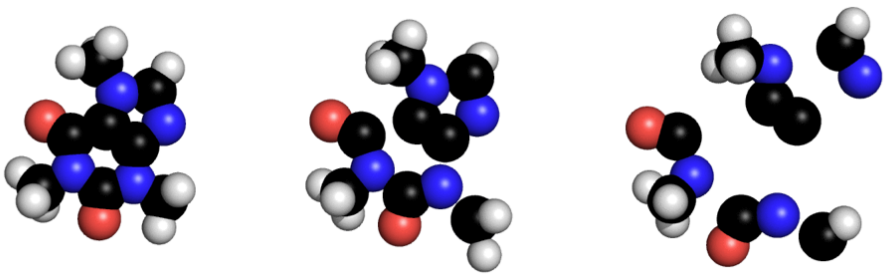
Thesis work in computational biology

To determine the molecular the structure of complex biological molecules, such as proteins, in sub-micrometer sized crystals, intense X-ray pulses generated by free electron lasers are used. The X-ray pulses generates a diffraction pattern containing the information of the molecular structure of the sample. The intensity of the pulse, needed to collect enough diffraction statistics, causes the molecule to heavy ionize and it turns into a plasma in a matter of femtoseconds. Before that time, an accurate diffraction pattern needs to be resolved.
The aim of the project is to understand the dissociation pathways of small protein components, such as peptides and groups containing heavier atoms, in order to improve the imaging of larger proteins. The ionization process successively breaks bonds within, and between, the building blocks of the protein. Bond-breaking of organic molecules is dictated by inherently quantum mechanical phenomena. As such, we resort to first-principles modeling of the process. Starting with the neutral molecule, ionization and subsequent optimization of the structure is performed in steps, until a map of ionization stage vs. bonds dissociation is acquired. This allows us to track the dissociation of bonds throughout the process of ionizing the molecule to a plasma, aiding reconstruction of real-space images of large proteins from diffraction patterns.
The first-principles calculations will be performed using Quantum Mechanical Molecular Dynamics, starting from available structures of amino acids.
Initially the project aims to study three small amino-acids, alanine, glycine and valine. For summer projects or Bachelor projects this is a suitable task. As a successful workflow is established, a complete study of the 20 available amino acids will be performed. Ideally, peptides consisting of several amino-acids will be addressed, suitable for Master thesis work.

A continuation of the project, to study the influence of external fields on the structure in real-time dynamics within the time-dependent density functional formalism, for a detailed understanding of the non-equilibrium dynamics is also possible.

Optimized software for these tasks is developed within the department, and is running on Swedish high-performance computing resources, made available for students undertaking this project. Calculations are setup and run in a linux based environment, previous knowledge of the linux operating system and basic scripting languages is strongly beneficial.



Coffein molecule exploding due to ionization.

If you are interested please contact Oscar Grånäs (oscar.granas@physics.uu.se) or Carl Caleman (carl.caleman@physics.uu.se) at the Department of Physics and Astronomy.