Abstract: NS3 helicase is a protein that unwinds and translocates along ssRNA. From X-ray structures and single molecule experiments an inchworm-like mechanism has been proposed for the translocation process. However, the details of this mechanism are not still very clear.

In this work, we used a GPU accelerated molecular dynamics software to perform microsecond time scale molecular dynamics simulation in explicit solvent in order to obtain the atomistic details of the translocation mechanism. We simulated crystal structures and also built some intermediate ones considering different conformers in the presence and the absence of ATP/ADP. For the simulated structures we study the hydrogen bonds network and the contacts between peptide, RNA and ligand. From this analysis we observed an ATP-dependent stabilization of one of the NS3 conformers.

We also used enhanced sampling simulations (metadynamics) to accelerate the conformational changes. In this context, it is useful to introduce a multiple time-step scheme that allows to significantly decrease the computational cost of expensive collective variables by optimizing the load between the CPU and the GPU.