# easyAmber: a step away from inefficient “static” approaches towards a deeper understanding of protein dynamics

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Molecular dynamics (MD) can improve the success rate of *in silico* tools for drug discovery and protein engineering by accounting for protein structure flexibility/plasticity and predicting the time-dependent behavior of a molecular system, but requires specialized training and skills, what impedes practical use by many investigators. We have developed the easyAmber – a set of wrapper scripts to assist the MD simulation using the Amber suite. The automated workflow supports all steps from the initial “static” molecular model to the MD “production run”. The software is freely available at https://biokinet.belozersky.msu.ru/easyAmber.

**Step-by-step practical guide** to the easyAmber software was published in
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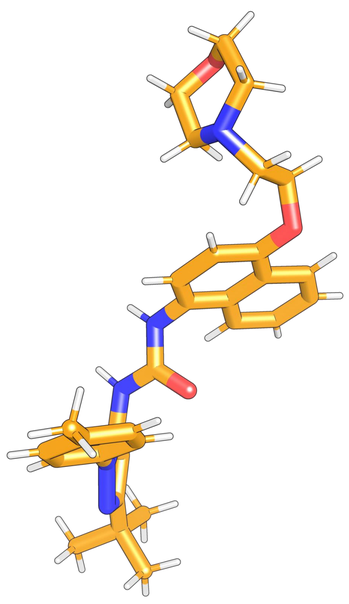
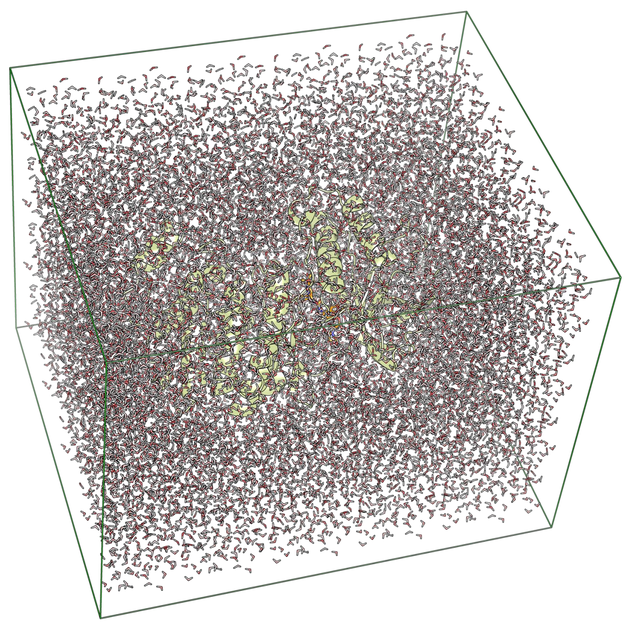
## Step 1: `autoligand.pl`



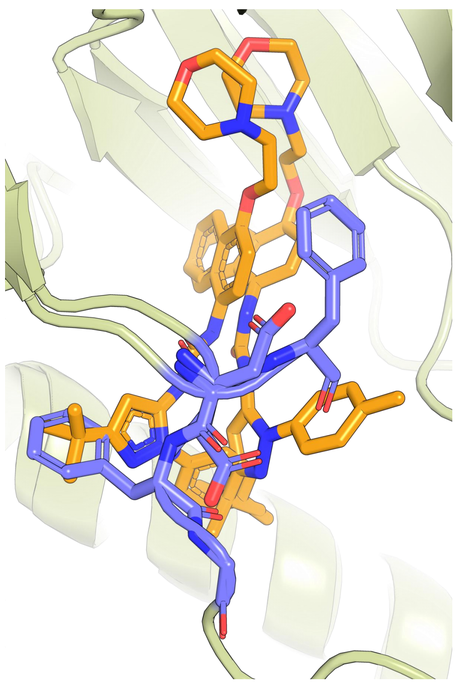
- The **`autoligand.pl` master-script** assists the preparation of a **draft version of Amber parameter files for a custom low-molecular-weight ligand**;
- a fully automatic approach attempts to calculate AM1-BCC charges on atoms using the `am1bcc` utility and the quantum chemistry program `sqm` called via the `antechamber` tool;
- a supposedly more precise approach using the **R.E.D. web-server** is recommended for advanced users and is described in detail in the on-line tutorial.

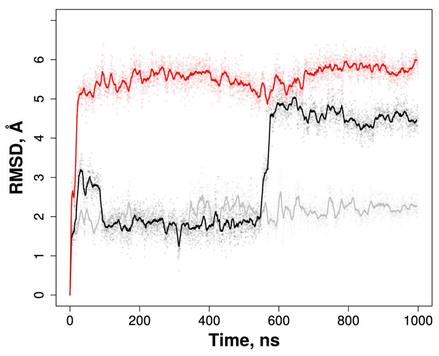
## Step 2: `automodel.pl`



- The **`automodel.pl` master-script** assists the preparation of the **Amber parameter files for full-atom molecular system** of a protein or a protein-ligand complex in a cubic water box;
- Two general-purpose combinations of Amber force-fields and water models are supported: the conventional *FF14SB* force-field with the three-point *TIP3P* or four-point *TIP4P-EW* solvent and *FF15IPQ* force-field with the three-point *SPC/Eb* solvent;
- Additional covalent bonds (e.g., disulfide bridges), new atom types, and auxiliary force-fields can be set by the user.

## Step 3: `autorun.pl`

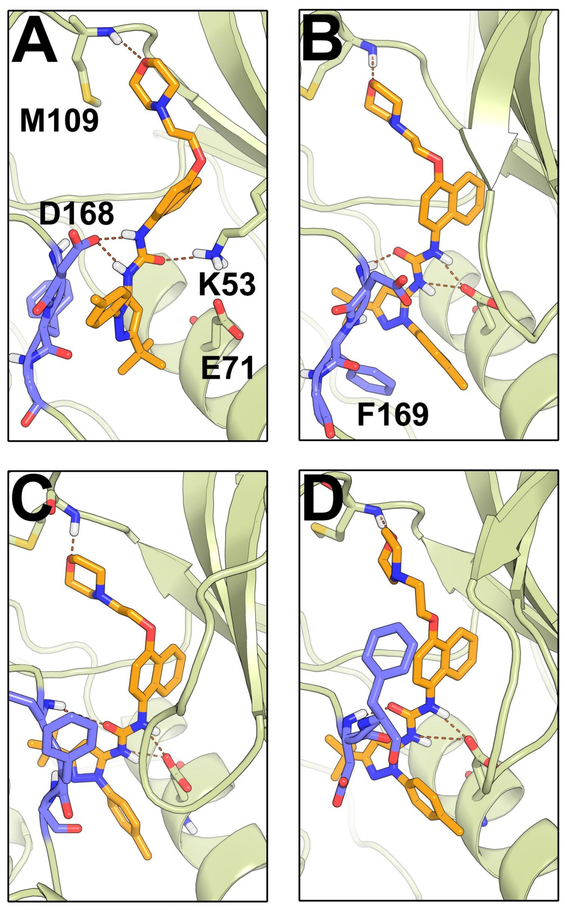






- The **`autorun.pl` master-script** accommodates the **seven-step MD simulation pipeline**: the initial optimization of the molecular system (i.e., three-step energy minimization with water relaxation), heating (in the NVT ensemble), equilibration (in the NPT ensemble), followed by the classical/conventional MD (in the NVT ensemble), and optionally concluded by the accelerated MD simulation (in the NVT ensemble);
- The two major MD methods (classical MD and accelerated MD) together can help to assess protein structure flexibility on a wide range of timescales;
- The script can be used to execute “production runs” on a personal desktop station equipped with a compatible gaming GPU-accelerator, as well as help to manage huge workloads on a powerful supercomputer;
- Auxiliary scripts are available to assist the postprocessing of the finally calculated MD trajectories.

## Examples

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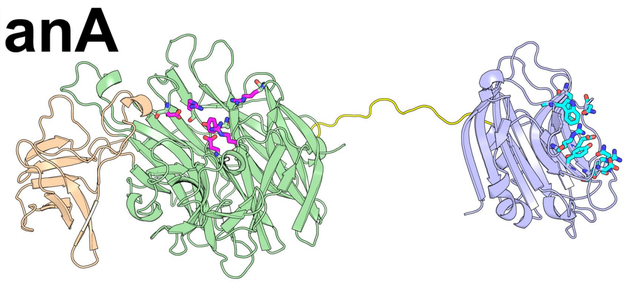
10.1080/07391102.2018.1475260

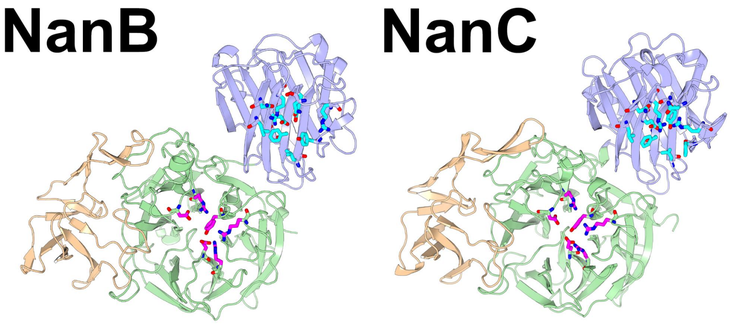
Molecular modeling assisted by the *easyAmber* showed that the type II inhibitor Doramapimod can bind to the human p38α mitogen-activated protein kinase even when the activation loop is in the DFG-‘in’ state (A) what is followed by the ligand-induced conformational changes, which finally improve accommodation of the inhibitor (B-D).

**NanA**



Molecular modeling assisted by the *easyAmber* revealed a significant difference in spatial organization of homologous neuraminidases of the pathogen *Streptococcus pneumoniae*: the lectin and catalytic domains of NanB and NanC form rigid globules stabilized by multiple interdomain interactions, whereas in NanA, the two domains are separated by a 16 amino acids long flexible linker – a characteristic of proteins that require conformational flexibility for their functioning.

**NanB** **NanC**



*FEBS J.*, 2018 10.1111/febs.14486

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