SCIENTIFDIC REPORT - Stage I – 2021 -

"*Method development (part I). Module externalization (part I).*"

Project: PN-III-P4-ID-PCE-2020-2444

Content

Stage 1 – Method Development (Part I). Module Outsourcing (Part I).

Results:
1.1 Deca-alanine folding times for new types of molecular robotic joints.
1.2 Non-equilibrium HMC sampling modules.
1.3 Data transmission modules between Robosample and OpenMM simulation packages.

Act 1.1 Act 1.1 Development and Testing of New Molecular Robotic Joints: Hinge, Cardanic, and Spherical.
Subactivitatea 1.1.1 Dezvoltarea articulatiilor robotice moleculare: Balama, Cardanica si Sferica si testarea lor prin timpul de impachetare pe sisteme model.

Theory

The three new joints (Hinge, Cardanic, and Spherical) are defined within the cinematic and dynamic framework developed by Jain and Rodriguez [1] under the nomenclature of Featherstone [2]. Robosample relies on a chain of rigid bodies represented in four reference frames to describe the topology, kinematics, and dynamics of the rigid body tree. Each joint in such a structure provides specific degrees of freedom: Hinge - rotation about the molecular angle axis, Cardanic - two degrees of rotational freedom – angle and bond, Spherical - three degrees of rotational freedom.

Implementation and Testing

Robosample integrates three libraries: Simbody, Molmodel, and gMolmodel, handling articulated body mechanics, rigid molecular systems, and Markov Chain Monte Carlo sampling, respectively. Implementation of the joints involved adapting Simbody's theoretical mechanics to the chemical domain, where certain atoms serve as reference systems for rigid bodies. The three joints are now part of new Molmodel classes, with dedicated functions in gMolmodel for constructing molecular graphs. IO modules have been added for user-friendly externalization of the new joints.
The implementation was tested on model systems suc as alanine dipeptide and decalanine through the analysis of the end-to-end distance.

Act 1.2 Implementation of the Non-Equilibrium Hamiltonian Monte Carlo Method (NEHMC) - Part I.

Subactivity 1.2.1 Development of Non-Equilibrium Hamiltonian Monte Carlo in Robosample and quantification through passage times in model systems.

Theory

The Non-Equilibrium Hybrid Monte Carlo Sampling Method (NEHMC) aims to overcome energy barriers through mechanical work. One option involves directing a subset of coordinates away from equilibrium to penetrate potential barriers, while the remaining coordinates can relax.

In the phase space defined by position coordinates (q) and momentum (p):, perturbing α in a Markov Chain Monte Carlo (MCMC) method, while maintaining detailed balance through a probability distribution in a subspace Γ_α, typically results in very low acceptance rates. Nilmeier, Crooks, Minh, and Chodera [17] proposed applying a gradual perturbation in T steps in tandem with Hybrid Monte Carlo (HMC) steps, K: In this study, the von Mises circular distribution was chosen as a perturbation, acting on a single torsional angle in the system. To satisfy detailed balance, the Λ protocol is applied with the following probability of accepting a move.

Implementation and Results

Perturbation through von Mises circular distribution.

Initially, von Mises sampling was implemented in the gMolmodel library within Robosample. This distribution is the equivalent of the normal distribution in an angular space. The sampling method used is described by Best and Fisher [18], starting from the Cauchy distribution and employing the following algorithm:

The correctness of the NEHMC sampling implementation was verified by estimating the free energy surface and the mean first passage times of alanine dipeptide, comparing it with an already implemented equilibrium HMC method in Robosample. The minima of the free energy, represented on a surface parameterized by the angles φ and ψ, exhibit correct positioning compared to an HMC simulation.

Act 1.3 Externalization of Molecular Configurations for Other Programs - Part I.

Subactivity 1.3.1 Development of code for externalizing molecular configurations for other programs in the form of auxiliary modules in Robosample.

Introducere si context

Robosample models molecules with internal coordinates, optimizing performance by transitioning between different molecular models. It now employs GPU acceleration for both bonded and nonbonded energy calculations through Molmodel and OpenMM libraries.

Implementation and Testing

To integrate OpenMM's energy calculation functionalities with CUDA or OpenCL acceleration, the molecular system was defined compatibly with OpenMM. Correspondence mechanisms between Robosample and OpenMM classes were established. The initialization function in the OpenMMPluginInterface class now fully defines the molecular object, allowing multiple customization options. The OpenMM::System class models the molecular system with rigid bodies, utilizing various bond and nonbond interaction types. Functions were adapted for multi-GPU systems and introduced parameters for user customization. These functionalities are exposed for direct use in Robosample, allowing users to pass parameters from the configuration file.

	Durata totala medie de calcul al fortelor si energie (μs)*	2-ALA	100-ALA
OLD	**Bonded + Nonbonded**	**246**	**7086**
	Bonded (CPU 1 core)	*246*	*7086*
	Nonbonded (GPU CUDA)	*112*	*149*
NEW	**Bonded + Nonbonded (GPU CUDA)**	**113**	**163**

×2 mai rapid: **2-ALA**

×43 mai rapid: **100-ALA**

* Mediile prezentate sunt realizate pe un set de de 70 de valori. Deviatiile standard sunt in intervalul 2-8% fata de medie

Calculele au fost realizate pe un sistem cu Intel(R) Core(TM) i9-9900K CPU @ 3.60GHz si GeForce RTX 2080TI GPU

Fig. 3.1 Comparison of the improved computation time for the forces and total energy of the system following the externalization of the complete energy calculation using GPU acceleration (CUDA 11.2) on two reference molecular systems: di-alanine (2-ALA) and cento-alanine (100-ALA)..

Presentations

Teodor A. Şulea, Victor G. Ungureanu, Eliza C. Martin, Andrei J. Petrescu, Laurentiu Spiridon: "Robosample - platforma de noua genaratie pentru eșantionarea spațiilor conformaționale ale biomoleculelor". Conferința Cercetării Științifice din Academia Română (CCSAR-2021). Academia Romana, București, 22-23 noiembrie 2021.

Teodor A. Şulea, Eliza C. Martin, Victor G. Ungureanu, Laurențiu Spiridon, Andrei-Jose Petrescu: "ROBOSAMPLE: robotics-based Gibbs sampling of macro-molecular systems". MacroYouth2021 Scientific Communications of Young Researchers, Iasi, 19 noiembrie 2021.

References

[1] Jain, A.; Rodriguez, G. Recursive flexible multibody system dynamics using spatial operators. J. Guidance, Control, and Dynamics 15(6):1453-66 (1992).
[2] Featherstone, R. Rigid Body Dynamics Algorithms, Springer (2008).
[3] Jain, A.; Vaidehi, N.; Rodriguez, G. A fast recursive algorithm for molecular dynamics simulation. J. Comput. Phys. 106(2):258-268 (1993).
[4] Schwieters, C.D.; Clore, G.M. Internal coordinates for molecular dynamics and minimization in structure determination and refinement. J. Magnetic Resonance 152:288-302 (2001).
[5] Jain, A.; Rodriguez, G. Recursive dynamics algorithm for multibody systems with prescribed motion. J. Guidance, Control, and Dynamics 16(5):830-837 (1993).
[6] Mitiguy, P.C.; Banerjee, A.K. Efficient simulation of motions involving Coulomb friction. J. Guidance, Control, and Dynamics 22(1):78-86 (1999).
[7] Ascher, U.M.; Chin, H.; Petzold, L.R.; Reich, S. Stabilization of constrained mechanical systems with DAEs and invariant manifolds. Mechanics of Structures and Machines 23(2):135-157 (1995).
[8] Eich, E. Convergence results for a coordinate projection method applied to mechanical systems with algebraic constraints. SIAM J. on Numerical Analysis 30(5):1467-1482 (1993).
[9] Baumgarte, J. Stabilization of constraints and integrals of motion in dynamic systems. Computer Methods in Applied Mechanics and Engineering 1:1–16 (1972).
[10] von Schwerin, R. Multibody System Simulation: numerical methods, algorithms, and software. Springer-Verlag Lecture Notes in Computational Science and Engineering (1999).
[11] Johnson, K.L. Contact Mechanics, Cambridge University Press (1985). Chapter 4, especially section 4.2.
[12] Hunt, K.H.; Crossley, F.R.E. Coefficient of restitution interpreted as damping in vibroimpact. ASME Journal of Applied Mechanics, Series E 42:440-445 (1975).
[13] Goldsmith, W. Impact, London: Arnold (1960).
[14] Marhefka, D.W.; Orin, D.E. Simulation of contact using a nonlinear damping model, Proc. of the 1996 IEEE Intl. Conf. on Robotics and Automation, Minneapolis, Minnesota (1996).
[15] Dupont, P.; Hayward, V.; Armstrong, B.; Altpeter, F. Single state elastoplastic friction models. IEEE Trans. On Automatic Control, 47(5):787-792 (2002).
[16] Chang, K.S.; Khatib, O. Efficient algorithm for extended operational space inertia matrix. Proc. of the 1999 IEEE/RSJ Intl. Conf. on Intelligent Robots and Systems (1999). The TAO source code is available in its original form under an unrestrictive license on Simtk.org here: https://simtk.org/home/tao_de.
[17] Nilmeier JP, Crooks GE, Minh DD, Chodera JD. Nonequilibrium candidate Monte Carlo is an efficient tool for equilibrium simulation. Proc Natl Acad Sci U S A. 2011 Nov 8;108(45):E1009-18. doi: 10.1073/pnas.1106094108. Epub 2011 Oct 24. Erratum in: Proc Natl Acad Sci U S A. 2012 Jun 12;109(24):9665.
[18] Best DJ, Fisher NI, "Efficient Simulation of the von Mises Distribution", Appl. Statist. 28, no. 2, p. 152-157, 1979