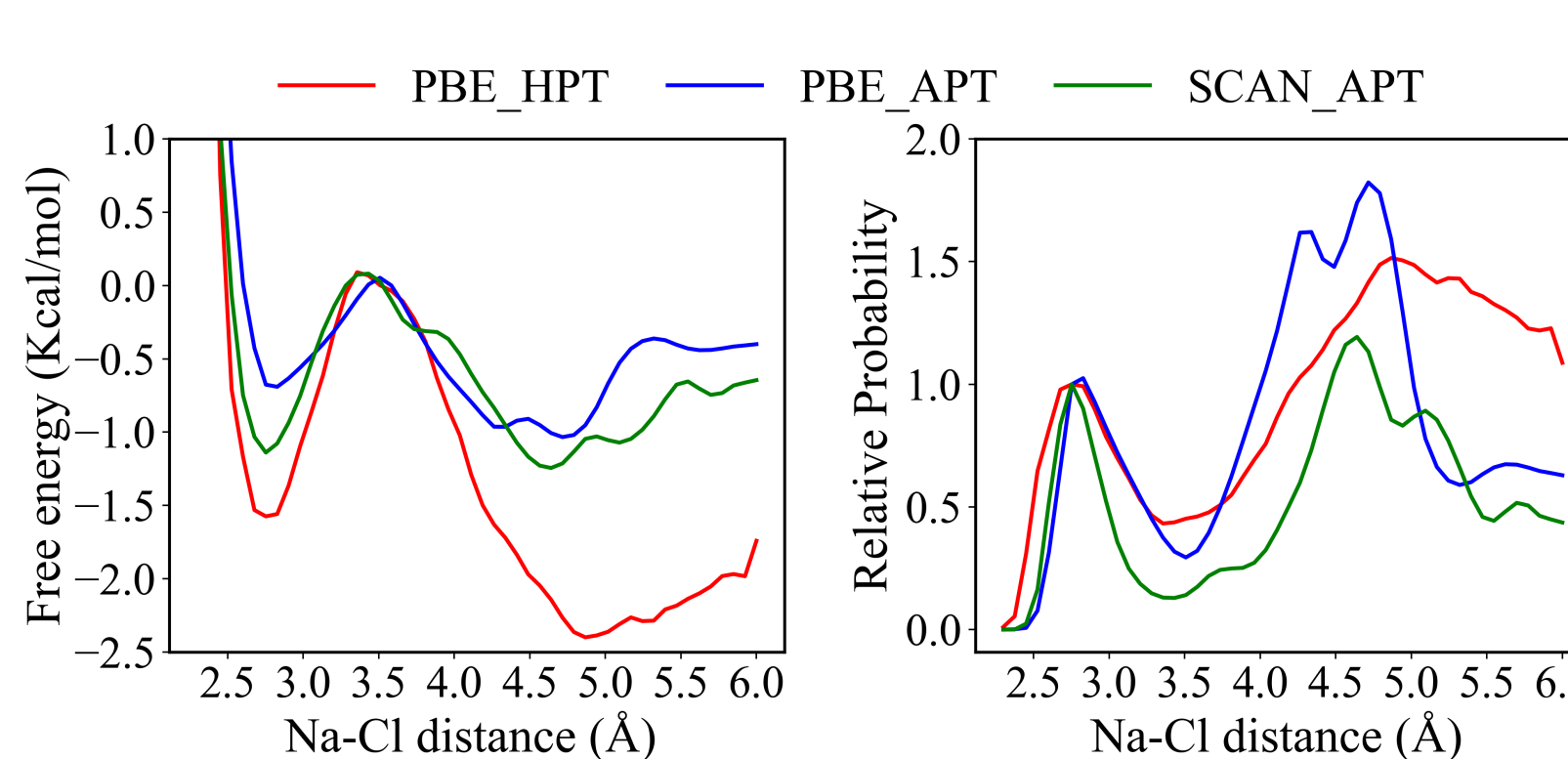


1D Free Energy Surface of PBE high P/T, PBE ambient P/T, SCAN ambient P/T

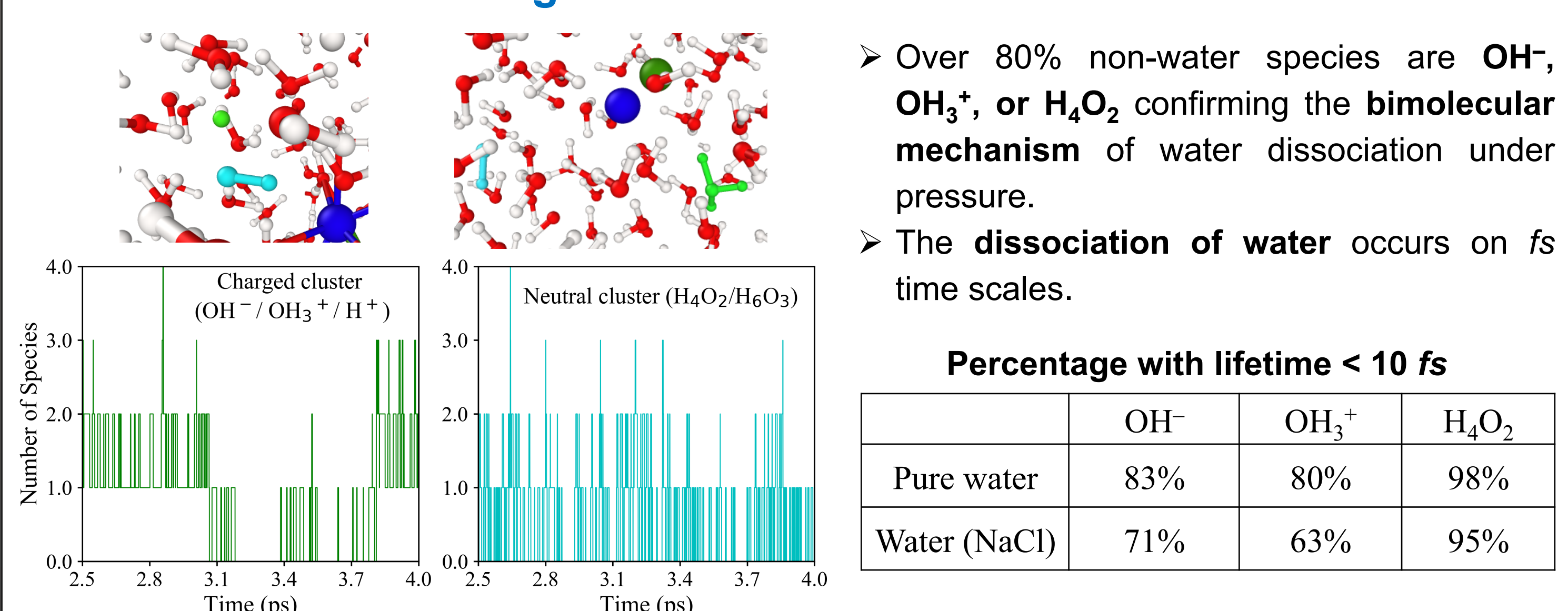
Our **PBE_HPT (11 GPa/ 1000 K) results** is compared to **PBE_APT (1atm/ 300 K)** and **SCAN_APT (1atm/ 300 K)** results from reference [4].

➤ PBE_HPT has **lower CIP and SSIP** minima, with respect to transition state, than PBE_APT and SCAN_APT.

➤ PBE_HPT exhibits a **larger probability** of visiting **SSIP** state than SCAN_APT.



Water dissociation at high P/T

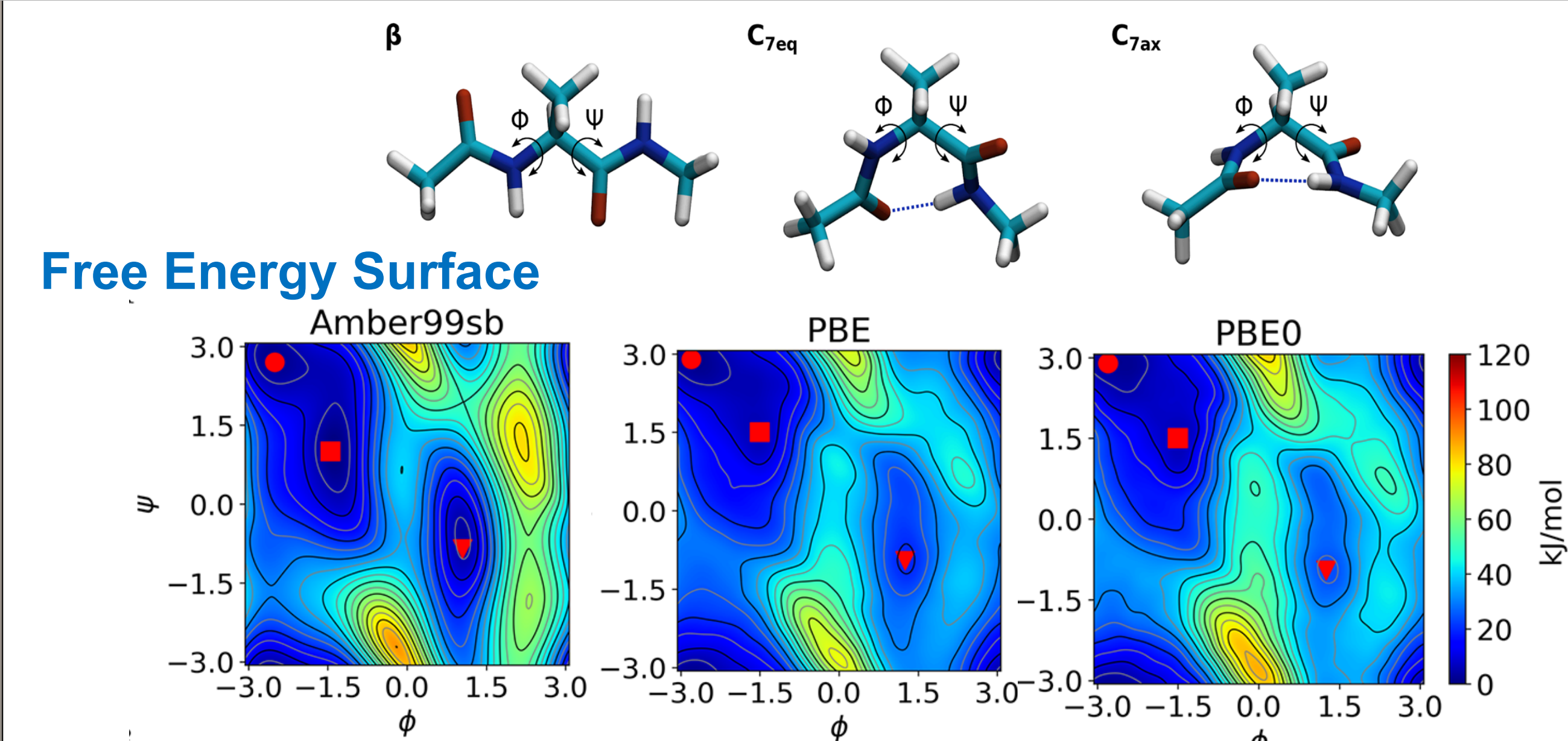


➤ Over 80% non-water species are **OH⁻, OH₃⁺, or H₄O₂** confirming the **bimolecular mechanism** of water dissociation under pressure.

➤ The **dissociation of water** occurs on **fs** time scales.

Free energy of alanine dipeptide isomerization

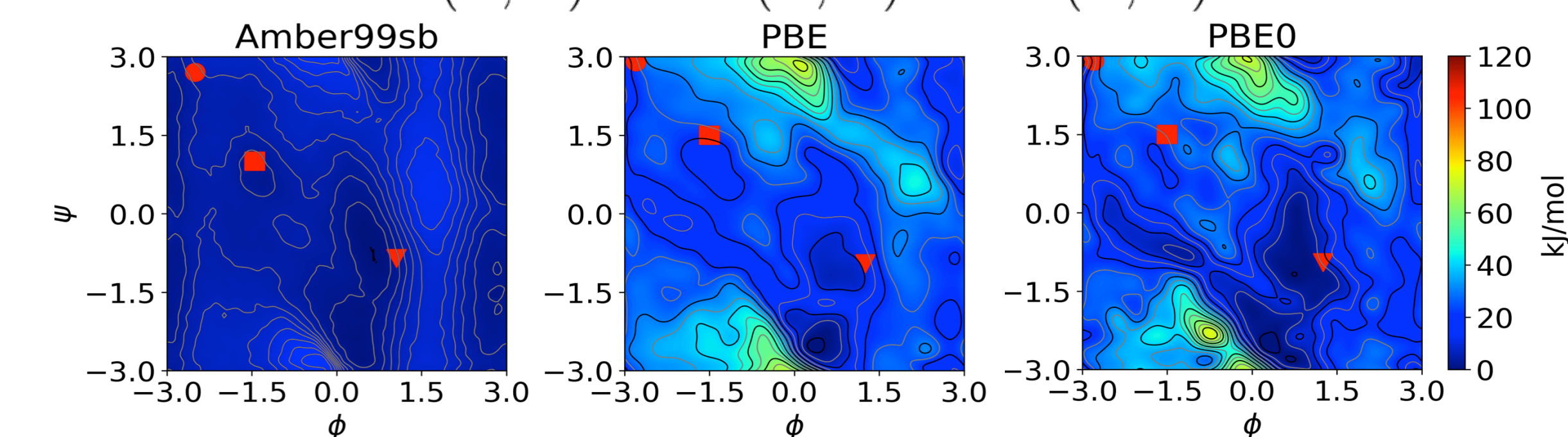
We calculated the free energy of isomerization using both classical and first principle Molecular Dynamics [5]. DFT results are compared to a frequently used force fields. We also demonstrated the power of hierarchical coupling: we obtained PBE0 FES by restarting from PBE results.



➤ We carried out **hierarchical calculations** of free energy surface: from empirical to PBE and eventually PBE0.

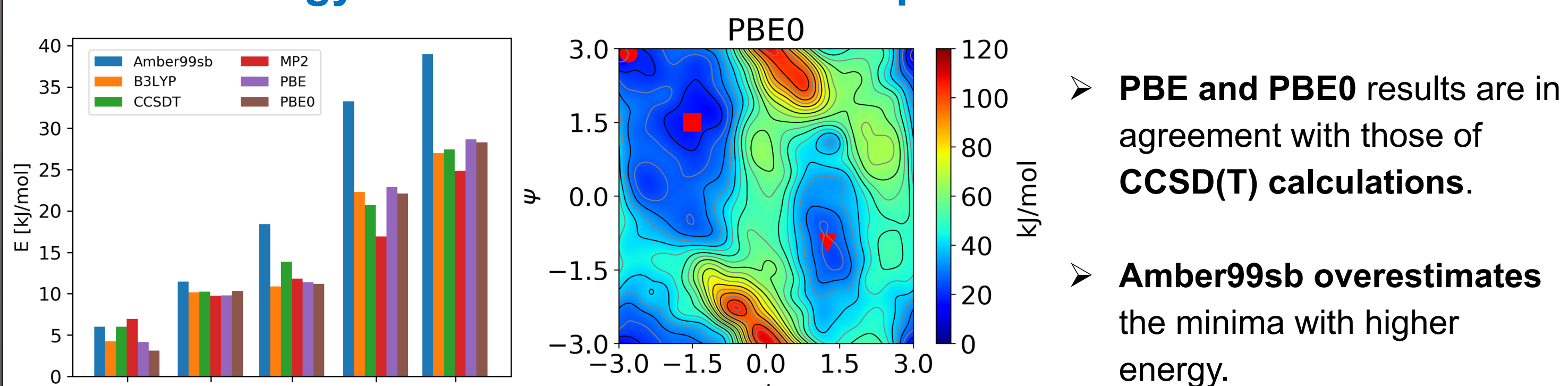
Entropic contribution ($T\Delta S$)

$$T\Delta S(\Phi, \Psi) = \Delta U(\Phi, \Psi) - \Delta G(\Phi, \Psi)$$



➤ **Amber99sb overestimates the internal energy** for configurations other than minima.
➤ **Amber99sb underestimates the entropic contribution** to free energy.
➤ These differences may affect folding and unfolding of longer peptides.

Internal energy contribution of different potential



➤ **PBE and PBE0 results** are in agreement with those of **CCSD(T) calculations**.

➤ **Amber99sb overestimates the minima** with higher energy.

References and Acknowledgements

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