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MDWeb and MDMoby: an integrated web-based platform for molecular dynamics simulations

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ABSTRACT

Summary: MDWeb and MDMoby constitute a web-based platform to help access to molecular dynamics (MD) in the standard and high-throughput regime. The platform provides tools to prepare systems from PDB structures mimicking the procedures followed by human experts. It provides inputs and can send simulations for three of the most popular MD packages (Amber, NAMD and Gromacs). Tools for analysis of trajectories, either provided by the user or retrieved from our MoDEL database (http://mmb.pcb.ub.es/MoDEL) are also incorporated. The platform has two ways of access, a set of web-services based on the BioMoby framework (MDMoby), programmatically accessible and a web portal (MDWeb).

Availability: http://mmb.irbbarcelona.org/MDWeb; additional information and methodology details can be found at the web site (http://mmb.irbbarcelona.org/MDWeb/help.php)

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1 INTRODUCTION

Molecular dynamics (MD) has experienced a long evolution since its origins (McCammon *et al.*, 1977), being now a mature technique that allows to obtain accurate pictures of the dynamics of proteins and nucleic acids. Unfortunately, the practical use of MD is limited by three factors: (i) force-fields uncertainties; (ii) the need of large computational resources; and (iii) the high-level expertise needed to use efficiently the technique. Indeed, setting up a system for simulation requires a large series of operations, and a number of decisions that demand a significant degree of expertise and large amounts of human time, in most cases similar to that of computing the trajectory. The end result is that newcomers to the field face a stiff learning curve. These problems reach a maximum in high-throughput projects (Meyer *et al.*, 2010; Rueda *et al.*, 2007; Van der Kamp *et al.*, 2010), where thousands of trajectories need to be launched and supercomputer resources are required.

We present here a tool designed to help naïve users to completely prepare systems for simulation, and that allows expert users to use MD in the high-throughput regime. The tool is presented in two different versions: a web-services-oriented software platform (MDMoby), and a web portal MDWeb. The technology has been adapted to be accessed as web-services following BioMoby (www.biomoby.org; BioMoby Consortium, 2008). MDMoby can be run with usual web-services clients and also programmatically through suitable APIs (http://inb.bsc.es). In turn, the web portal MDWeb provides a friendly environment to setup new systems, run test simulations and perform analysis within a guided interface. Setup files can be prepared, at present time, for Amber (Case *et al.*, 2010), NAMD (Phillips *et al.*, 2005) and Gromacs (Hess *et al.*, 2008), and analyses can be carried out from trajectories written in the most usual formats. Additionally, the platform is interfaced to our flexibility analysis software FlexServ, so providing coarse-grained simulation, and advanced analysis tools (Camps *et al.*, 2009; Emperador *et al.*, 2008), and also with our MoDEL database (Meyer *et al.*, 2010).

2 IMPLEMENTATION

2.1 MDMoby

MDMoby services have been developed under the BioMoby framework (www.biomoby.org; BioMoby Consortium, 2008). To this end, a complete new set of data types was designed (see MDWeb help section for a detailed information about MDMoby ontology). Among them, the most relevant are MD_Topology, MD_Structure and MD_Trajectory, that contain information on topologies, structures and trajectory files, respectively. Those data types have been defined in an abstract form, and specialized in the inherited objects. Hence, data formats are inferred from object name and handled without user intervention. Setup services cover operations like structure repair, titration of ionizable residues and relevant water molecules, neutralization of the system, addition of salt and solvent, energy minimization, thermalization and system equilibration. A limited set of parameterized ligands are available to

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be included in the setup process. Full automatic setup procedures in standard conditions for the software packages covered are offered as pre-packed workflows. Underlying software is based in the Ambertools (Case *et al.* 2010) and VMD (Humphrey *et al.* 1996) packages, combined with in-house and publicly available programs (Supplementary Table S1). The tool allows launching test simulations in our servers, and provides the necessary scripts for running production simulations at the user side. Scripts provided contain the necessary instructions to be customized to match the users' configuration. Basic analysis results are provided from Ambertools and Gromacs tools, complemented with in-house software. Tools for conversion between trajectory formats are available to facilitate trajectory sharing, extension and analysis. Supplementary Tables S2 and S3, and MDWeb site's help show the full offer of web-services and operations available.

MDMoby is accessible through Perl and Java APIs provided by the Spanish National Institute of Bioinformatics (http://inb.bsc.es), and, in a limited extent, using clients like Taverna (Hull *et al.*, 2006) or Jorca (Martín-Requena *et al.*, 2010). Supplementary Figure S1 shows a sample Perl script to prepare of a protein system using MDMoby.

2.2 MDWeb

MDWeb is a web portal implemented in PHP and MySQL that provides a GUI to MDMoby. It provides users with a personal workspace where intermediate data, trajectories and analysis results can be stored. Registration is free but necessary to maintain a permanent workspace. The primary entry is a structure (uploaded or obtained from PDB) for setup or a trajectory for analysis. The input structure or trajectory acts as the root of a tree (see Supplementary Figure S2 for some screenshots) to that new sets of data are added according to the operations performed. Every new component of the tree is identified by its BioMoby's data-type, and can be visualized (with JMol, http://www.jmol.org), or downloaded. For every component the appropriate choice of operations is presented. To guide the non-experts, pre-packed workflows including recommended options are also available. However, all web-services in MDMoby are available separately, allowing more experienced users to finely tune the procedures. Results of trajectory analysis are presented through alphanumerical values, 2D plots or Jmol-based 3D visualizations, as appropriate. Analysis results can also be downloaded for further processing. Trajectories from the MoDEL library (Meyer *et al.*, 2010) can also be loaded in MDWeb and analyzed. MDWeb handles efficiently potentially slow operations, which are derived to a batch queue to be executed. Results become available in the workspace as soon as calculations are finished and can be recovered at a later time.

3 CONCLUSIONS

The software platform formed by MDMoby and its portal MDWeb provides a step forward in the current offer of software to help in the use of MD. It is a consequence of the automation required to develop the MoDEL project and integrates the expertise accumulated over the years on massive setup of systems and analysis of MD trajectories. The modular nature of the web-service paradigm in which the platform is created assures that the system can grow to incorporate new operations without a significant change of the interface or even to incorporate MDMoby services to user's codes. The platform provides non-experts users of pre-packed tools allowing to do complete MD analysis without a deep knowledge of the details involved. At the same time, the platform is flexible enough as to allow expert users to perform finely tuned simulations. The platform is not tied to a specific software package, therefore increasing the number of potential users and helping them in code-migration and re-use of trajectories. MDMoby and MDWeb constitute a growing platform where eventually new operations and scenarios will be included in the future.

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