

# Chemistry Matryoushka

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## **Computational chemistry**

Use models and computer simulations to solve complex chemical problems, offering insight into molecular structure, properties and reactivity.

Study interactions, energetics, reaction pathways

→ New molecules and materials design, support experiments, improve chemical processes, understand biochemical processes





https://pubs.acs.org/doi/10.1021/ja5112749



# The problem...

- How many atoms does an "interesting" molecule has?
- How small does the simulation time step needs to be to ensure numerical stability?
- What is the time scale of interest?
- What is the level of theory needed to capture the properties of interest?







https://search.asu.edu/media/8347

## Let's consider an example..

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- PYP is a protein involved in a negative response to blue light of a bacteria
- It has 125 aminoacids; each aminoacid has on average ~20 atoms
- Upon absorbing blue light the PYP undergoes a photocycle that takes hundreds of ms.

Assuming we represent the system just as "balls" moving under Newton's laws:

 $\rightarrow$  We need to calculate forces between ~2500 atoms per frame (excluding the environment)

 $\rightarrow\,$  If a timestep of 1ns is used we need ~million frames to reach 1ms

 $\rightarrow$  In a desktop computer this will take hundreds of thousands of years







### How are these systems simulate currently?

- Specialized hardware (HPC, GPUs, etc)
- Optimization of software
- Special techniques to "accelerate" dynamics (collective variable, path sampling, replica exchange, parallel, tempering, etc.)
- Implicit solvent: represent it as a continuous
- Coarse graining: represent atoms as fewer larger beads













### What about phenomena across a range scales?

- Multiscale modelling: couple different models with scale-bridging techniques that accurately preserve the physics
- Exploit local character of chemical reaction in condensed matter
- Molecular embedding: QM/MM

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Fig. 1. Illustration of the QM/MM concept. A small region, in which a chemical reaction occurs and therefore cannot be described with a force field, is treated at a sufficiently high level of QM theory. The remainder of the system is modelled at the MM level.



Katja-Sophia Csizi, Markus Reiher, Universal QM/MM approaches for general nanoscale applications, WIREs, 2023



### QM-MM

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Fig. 4. Flow scheme of a QM/MM energy calculation within the electrostatic embedding scheme. Interactions between atoms in the MM subsystem are handled at the force field level (*third branch*). The QM atoms enter the self-consistent field routine, with the charged MM atoms included as point charges (*first branch*). Diagonalization of the augmented Fock matrix yields the energy of the QM atoms as well as the electrostatic interaction energy between the subsystems. All other interactions involving QM and MM atoms are described by the force field terms (*second branch*).

https://pure.mpg.de/rest/items/item\_1562917/component/file\_1744080/content

# MM QM

### What level of theory do we use for QM?

 Most methods are good for "single reference states" meaning there is a dominant electronic structure but have issues where multiple electronic configurations come to play "multireference states"







https://pubs.acs.org/doi/10.1021/acs.jctc.2c00286



### QM-QM-MM?

**Divided molecule into regions:** 

- a classical region where interatomic interaction can be treated with classical force fields;

- a quantum region where mean-field approximations are sufficient;

- and a strongly correlated region where high-level methods are needed



Cheng HP, Deumens E, Freericks JK, Li C, Sanders BA. Application of Quantum Computing to Biochemical Systems: A Look to the Future. Front Chem. 2020 Nov 24



### Quantum Computing (QC-QM-MM?)

The exponential growth in the multi-body Hilbert space with system size limits the application of highly-accurate methods (multi reference methods)

→ Feynman's idea: the chemistry and physics of molecules and materials is best described using quantum mechanics

Can we further divide the QC part in even smaller pieces?

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MM

QC





https://arxiv.org/html/2409.06813v1

### Quantum computing algorithms

**Quantum Phase Estimation (QPE): It estimates** the phase corresponding to an eigenvalue of a given unitary operator therefore enabling high-precision measurements of the ground and excited energy levels of a system.

Variation Quantum Eigensolver (VQE): hybrid classical-quantum (family?) algorithm that is finds the minimum value of some target. In this case, it minimizes the system's energy.

operators to gubits mean-field Generate initial guess calculation  $\vec{t}(0)$  $H = \sum H_i$   $\vec{f}(n+1)$  $\Phi_0$ Measurement State preparation

**Classical** preparation

FIG. 14. Workflow of the variational quantum eigensolver algorithm. The classical optimization routine adds expectation values of the Hamiltonian Pauli terms to calculate the energy and estimates new values for the unitary parameters. The process is repeated until convergence. From [211].





**Classical feedback** 



#### QC-QM-MM

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# **Questions**?

