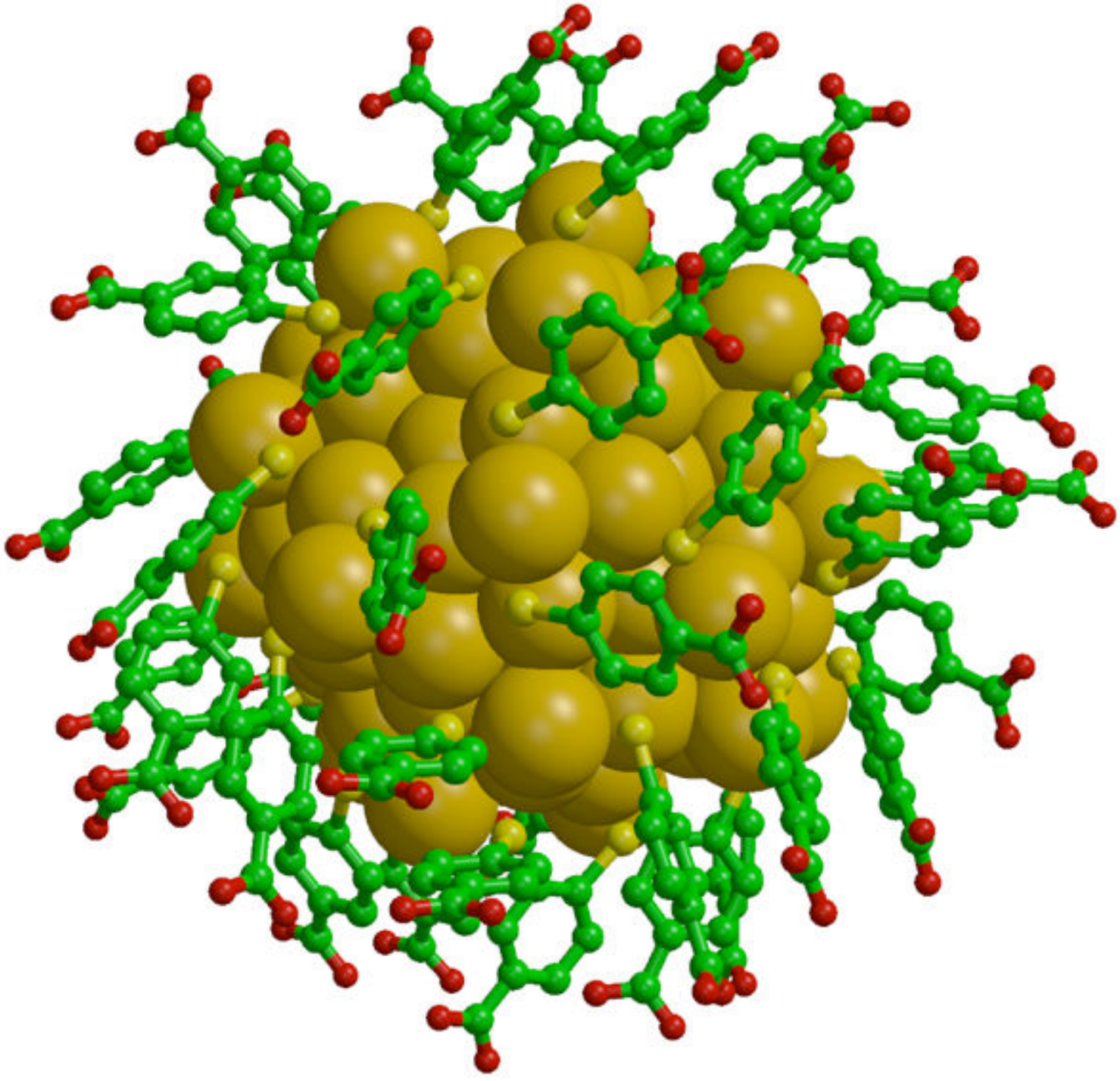
Bling Bling particles

Gerrit Groenhof
Nanoscience Center & Department of Chemistry



Molecular dynamics simulations

Isaac Newton

classical nuclei

$$\mathbf{F}_i = -\nabla_{\mathbf{R}_i} V(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) = m_i \frac{d^2}{dt^2} \mathbf{R}_i$$

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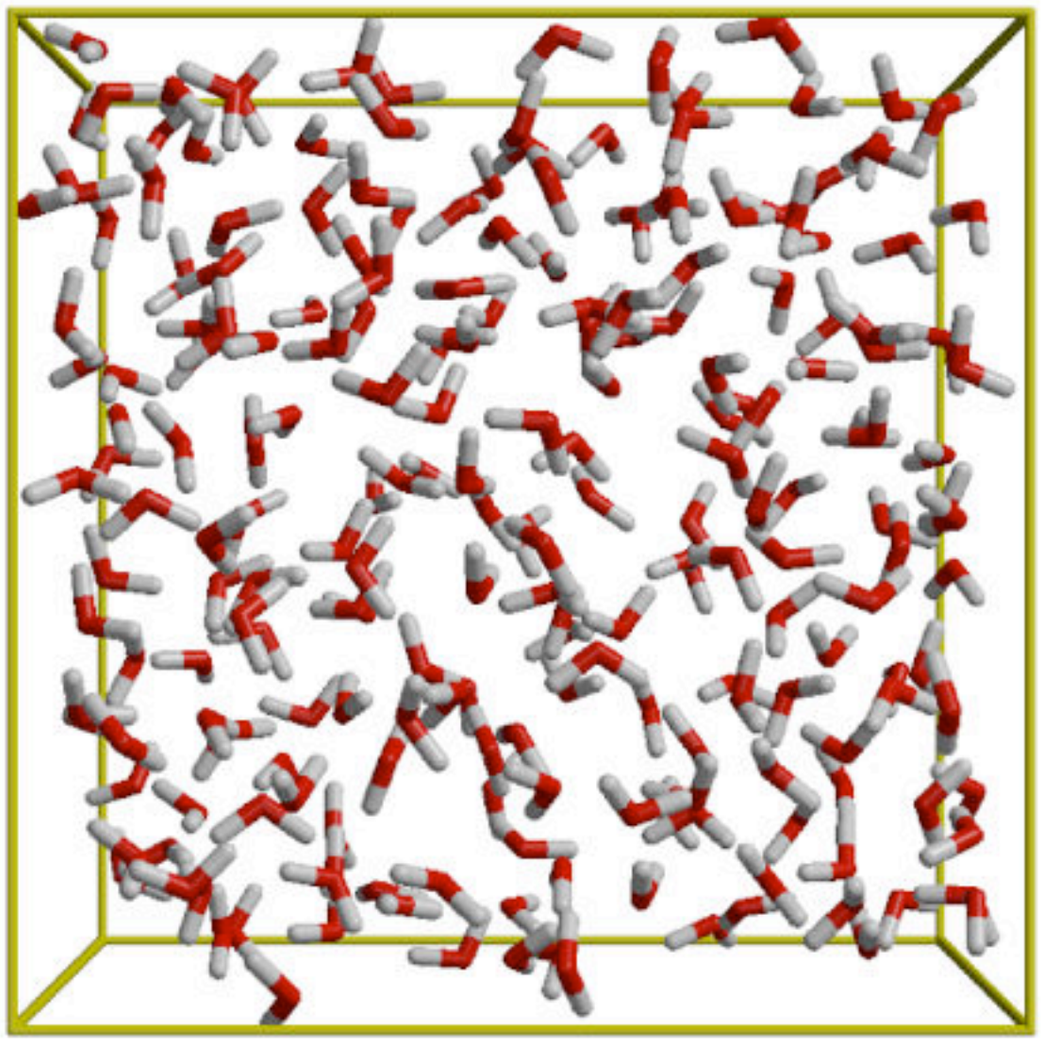
trajectory

jiggling & wiggling



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potential energy functions

Molecular dynamics simulations

Isaac Newton

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potential energy functions

quantum chemistry

Erwin Schrödinger

$$V^{\mathrm{QM}}(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) =$$

$$\langle \Psi_e(\mathbf{r}_1, \mathbf{r}_2, ...\mathbf{r}_n) | \hat{H}_e(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) | \Psi_e(\mathbf{r}_1, \mathbf{r}_2, ...\mathbf{r}_n) \rangle$$

Molecular dynamics simulations

Isaac Newton

classical nuclei

$$\mathbf{F}_i = -\nabla_{\mathbf{R}_i} V(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) = m_i \frac{d^2}{dt^2} \mathbf{R}_i$$

potential energy functions

Erwin Schrödinger

quantum chemistry (QM)

$$V^{\mathrm{QM}}(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) =$$

$$\langle \Psi_e(\mathbf{r}_1, \mathbf{r}_2, ...\mathbf{r}_n) | \hat{H}_e(\mathbf{R}_1, \mathbf{R}_2, ..., \mathbf{R}_N) | \Psi_e(\mathbf{r}_1, \mathbf{r}_2, ...\mathbf{r}_n) \rangle$$

molecular mechanics (MM)

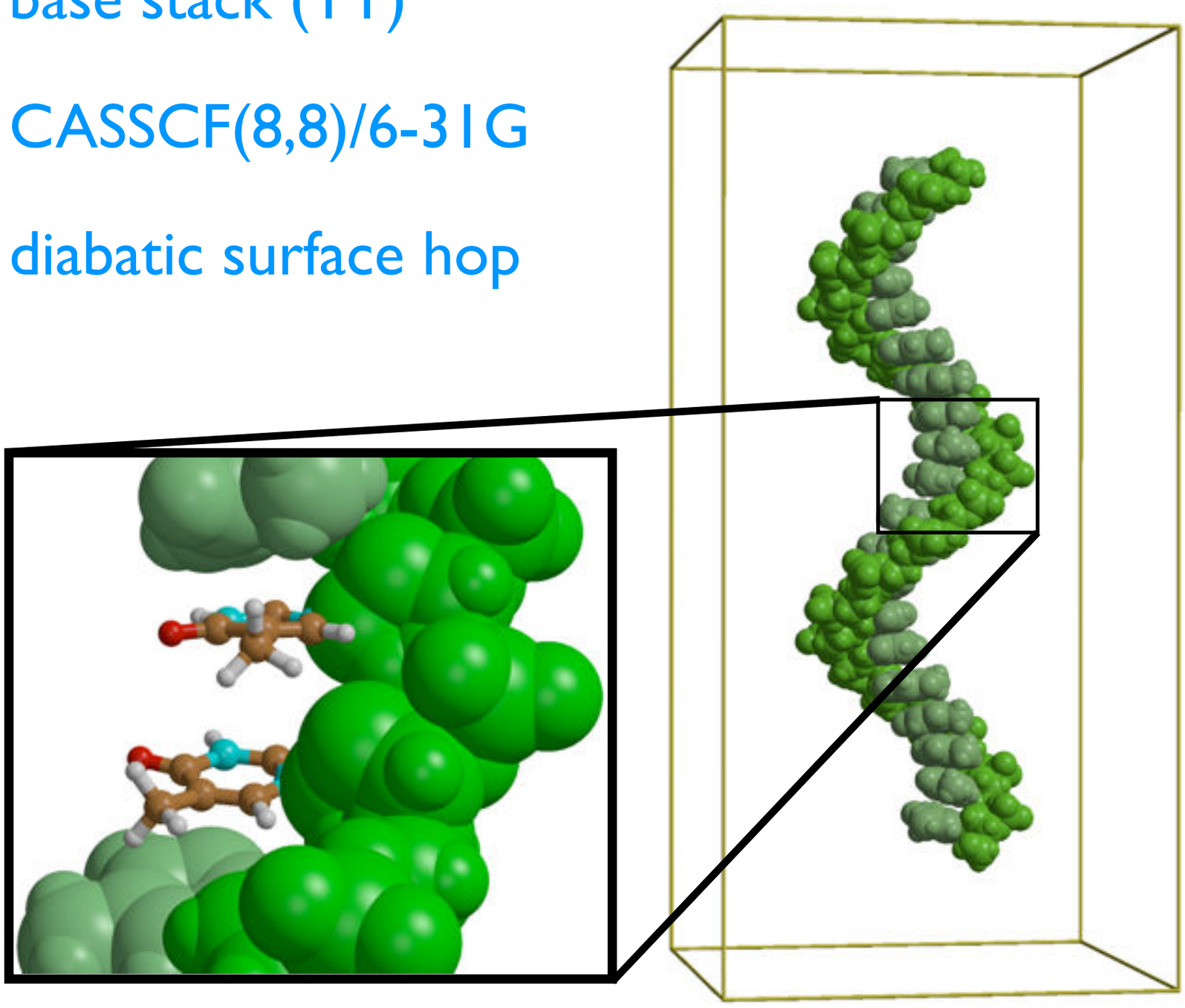
empirical functions with parameters

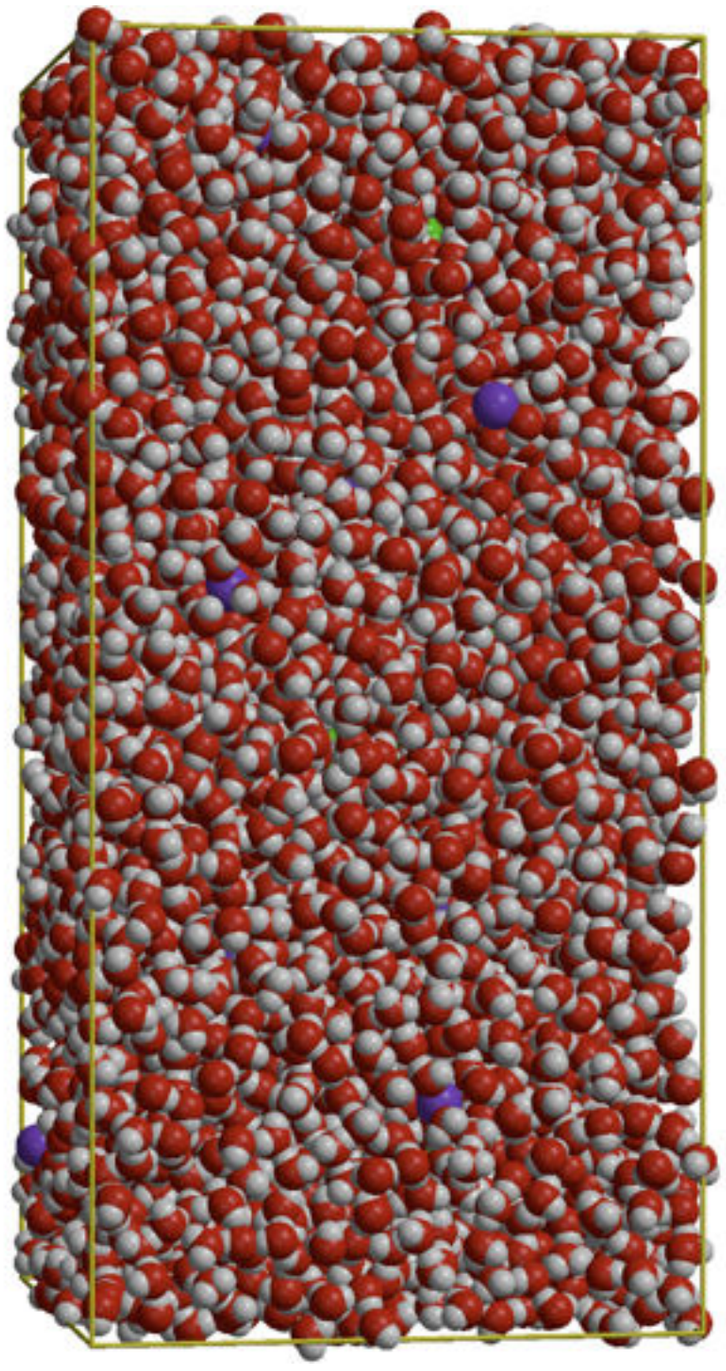
$$V^{\mathrm{MM}}(R_1, R_2, ..., R_N) = \sum_k v_k(R_i, R_j, R_k, R_l; \{p_k\})$$

Observe while it all happens

computer simulations of DNA photodamage

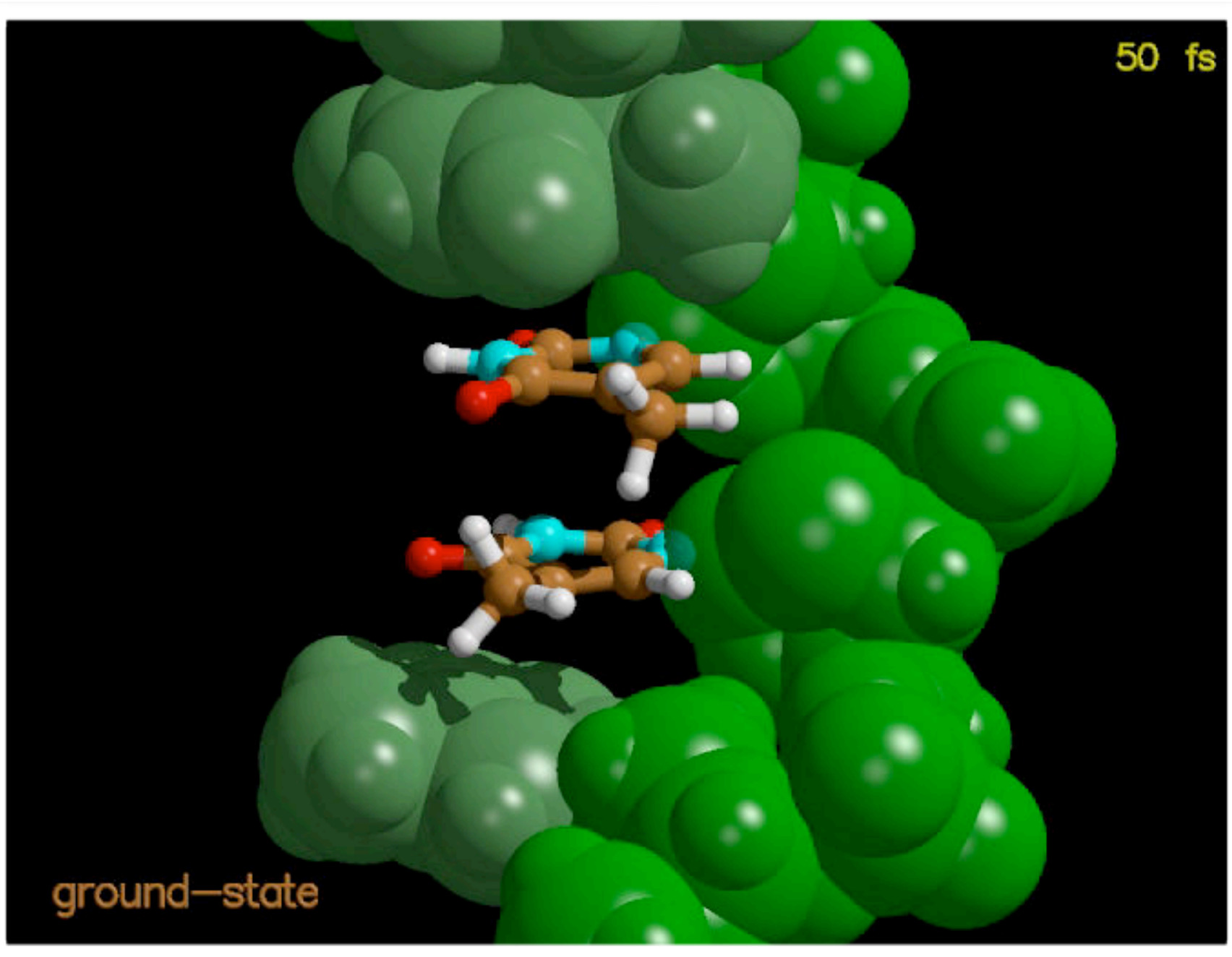
- base stack (TT)
- CASSCF(8,8)/6-31G
- diabatic surface hop





Observe while it all happens

excited-state simulation of TT base stack



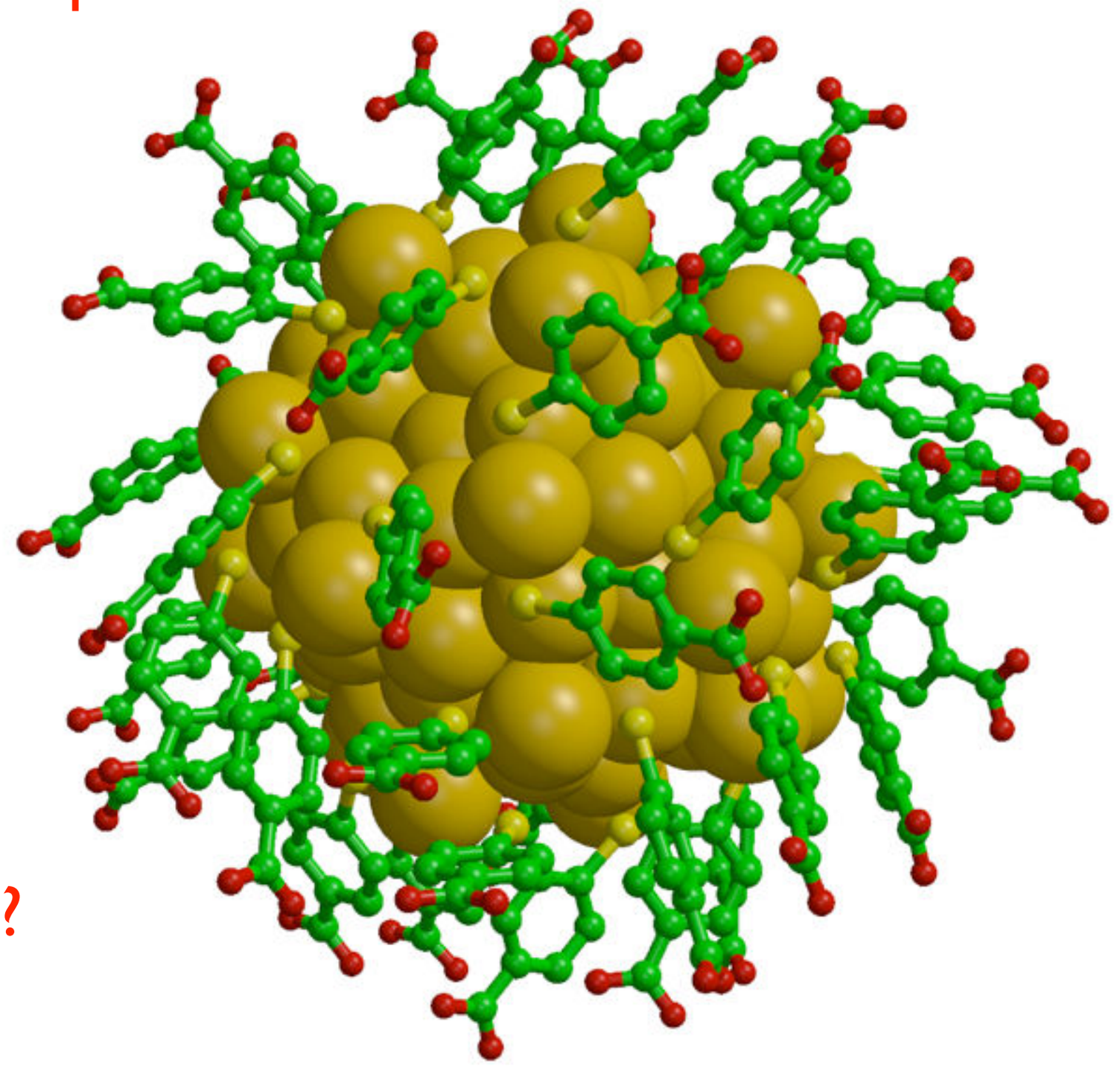
Today's project

Monolayer protected gold nanoparticles

claim: these are very important

who knows?

easy to publish



pK_a of nanoparticle?

44 protanatable sites

anti-cooperativity

microscopic pK_a's

What's actually a pK_a?

who knows?

Constant pH molecular dynamics simulations

requirements

sample of configuration & protonation state space

control rate of transition between protonation states

fully atomistic description

explicit solvent

Serena Donnini

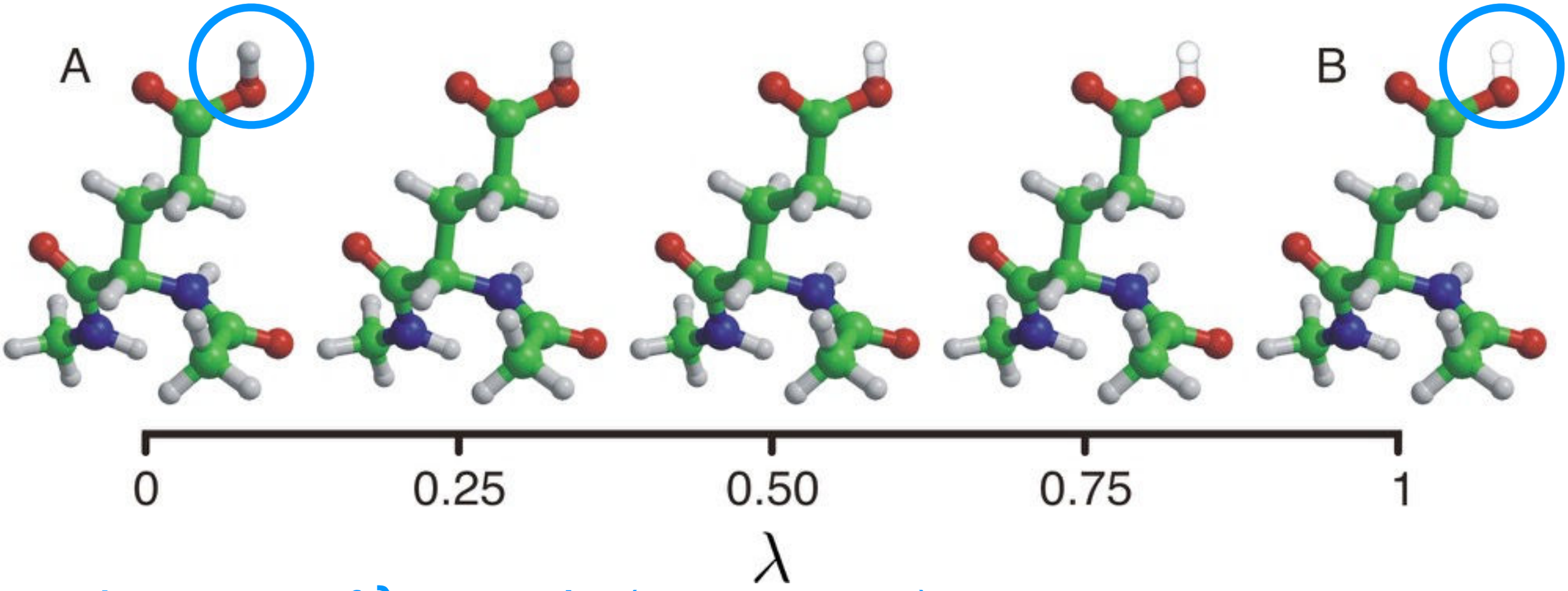
Florian Tegeler

Helmut Grubmüller

Donnini et al. *J. Chem. Theory. Comp.* 7 (2011) 1962

Molecular dynamics at constant pH

protons as extra degrees of freedom



dynamics of λ-particle (protonation)

$$m_\lambda d^2\lambda/dt^2 = -\partial V(\mathbf{x},\lambda)/\partial\lambda$$

X. Kong & C.L. Brooks J. Chem. Phys. 105 (1996) 2414

M.S. Lee, J.F.R. Salsbury, C.L. Brooks Proteins 56 (2004) 738

Molecular dynamics at constant pH

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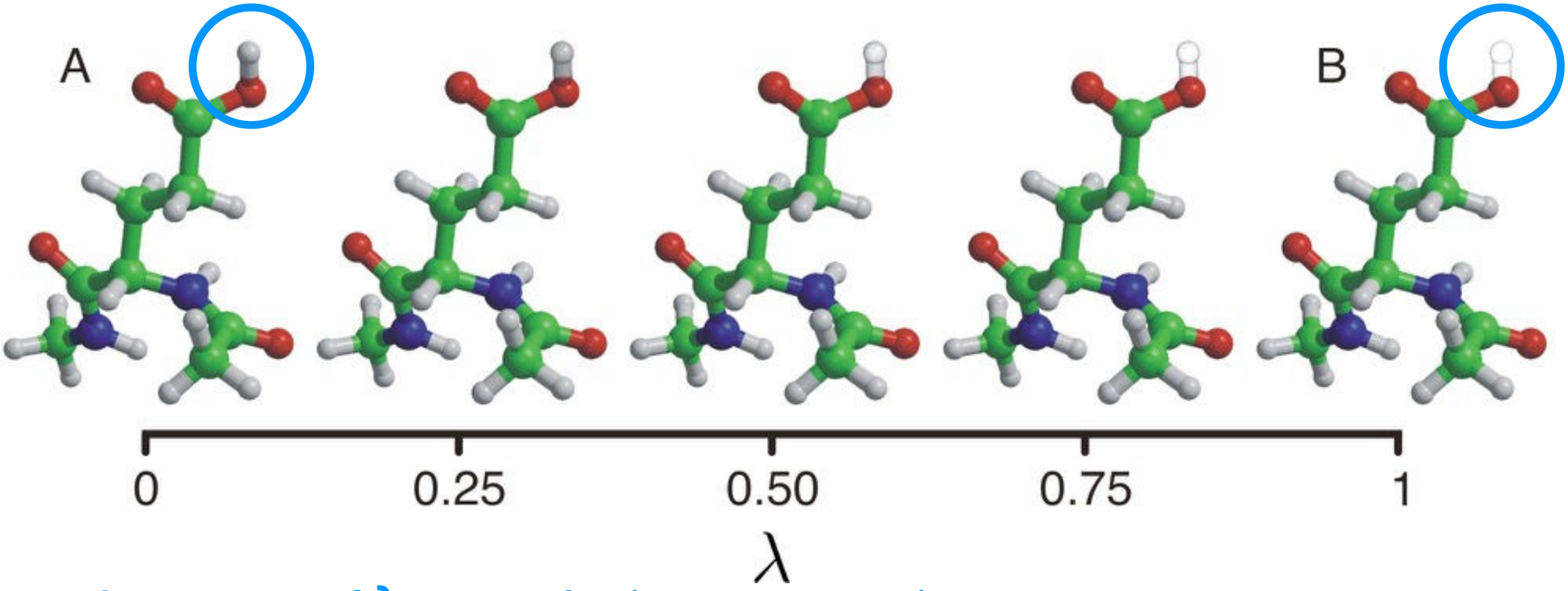

dynamics of λ-particle (protonation)

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$$V(\mathbf{x},\lambda) = (1-\lambda)V^{\mathrm{A}}(\mathbf{x}) + \lambda V^{\mathrm{B}}(\mathbf{x}) + U(\lambda) +$$

$$\lambda RT\ln(10)[pK^{\mathrm{exp}}_{\mathrm{a,\ ref}} - pH] + \Delta\tilde{G}^{\mathrm{corr}}_{\mathrm{MM}}(\lambda)$$

$$V(\mathbf{x},\lambda) \quad = \quad (1-\lambda)V^{\mathrm{A}}(\mathbf{x}) + \lambda V^{\mathrm{B}}(\mathbf{x}) + U(\lambda) +$$

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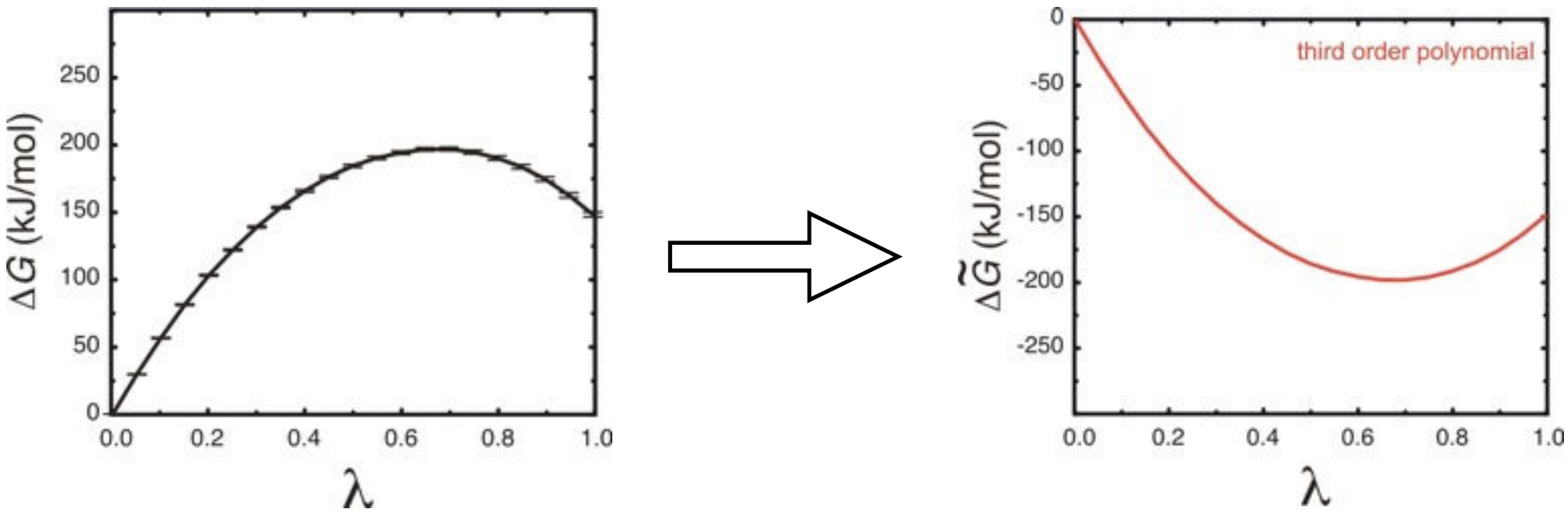
$\Delta\tilde{G}_{\mathrm{MM}}^{\mathrm{corr}}(\lambda)$ obtained by thermodynamic integration (pH = pK_a)



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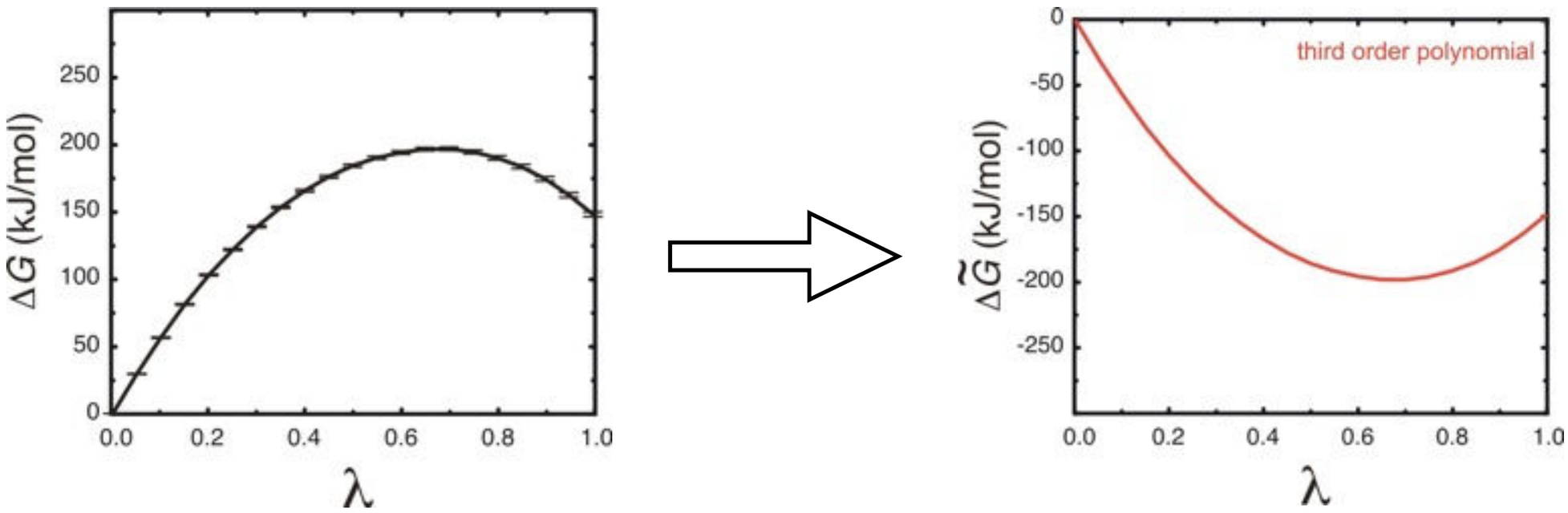
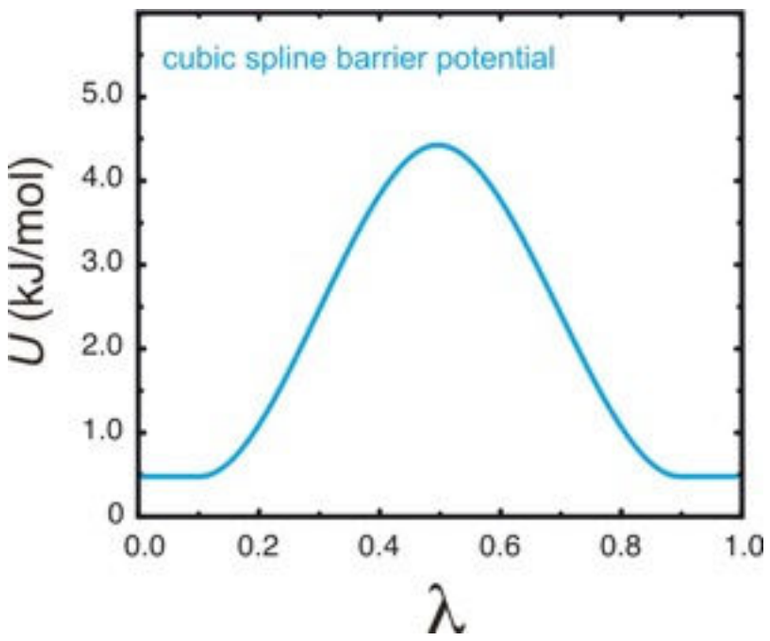


barrier potential



$$V(\mathbf{x},\lambda) = (1-\lambda)V^{\mathrm{A}}(\mathbf{x}) + \lambda V^{\mathrm{B}}(\mathbf{x}) + U(\lambda) + \lambda RT\ln(10)[pK_{\mathrm{a,\,ref}}^{\mathrm{exp}} - pH] + \Delta\tilde{G}_{\mathrm{MM}}^{\mathrm{corr}}(\lambda)$$

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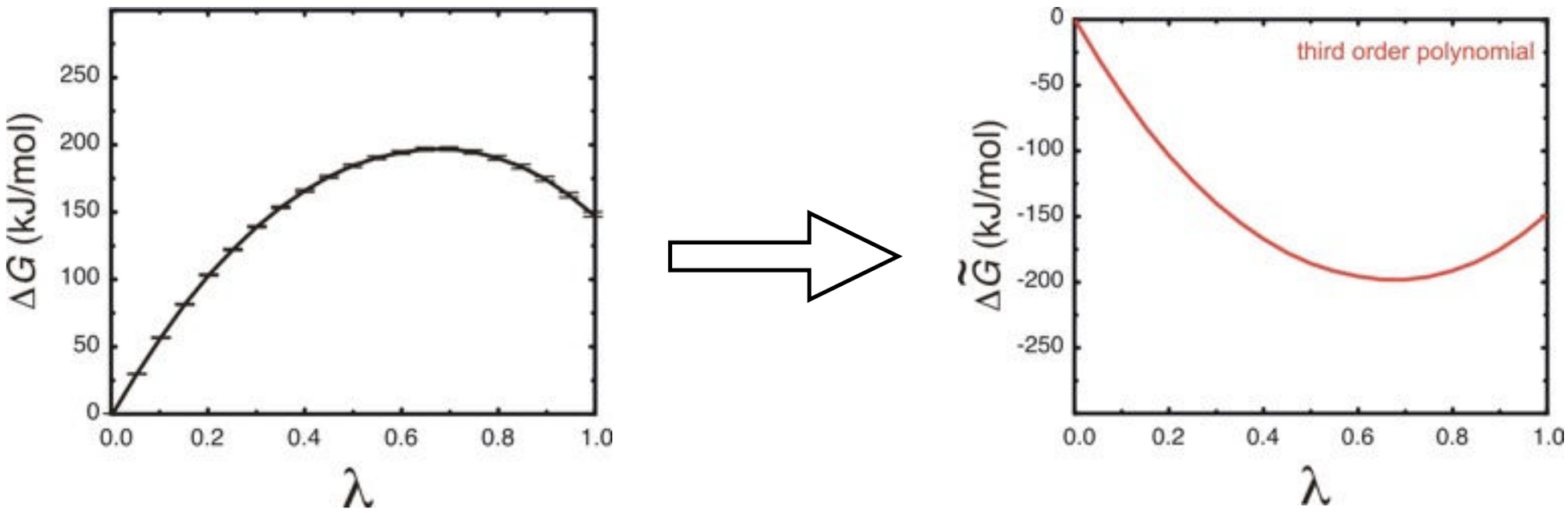
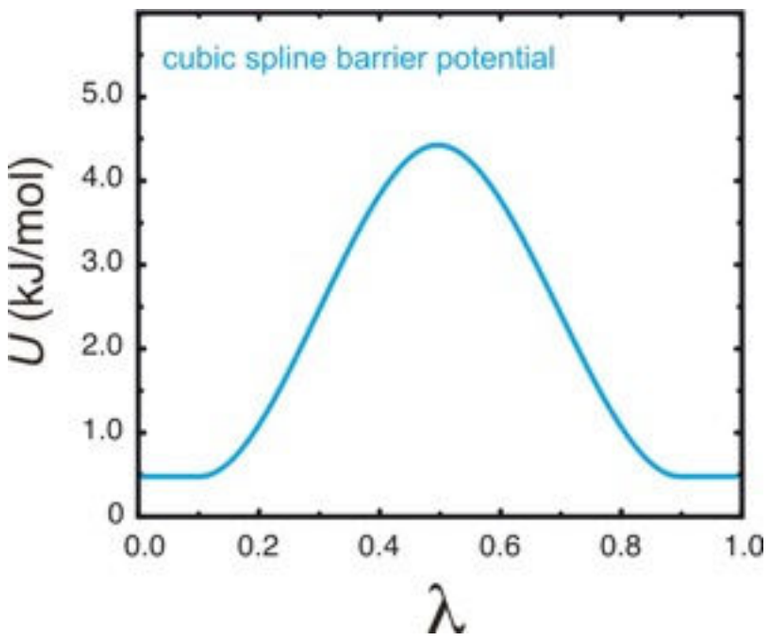
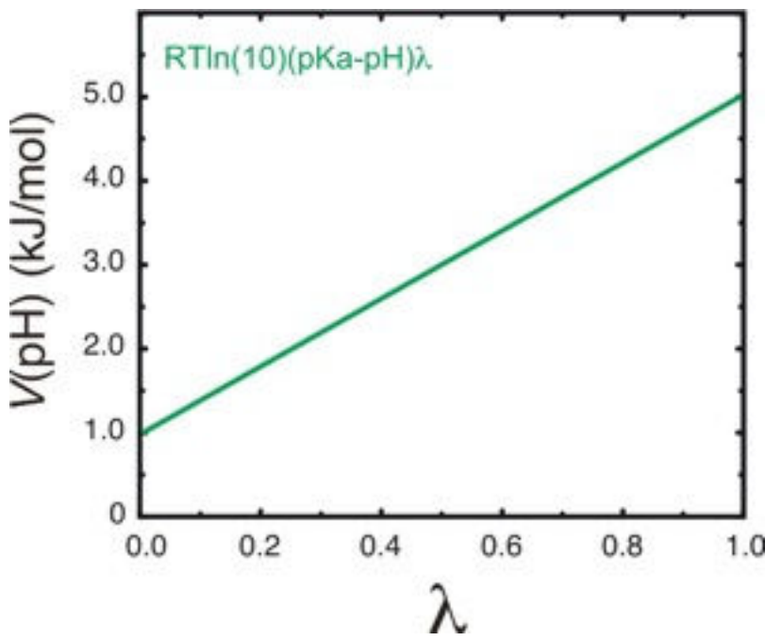


barrier potential

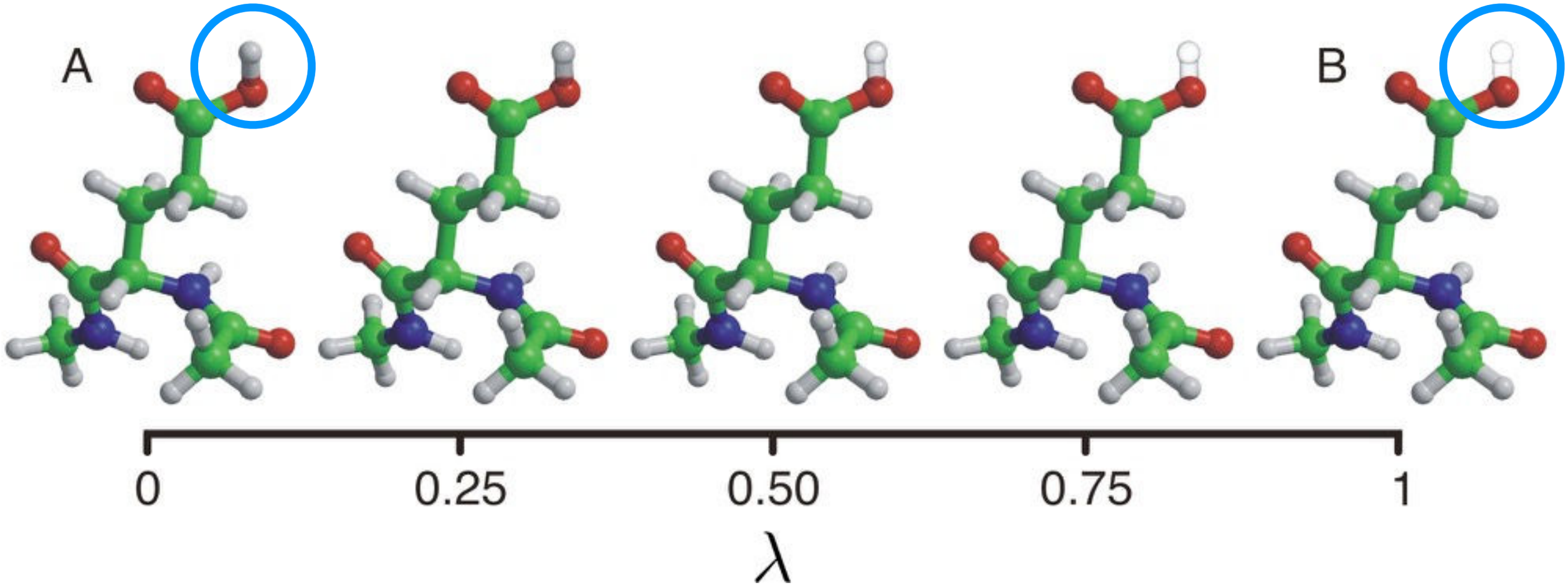


pH dependence



Molecular dynamics at constant pH

protons as extra degrees of freedom



dynamics of multiple λ-particles (protonation states)

$$m_{\lambda_i} d^2\lambda_i/dt^2 = -\partial V(\mathbf{x}, \lambda_i)/\partial\lambda_i$$

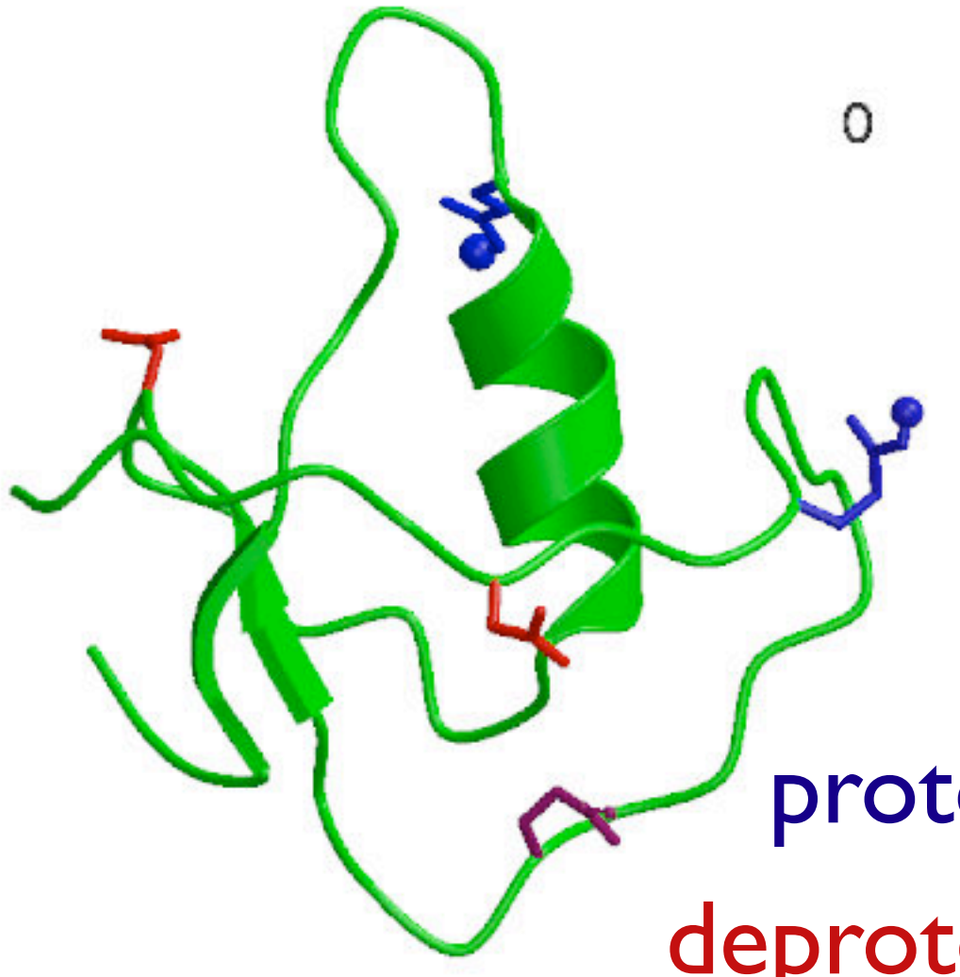
$$V(\mathbf{x}, \lambda_i) = (1-\lambda_i)V^{\mathrm{A}}(\mathbf{x}, \boldsymbol{\lambda}) + \lambda_i V^{\mathrm{B}}(\mathbf{x}, \boldsymbol{\lambda}) + U(\lambda_i) +$$

$$\lambda_i RT \ln(10)[pK_{\mathrm{a,\ ref}}^{\mathrm{exp}} - pH] + \Delta\tilde{G}_{\mathrm{MM}}^{\mathrm{corr}}(\lambda_i, \boldsymbol{\lambda})$$

Molecular dynamics at constant pH

time-dependent protonation states

third domain of turkey ovomucoid inhibitor at pH = 4



protonated

deprotonated

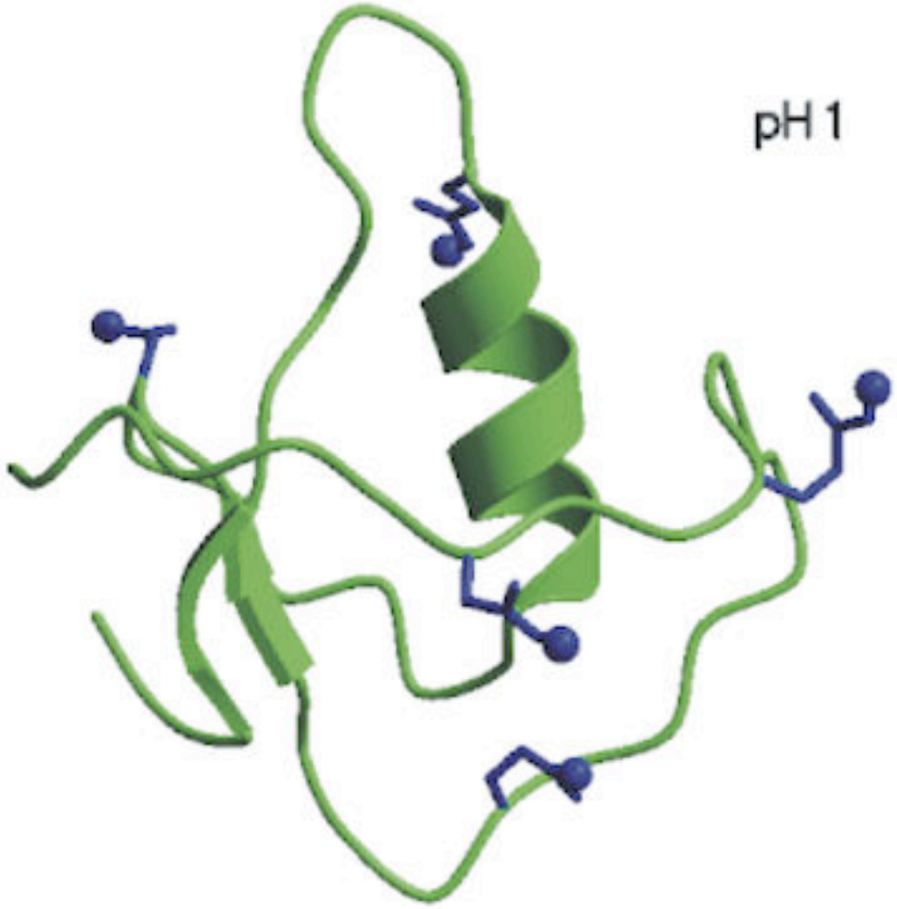
Molecular dynamics at constant pH

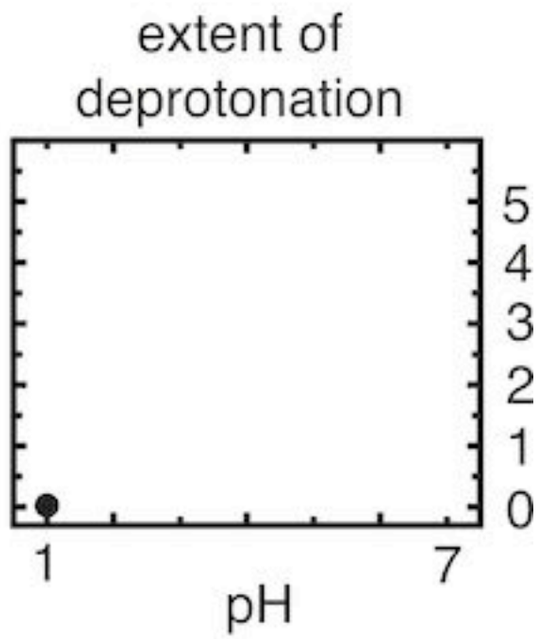
in silico titration experiment

MD simulations at different solvent pH values

Henderson-Hasselbalch

$$\frac{[\mathrm{A}^-]}{[\mathrm{A}^-]+[\mathrm{AH}]} = \frac{1}{10^{n(\mathrm{pK_a}-\mathrm{pH})}+1}$$

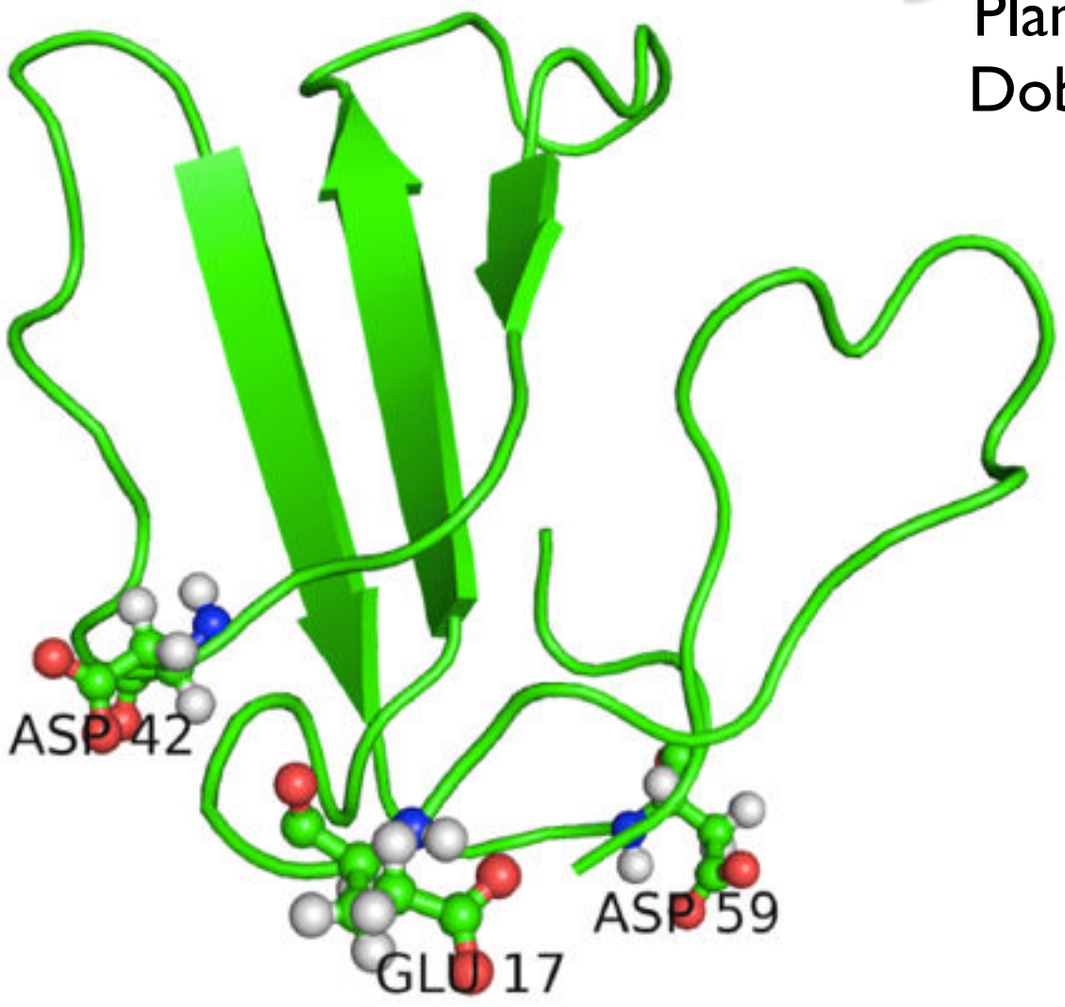


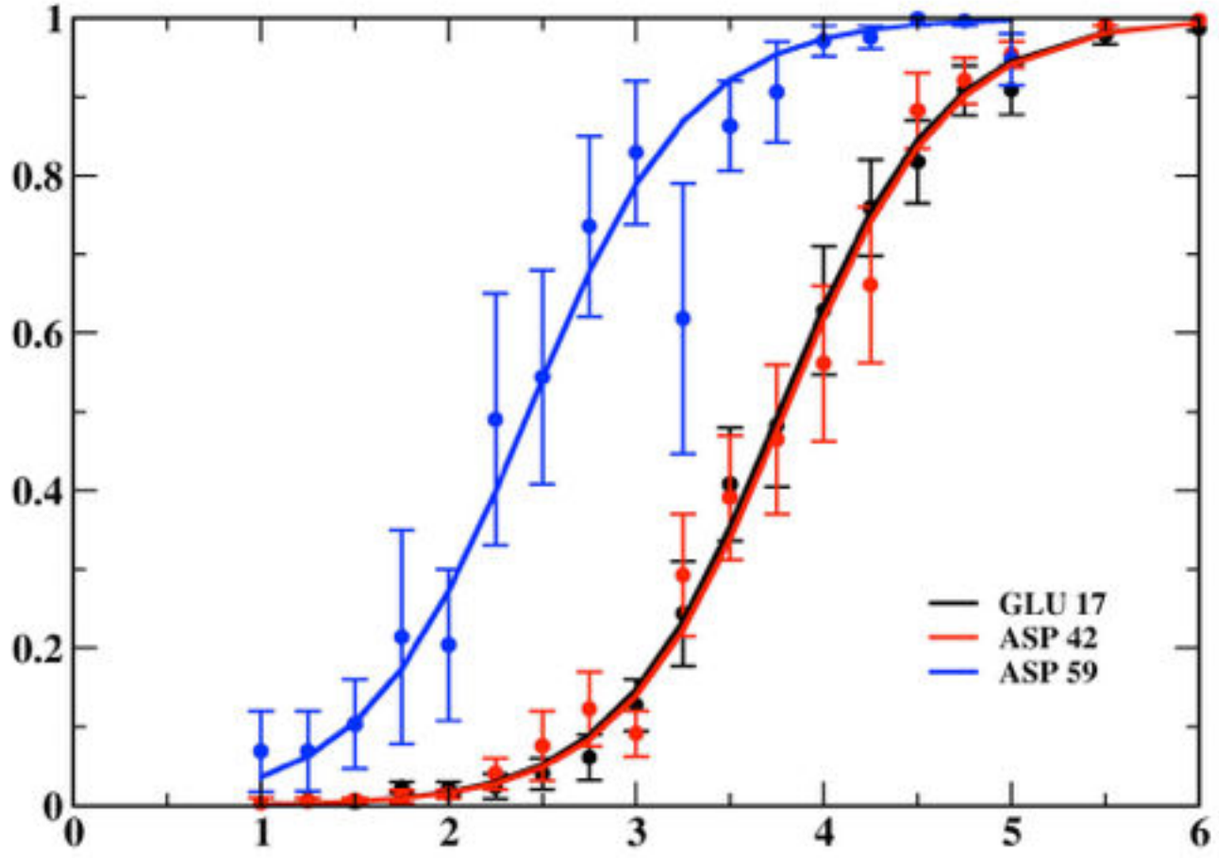


pK_a's in proteins

cardiotoxin V

Plamen Dobrev



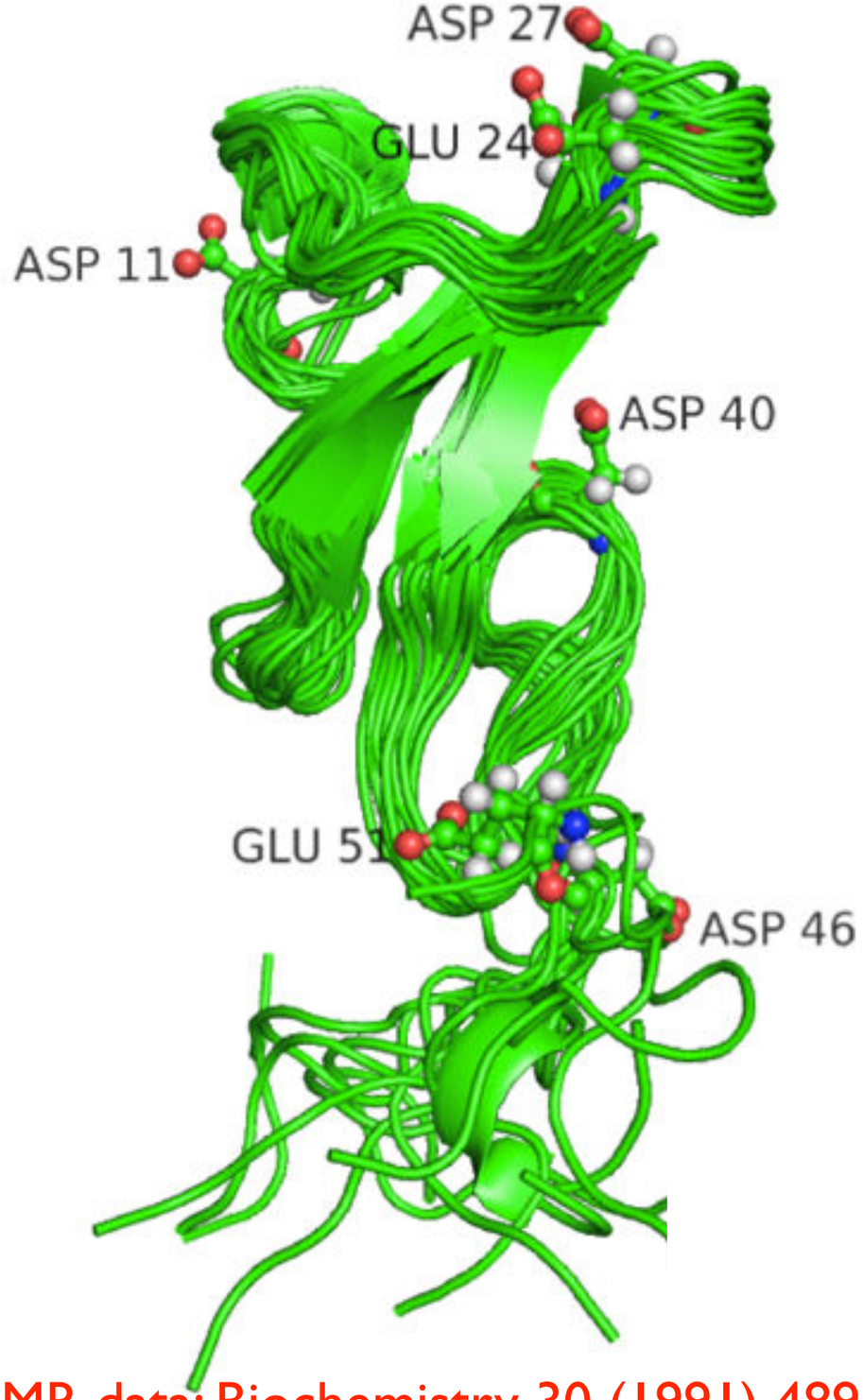


residue	CPHMD	PB	NMR
Glu17	3.77 (0.06)	3,73	4
Asp42	3.8 (0.07)	3,64	3,2
Asp59	2.44 (0.12)	2,84	< 2.3

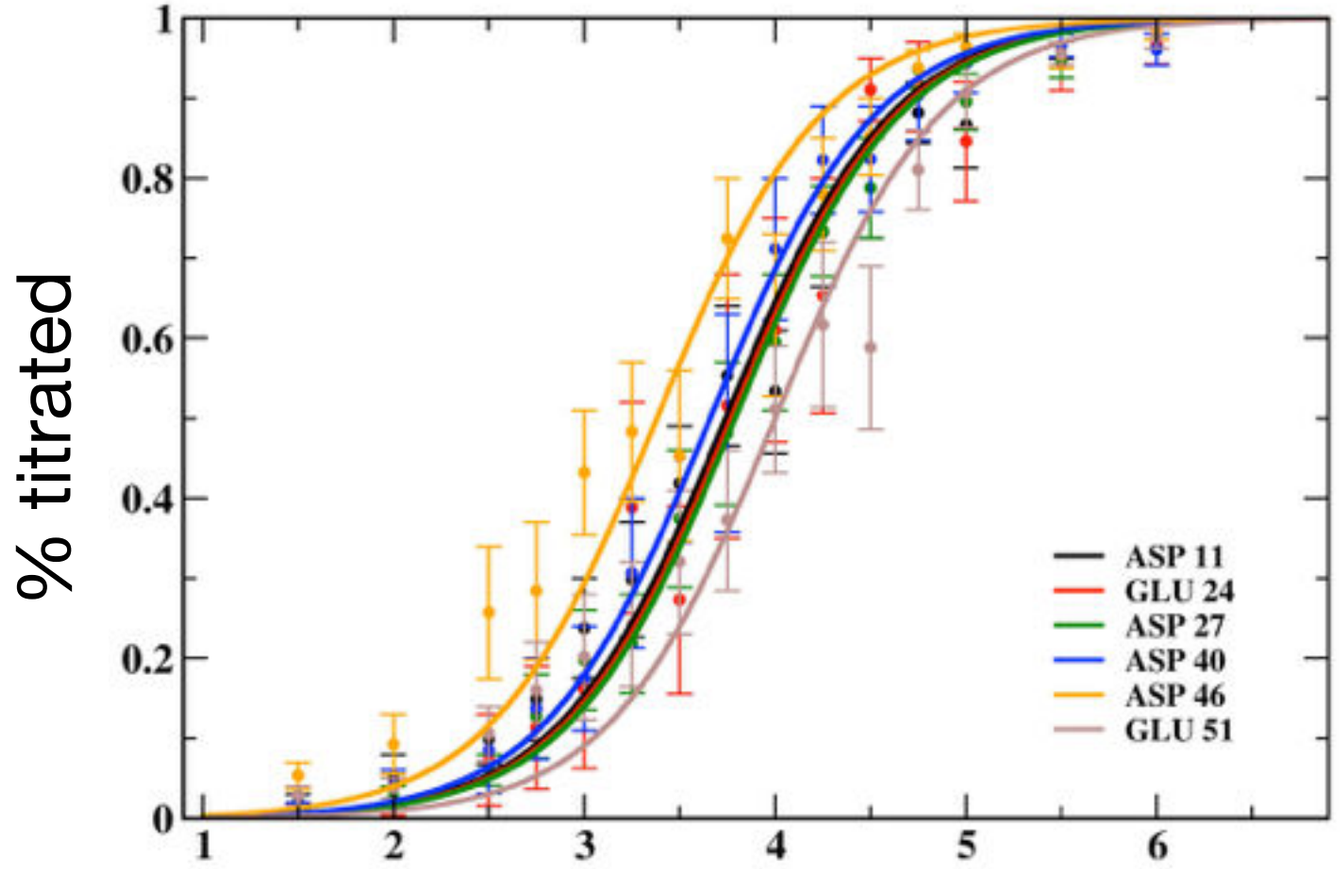
NMR data: Biochemistry 35 (1996) 9167

pK_a's in proteins

epidermal growth factor



NMR data: Biochemistry 30 (1991) 4896



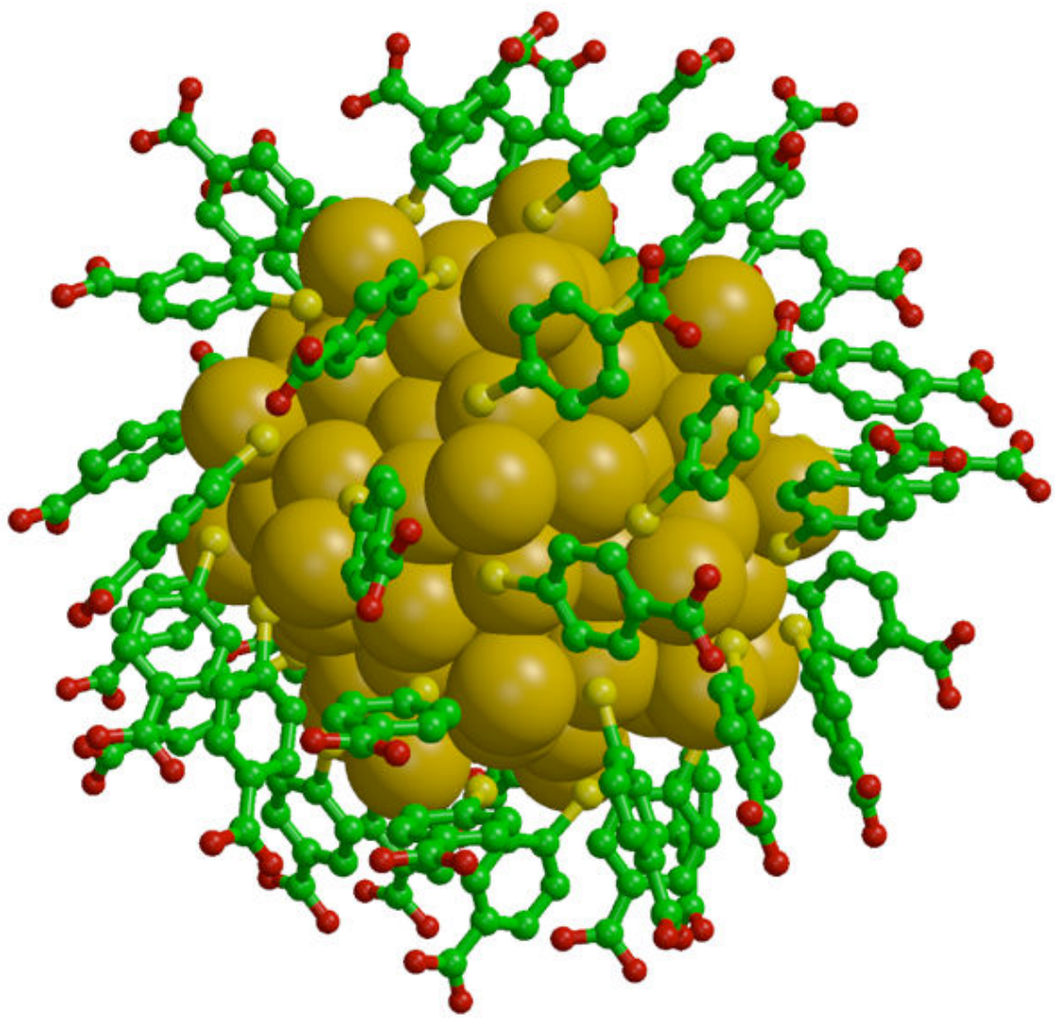
residue	CPHMD	PB	NMR
Asp11	3.74 (0.07)	4.2 (0.13)	3,9
Glu24	3.77 (0.12)	3.78 (0.15)	4,1
Asp27	3.79 (0.07)	3.8 (0.08)	4
Asp40	3.66 (0.09)	5.33 (0.28)	3,6
Asp46	3.38 (0.09)	4.1 (0.34)	3,8
Glu51	4.0 (0.09)	4.1 (0.24)	4

Analysis of constant pH MD of Au particles

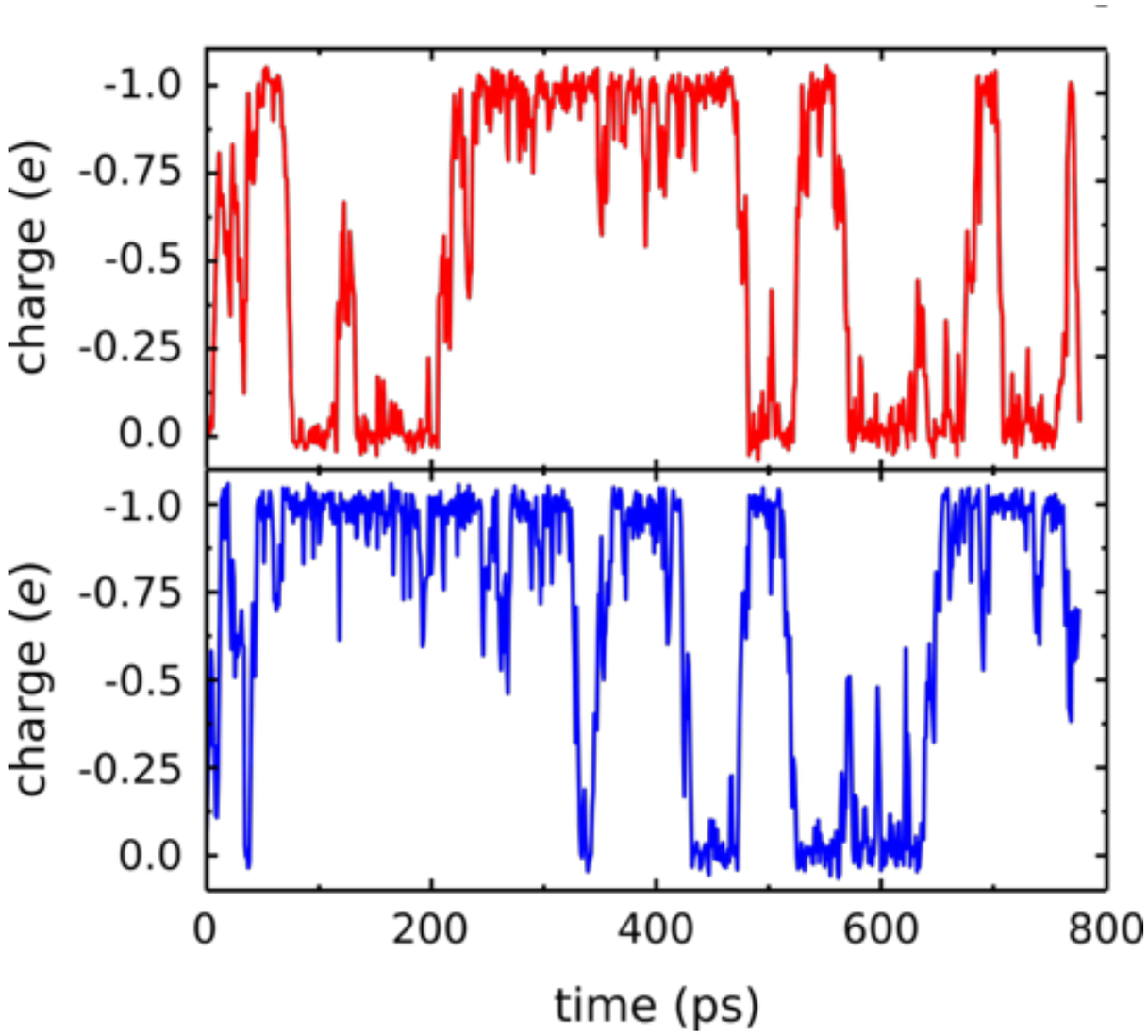
charge fluctuations

many protonations & deprotonation events

44 titratable sites



trajectory for sites 9 & 10

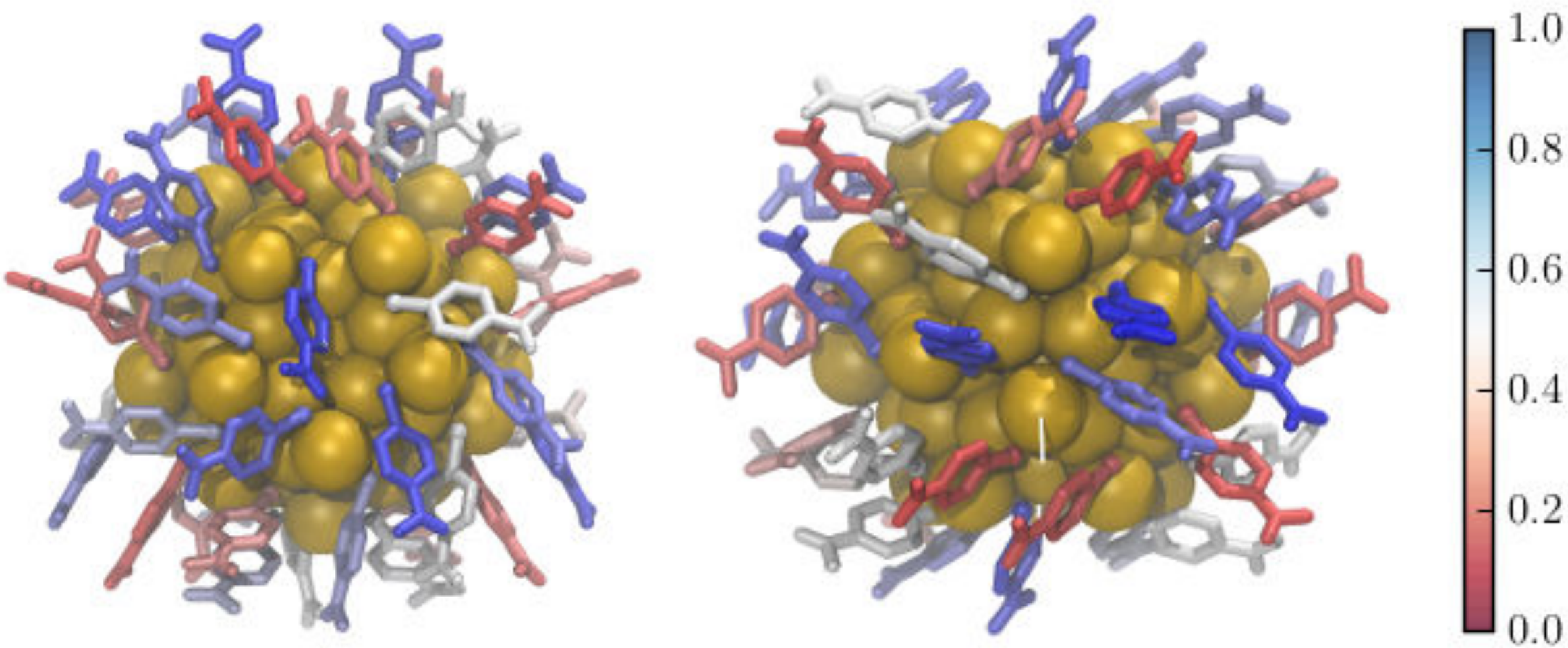


protonation of nanoparticles

are there patterns

important for interactions/recognition/biocompatability

average



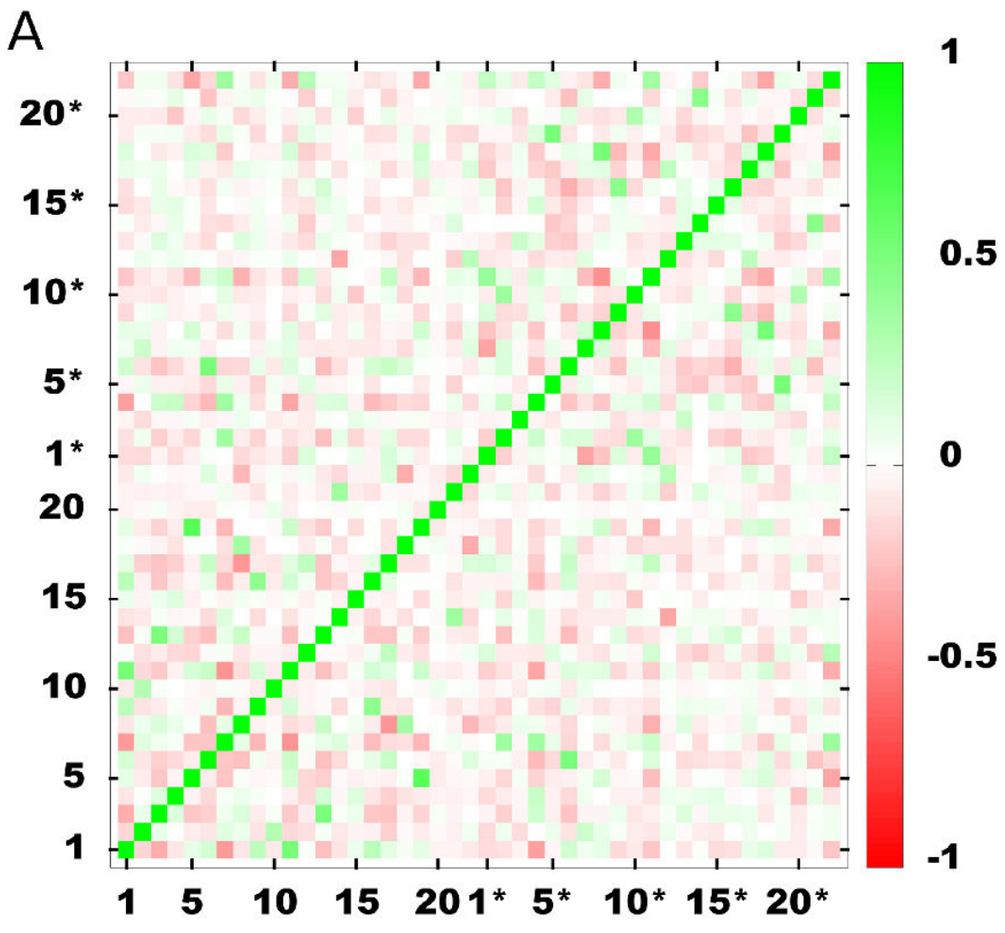
anyone sees a pattern?

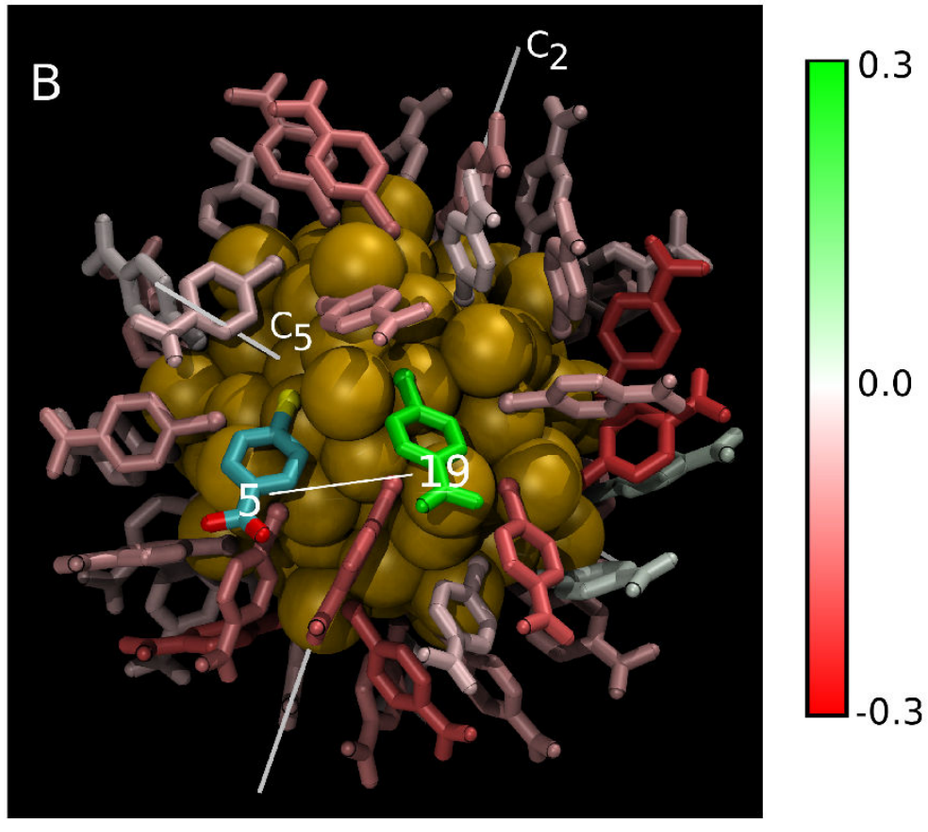
protonation nanoparticles

correlations

cooperative/anti cooperative proton binding

Pearson correlation plot



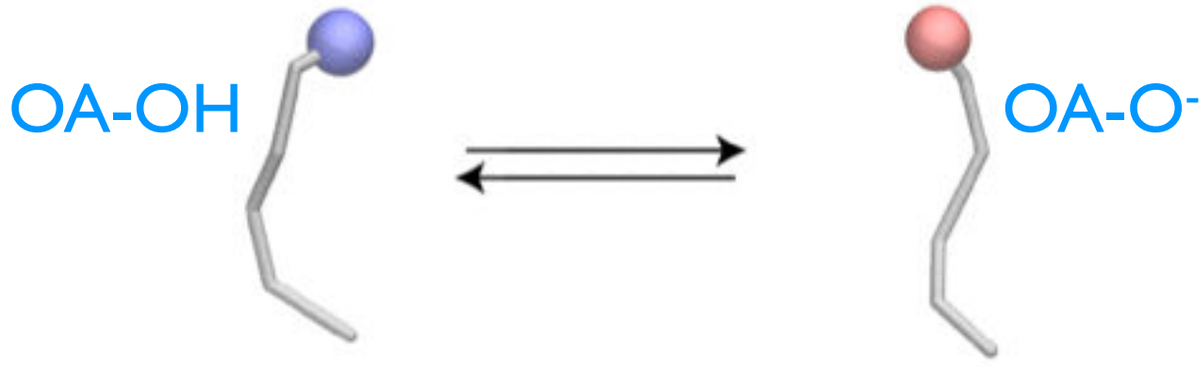


anyone sees a pattern?

Coarse grained simulations at constant pH

Oleic acid aggregates

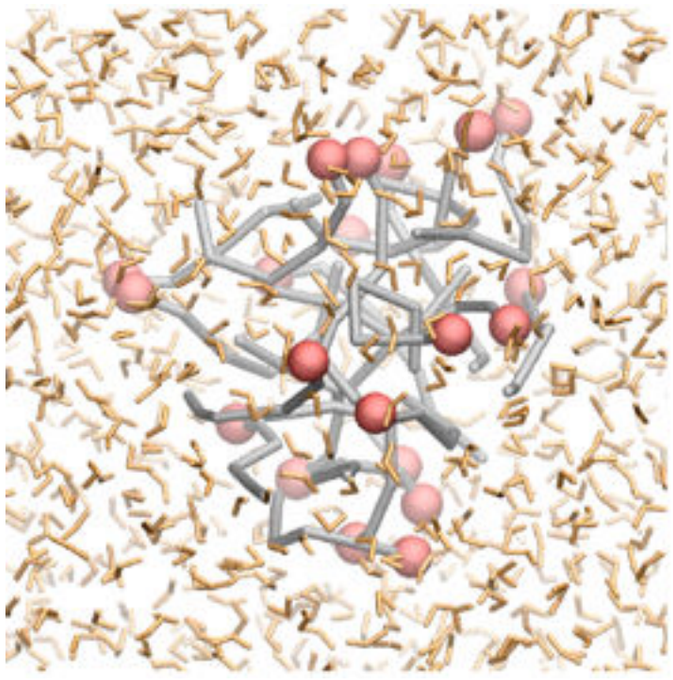
MARTINI coarse grainedforce field (Marrink *et al.*)



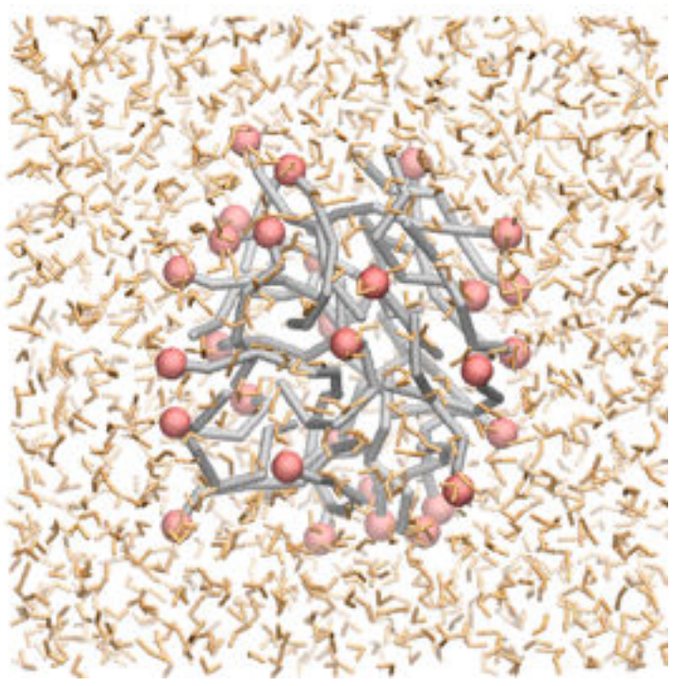
Drew Bennett

Peter Tieleman

micelle systems (self-aggregation)



20-mer



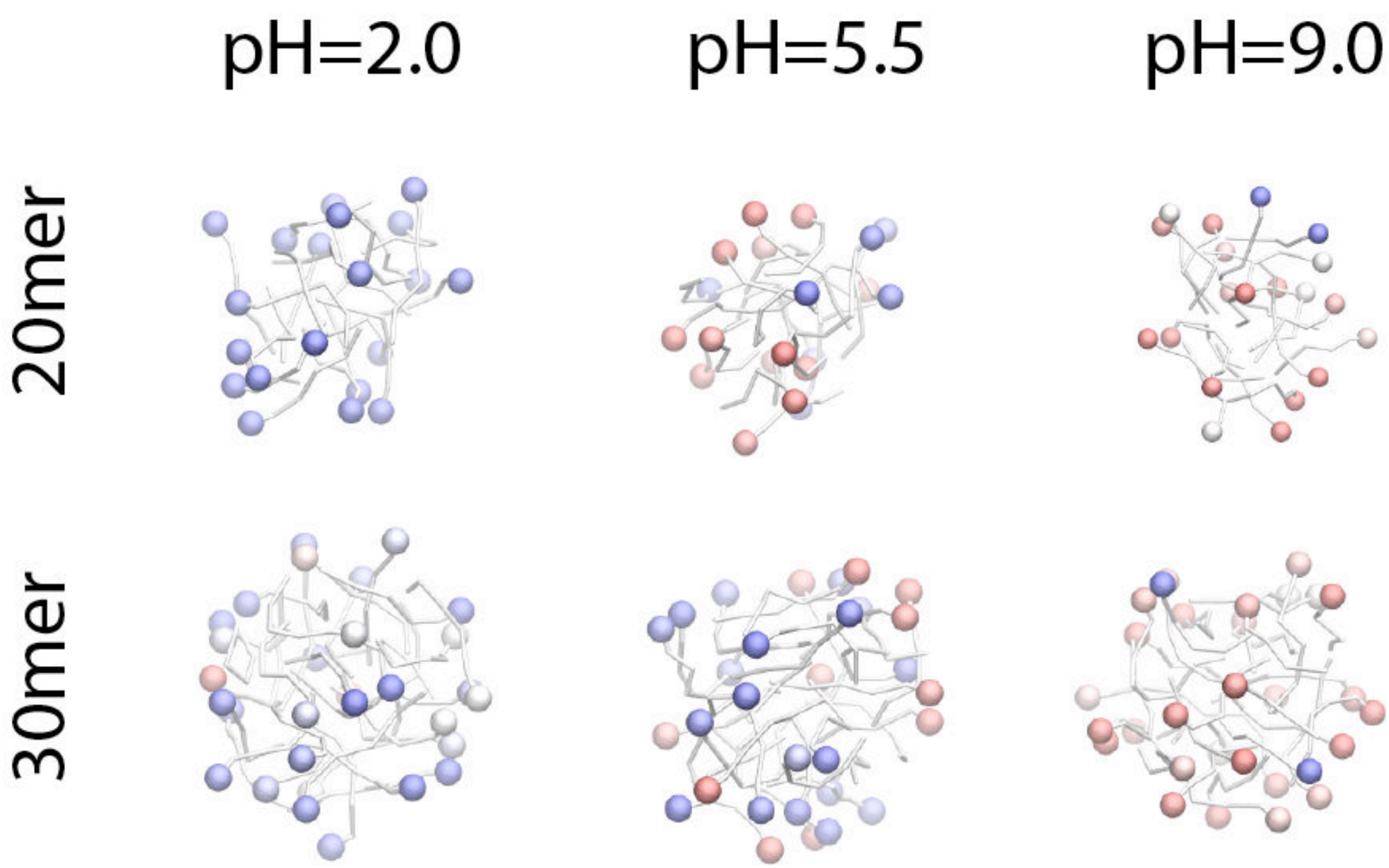
30-mer

Can. J. Chem. 91 (2013) 839

Coarse grained constant pH simulations

Oleic acids aggregates

micelles at different pH

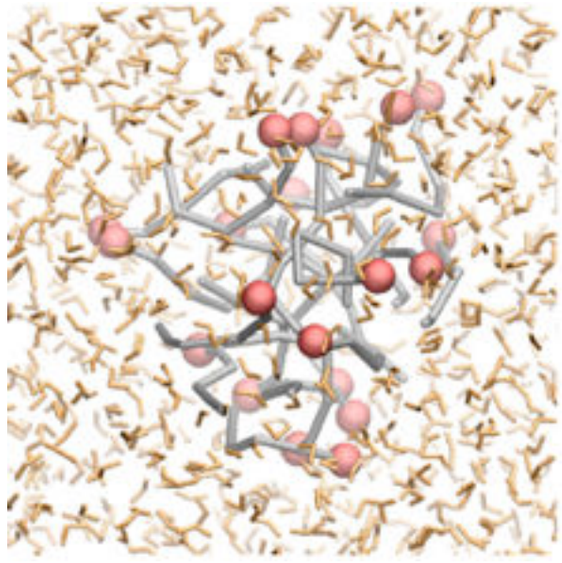


Coarse grained constant pH simulations

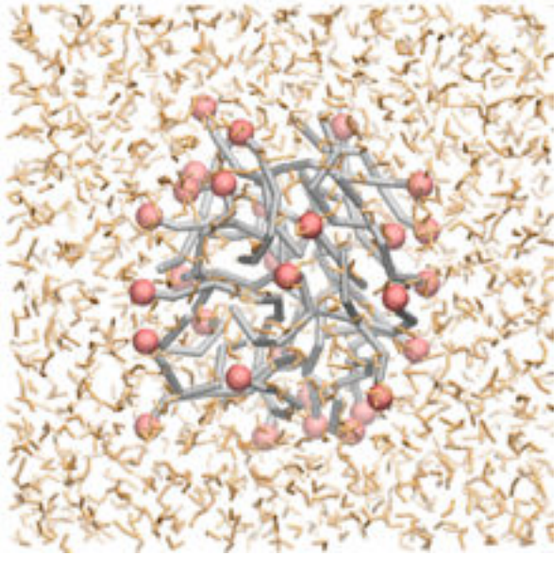
Oleic acids aggregates

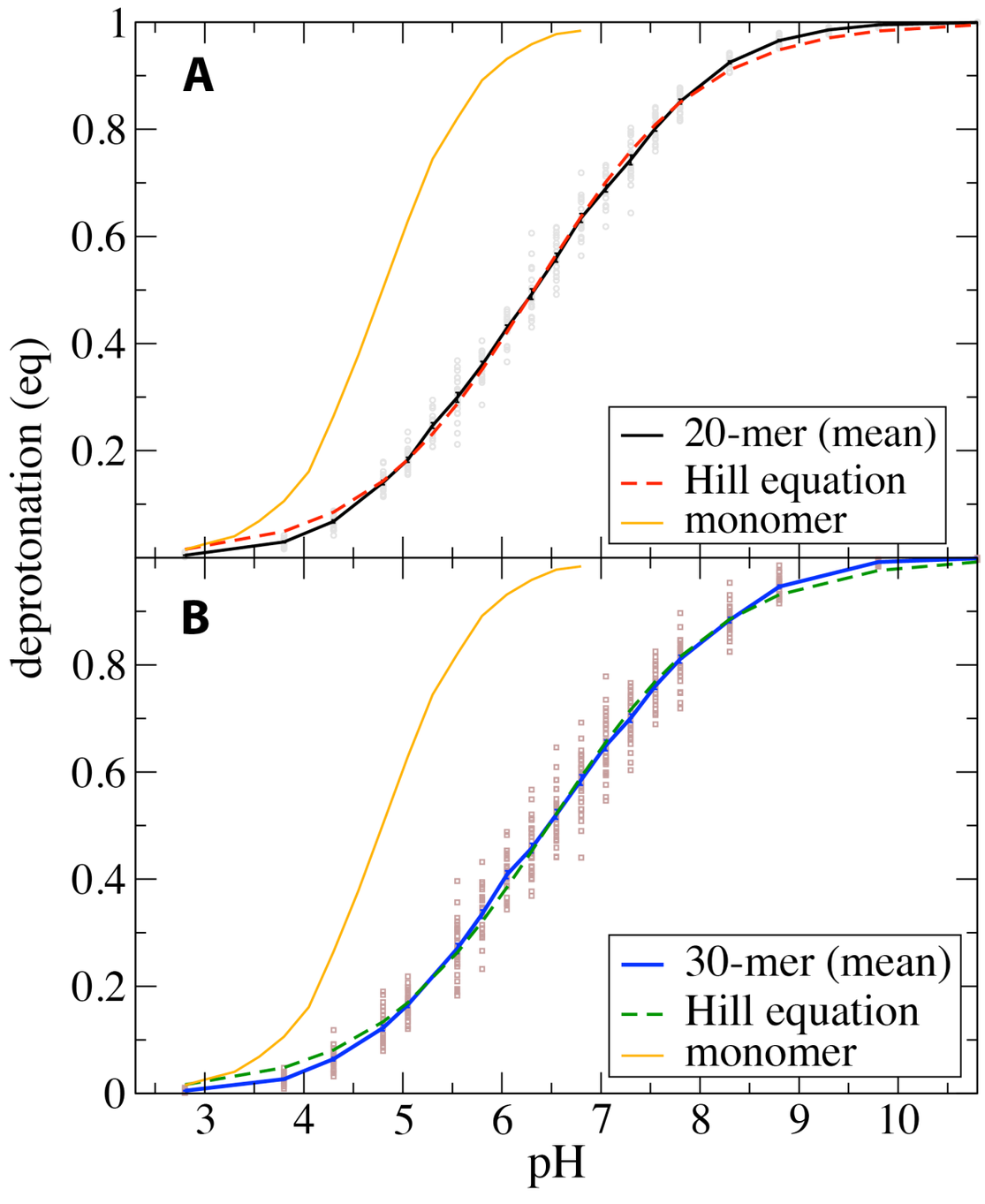
upward pK_a shift of OA in micelles

20-mer



30-mer



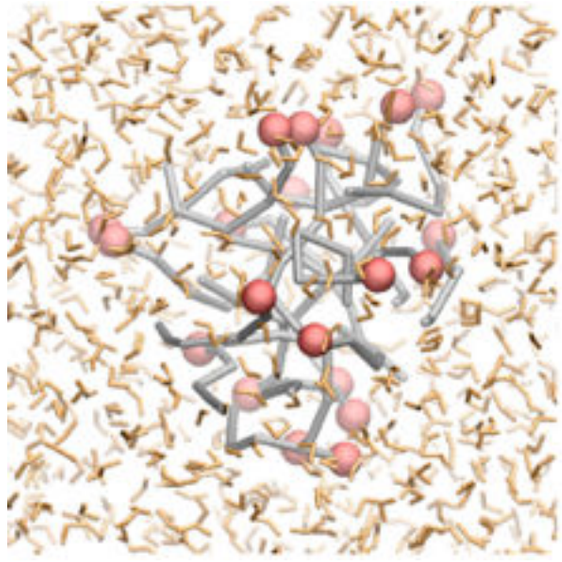


Coarse grained constant pH simulations

Oleic acids aggregates

pK_a shift correlates with micelle radius

20-mer



30-mer