

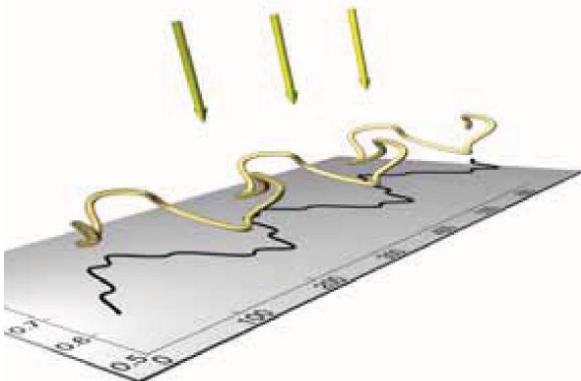


Oliver Lange (Autor)

Collective Langevin Dynamics of Conformational Motions in Protein

Oliver Lange

Collective Langevin Dynamics of Conformational Motions in Proteins



Cuvillier Verlag Göttingen

<https://cuvillier.de/de/shop/publications/2304>

Copyright:

Cuvillier Verlag, Inhaberin Annette Jentzsch-Cuvillier, Nonnenstieg 8, 37075 Göttingen,
Germany

Telefon: +49 (0)551 54724-0, E-Mail: info@cuvillier.de, Website: <https://cuvillier.de>

Contents

1	Introduction	7
2	Principal Component Analysis	13
2.1	Theory of principal component analysis	14
2.2	Principles of Molecular Dynamics Simulation	16
2.3	Methods	18
2.3.1	Generation of MD ensembles	18
2.3.2	Recording of trajectory data	19
2.3.3	Convergence of conformational subspaces	20
2.3.4	Frequency Spectra	21
2.4	Separation of timescales	21
2.5	Convergence of conformational subspaces	24
2.6	Conclusions	25
3	Generalized Correlation of Biomolecular Dynamics	27
3.1	Theory of correlation measures	29
3.1.1	Pearson correlation coefficient	29
3.1.2	Mutual information	30
3.1.3	Linear mutual information	32
3.2	Methods	33
3.3	Correlated motion in Protein G	34
3.4	Correlated motion in Lysozyme	36
3.5	Analysis of the failures of the Pearson coefficient	38
3.6	Conclusions	41
4	Full Correlation Analysis	43
4.1	An Algorithm for Full Correlation Analysis (FCA)	45
4.1.1	Minimization of mutual information	45
4.1.2	An efficient selection of rotation planes	46
4.1.3	Estimation of mutual information	46

4.2	Methods	47
4.2.1	Preprocessing of FCA	47
4.2.2	Selection of essential FCA modes	47
4.2.3	Selection of pairs of FCA modes	47
4.2.4	A test-system for FCA	48
4.2.5	Collectivity of modes	48
4.2.6	Free energy surface for projected motion of neurotensin	48
4.3	Checks of FCA Algorithm	49
4.3.1	Check of entropy estimation	49
4.3.2	Application of FCA to test-case with known result	50
4.4	Extraction of functional motion with FCA	53
4.4.1	Conformational motion of lysozyme analyzed with FCA	53
4.4.2	Reduced description of conformational transitions of neurotensin with FCA .	57
4.4.3	Comparative analysis of PCA and FCA modes	59
4.4.4	Remaining correlations between modes	62
4.4.5	Convergence of FCA	64
4.5	Conclusions	65
5	Covariation of protein backbone motion: a comparison between NMR relaxation measurements and MD simulations	67
5.1	Methods	68
5.1.1	Generation of structure ensembles from NMR NOE data	68
5.1.2	Root mean square fluctuations	68
5.1.3	Generalized correlation coefficients	68
5.1.4	Order parameters	69
5.2	Comparison of NMR covariance with correlations in MD simulations	69
5.3	Verification of molecular dynamics simulation	71
5.4	Rotational correlation	75
5.5	Conclusions	75
6	Equations of Motion for Collective Langevin Dynamics	77
6.1	Projection Operator Formalism	78
6.2	Definition of Motion along Conformational Coordinate(s) as the Observable	80
6.3	Equations of Motion for Conformational Coordinate(s)	81
6.4	Integration of the generalized Langevin equation	83
6.4.1	Generation of a random force	83
6.4.2	Integration of the GLE	84
6.4.3	Treatment of the convolution integral with FFT	85
6.5	Appendix	86

CONTENTS	5
7 Extraction of Memory Kernels from Molecular Dynamics Simulations	89
7.1 The Memory equation	90
7.2 Ill-posedness of the Memory equation	91
7.3 Regularization of Inverse Problems	92
7.3.1 Discretization of Memory equation	94
7.3.2 Straightforward recursion formulas without regularization	94
7.3.3 Strong regularization by projection	96
7.3.4 Weak regularization by projection to auto-regressive models	96
7.3.5 Regularization by Landweber's iterations	97
7.3.6 Tikhonov regularization	98
7.3.7 Sequential Tikhonov regularization	99
7.3.8 Choice of regularization parameter by means of L-curve	101
7.4 Evaluation of methods to solve the Memory equation	101
7.4.1 Method of Evaluation	102
7.4.2 Results	103
7.4.3 Discussion and Outlook	106
7.5 Determination of memory via force autocorrelation functions	107
7.5.1 Methods	108
7.5.2 Memory kernel from constrained particle force autocorrelation function . . .	108
7.5.3 Spatial dependence of memory functions	112
7.5.4 Discussion	112
7.6 Summary and Conclusions	113
8 Collective Langevin Dynamics (CLD) of a Conformational Transition in Neurotensin	115
8.1 Transition rates	116
8.2 Methods	117
8.2.1 Definition of a one-dimensional curved conformational coordinate	117
8.2.2 Projection onto the conformational coordinate	117
8.2.3 Solution of the memory equation	118
8.2.4 Potential of mean force	118
8.2.5 Statistics of conformational transitions	119
8.3 Conformational dynamics of reference MD simulation	119
8.4 Construction of a curved conformational coordinate	120
8.5 Velocity autocorrelation function of collective motion	123
8.6 Extraction of memory kernels	124
8.7 Conformational dynamics by CLD	126
8.8 Prediction of Transition Rates by CLD	128
8.9 Prediction of positional autocorrelation functions by CLD	131
8.10 Discussion and Conclusions	132

9 Summary and Conclusions	135
10 Acknowledgments	141
Bibliography	143