Večskalne simulacije mehke in biološke snovi
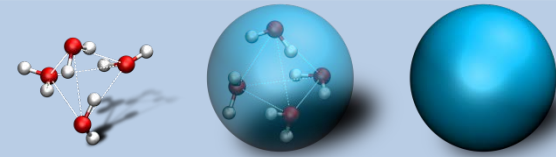
Matej Praprotnik

Računske in statistične metode v kemiji

Kemijski inštitut, 19.-21. oktober 2021

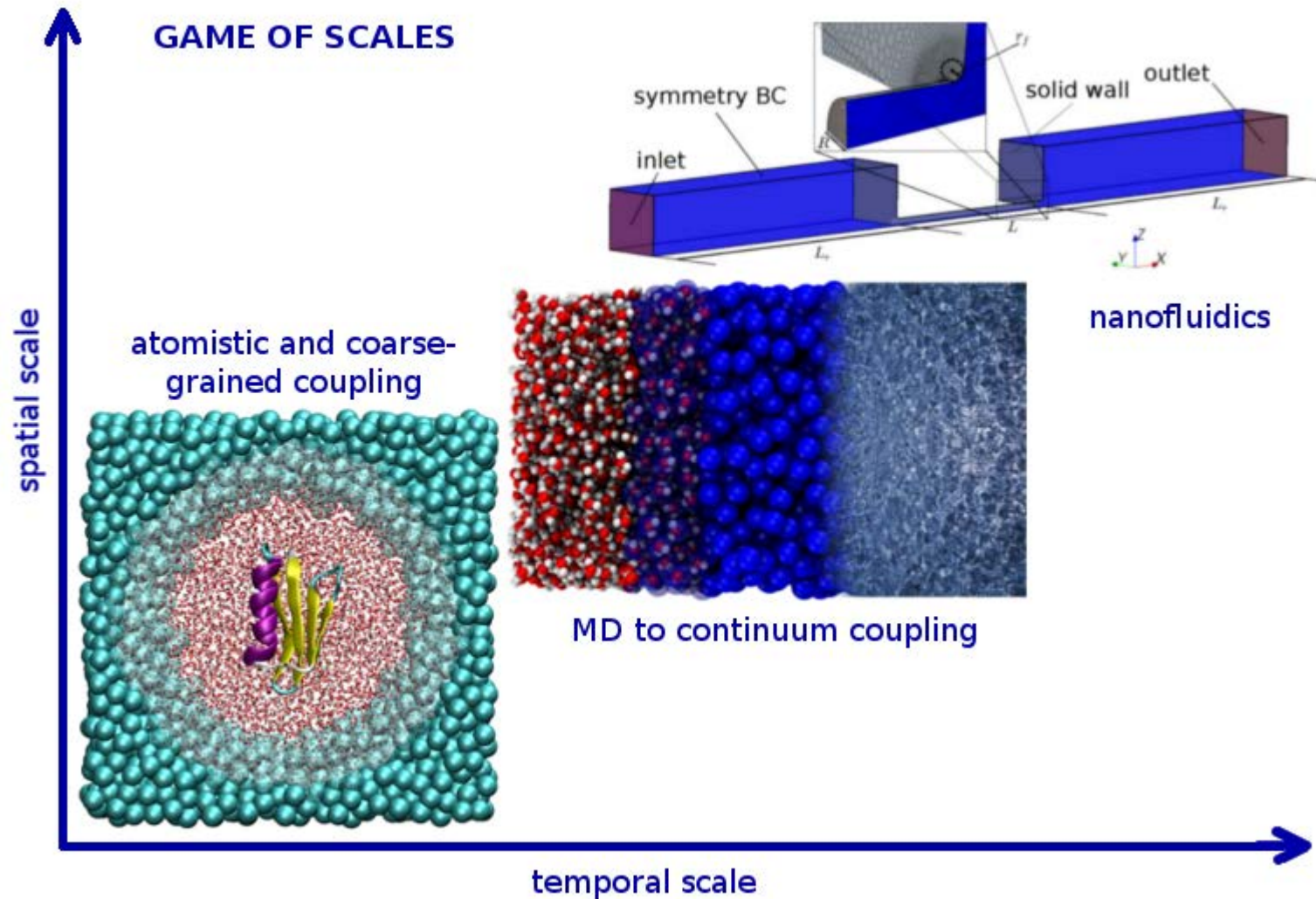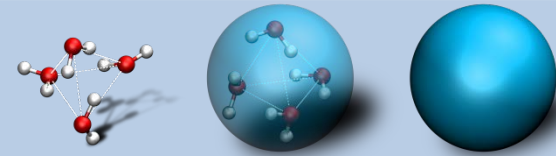NATIONAL INSTITUTE OF CHEMISTRY

Outline

➢ multiscale simulations:

    1.   Adaptive Resolution Scheme (AdResS)

    2.   coupling to supramolecular coarse-grained models
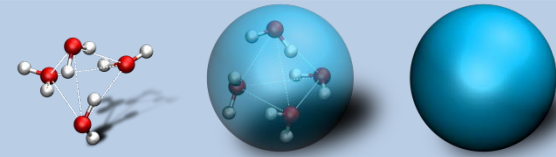
    3.   Open Boundary Molecular Dynamics (OBMD)

➢ biomolecular applications:

    1.   DNA molecule in salt solution

    2.   columnar phases of DNA

    3.   OBMD of a DNA molecule

Multiscale modeling & simulation

GAME OF SCALES

spatial scale

atomistic and coarse-grained coupling

symmetry BC

inlet

solid wall

outlet

nanofluidics

MD to continuum coupling

temporal scale

Multiscale simulation
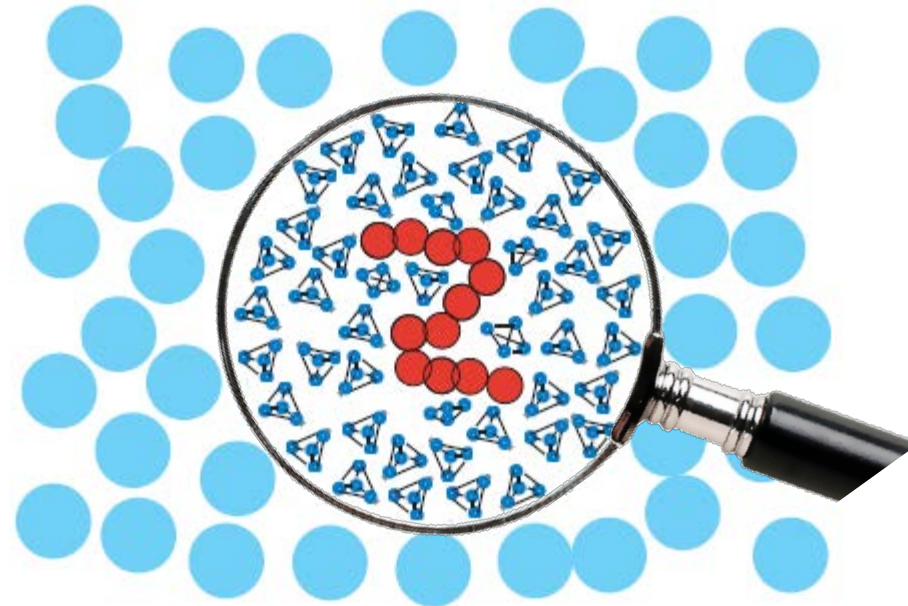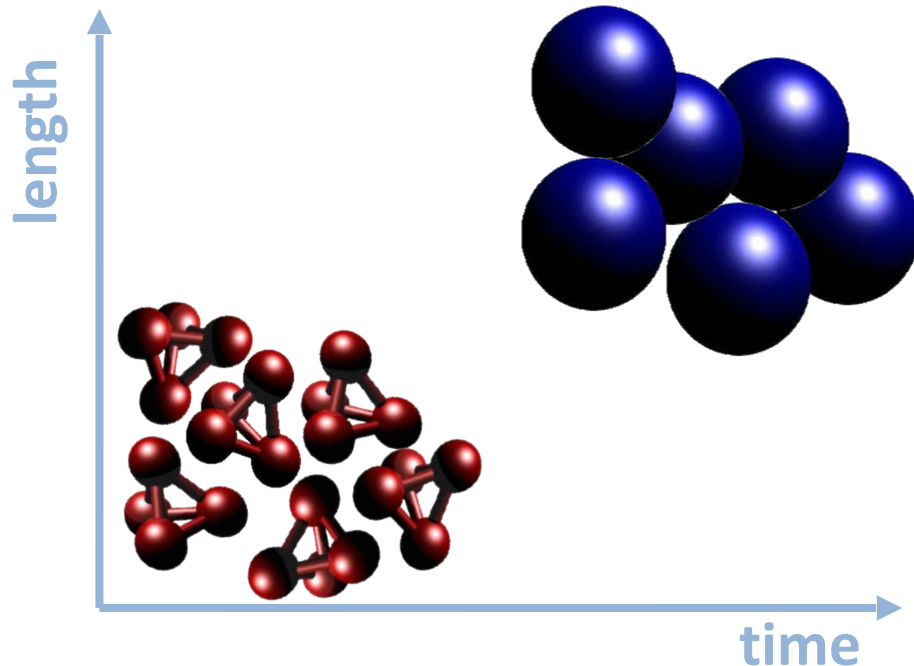
➢ atomistic simulation

- large length and time scales are difficult to capture

➢ coarse-grain simulation

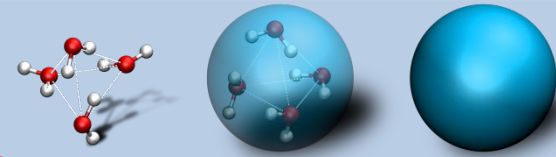- atomistic details are lost

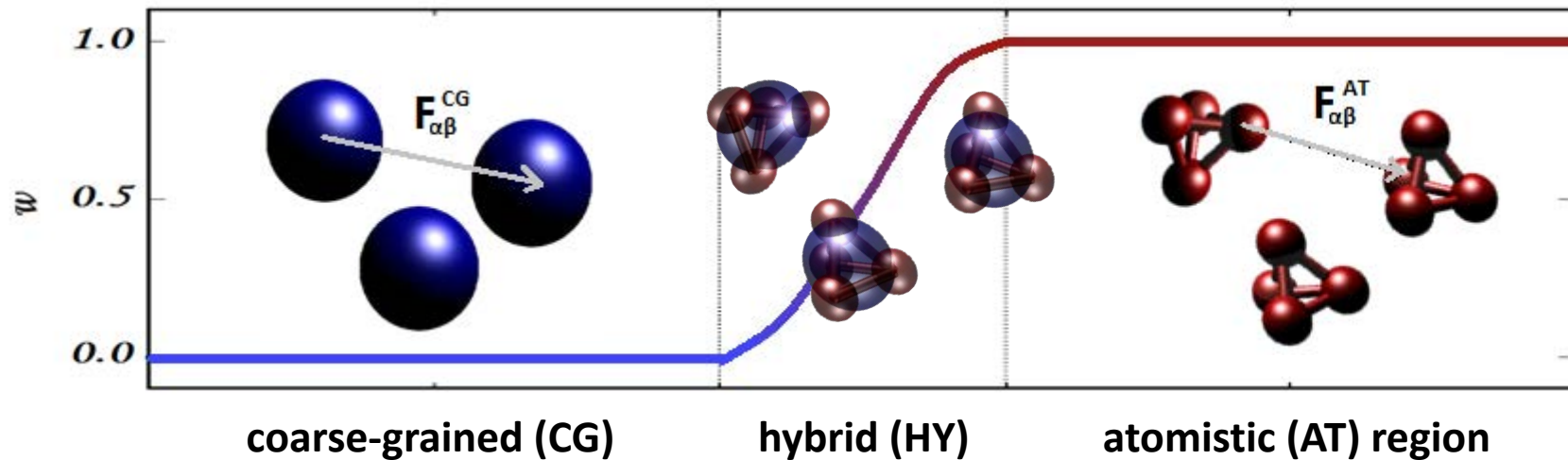➢ multiscale simulation

Molecular Dynamics

$$F = m \cdot a$$

"hard core"

Noise

Langevin–Thermostat

Damping

V

Electrostatic

$P^{3}M$–Algorithm
(Mesh–Ewald)

Periodic Boundary Conditions

Geometry

hexagonal cell

Adaptive Resolution Scheme (AdResS)

coarse-grained (CG)   **hybrid (HY)**   **atomistic (AT) region**
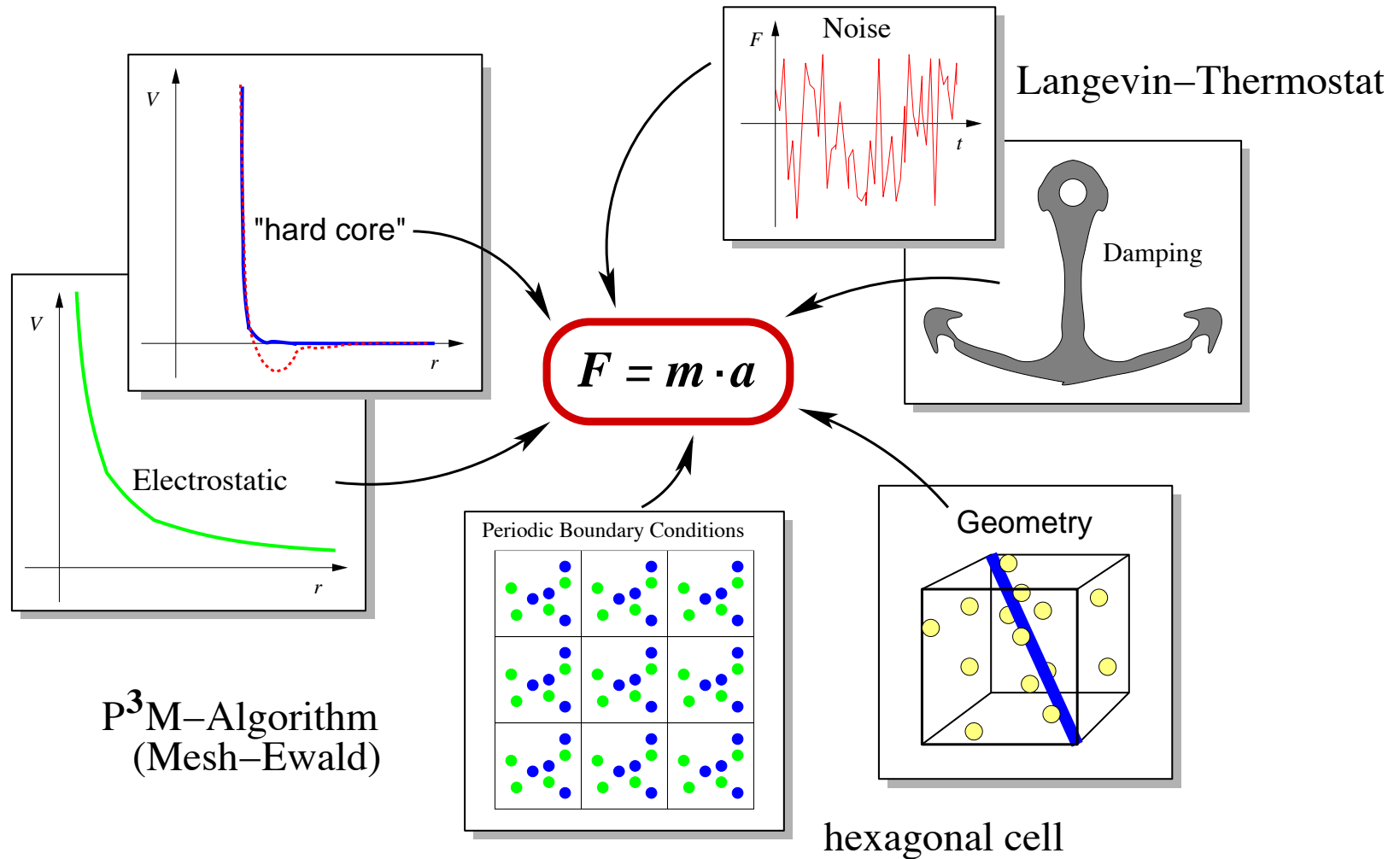
➢ force between particle α and β:

$$F_\alpha^{AdResS} = \sum_{\beta \neq \alpha} w\left(\left|R_\alpha - R\right|\right) w\left(\left|R_\beta - R\right|\right) F_{\alpha\beta}^{AT} + \sum_{\beta \neq \alpha} \left[1 - w\left(\left|R_\alpha - R\right|\right) w\left(\left|R_\beta - R\right|\right)\right] F_{\alpha\beta}^{CG} - F_\alpha^{TD}\left(\left|R_\alpha - R\right|\right)$$

$w(r)$… position dependent weighting function

➢ above force coupling scheme obeys Newton's third law

Praprotnik, Delle Site, Kremer; Annu. Rev. Phys. Chem. (2008)
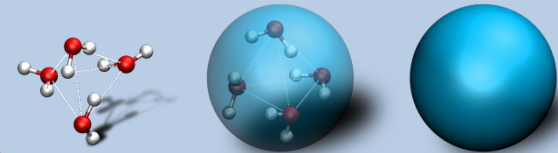
Multiscale 1M NaCl salt solution

➢ atomistic force field:

   TIP3P + Amber 03

➢ coarse-grained force field:

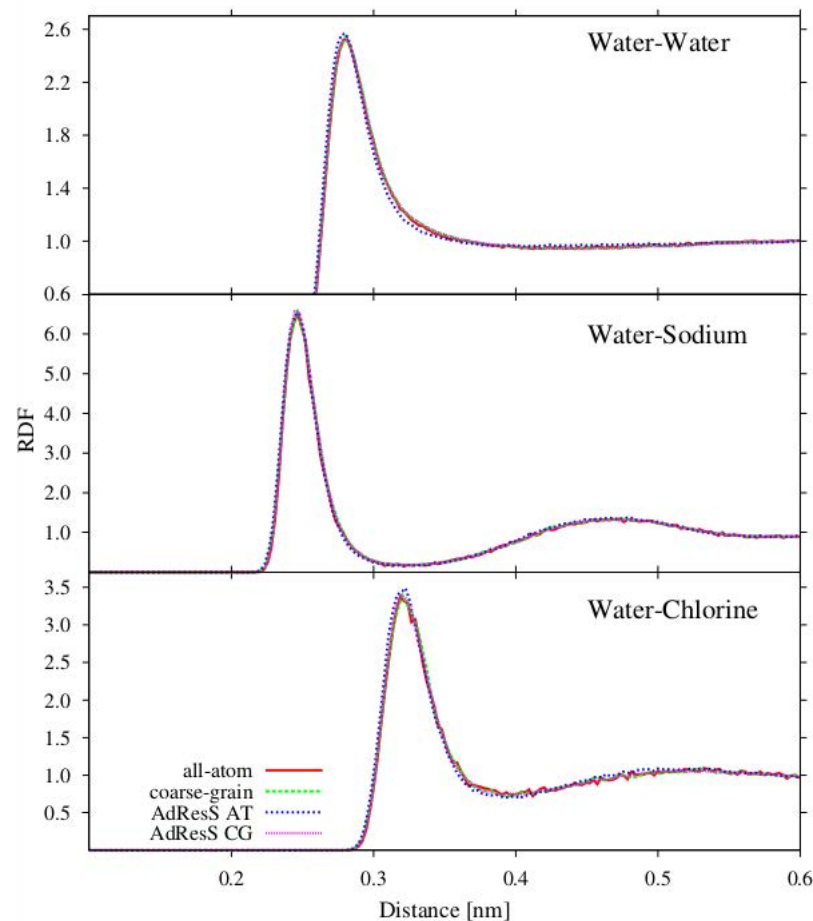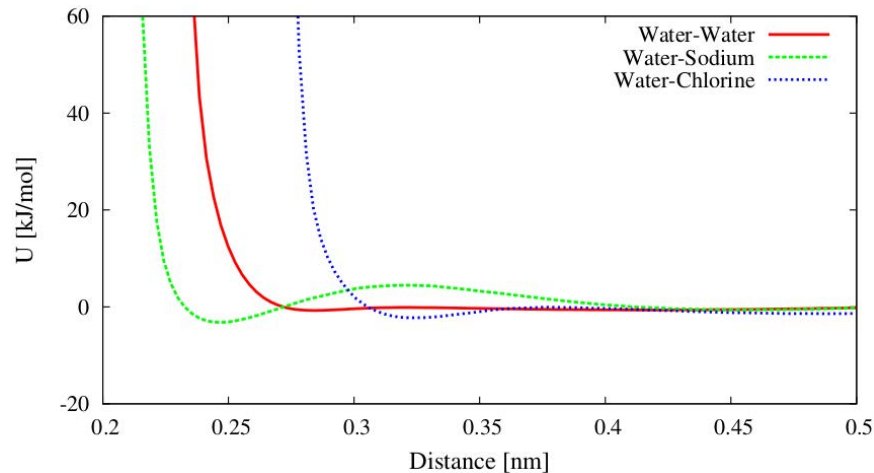   derived with Boltzmann inversion
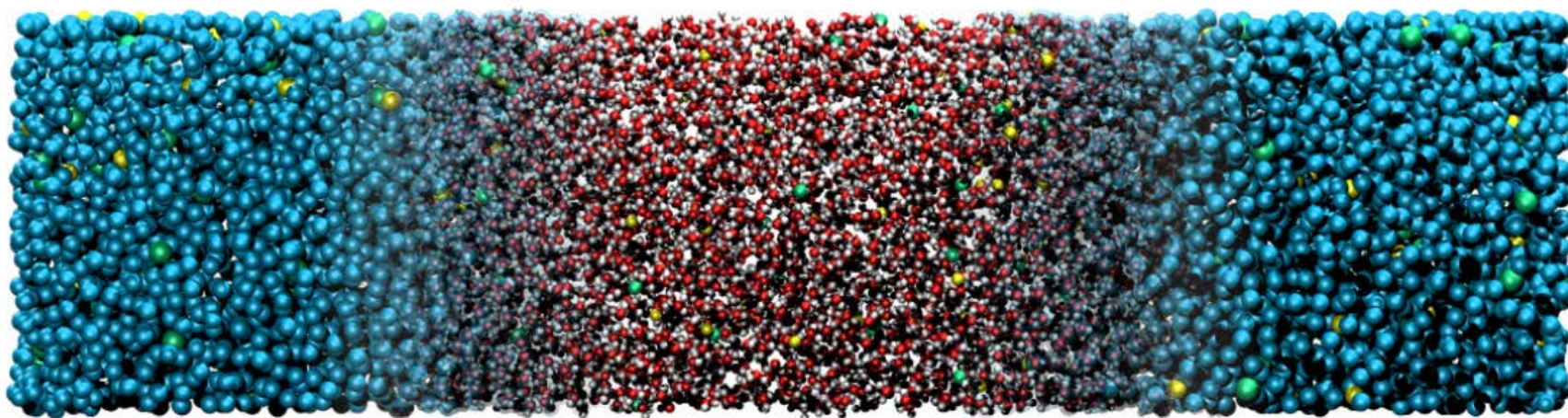
Bevc, Junghans, Kremer, Praprotnik; *New. J. Phys.* (2013)
Zavadlav, Podgornik, Praprotnik; *JCTC* (2015)

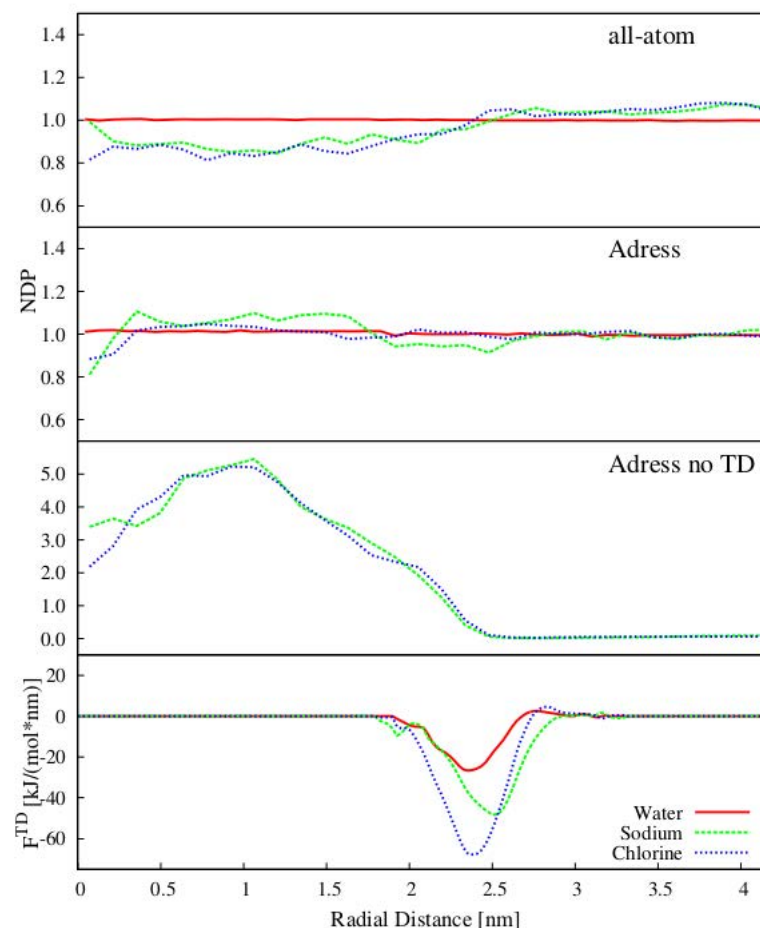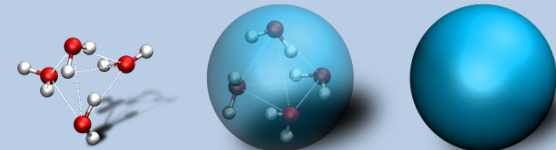# Multiscale 1M NaCl salt solution

➢ derived CG potential

Zavadlav, Podgornik, Praprotnik; *JCTC* (2015)
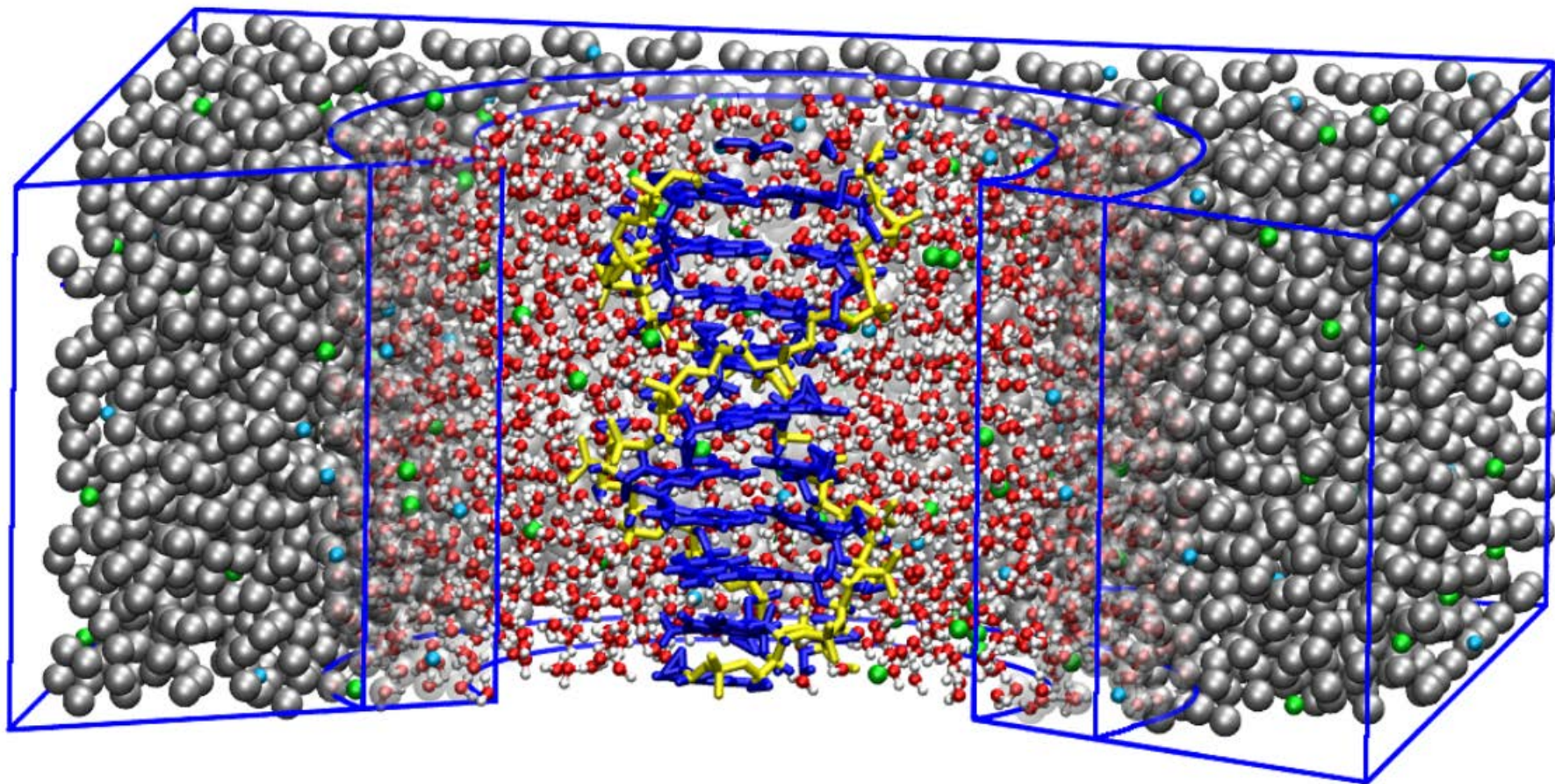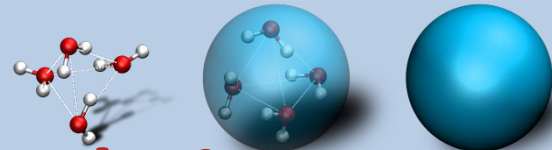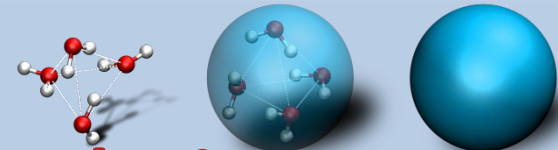
Multiscale 1M NaCl salt solution

➢ density profile
➢ thermodynamic (TD) force
on CG beads in HY region
➢ calculated iteratively

$$F_{TD}{}^{i+1} = F_{TD}{}^{i} - \frac{M_{\alpha}}{\rho_0{}^2 \kappa_T} \nabla \rho^i(x)$$

Zavadlav, Podgornik, Praprotnik; *JCTC* (2015)

Atomistic DNA in multiscale salt solution

Zavadlav, Podgornik, Praprotnik; *J. Chem. Theory Comput.* (2015)

DNA molecule in multiscale salt solution

➢ dielectric constant of DNA molecule

Group	ε (1.5 nm)	ε (1.8 nm)	ε (2.1 nm)	ε (2.4 nm)	ε (∞)
Phosphate	18.3	21.1	17.3	15.7	17.0
Sugar	2.7	2.8	2.7	2.4	2.6
Base	2.1	2.1	2.0	2.0	2.1
DNA	5.6	5.9	5.4	4.5	5.0
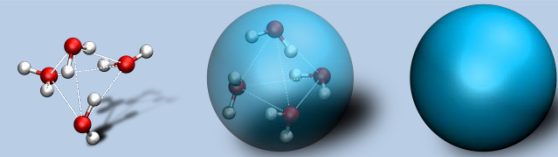
Zavadlav, Podgornik, Praprotnik; *JCTC* (2015)

DNA molecule in multiscale salt solution

➢ dielectric constant of water

Zavadlav, Podgornik, Praprotnik; *JCTC* (2015)

Columnar phases of DNA arrays

Isotropic	Cholesteric	Hexagonal 2D progressive 3D longitudinal ordering			Orthorhombic
C(mg/ml) ≈ 160 (*)	380			670	1055
	mean interhelices distance a_m	intermolecular distance a_H			lattice parameters
	49 Å 32 Å	31.5 Å 29 Å	23.7 Å		a = 24.09 Å a = 20.77 Å b = 39.33 Å b = 29.72 Å
			helix pitch P		
34.6 Å	....				30.2 Å

Durand, Doucet, Livolant, *J. Phys. II France* (1992)

(A)
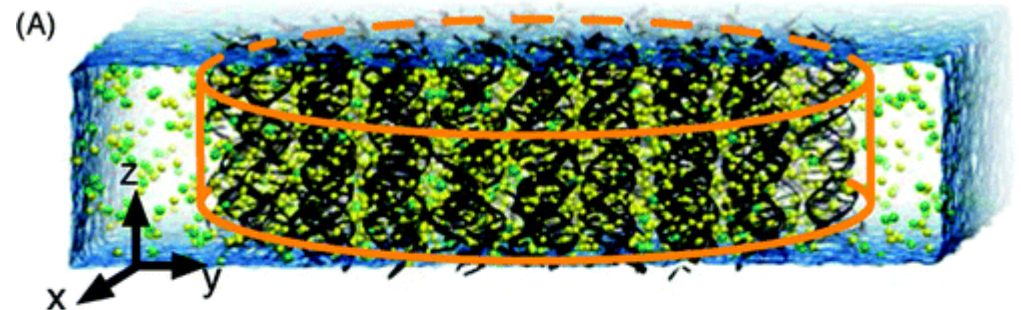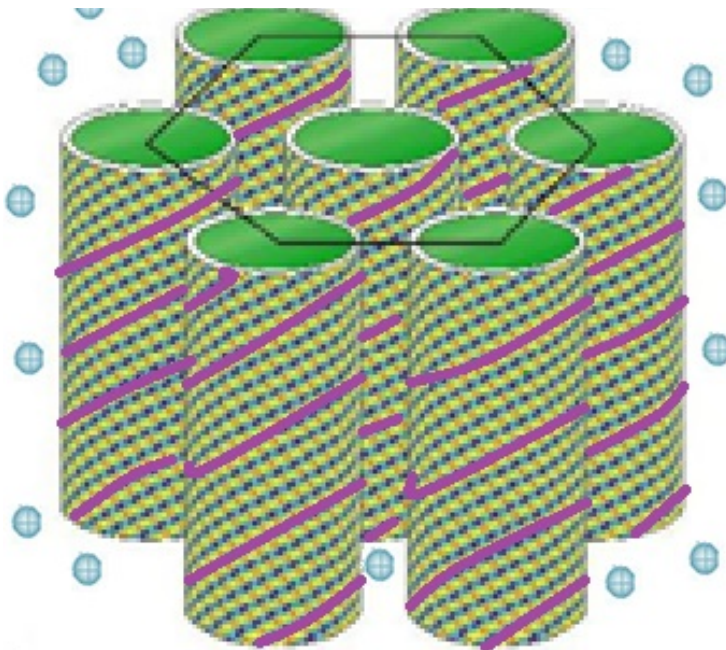
Lyubartsev, Nordenskiöld, *J. Phys. Chem.* (1995), Yoo, Aksimentiev, *J. Phys. Chem. Lett. (2011)*
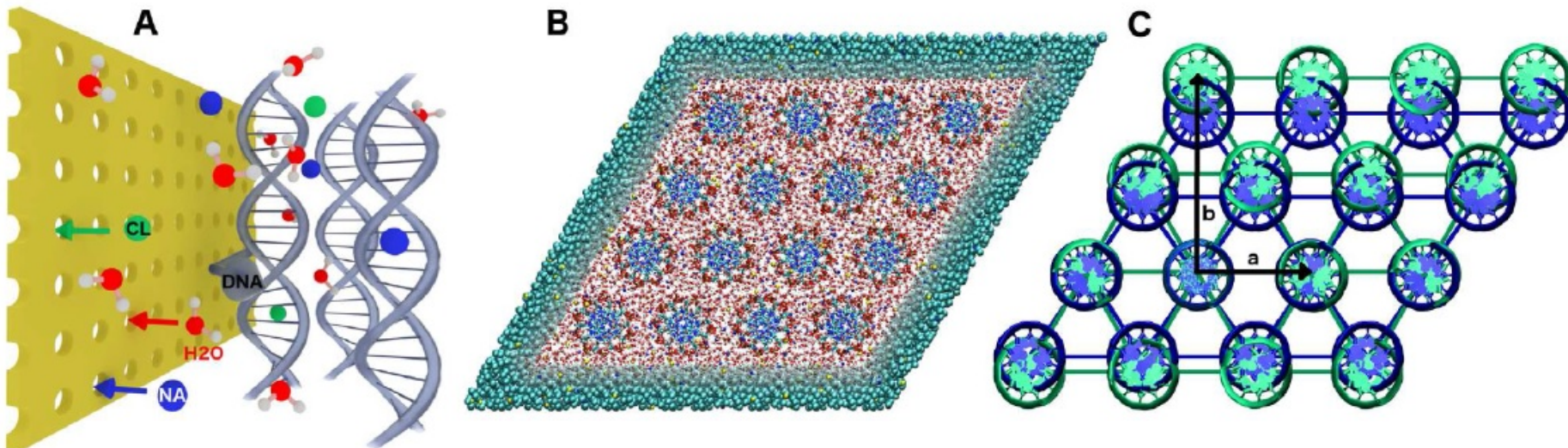
Columnar phases of DNA arrays

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			helix pitch P		
		34.6 Å			30.2 Å

Durand, Doucet, Livolant, *J. Phys. II France* (1992)

➢ system of 16 DNA molecules
➢ hexagonal/orthorhombic
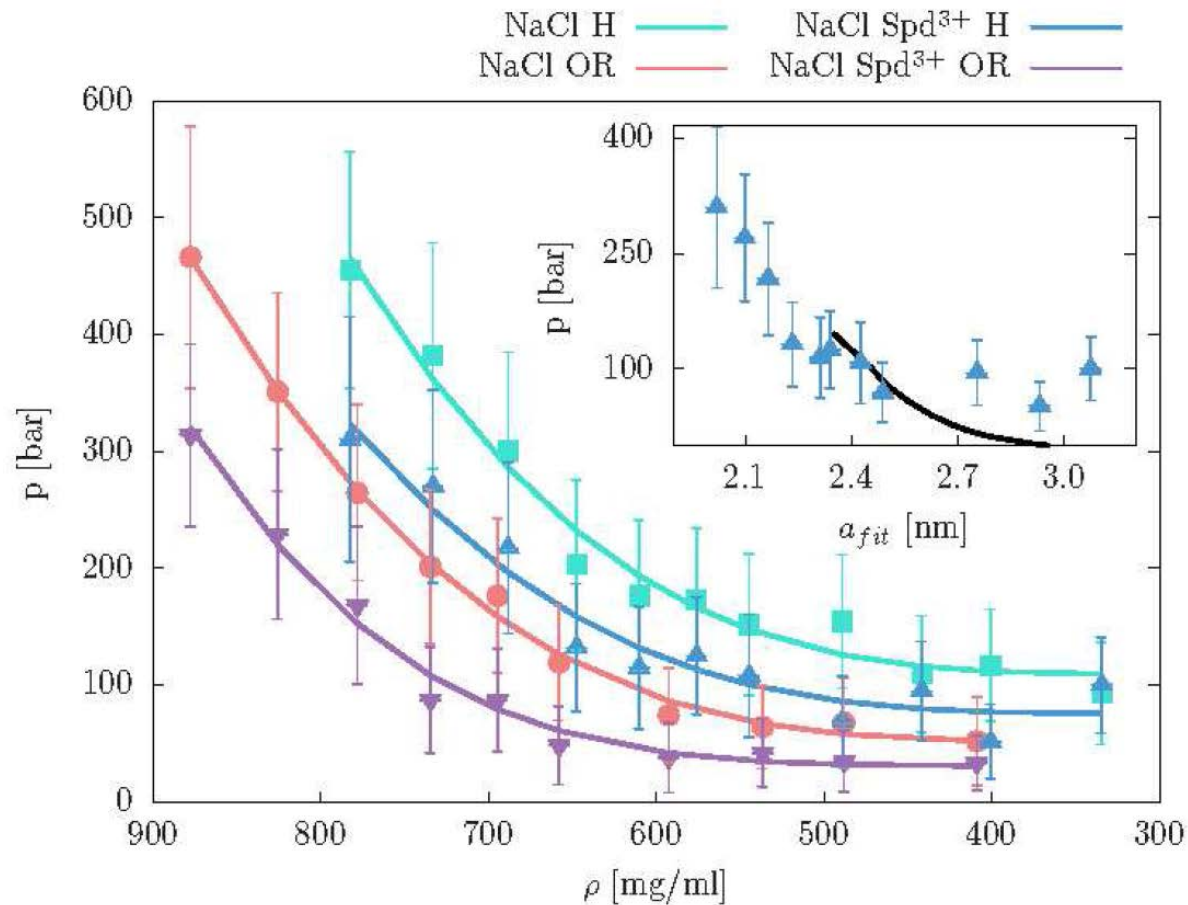➢ Na^+/Spd^{3+}
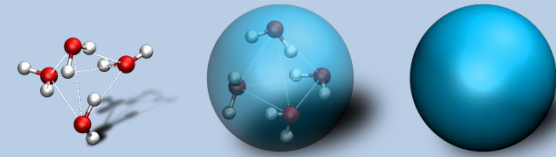

Zavadlav, Podgornik, Praprotnik; *Sci. Rep.* (2017)
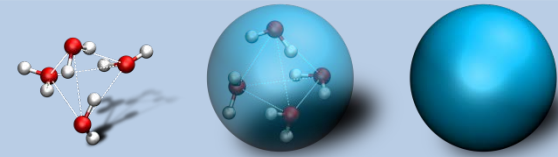
Columnar phases of DNA arrays

➢ osmotic pressure vs. DNA density

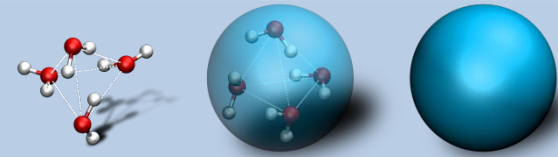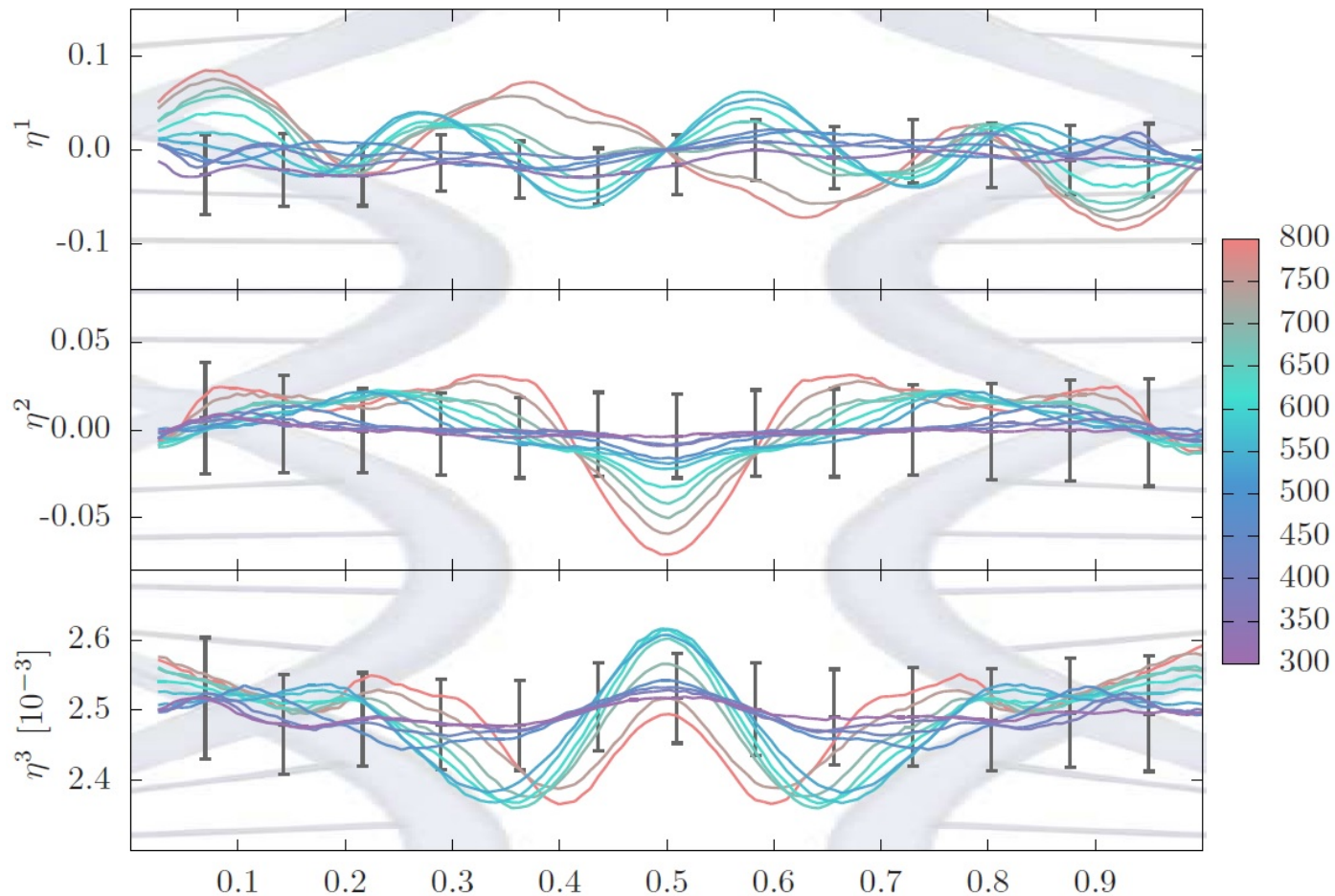Zavadlav, Podgornik, Praprotnik; *Sci. Rep.* (2017)

Columnar phases of DNA arrays

➢ positional and orientational correlations

Zavadlav, Podgornik, Praprotnik; *Sci. Rep.* (2017)
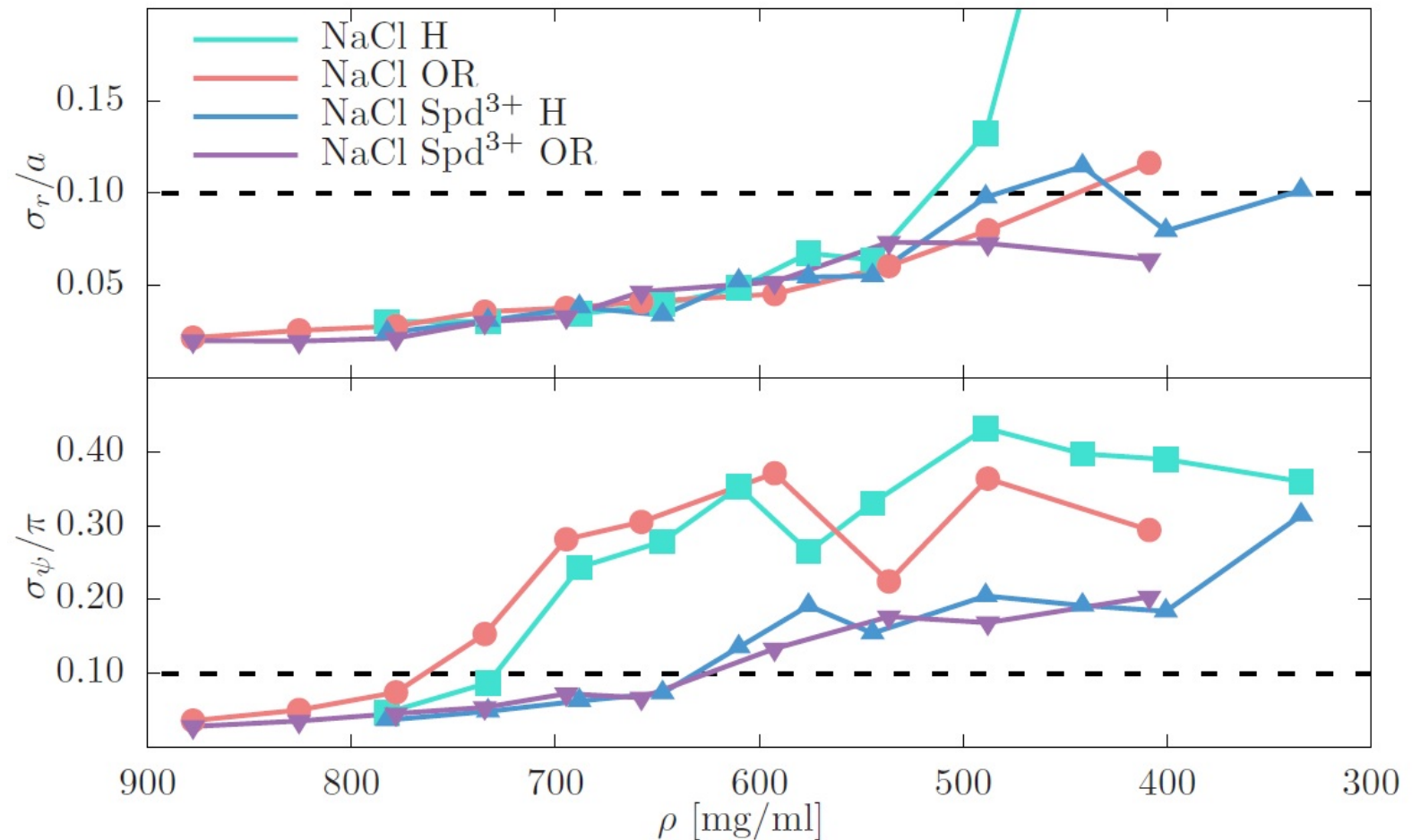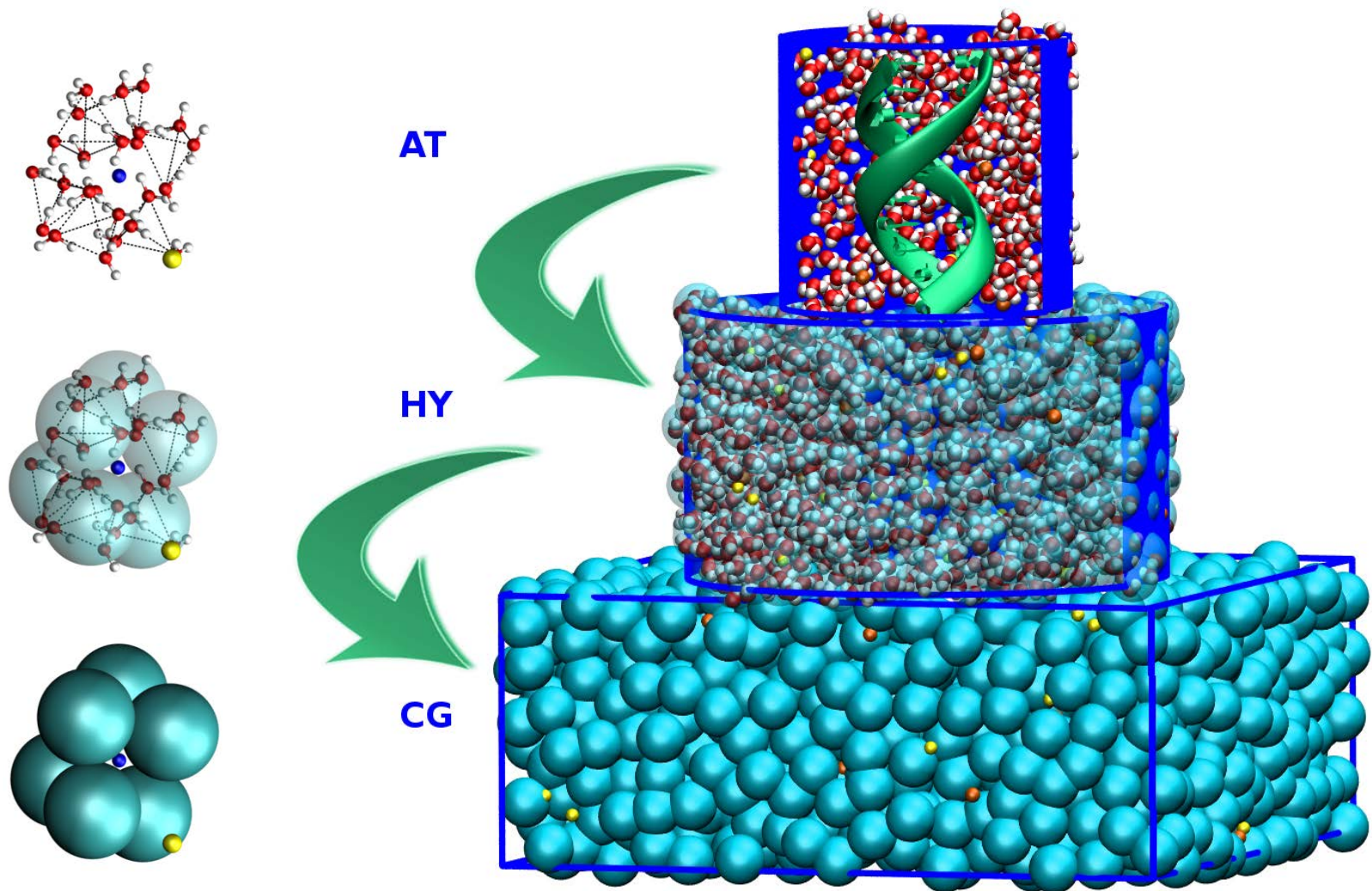
Columnar phases of DNA arrays

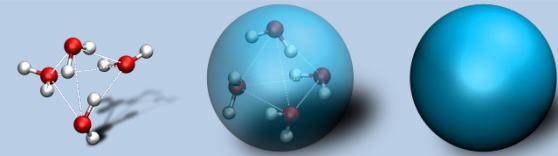➢ order parameters

Zavadlav, Podgornik, Praprotnik; *Sci. Rep.* (2017)

DNA molecule in bundled-SPC/MARTINI salt solution

AT

HY

CG

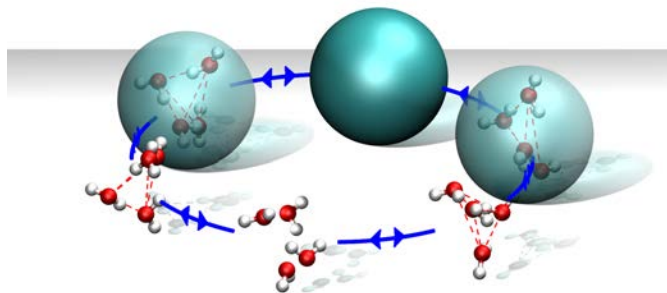Zavadlav, Podgornik, Melo, Marrink, Praprotnik; *EPJST* (2016)

Free SPC/MARTINI water and DPD
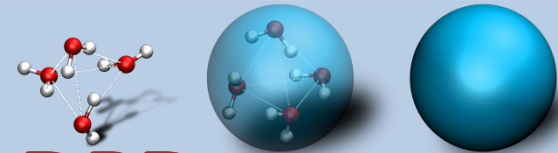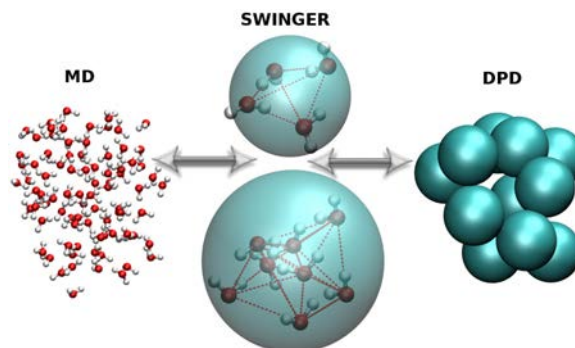
➢ Algorithm SWINGER:

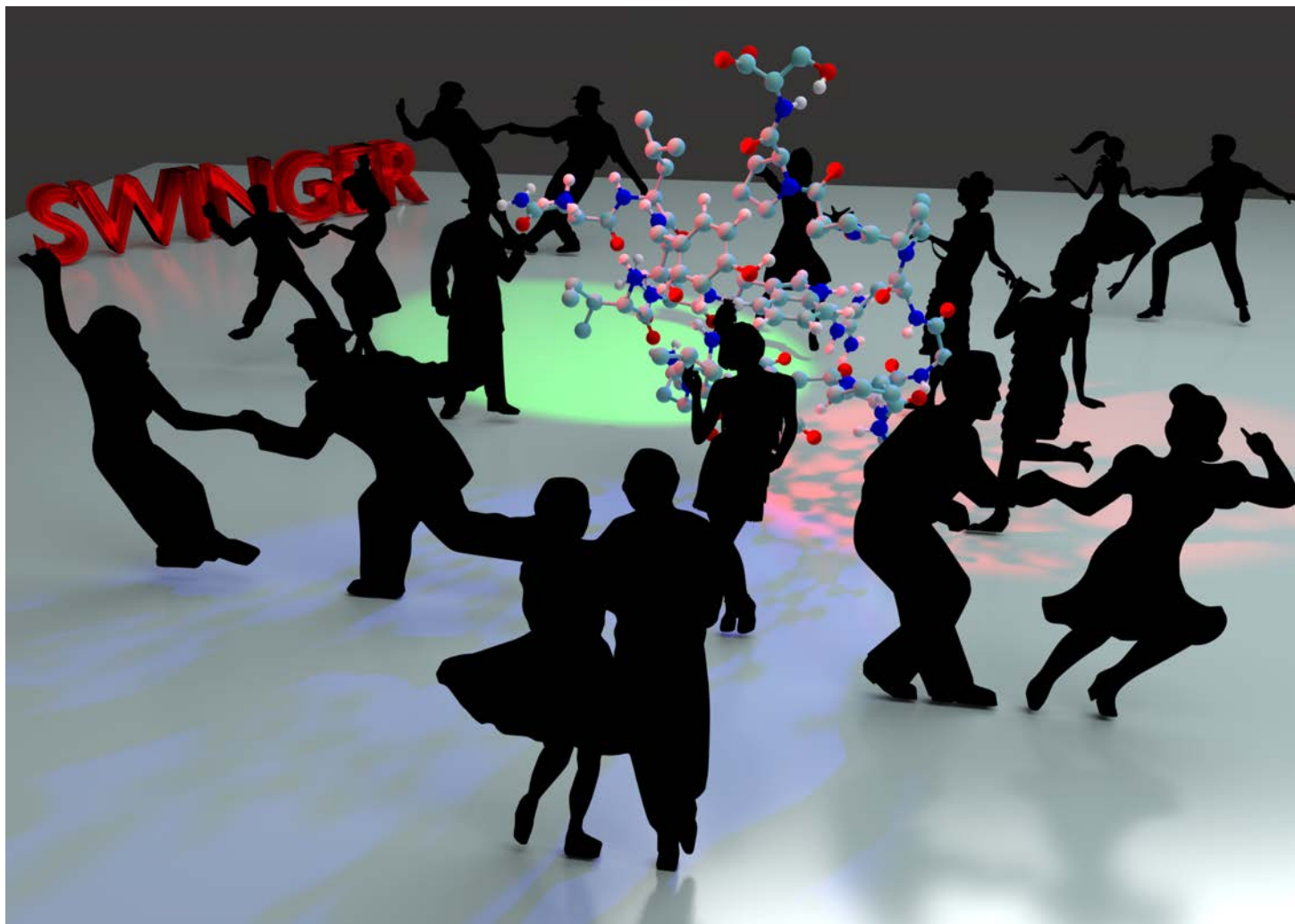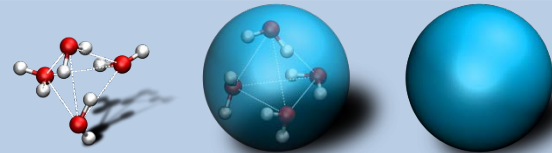- concurrently assembles, disassembles and reassembles water clusters

➢ DPD:

- supramolecular coupling of atomistic water with DPD

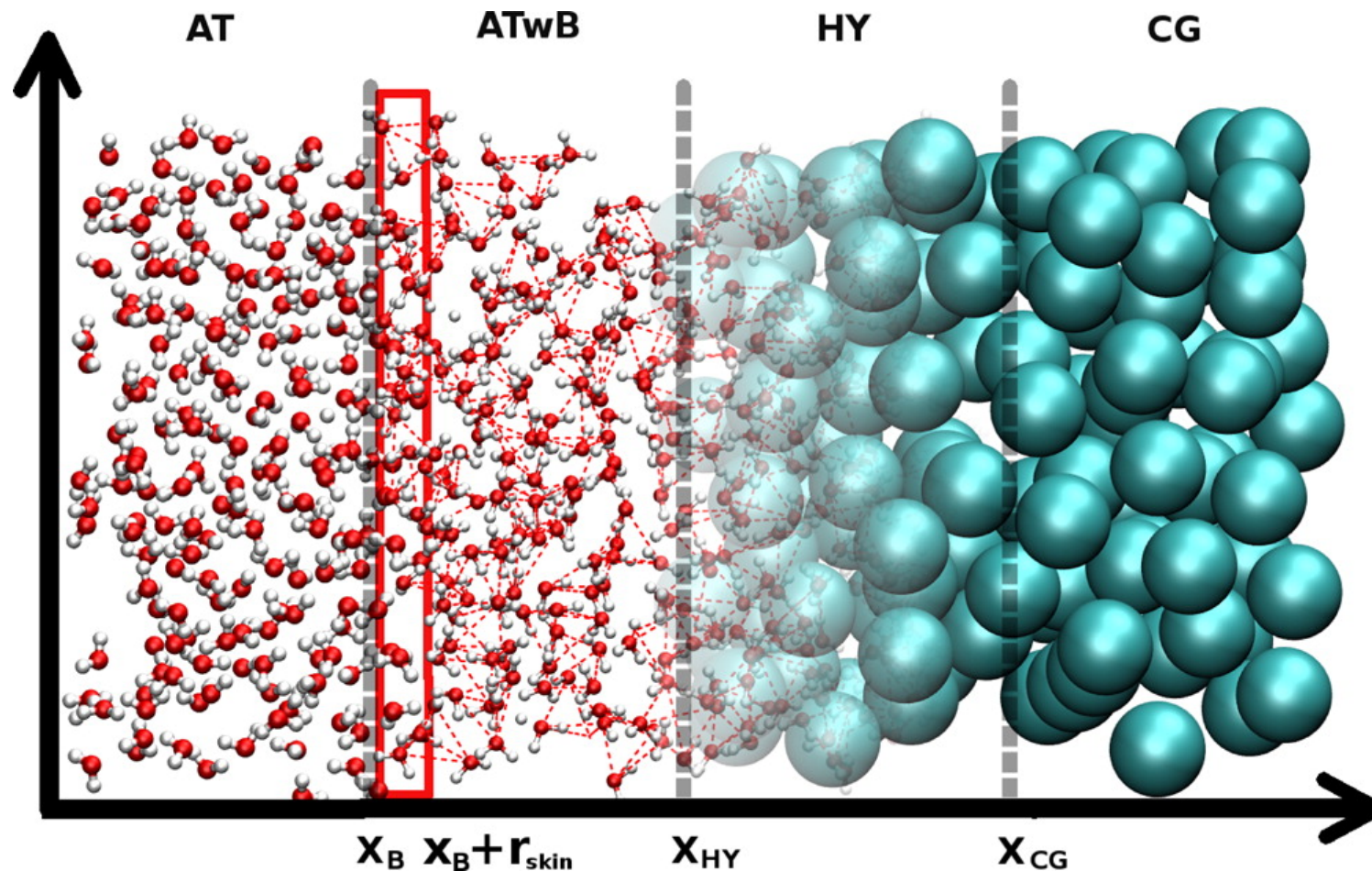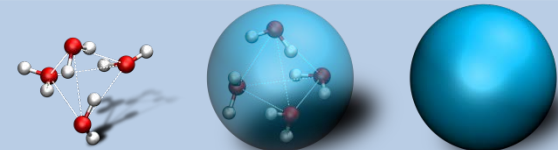Zavadlav, Marrink, Praprotnik; *J. Chem. Theory Comput*. (2016)
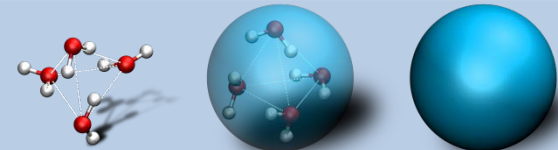Zavadlav, Praprotnik; *J. Chem. Phys*. (2017)

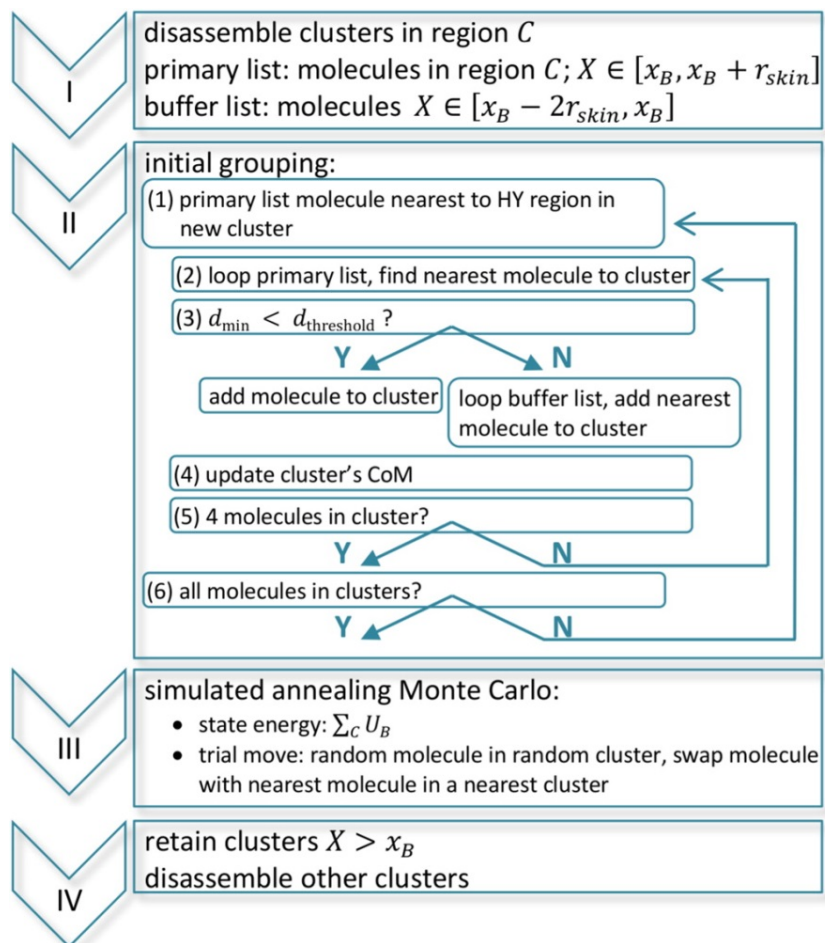# SWINGER algorithm

Zavadlav, Marrink, Praprotnik; *JCTC* (2018)

Free SPC/MARTINI water

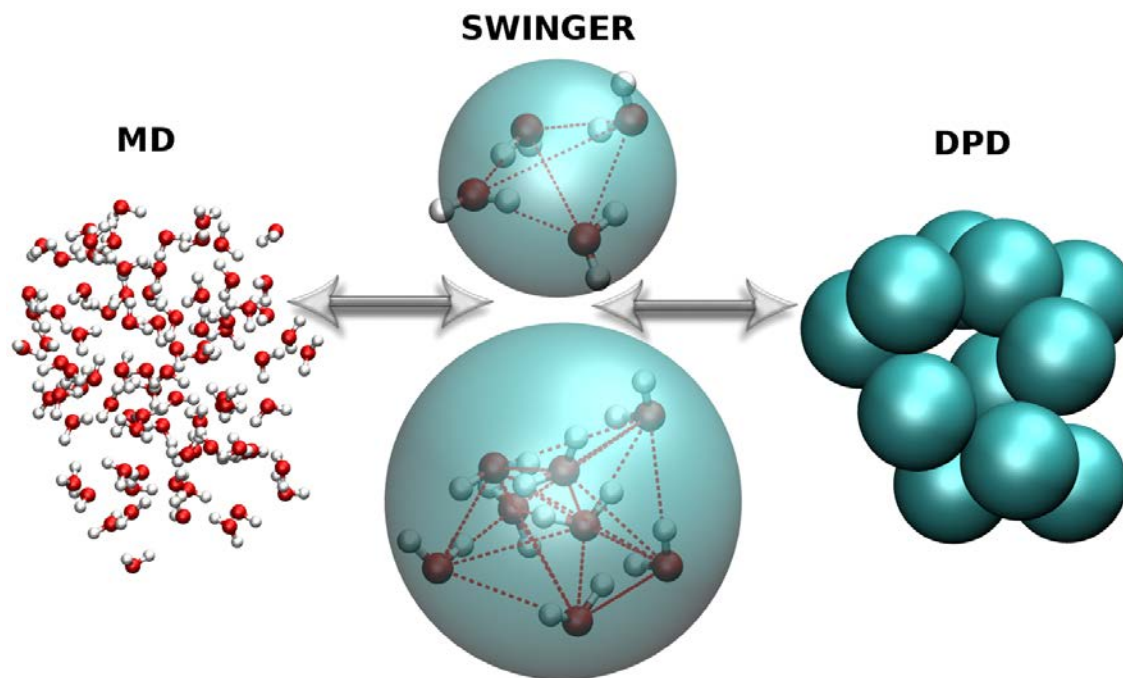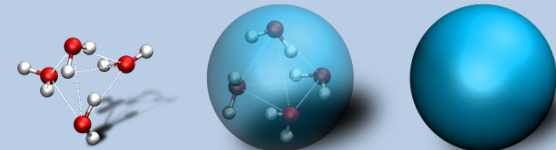Zavadlav, Marrink, Praprotnik; *J. Chem. Theory Comput*. (2016)

Free SPC/MARTINI water

➢ SWINGER algorithm

Zavadlav, Marrink, Praprotnik; *J. Chem. Theory Comput*. (2016)

MD/DPD water

MD   **SWINGER**   **DPD**

MD:

$$\mathbf{F}_{ij}^{MD,C}(\mathbf{r}_{ij}) = -\frac{\partial U^{MD}}{\partial \boldsymbol{r}_{ij}}$$
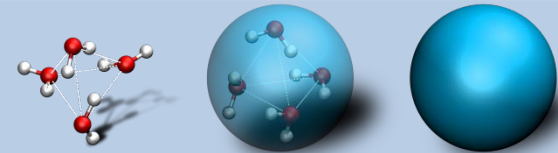
DPD:

$$\mathbf{F}_{\alpha\beta}^{DPD,C}(\mathbf{R}_{\alpha\beta}) = a_{\alpha\beta}(1 - R_{\alpha\beta}/R_c)\hat{\mathbf{R}}_{\alpha\beta}$$

$$\mathbf{F}_{\alpha\beta}^{DPD,R}(\mathbf{R}_{\alpha\beta}) = \sqrt{2\gamma_{\alpha\beta}k_B T}(1 - R_{\alpha\beta}/R_c)\zeta_{ij}\hat{\mathbf{R}}_{\alpha\beta}$$
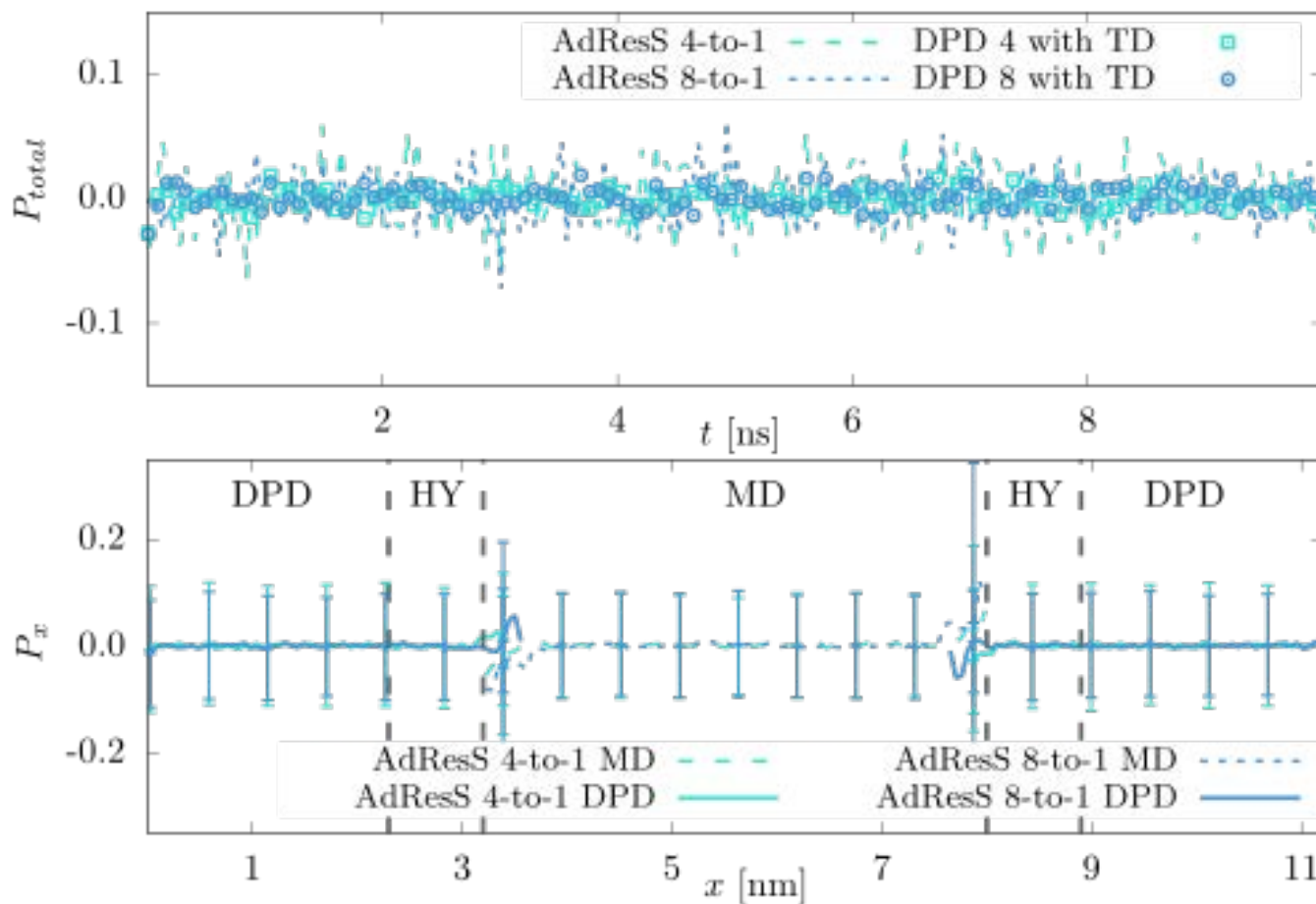
$$\mathbf{F}_{\alpha\beta}^{DPD,D}(\mathbf{R}_{\alpha\beta}) = -\gamma_{\alpha\beta}(1 - R_{ij}/R_c)^2(\hat{\mathbf{R}}_{\alpha\beta} \cdot \mathbf{V}_{\alpha\beta})\hat{\mathbf{R}}_{\alpha\beta}$$
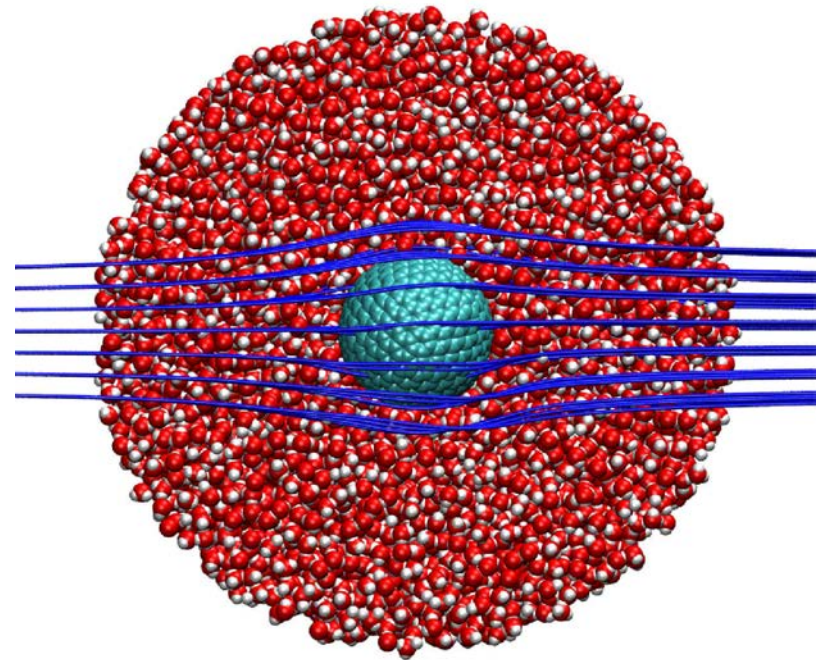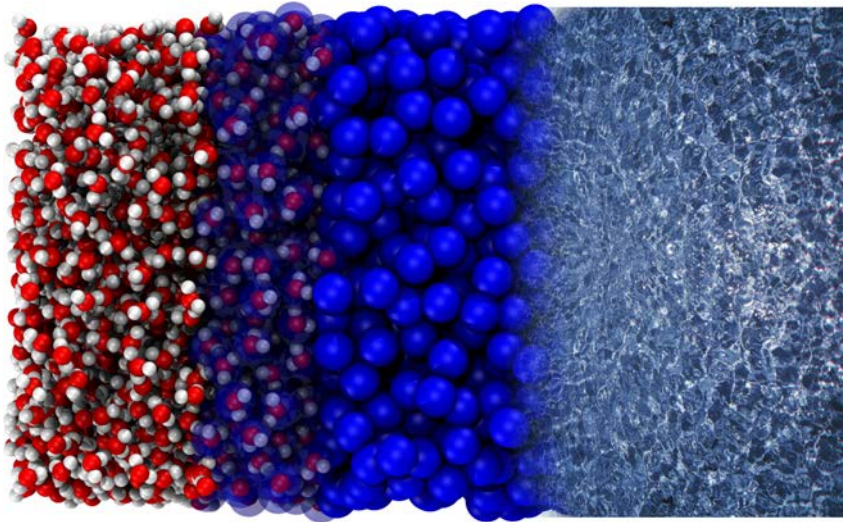
Zavadlav, Praprotnik; *J. Chem. Phys. (2017)*

MD/DPD water

➢ conservation of linear momentum

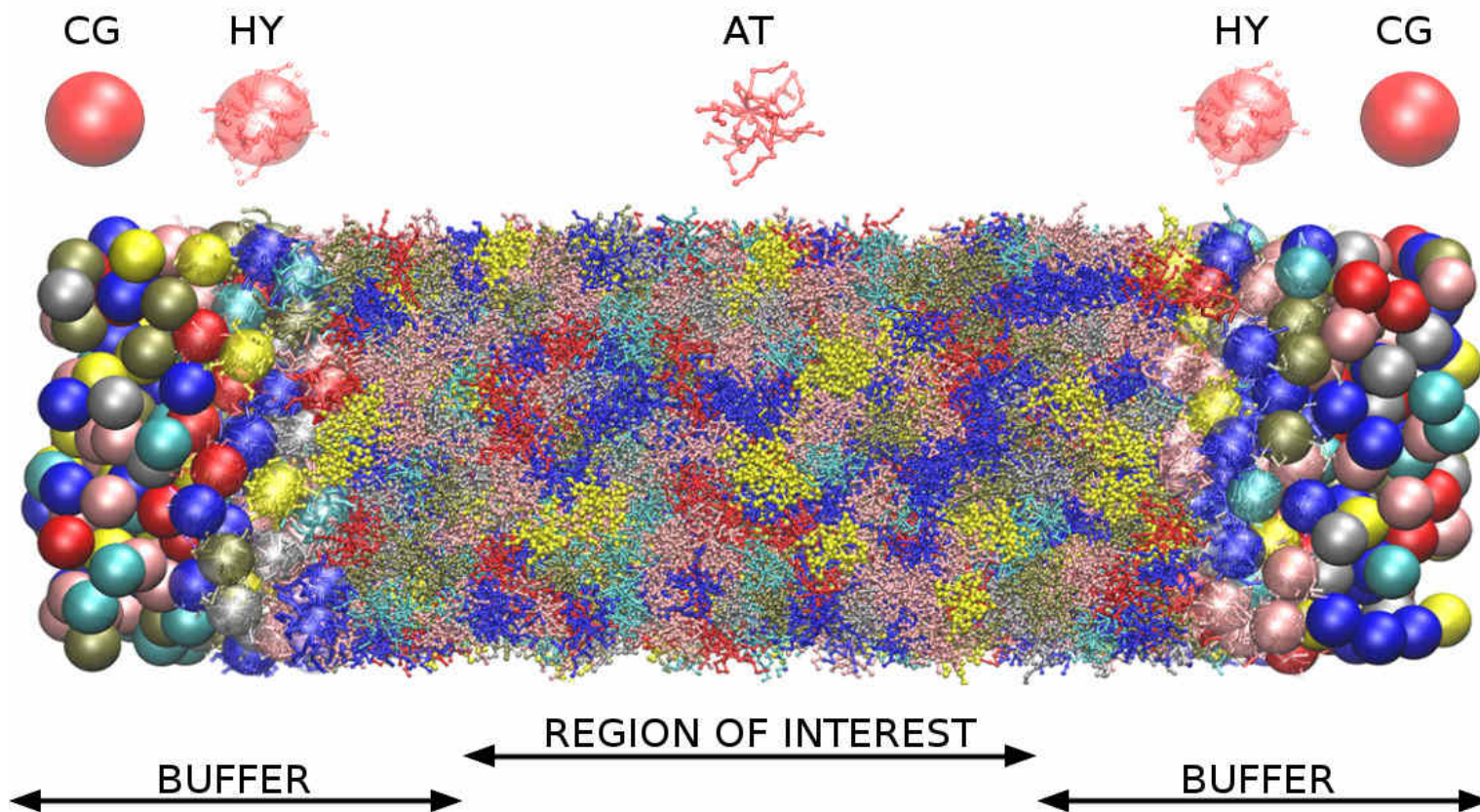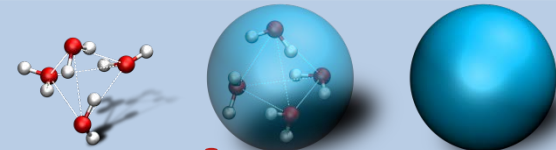Zavadlav, Praprotnik; *J. Chem. Phys. (2017)*

Coupling to CFD
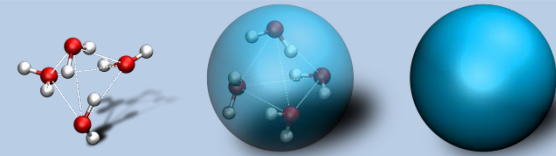
Delgado-Buscalioni, Sablić, Praprotnik; *Eur. Phys. J. Special Topics* (2015)
Walther et al.; *J. Comput. Phys.* (2012)

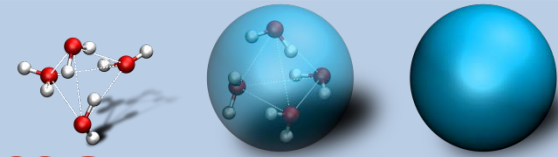# Open Boundary Molecular Dynamics

Delgado-Buscalioni, Sablić, Praprotnik; *Eur. Phys. J. Special Topics* (2015)

Sablić, Praprotnik, Delgado-Buscalioni; *Soft Matter* (2016)

Delle Site, Praprotnik; Phys. Rep. (2017)
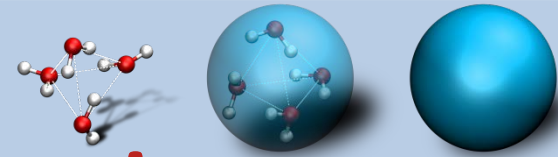
Thermodynamic systems

➢ isolated systems:

  1. no exchange of matter and energy with the surroundings

➢ closed systems:

  1. exchange of energy, no exchange of matter

  2. constant number of particles

➢ open systems:

  1. exchange of matter and energy

  2. number of particles fluctuates

Open Boundary Molecular Dynamics

➢ system exchanges mass, momentum, and energy with its

surroundings

1. Insertion of molecules: $\Delta N_B = \dfrac{\Delta t}{\tau_r}\left(\alpha\langle N_B\rangle - N_B\right)$

2. Multiscale buffers -> facilitates insertion

➢ external boundary condition

1. Linear momentum conservation

2. Additional force in buffers: $F^{ext} = J \cdot n_B A + \dfrac{P_{out} - P_{in}}{\Delta t} + \sum_\alpha F_\alpha^{TD}$

➢ DPD thermostat: $F_\alpha^{thermo} = \sum_{i\in\alpha; j\in\beta, \alpha\neq\beta} \sigma\omega^R(r_{ij})\zeta_{ij}\hat{r}_{ij} - \gamma\omega^D(r_{ij})(\hat{r}_{ij}\cdot v_{ij})\hat{r}_{ij}$
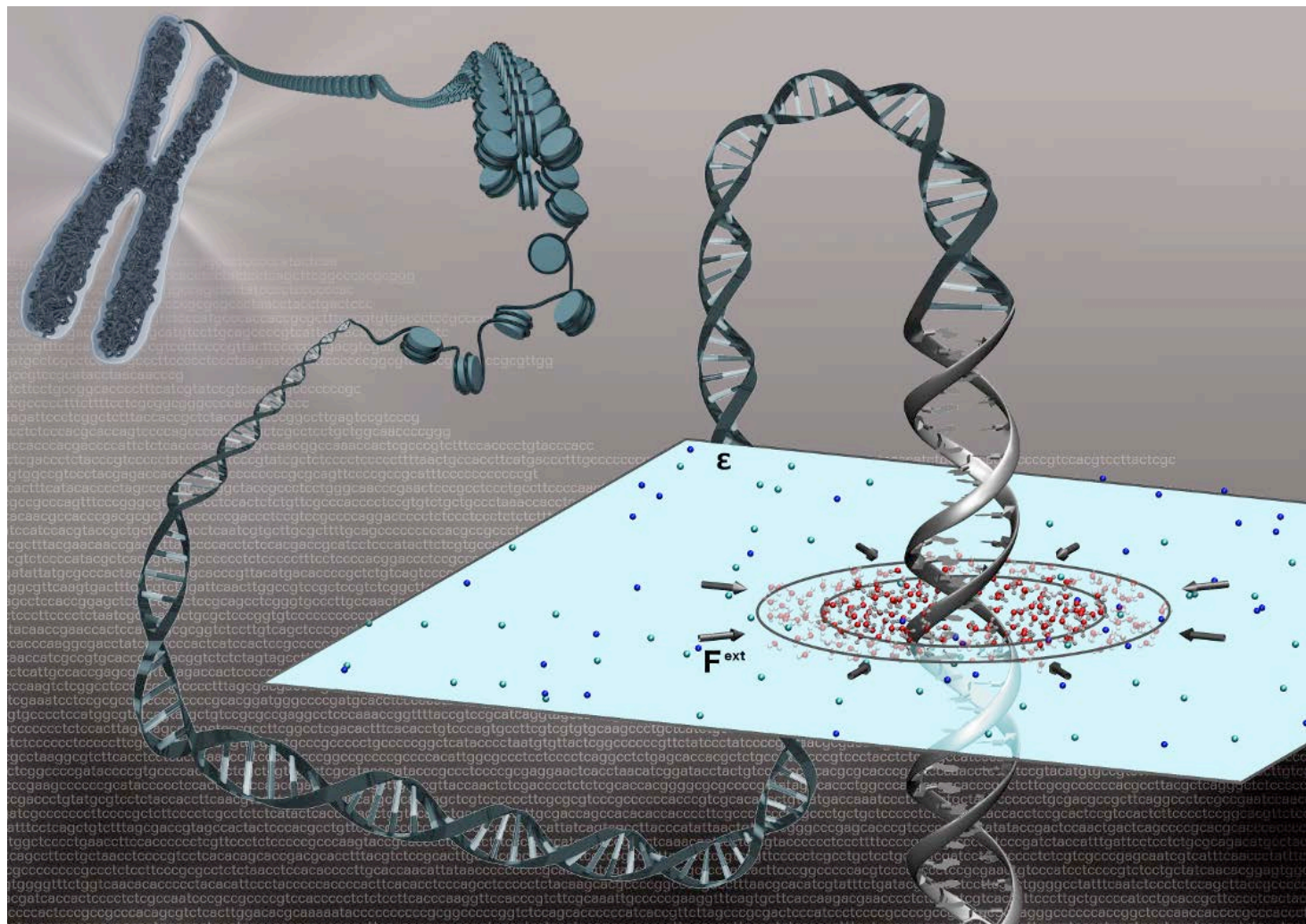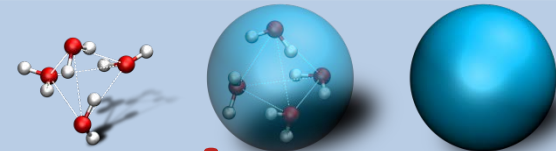
➢ total force on each particle:

$$\omega^D(r_{ij}) = \left[\omega^R(r_{ij})\right]^2 \sigma^2 = 2k_B T\gamma$$

$$F_\alpha = F_\alpha^{AdResS} + F_\alpha^{ext} + F_\alpha^{thermo}$$

Open Boundary Molecular Dynamics

Zavadlav, Sablić, Podgornik, Praprotnik; *Biophys. J.* (2018)

Open Boundary Molecular Dynamics
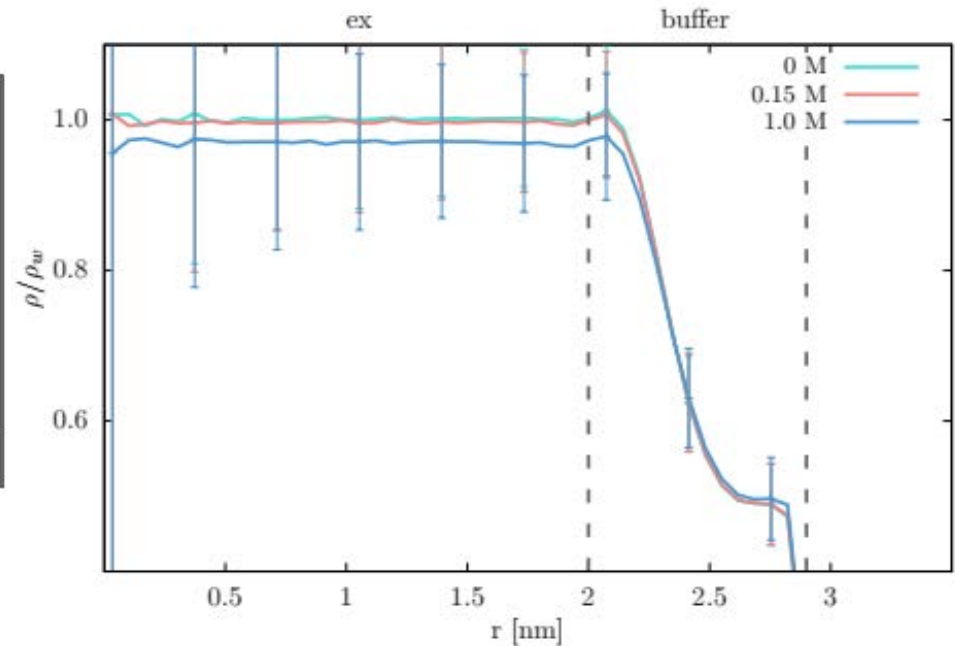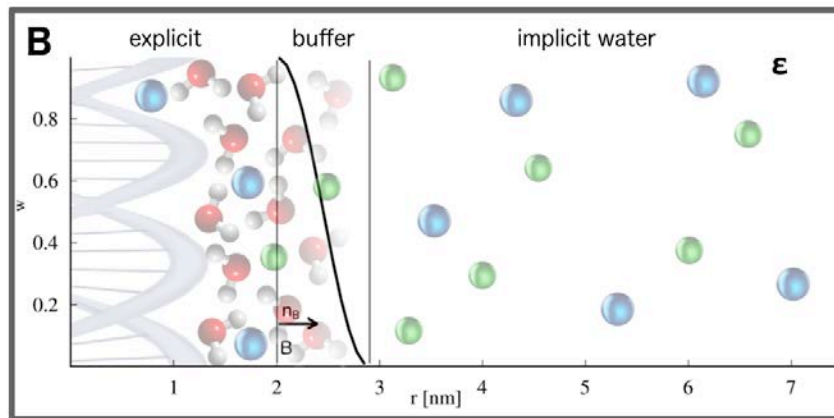

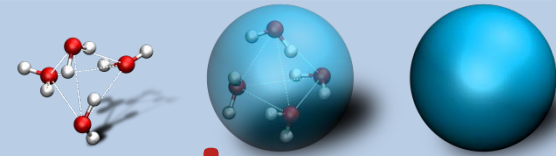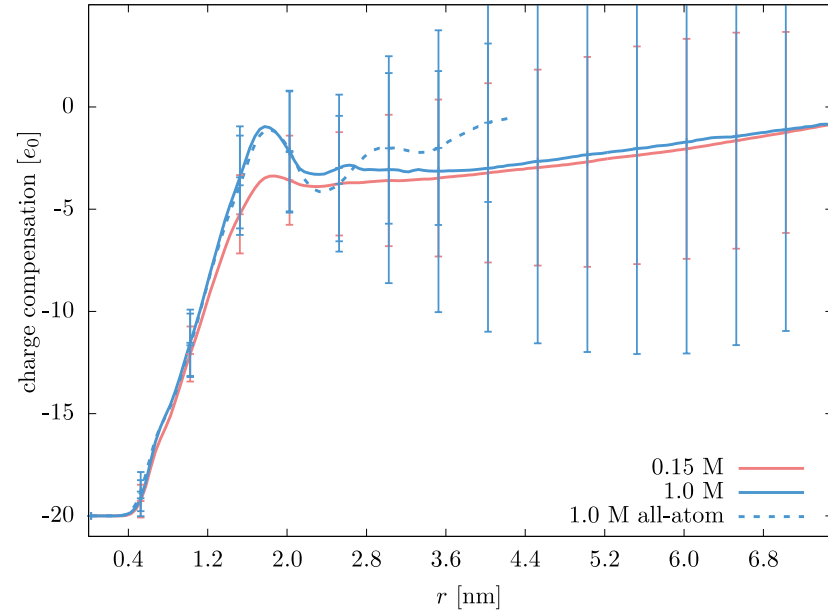Zavadlav, Sablić, Podgornik, Praprotnik; *Biophys. J.* (2018)

Open Boundary Molecular Dynamics

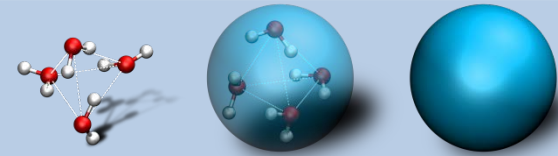Zavadlav, Sablić, Podgornik, Praprotnik; *Biophys. J.* (2018)
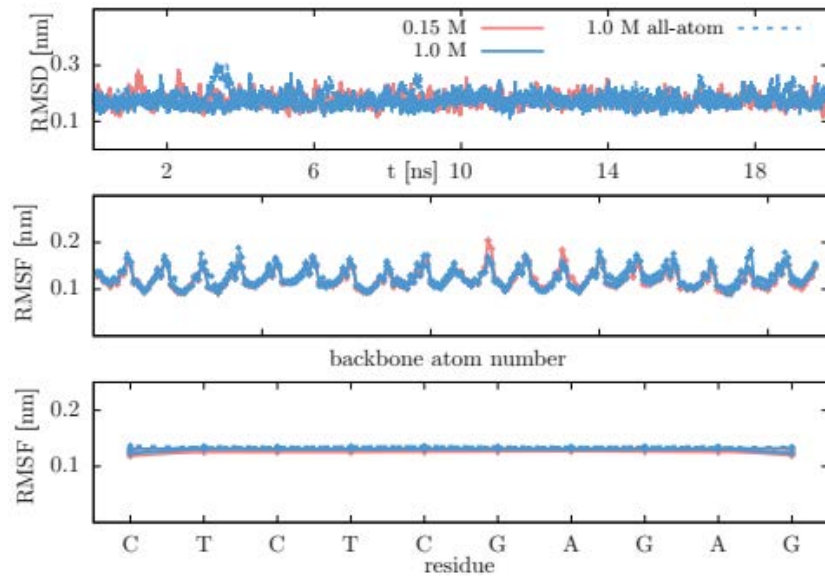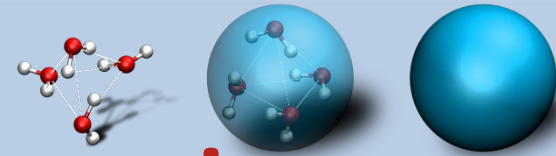
Conclusions

➢ OBMD:

- Allows for simulation of open systems that can exchange mass, energy, and linear momentum with the environment.

- Enables us to perform efficient molecular dynamics simulations of molecular liquids in the grand-canonical ensemble or under non-equilibrium flows.

- In the explicit domain, the water molecules and ions are both overtly present in the system, whereas in the implicit water domain, only the ions are explicitly present and the water is described as a continuous dielectric medium.

- Water molecules are inserted and deleted into/from the system in the intermediate buffer domain that acts as a water reservoir to the explicit domain, with both water molecules and ions free to enter or leave the explicit domain.

- Our approach is general and allows for efficient molecular simulations of biomolecules solvated in bathing salt solutions at any ionic strength condition.

Acknowledgements
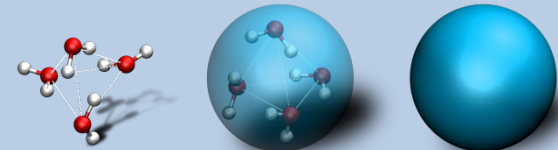
➢ **Staš Bevc**; Gocan d.o.o., Slovenia

➢ **Julija Zavadlav**; TUM, Germany

➢ **Jurij Sablić**; National Institute of Chemistry, Slovenia

➢ **Rudolf Podgornik**; University of CAS, China

➢ **Siewert J. Marrink**; University of Groningen, The Netherlands

➢ **Rafael Delgado-Buscalioni**; UAM, Madrid, Spain