Causality Analysis of Structural Changes from Molecular Dynamics Simulation Data

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Detecting causality relationships between events which are observed in molecular dynamics (MD) simulations of biomolecular systems is of crucial importance for the description of molecular mechanisms and understanding the logic of their functioning, for an overview see: A. Gorecki, J. Trylska & B. Lesyng, Causality and Correlation Analyses of Molecular Dynamics, in “Computational Biophysics to Systems Biology”, NIC Series, 36, pp. 25-30, 2007 (ISBN 978-3-9810843-2-0, http://www.fz-juelich.de/nic-series/volume36/). Signals extracted from MD simulation data are time-dependent atomic positions, momenta, forces or their functions. Quantum degrees of freedom can also be incorporated in the analysis. In multidimensional cases (larger systems) selection or construction of the most important information channels to be analyzed is nontrivial mathematical and computational problem.

Based on Mathematica 7 a computational environment (CausalMD) for the time-series analysis extracted from MD simulation data was designed and tested for a model molecular system with intramolecular proton transfer. Parallel solutions using Grid Mathematica were implemented.

In the current study three different methodologies were applied – two parametric approaches:

• a conventional Granger causality method,
• a Multi-Variate Autoregressive Model (MVAR) with a Directed Transfer Function (DTF) method, and
• a nonparametric wavelet approach.

The first two approaches appeared to be effective to study stationary time-series, the third one also to study nonstationary ones – this, in particular, accounts for proton transfer processes in (bio)molecular systems. Examples of the analyses will be presented for the proton transfer process in malonaldehyde and for conformational changes in an enzyme molecule.

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