



Philipp Nicolas Depta (Autor)
**Physics-Based and Data-Driven Multiscale Modeling
of the Structural Formation in Macromolecular
Systems**

SPE INSTITUTE OF
SOLIDS PROCESS
ENGINEERING &
TUHH PARTICLE TECHNOLOGY

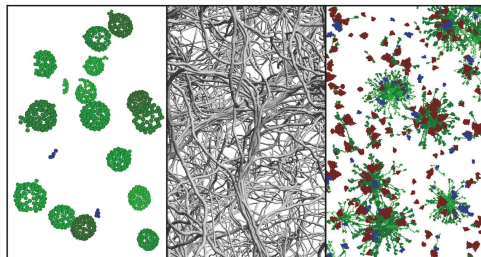
SPE-Schriftenreihe

25

Herausgegeben von Prof. Dr.-Ing. habil. Prof. E.h. Dr. h.c. Stefan Heinrich

Philipp Nicolas Depta

**Physics-Based and Data-Driven Multiscale
Modeling of the Structural Formation in
Macromolecular Systems**



Cuvillier Verlag Göttingen
Internationaler wissenschaftlicher Fachverlag

<https://cuvillier.de/de/shop/publications/9000>

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

Acknowledgments	i
Abstract	iii
Contents	v
Symbols	ix
1 Introduction	1
1.1 Motivation	1
1.2 Theory and State of the Art in Molecular Mechanics	3
1.2.1 Molecular Dynamics (MD)	3
1.2.2 Coarse-Graining in Space and Time	8
1.2.3 Other Derivatives and Related Methods: From Monte Carlo to Machine Learning	13
1.2.4 Scope of this Work	15
1.3 Model Systems	16
1.3.1 Alginate Gelation	17
1.3.2 Hepatitis B Core Antigen (HBcAg)	19
1.3.3 Pyruvate Dehydrogenase Complex (PDC)	20
1.4 Outline	23
2 Model Framework	25
2.1 Introduction and Framework Overview	25
2.2 MDEM Implementation	28
2.3 Molecular Reference Structures	30
3 Diffusion and Thermodynamics	33
3.1 Introduction	33
3.2 Model Description	34
3.2.1 Overview	34
3.2.2 Background	35
3.2.3 Simplification for Isotropic Diffusion	36
3.3 Parameterization	36
3.3.1 Approaches	36
3.3.2 Parameterization through Molecular Dynamics	37
3.4 Convergence	38
3.4.1 Critical Time Step	39

3.4.2	Thermal Equilibration Speed	40
3.4.3	Diffusion Coefficient	40
3.4.4	Kinetic Energy	41
3.5	Comparison with Molecular Dynamics Data	44
3.6	Enhanced Sampling of the Conformation Space through Simulated Annealing	46
4	Intermolecular Interaction	47
4.1	Introduction	47
4.2	Probabilistic Interaction Model for Calcium Mediated Alginate Gelation Based on Literature and Theory	49
4.2.1	Interaction Model	50
4.2.2	Ion Model	51
4.2.3	Critical Time Step	54
4.3	Data-Driven Interaction Potential Fields Based on MD	55
4.3.1	Molecular Dynamics Setup and Potential Groups	57
4.3.2	Spatial Descriptors	59
4.3.3	Basic Functions for Trend and Variogram Modeling	61
4.3.4	Multi-Variant Field Interpolation using Universal Kriging	63
4.3.4.1	Method	63
4.3.4.2	Grid Design	67
4.3.4.3	Initial Sampling and Iterative Refinement	69
4.3.4.4	2D Example	71
4.3.5	Biased MD and Insertion of Empirical Data	72
4.3.6	Molecular Collisions	75
4.3.7	Method Summary and Uncertainties	77
4.4	Derivation of Interaction Forces and Torques From Potential Fields	78
4.4.1	Direct Usage of Potential Field	79
4.4.2	Alternative Representations and Simplifications	80
4.5	Critical Time Step	81
5	Bonded Interaction	83
5.1	Introduction	83
5.2	Pairwise Elastic Bond Model (incl. Orientation)	84
5.2.1	Model Description	84
5.2.2	Bond Contact Point	87
5.2.3	Critical Time Step	87
5.3	Fiber Bond Model	88
5.3.1	Model Description	88
5.3.2	Critical Time Step	90
6	Results: Alginate System	93
6.1	Model Parameters	93
6.1.1	Structural Model	93
6.1.2	Functional Model	96
6.1.2.1	Diffusion and Thermodynamics	96
6.1.2.2	Intermolecular Interaction	97
6.1.2.3	Bonded Interaction	101

6.1.2.4	Critical Time Step	102
6.2	Simulation Setup and Procedure	102
6.3	Analysis and Postprocessing	103
6.4	Results	104
6.4.1	Base Case	106
6.4.2	Case Studies	109
6.4.2.1	Constant Temperature (No Annealing)	109
6.4.2.2	Annealing Procedure (AN2)	114
6.5	Comparison with Literature and Collaborator Data	117
7	Results: HBcAg System	125
7.1	Model Parameters	125
7.1.1	Structural Model	125
7.1.2	Functional Model	126
7.1.2.1	Diffusion and Thermodynamics	126
7.1.2.2	Intermolecular Interaction	126
7.1.2.3	Bonded Interaction	127
7.1.2.4	Critical Time Step	128
7.2	Simulation Setup and Procedure	128
7.3	Analysis and Postprocessing	129
7.4	Results	130
7.4.1	Intermolecular Interaction Potential and VLP Stability	131
7.4.1.1	Pure MD-Based Interaction Potential	131
7.4.1.2	Biased MD-Based Interaction Potential	135
7.4.1.3	MD-Based Interaction Potential with Empirical Data	136
7.4.2	VLP Self-Assembly	138
8	Results: PDC System	151
8.1	Model Parameters	151
8.1.1	Structural Model	151
8.1.2	Functional Model	152
8.1.2.1	Diffusion and Thermodynamics	152
8.1.2.2	Intermolecular Interaction	152
8.1.2.3	Bonded Interaction	155
8.1.2.4	Critical Time Step	155
8.2	Simulation Setup and Procedure	156
8.3	Analysis and Postprocessing	156
8.4	Results	158
8.4.1	Intermolecular Interaction Potentials	158
8.4.2	PDC Self-Assembly	164
8.4.2.1	Pure E2 System	164
8.4.2.2	Full Component PDC System	170
9	Conclusions	177

A	General Appendix	181
A.1	Euler Angle Definition	181
A.2	Detailed Framework Overview	182
A.3	Hydrodynamic Interaction	183
B	Diffusion Model Comparison with Molecular Dynamics Data	185
C	Kriging Algorithm Components	187
C.1	Variogram Binning Algorithm	187
C.2	Kriging Neighborhood Search and Convergence	188
C.3	Objective Function For Quantitative Structural Stability	190
C.4	MD Quality Criteria	191
D	HBcAg Results Supplementary	193
D.1	Spatial Descriptors	194
D.2	Biased MD-Based Interaction Potential	195
D.3	Kriging Statistical Data	195
E	PDC Results Supplementary	201
E.1	Binding Locations	202
E.2	Pure MD-Based Interaction Potentials	205
E.3	Repulsive-Only Interaction Potentials	206
E.4	Kriging Statistical Data	208
E.5	PDC Self-Assembly	221
E.5.1	Pure E2 System	221
E.5.2	Full Component PDC System	224
E.5.3	Enhanced E2 – E2 Arm Interaction	231
	Bibliography	239