

# **The INTERFACE Force Field to Unite Materials and Biomolecular Simulation in a Single Platform: Examples and Tutorial**



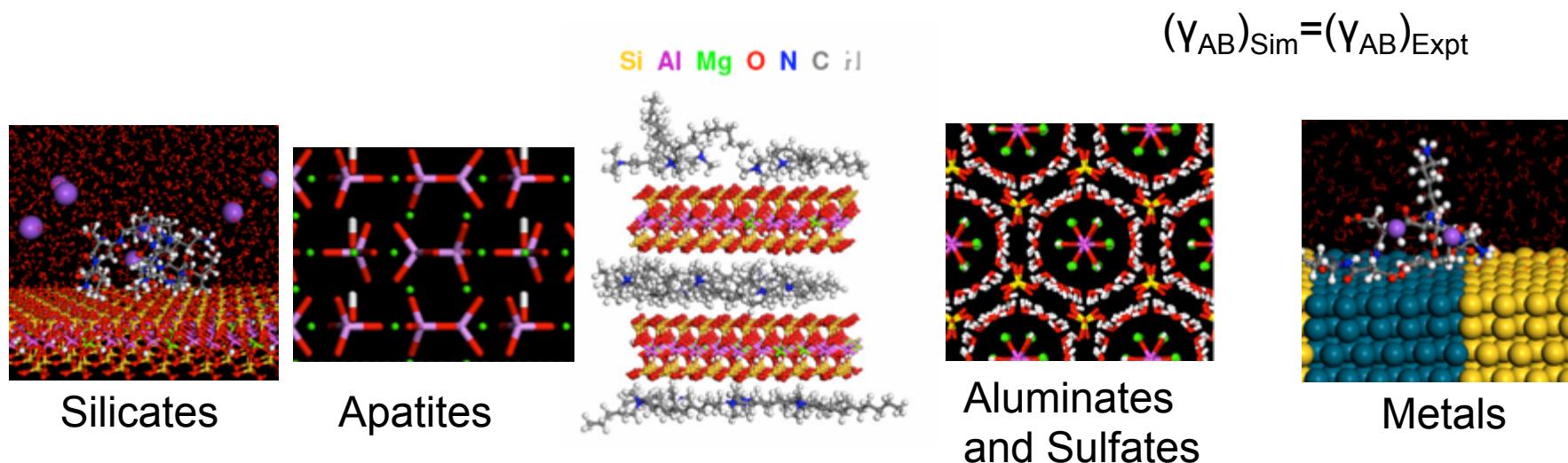
**An Overview Based on the NSF Summer  
School on Transformational Technologies in  
Molecular Simulation  
(U Wisconsin-Madison, May 18-22, 2014)**

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The University of Akron, Ohio**



# The INTERFACE Force Field

- A uniform classical simulation platform (force field parameters) for biomolecules and inorganic components at the 1-1000 nm scale



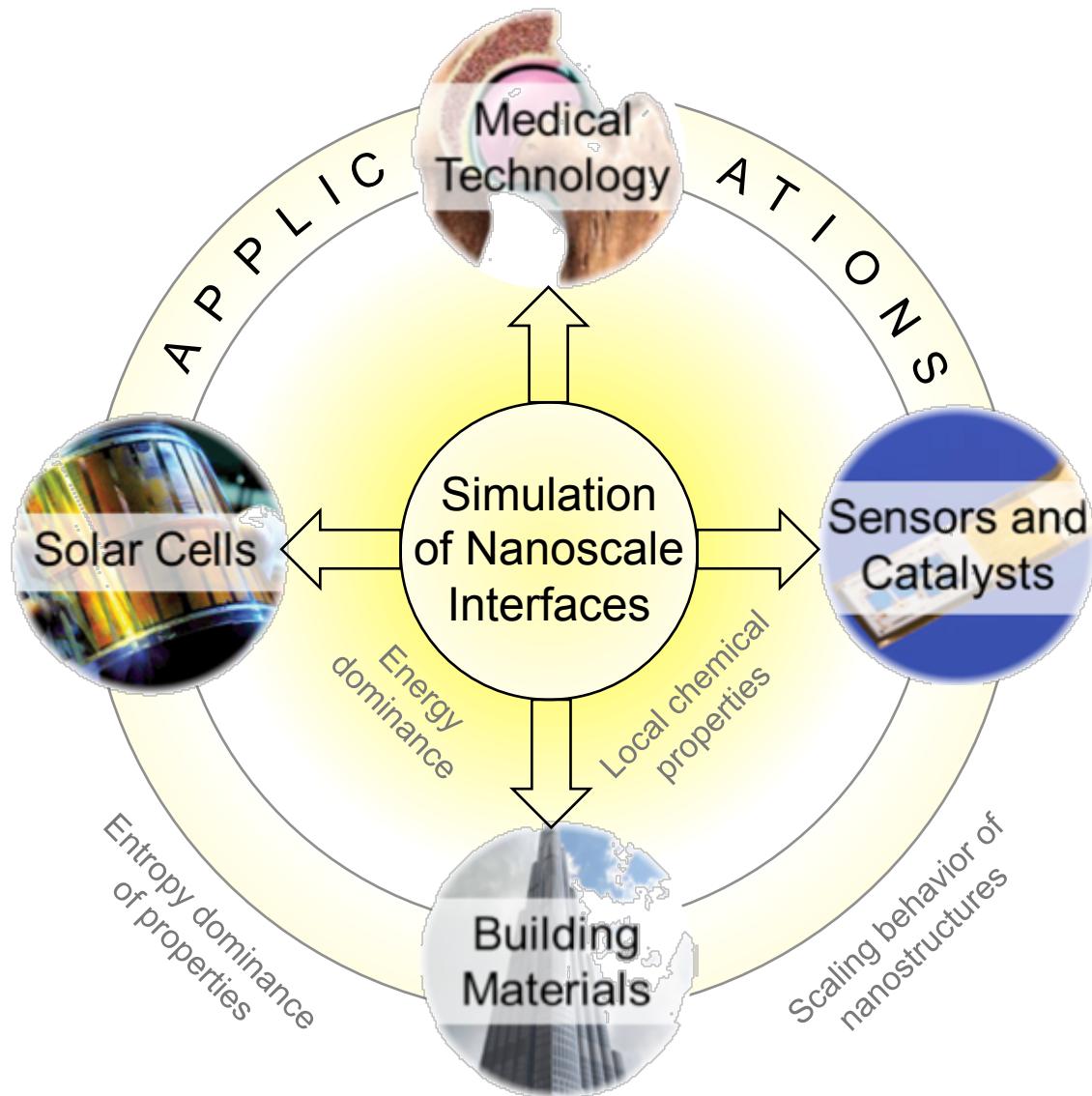
- Based on thermodynamic consistency of classical Hamiltonian for organic and inorganic components (extended PCFF, CVFF, CHARMM, AMBER, OPLS-AA, ...)
- Broad utility for biomaterials, polymer, energy, and construction materials (bone, teeth, biomarkers, polymer composites, nanometal catalysts, solar cells)

$$E_{pot}(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) = E_{bonds} + E_{angles} + E_{torsions} (+ E_{out-of-plane}) + E_{Coulomb} + E_{vdW}$$

Heinz, Emami et al. Langmuir Feature 2013, 29, 1754. Individual compounds 2003-2014.



# From Nanoscale Interfaces to Applications (Products)



Simulation at the 1 to 100 nm scale as a complimentary tool to synthesis, imaging, spectroscopy, and computation at other length scales



# Outline

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## Part I

- What is the INTERFACE force field and what can it do?
- Case studies: examples of protein recognition on metal nanoparticles, silica, apatites, and cement-organic interfaces

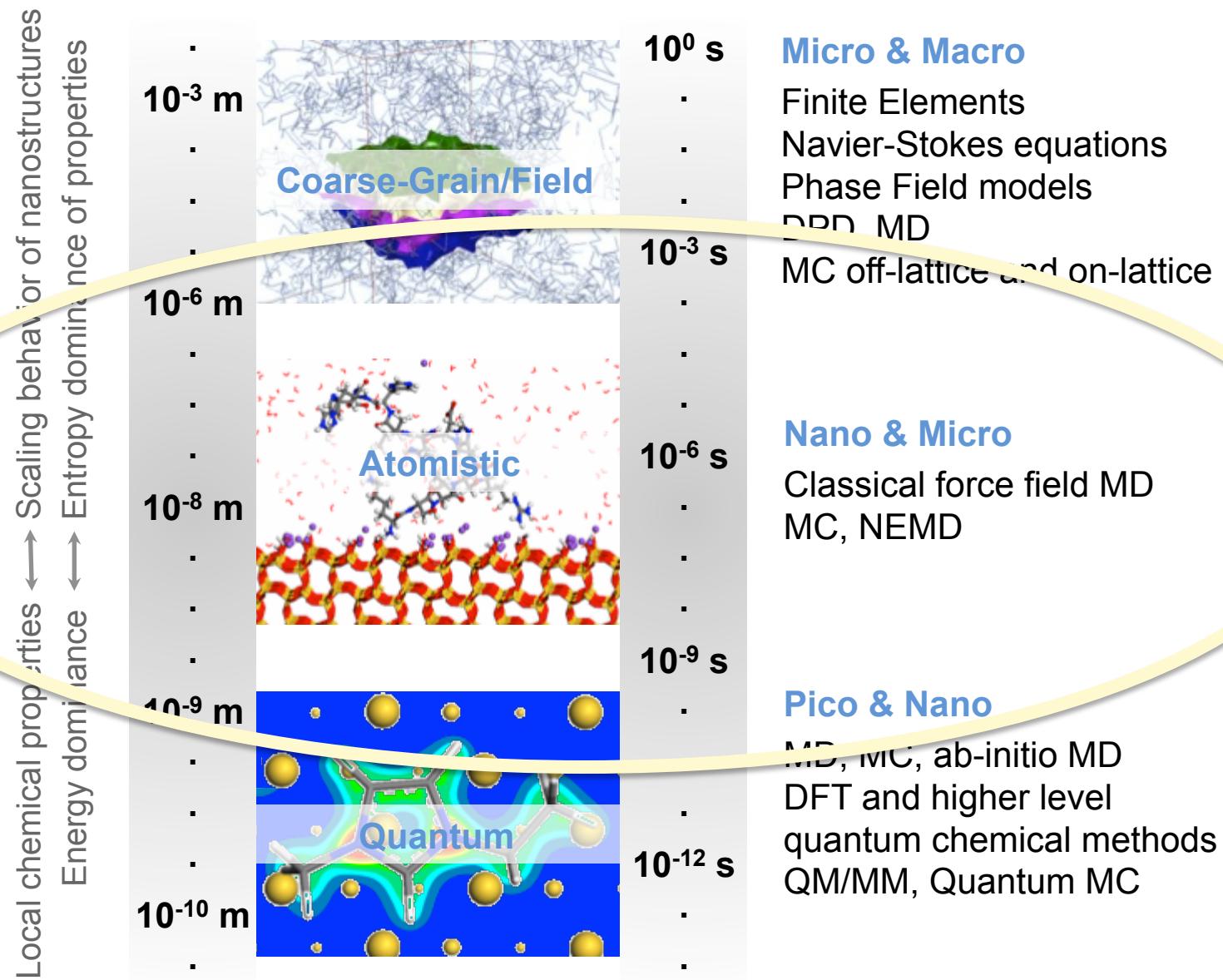
## Part II

- Approach to chemically accurate, thermodynamically consistent force field parameterizations, and examples
- Tutorial: how to use the INTERFACE force field, connect with laboratory tests and multi-scale simulation methods

*What is the INTERFACE Force Field  
and what can it do?*



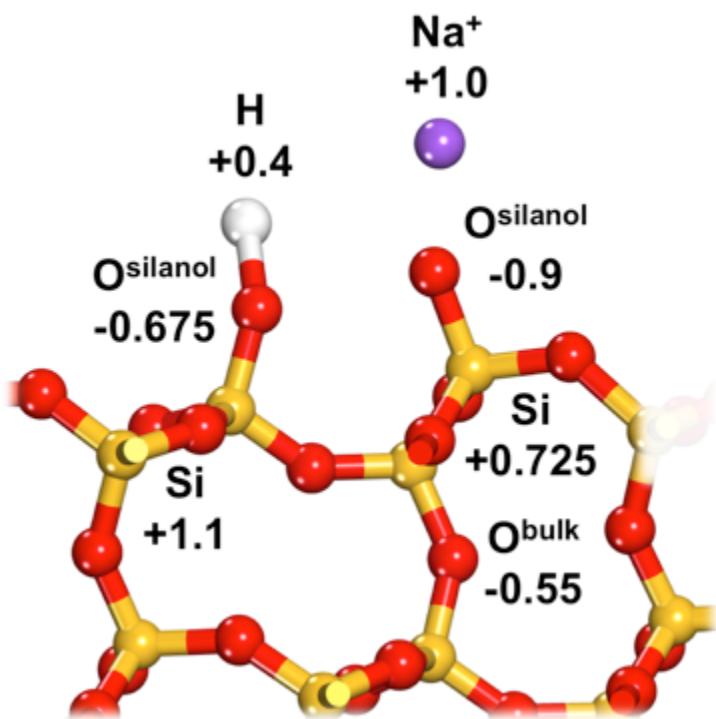
# Length and Time Scales in Simulations



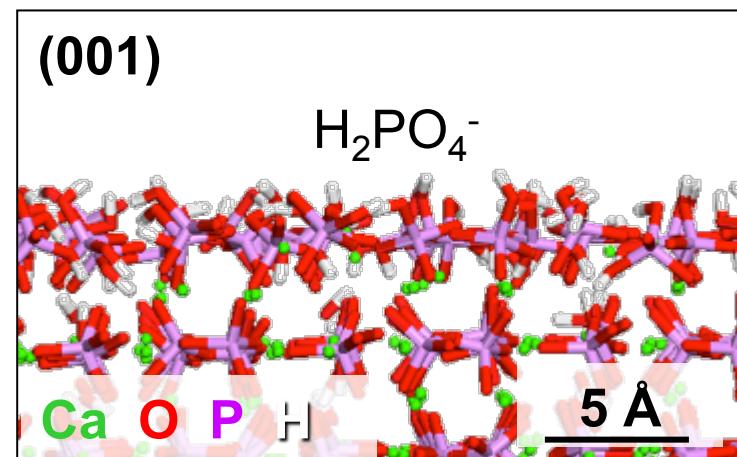


# Key Elements of Parameterization

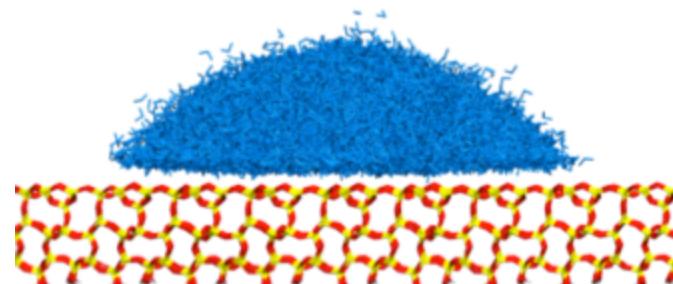
- Parameters in agreement with measured properties at the atomic and macroscopic scale: polarity ( $q$ ,  $\mu$ ), structure (XRD), and surface energy ( $\gamma$ ,  $\theta$ ,  $\Delta H_{imm}$ )



Atomic charges  
on silica



pH (surface protonation)



Contact angles & surface energies



## Unique Features and Capabilities

- Arguably most accurate parameters for inorganic compounds to date  
Reduction in >500% deviation in interfacial properties from experiment in earlier models to <10%
- A uniform platform to enable simulations of multiple materials classes  
Fully compatible with biomolecular and materials oriented force fields (energy expressions)  
Applicable to biointerfaces, metals, ceramics, polymers, construction materials
- Emphasis on chemically meaningful atomic charges and van-der-Waals parameters with thorough validation by measured atomic-scale and surface properties
- ***Open to parameterization of further compounds by users*** and integration in community simulation software (CHARMM, GROMACS, Accelrys, Tripos, ...)
- Limitations and further developments: reactions, polarizability, more compounds (graphene, organic semiconductors, quantum dots ..)

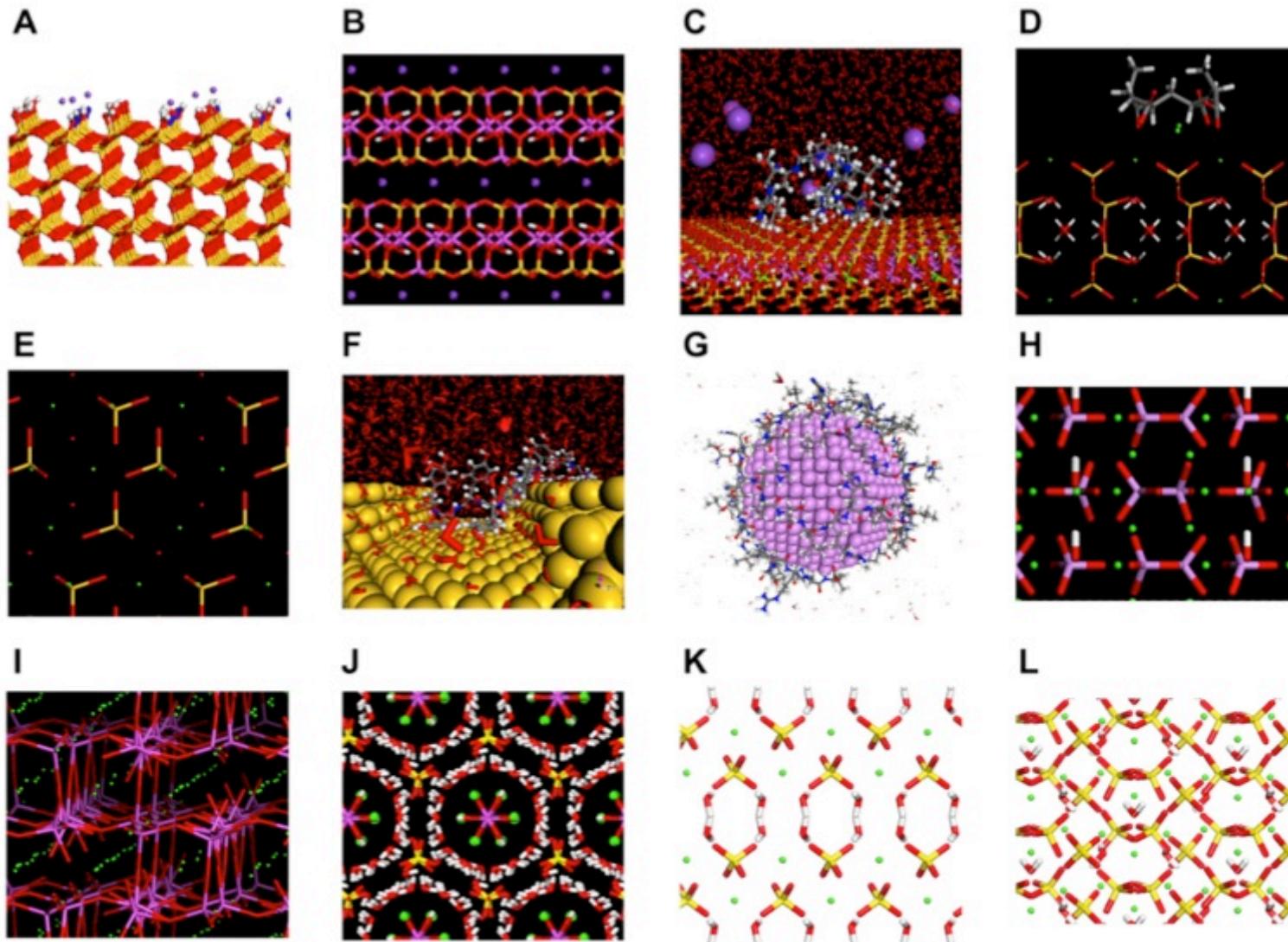


# Validation – Representative Examples

compound	property	experiment	INTERFACE force field	other force fields
1. Layered Silicates: Mica, Montmorillonite, and Pyrophyllite				
any in this group	average deviation of cell parameters ( $a$ , $b$ , $c$ , $\alpha$ , $\beta$ , $\gamma$ ) and density ( $\rho$ ) from experiment	$\pm 0.1\%$	$\pm 0.5\%$	1–5%, often amorphization
mica	cleavage energy {001} (mJ/m <sup>2</sup> )	375	380	–400 to +700
	surface tension, alkyl-modified (mJ/m <sup>2</sup> )	41–46	45 ± 3	NA
pyrophyllite	surface tension $\gamma = \gamma^{\text{el}} + \gamma^{\text{vdW}}$ (mJ/m <sup>2</sup> )	39.7 ± 1	40 ± 1	–1000 to +260
	electrostatic contribution $\gamma^{\text{el}}$ (mJ/m <sup>2</sup> )	5.8 ± 1	8 ± 1	2–155
	van der Waals contribution $\gamma^{\text{vdW}}$ (mJ/m <sup>2</sup> )	33.9 ± 1	32 ± 1	–1100 to +250
2. Silicates and Aluminates in Cement: Tricalcium Silicate, Tricalcium Aluminate, Ettringite, 11 and 14 Å Tobermorites, and Monosulfate				
any in this group	average deviation of cell parameters ( $a$ , $b$ , $c$ , $\alpha$ , $\beta$ , $\gamma$ ) and density ( $\rho$ ) from experiment	$\pm 0.1\%$	$\pm 0.5\%$	NA
tricalcium silicate	cleavage energy (mJ/m <sup>2</sup> )	1300 ± 100	1340 ± 20	NA
	bulk modulus (GPa)	105.2 ± 5	105 ± 2	NA
tobermorite 11 Å	water interfacial tension {100} (mJ/m <sup>2</sup> )	10–50	34 ± 5	NA
tobermorite 14 Å	facet-averaged surface energy (mJ/m <sup>2</sup> )	390 ± 20	390 ± 10	NA
	bulk modulus (GPa)	15 ± 2	15 ± 1	NA
3. FCC Metals: Ag, Al, Au, Cu, Ni, Pb, Pd, and Pt				
any in this group	average deviation of cell parameters ( $a$ , $b$ , $c$ , $\alpha$ , $\beta$ , $\gamma$ ) and density ( $\rho$ ) from experiment	$\pm 0.01\%$	$\pm 0.1\%$	0–5%
gold	surface tension $\gamma_{\text{SV}}\{111\}$ (mJ/m <sup>2</sup> )	1540	1540 ± 5	1000–3000
	water interfacial tension $\gamma_{\text{SL}}\{111\}$ (mJ/m <sup>2</sup> )	1470	1350 ± 10	1000–3000
	anisotropy $\gamma\{100\}/\gamma\{111\}$	1.04 ± 0.01	1.035 ± 0.01	1.03–1.07
	anisotropy $\gamma\{110\}/\gamma\{111\}$	1.10 ± 0.02	1.10 ± 0.02	1.08–1.20
	strongest-binding amino acids to {111}	R, W, Y	R, W, N	Y, F, H, or NA
palladium (with 12–6 LJ)	Young's modulus (GPa)	146 ± 1	146	90–240
	bulk modulus (GPa)	193 ± 1	182	120–280
	shear modulus (GPa)	53.2 ± 0.5	53	30–90
	specific molecular binding to {111}/{100}	yes	yes	NA
:	:	Heinz, Emami, et al. Langmuir Feature 2013, 29, 1754.	:	:



# Graphical Impression of Compounds Included: Clays, FCC Metals, Silica, Apatites, Cement Minerals





## List of Compounds Currently Included

- **Layered silicates:** mica, different montmorillonites, pyrophyllite, kaolinite including surfaces of different CEC and cation distributions according to NMR data
- **Fcc metals:** Ag, Al, Au, Cu, Ni, Pb, Pd, Pt, including {111}, {100}, and {110} surfaces
- **Silica:** bulk minerals (quartz, cristobalite) as well as surfaces of different degree of ionization for specific pH values and particle sizes (comprehensive database)
- **Hydroxyapatite:** bulk mineral, different cleavage planes, nanorods for various pH
- **Cement minerals/LDH:** tricalcium silicate, tricalcium aluminate, ettringite, monosulfate (hydrocalumite), tobermorite 11 Å, tobermorite 14 Å, including different cleavage planes
- **Calcium sulfates:** calcium sulfate hemihydrate and gypsum, including different cleavage planes
- **Poly(ethylene oxide):** crystal and polymer chain including gauche effect and approximate solubility (radius of gyration) in water

(Extensible to similar/other compounds)



# How to Use the INTERFACE Force Field

## 1) Download from Web (Heinz webpage)

<http://www2.uakron.edu/cpspe/dpe/web/nsi/interface-force-field.php>

Content:

- Force field files
- Surface model database
- Utility programs (to help file conversion in CHARMM)
- Documentation

## 2) Prepare structure for simulations

(using atom types and charges provided in models)

## 3) Perform MD/MC Simulations

LAMMPS, NAMD, Towhee, GROMACS, **Materials Studio Discover/Forcite (easiest)**, ...

Fully supported force fields:

CHARMM-INTERFACE, CVFF-INTERFACE, PCFF-INTERFACE; others in part  
(AMBER, OPLS-AA, ...)

**Case Studies:**

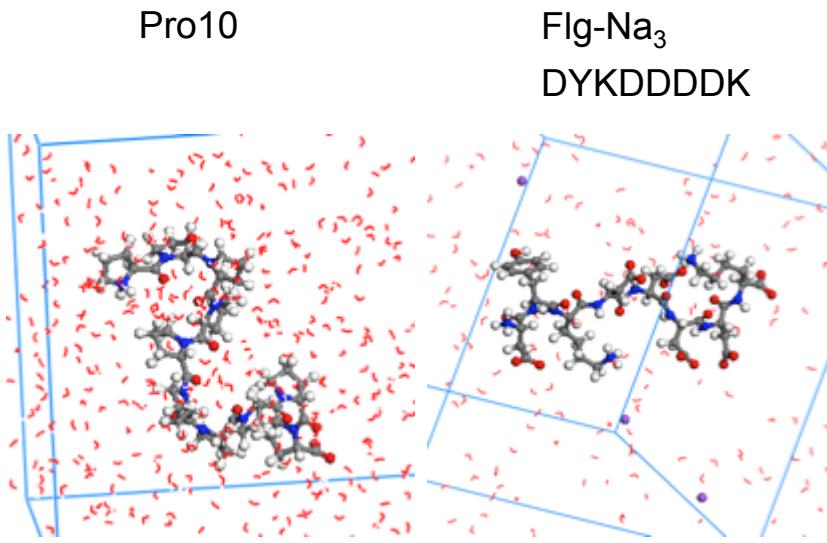
***Examples of Protein Recognition on Metal Nanoparticles, Silica, Apatites, and Cement-Organic Interfaces***



# Peptides in Solution and on Surfaces: Metals

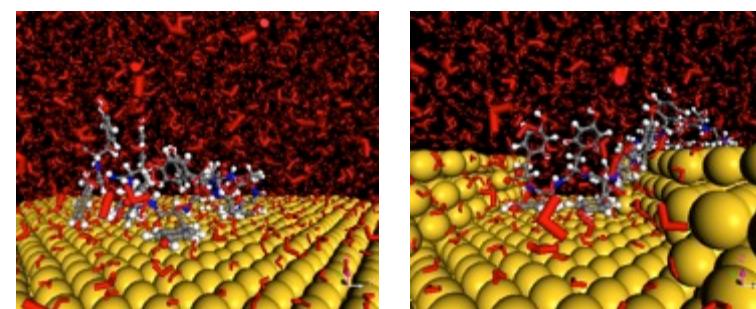
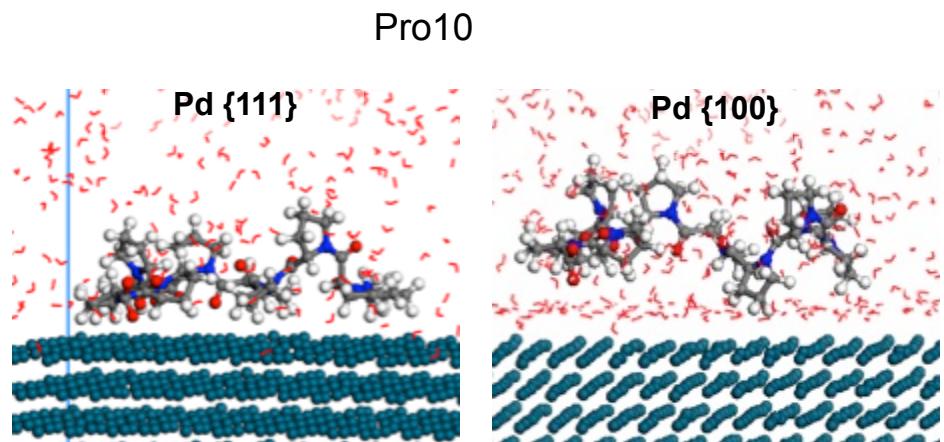
- All atom resolution, 1000-5000 molecules explicit water (SPC)
- NVT dynamics 10-100 ns and adsorption analysis Heinz J. Comp. Chem. 2010

## In solution: 3D conformation

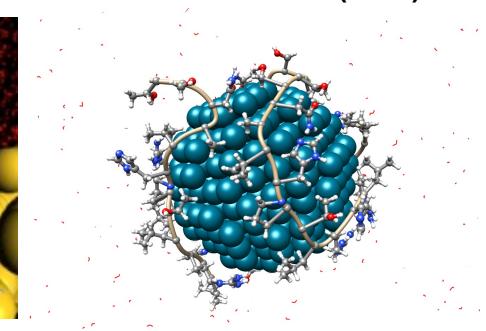


Heinz et al. JACS 2009, 131, 9704;  
JACS 2011; Small 2012

## On the surface: different 2D - 3D conformation

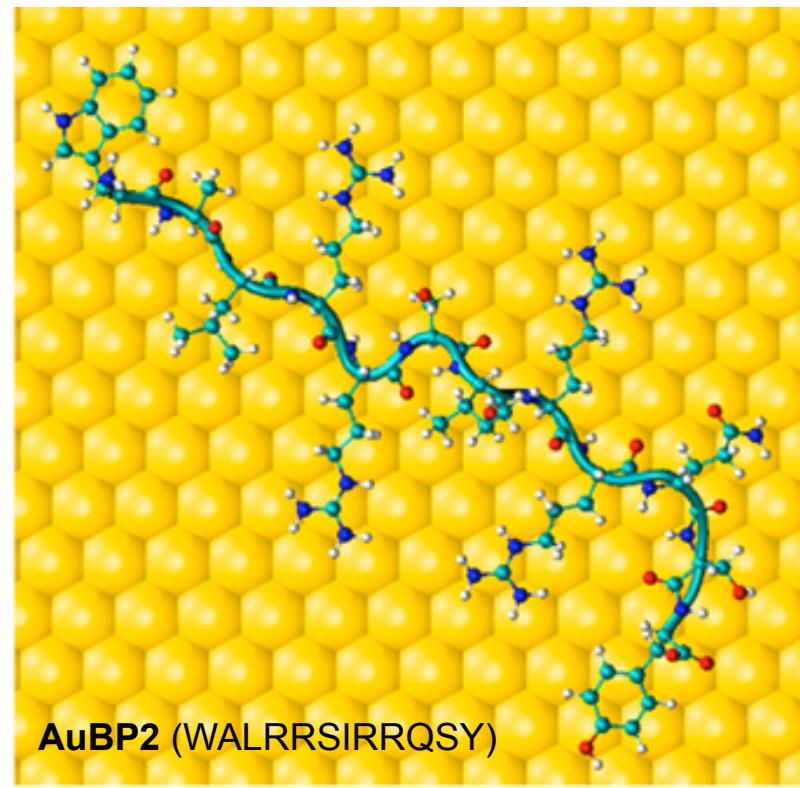
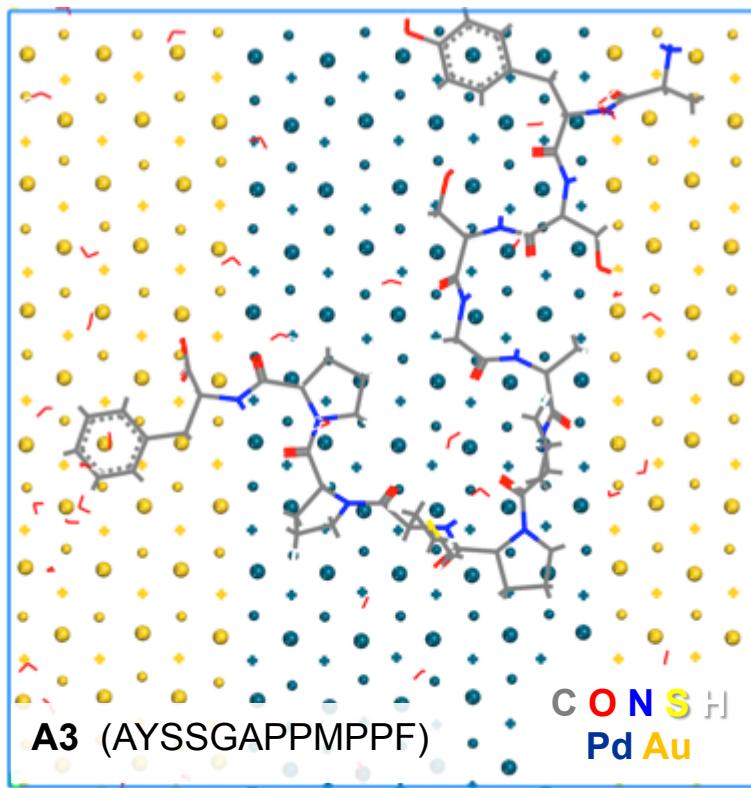


Pd - 2 nm NP (4 ns)



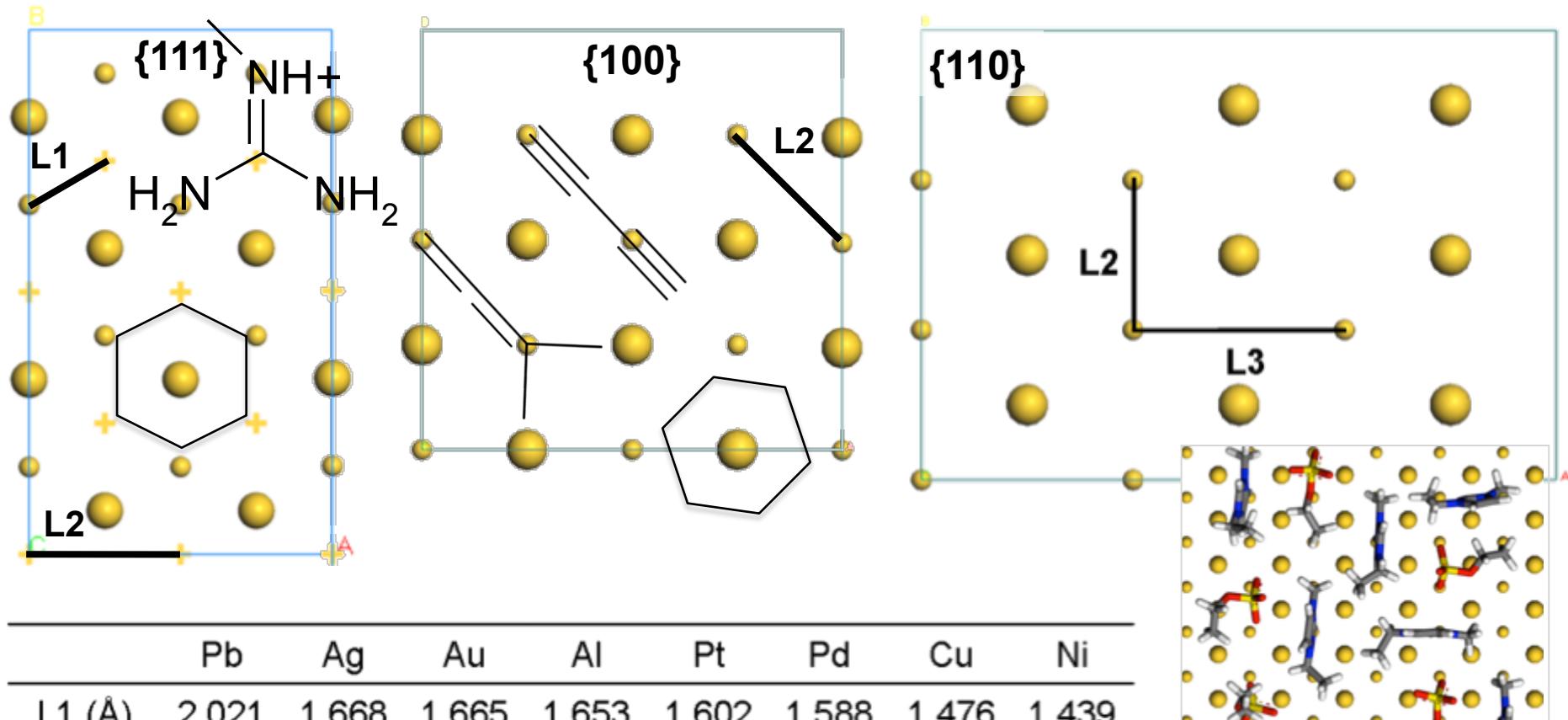


# Peptide Conformation on Au {111}





# Specific Facet Recognition of Molecular Features



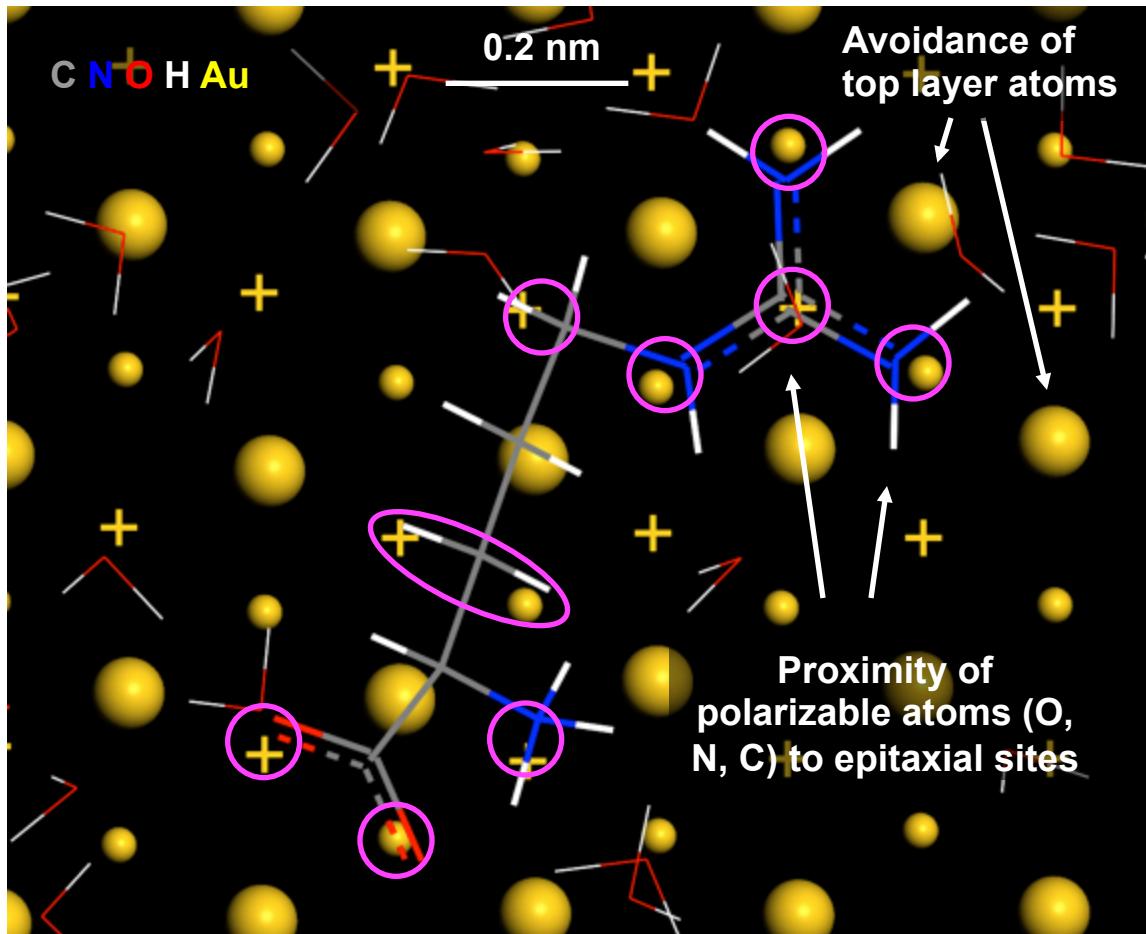
	Pb	Ag	Au	Al	Pt	Pd	Cu	Ni
L1 (Å)	2.021	1.668	1.665	1.653	1.602	1.588	1.476	1.439
L2 (Å)	3.5	2.889	2.884	2.863	2.774	2.751	2.556	2.492
L3 (Å)	4.95	4.086	4.078	4.05	3.924	3.89	3.615	3.524

Feng, Heinz et al. *Soft Matter* 2011, 7, 2113.

**Binding increases when polarizable atoms (C, N, O) in molecules and polymers coordinate a higher number of epitaxial sites**

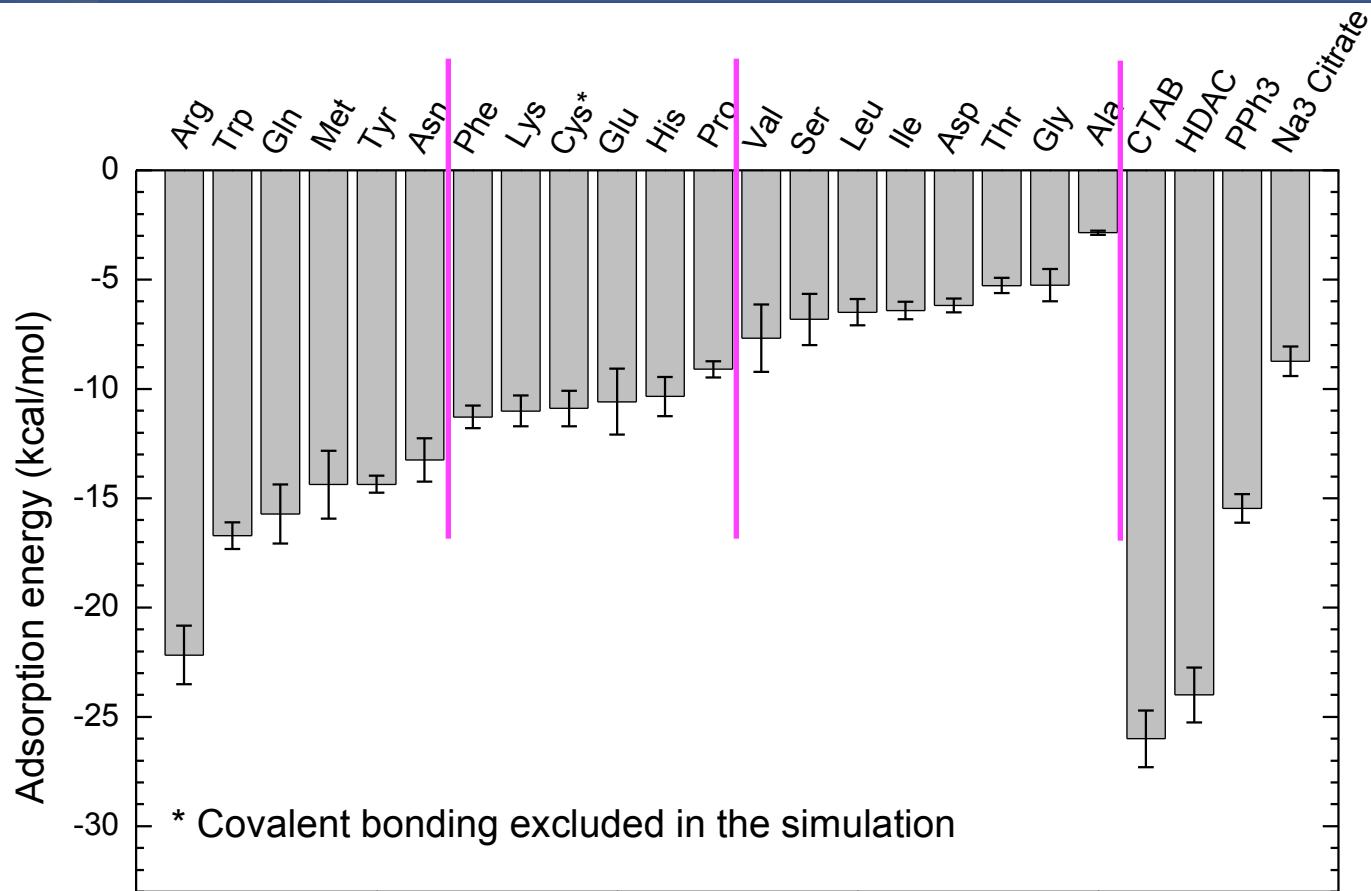


# Soft Epitaxial Binding Mechanism (Example: Arg on Gold {111})





# Computed Adsorption Energy of Single Amino Acids in Solution on Au {111}



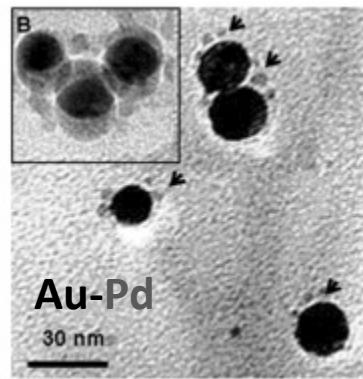
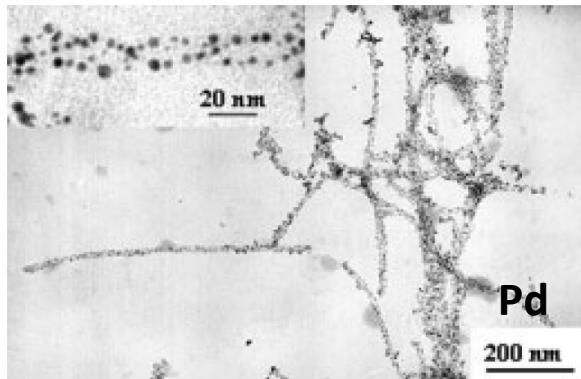
- Correlation with molecule size and geometry (less with chemistry)
- Coordination of multiple polarizable atoms (N, O, C) with epitaxial sites lowers adsorption energy
- Similarity between amino acids and surfactants in adsorption strength

J. Feng, HH , et al. PCCP 2009, 11, 1989; Soft Matter 2011, 7, 2113.



# Evidence by Experiment

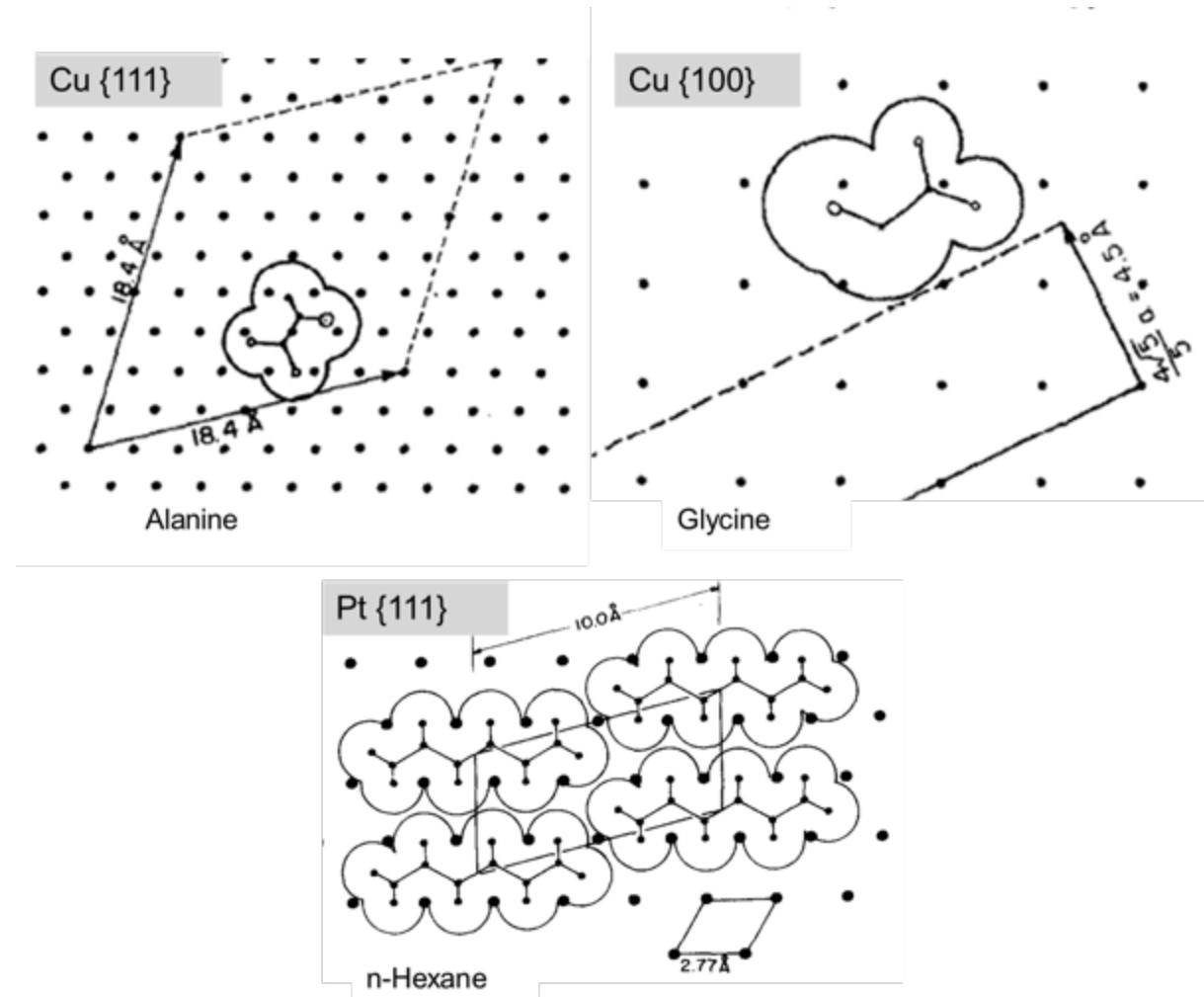
- Same relative strength of 20 amino acids on {111} surfaces in combinatorial peptide screening (phage display) and computation:  
Arg > Tyr > ... Phe ... His ... Ser ... > Ala
- No reported significant adsorption of peptides to {100} surfaces
- Metal binding peptides (A3, GBP, ...) are similarly attracted to Ag {111}, Au {111}, and Pd {111} surfaces – *similar L1 spacing*
- Only peptides containing strongly binding amino acids, or such amino acids alone, stabilize and control the shape of nanoparticles synthesized from metal salts



Data by several groups:  
R. Naik, M. Sarikaya, Z. Nie,  
Y. Huang, M. Knecht, H.  
Matsui  
LEEDS data of amino acid  
monolayers by Somorjai



# LEED Measurements Support Epitaxial Coordination



Packing data of alkane and amino acid monolayers on Cu and Pt surfaces support this mechanism (though no hard evidence possible by LEED)

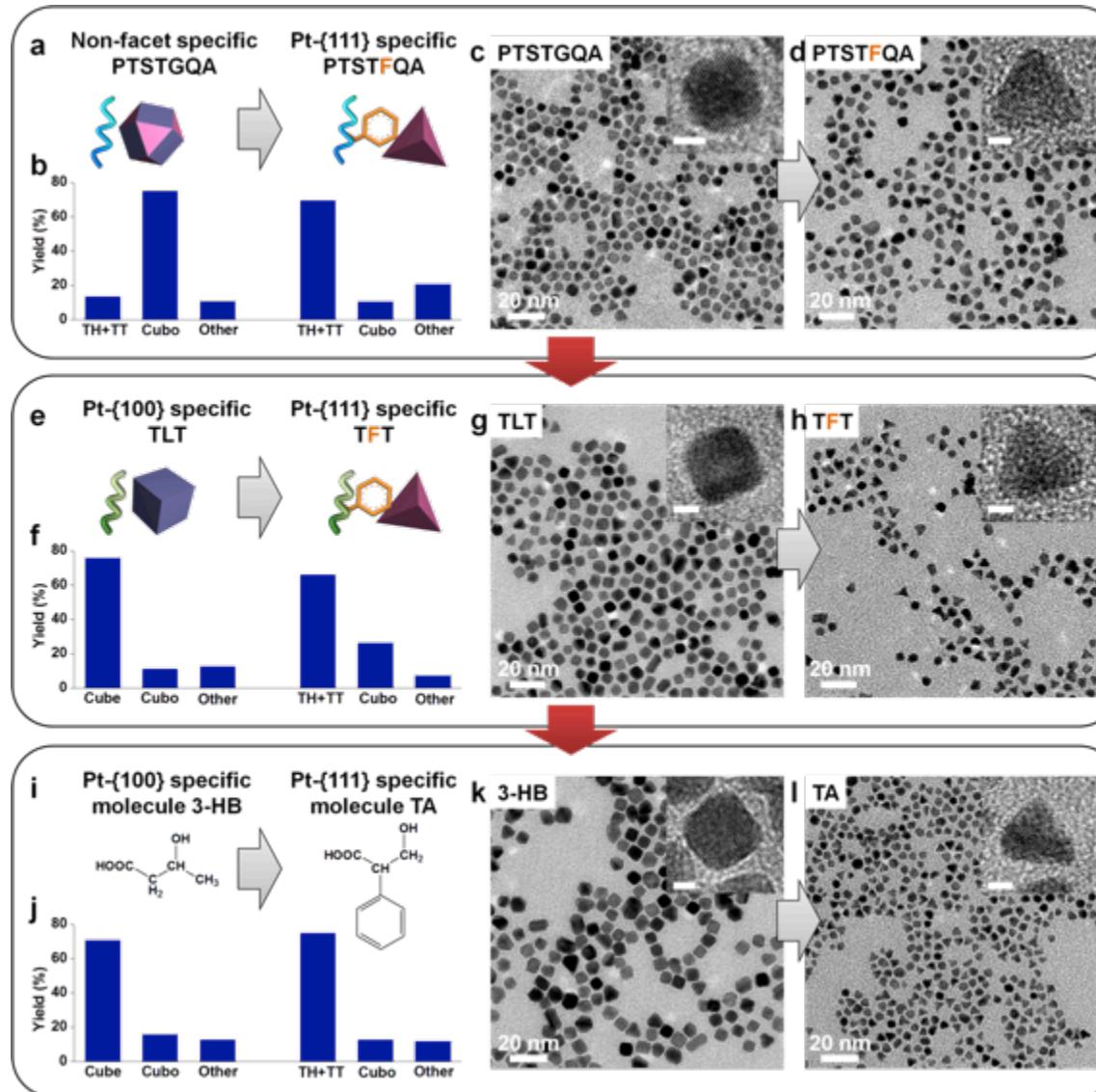
Atanasoska, Somorjai et al. *Surface Sci.* **72**, 189-207 (1978); Firment and Somorjai *J. Chem. Phys.* **66**, 2901 (1977).



# Molecular Control Over Pt Nanocrystal Shape Using a Phenyl Molecular Switch

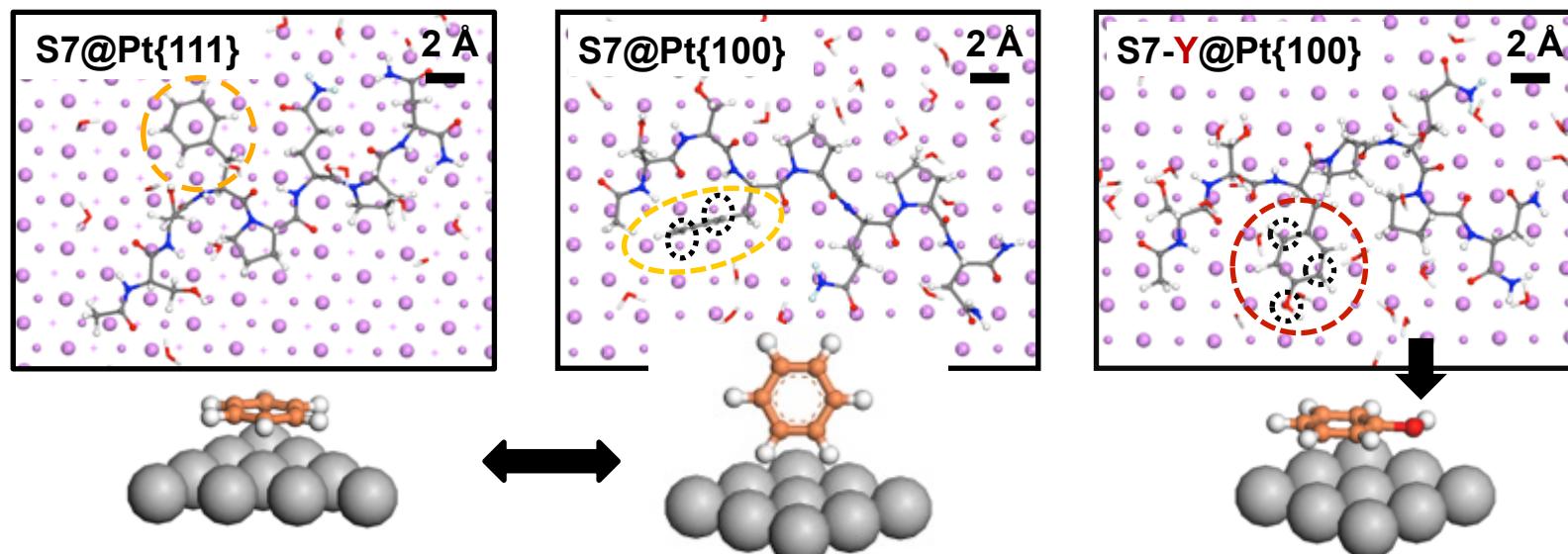
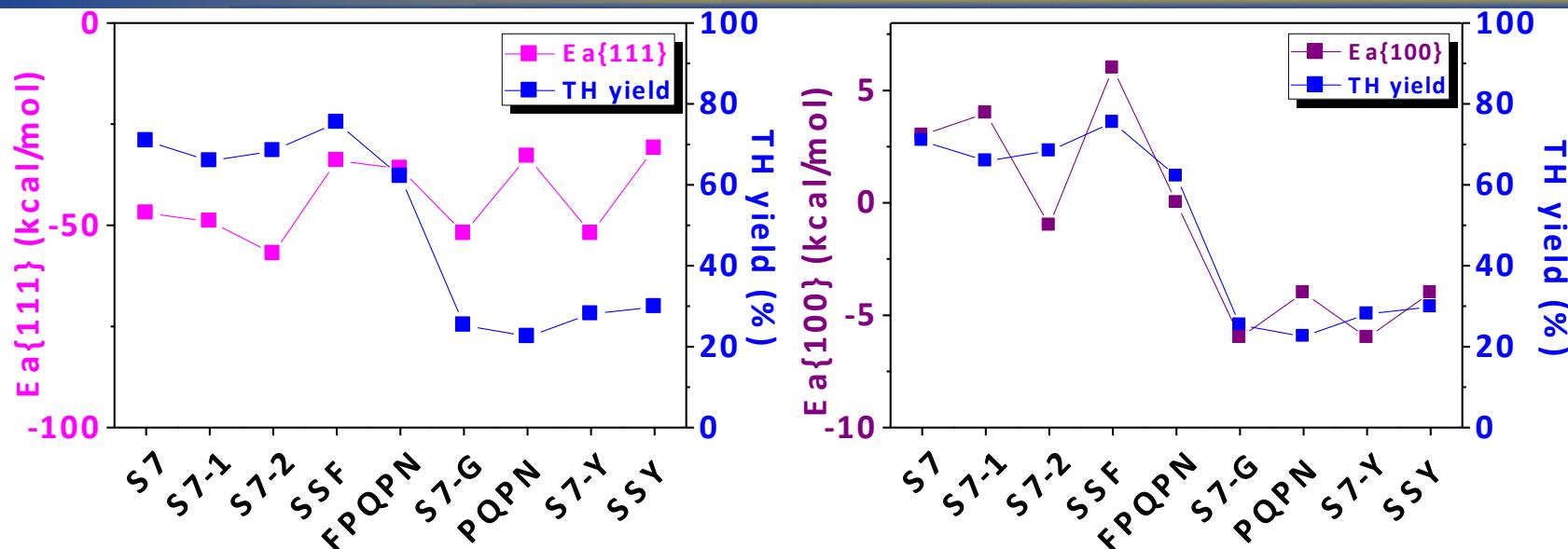
Binding contrast between {111} and {100} surfaces determines preferred shape

Synthesis from  $\text{H}_2\text{PtCl}_6$  with sodium borohydride and ascorbic acid in the presence of peptides





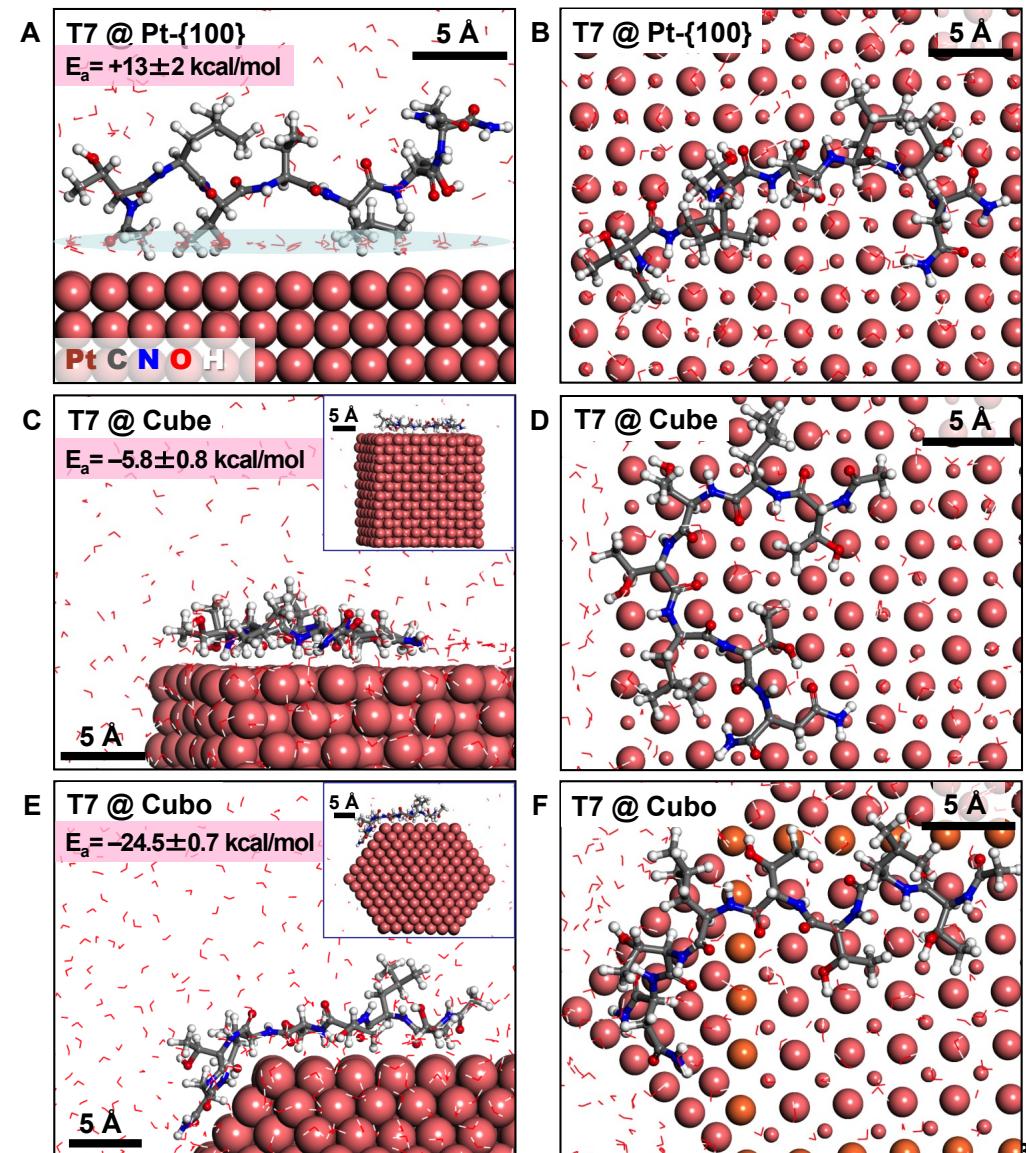
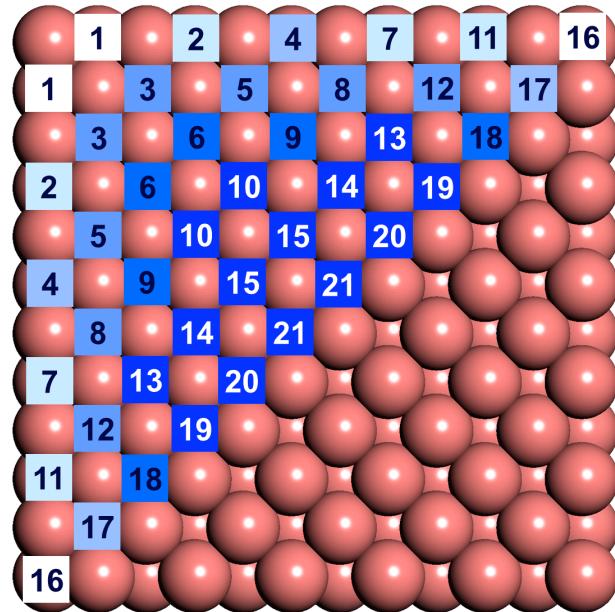
# Binding Contrast between Facets Determines Shape



Y. Huang and H. Heinz et al. Nano Letters 2013, 13, 840.

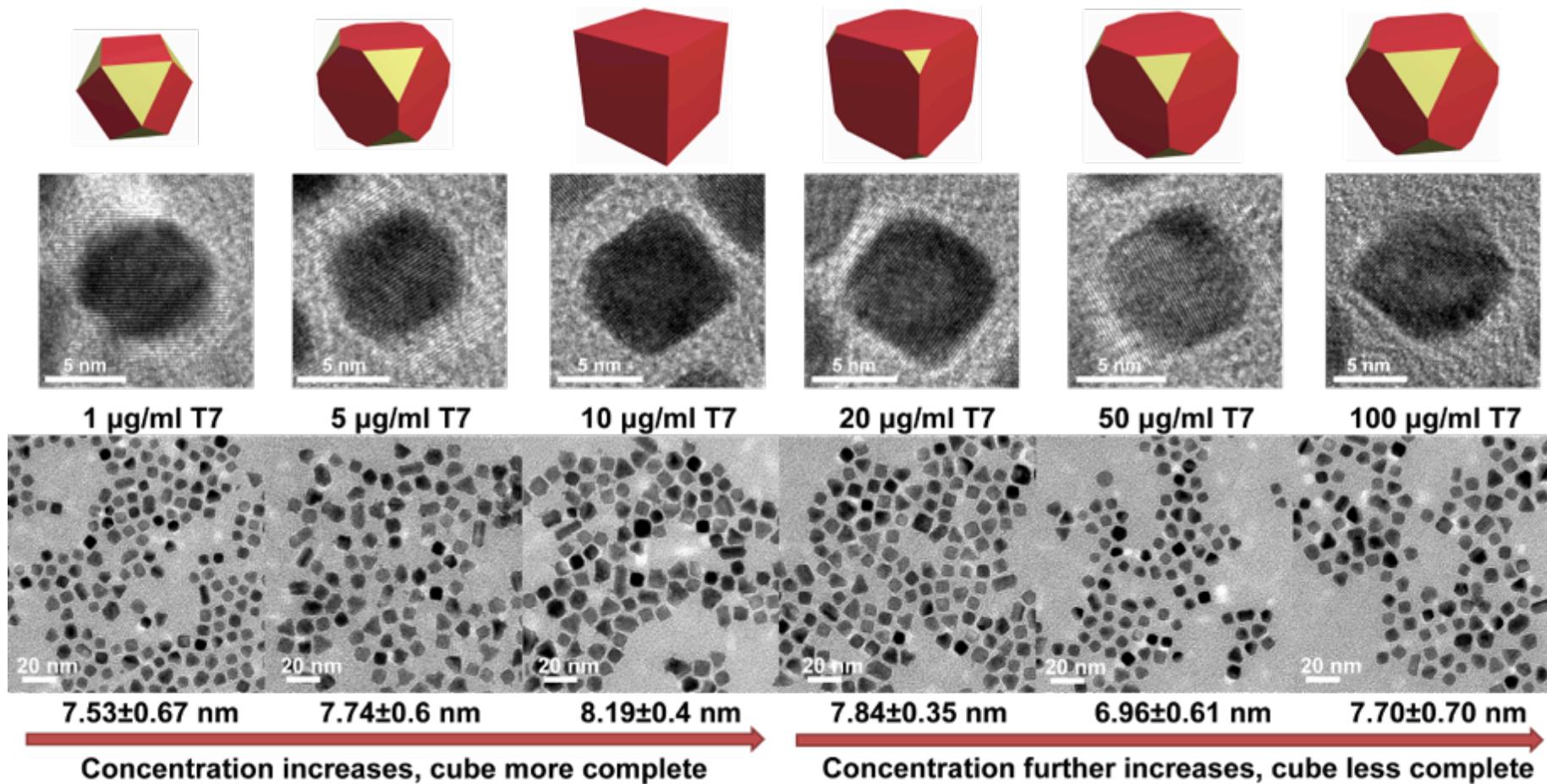


# Spatial Differences in Adsorption of Water and Peptides on Pt Nanocubes and Cuboctahedra





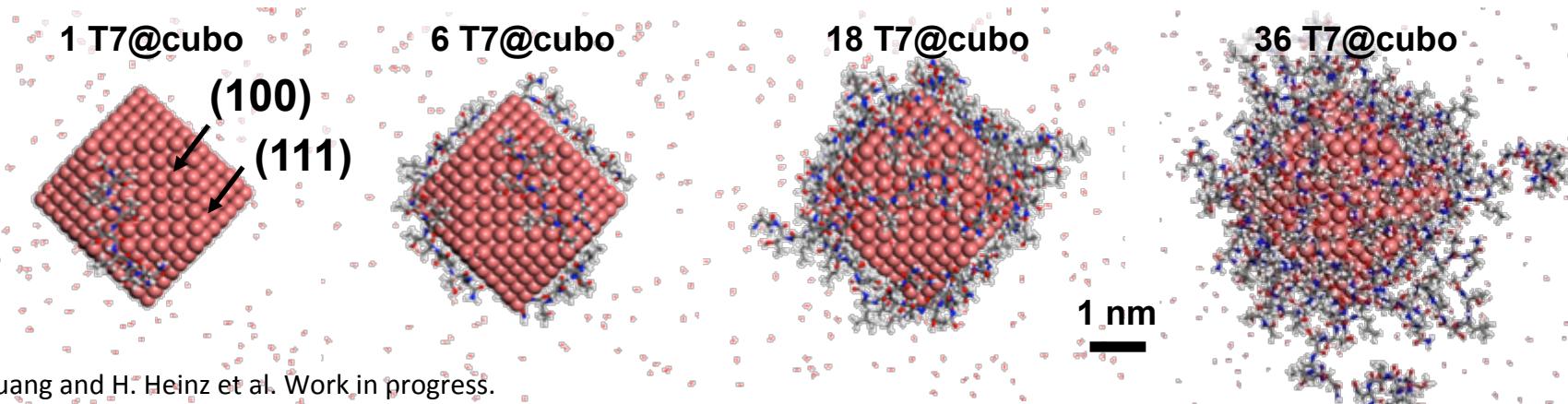
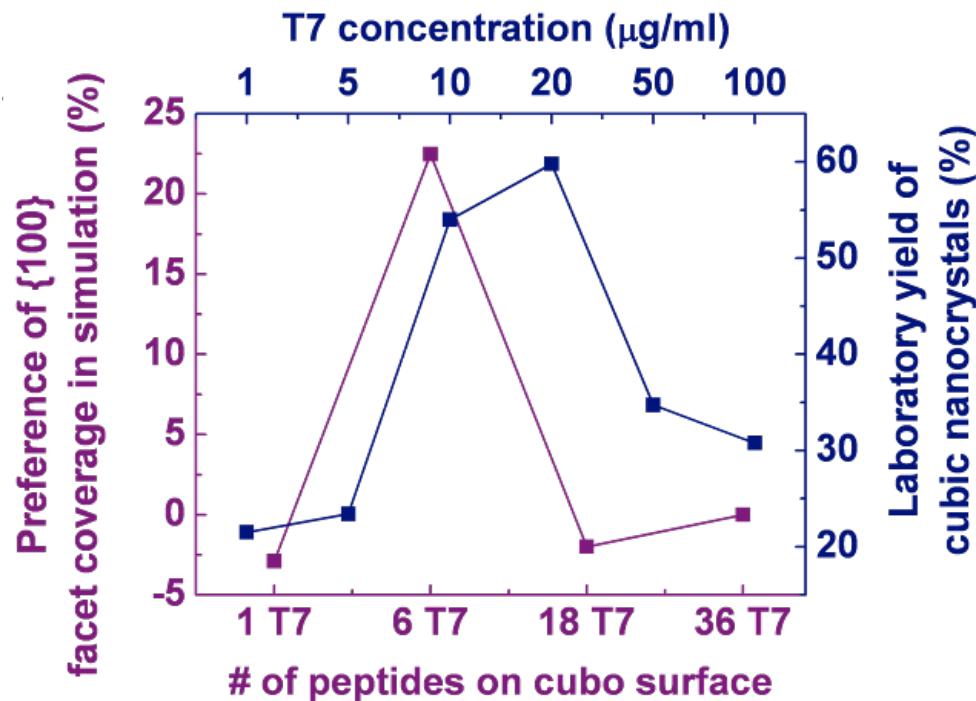
# Shape Development Depends on Surfactant (Peptide) Concentration



Peptide T7 = TLTTLTN



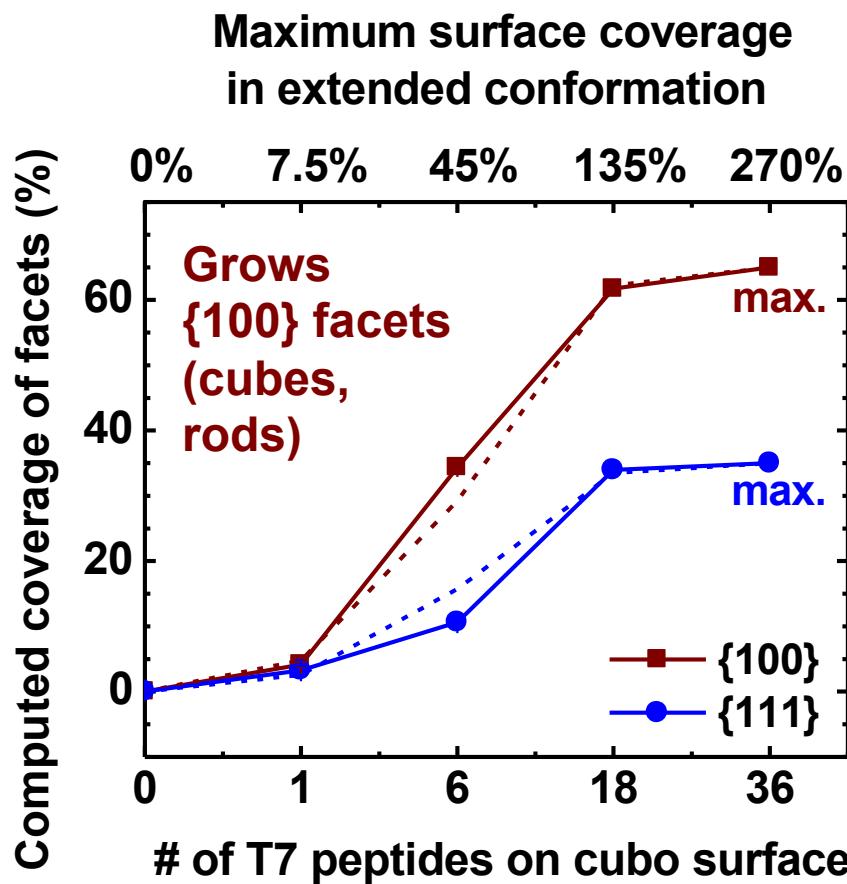
# Concentration Dependence Explained



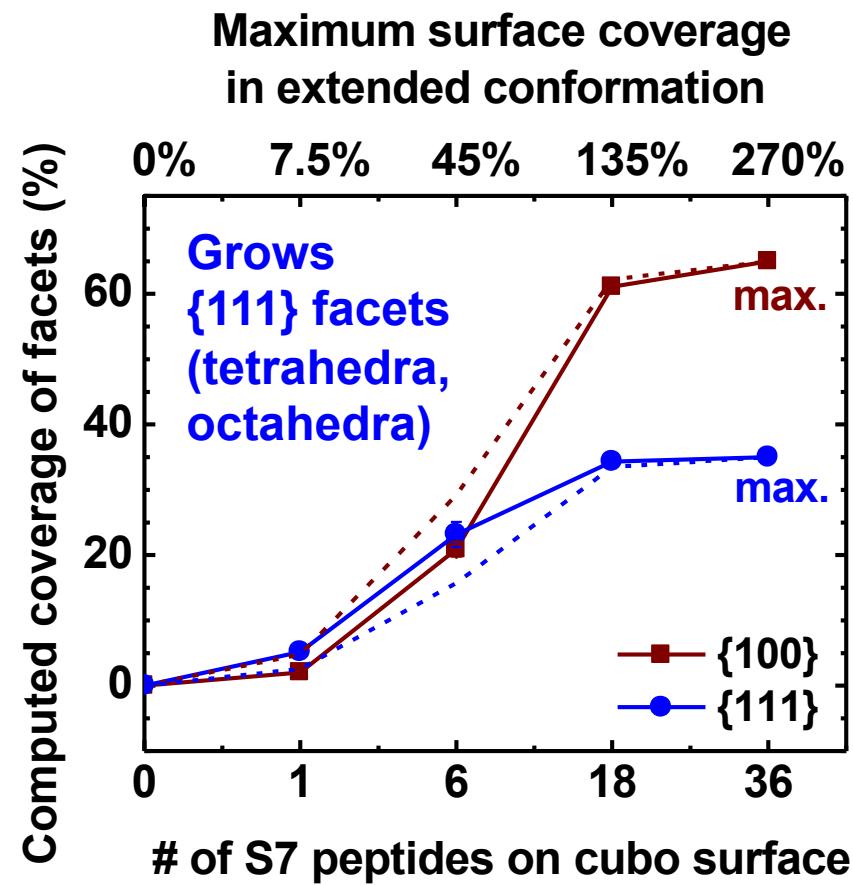


# Concentration Dependence Explained

Peptide T7  
(TLTTLTN)

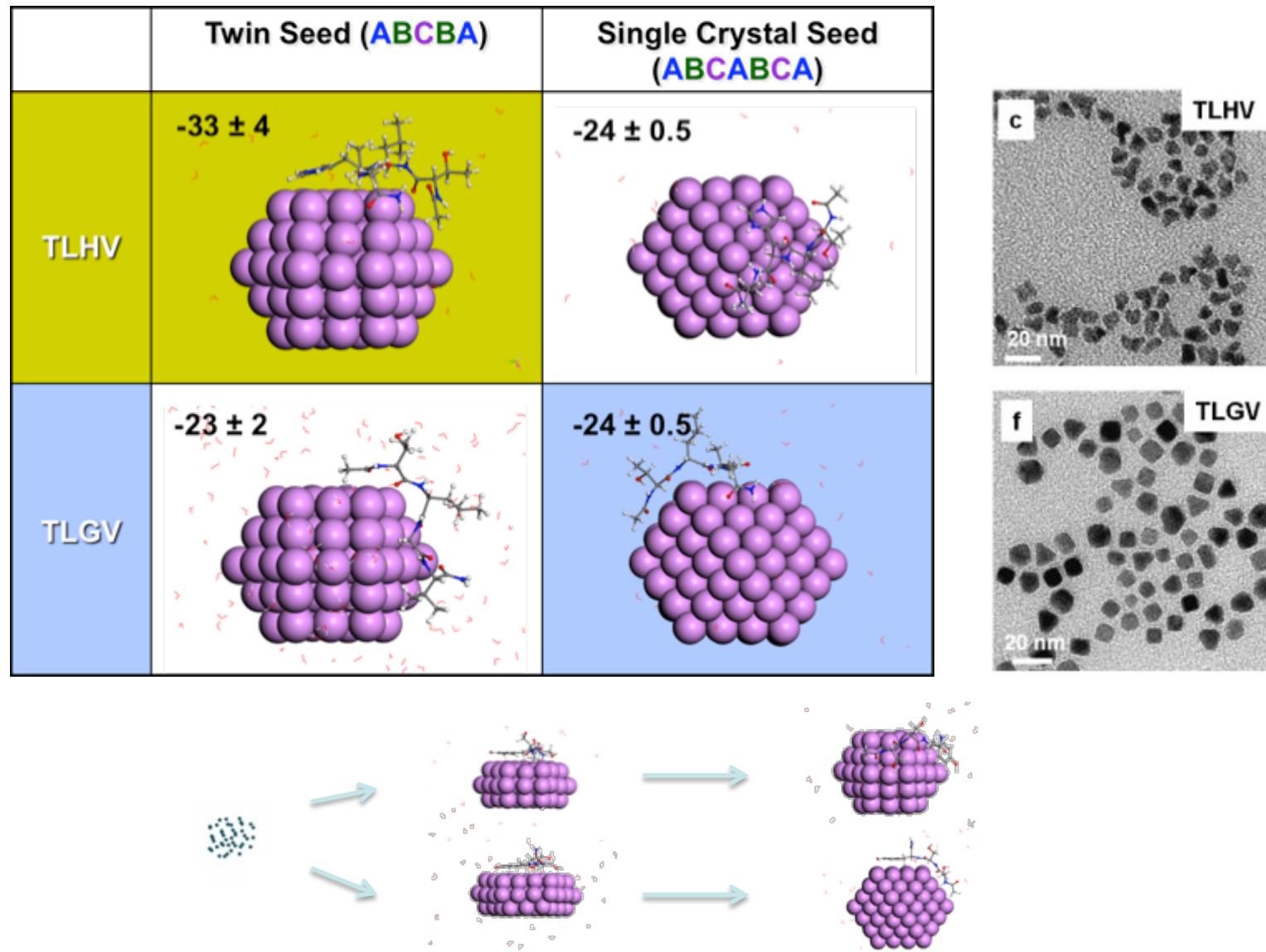


Peptide S7  
(SSFPQPN)





# Understanding Particle Shape II: Twin Versus Single Crystal





## Conclusions: Soft Epitaxial Concept and Application to Ligand/Nanostructure Design

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- Molecular epitaxy drives adsorption of peptides & organics on fcc metal surfaces
- {111} surfaces are a better fit to  $sp^2/sp^3$  hybridized groups than {100} and {110} surfaces
- Locally even surfaces lead to higher peptide adsorption than strongly curved or rough surfaces (difference to thiols))
- Polarization/induced charges enhance adsorption

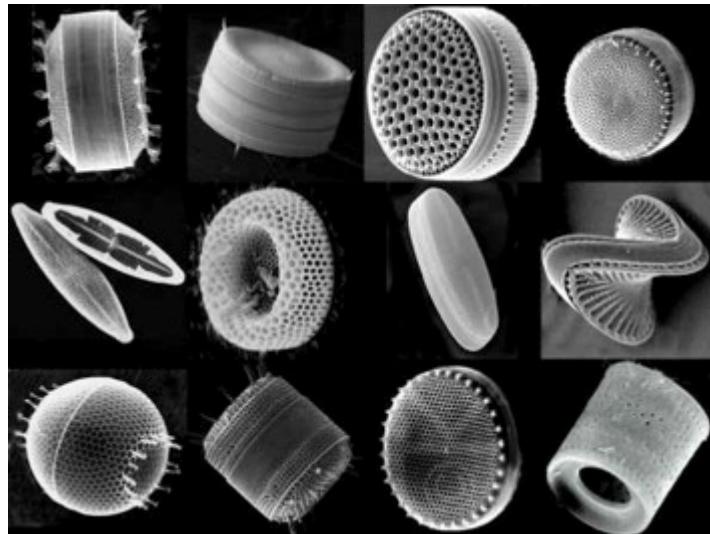


# Application to Design of Ligands and Nanoparticle Shape

Calculated property	Relation to experiment
Selectivity of peptides to extended and nanocrystals $\{h\ k\ l\}$ facets	Recognition of facet specific peptides using phage display
Facet coverage and relative facet coverage with peptides	Shapes and yields of nanocrystals
Binding energies	Binding constants and size of nanocrystals
Concentration dependence preference of peptides on the surface	Above properties as a function of concentration and surface coverage
Spatial location of peptides on $\{h\ k\ l\}$ facets, and average distance of residues to the surface	New information, and more accurate interpretation of observations
Tendency for peptide assembly on nanocrystal surfaces	New information, and more accurate interpretation of observations



# Silica ( $\text{SiO}_2$ )<sub>n</sub>



10  $\mu\text{m}$



10 cm

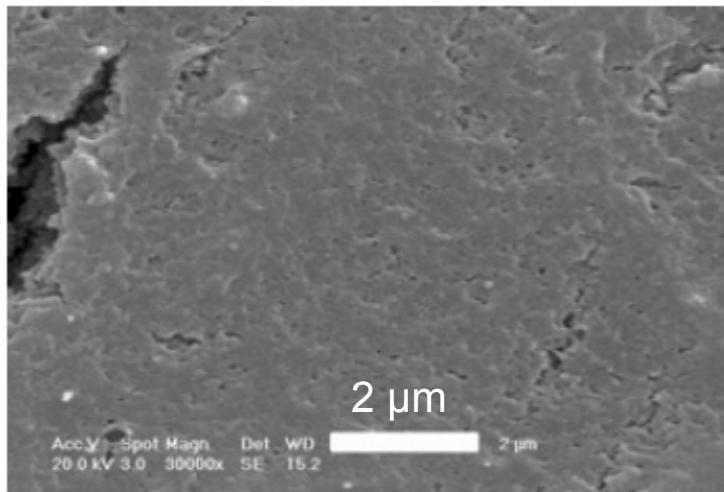
- Silica nanoparticles as drug carrier (FDA approved)
- Catalyst supports
- Separation media (chromatography)
- Templates for nanostructure overgrowth
- Interfacial control in silica/polymer composites
- Which silica particles (acidity, surface structure) are suited for a given application?



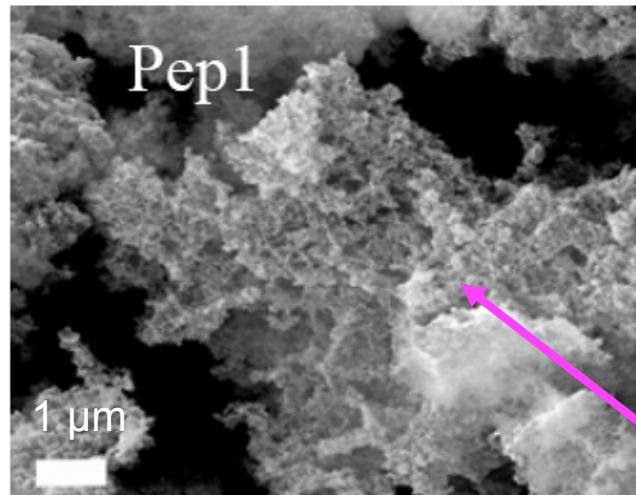
# How Can we Control Selective Binding of Biomolecules and Shape *in Vitro*?

Morphology upon acidic hydrolysis of  $(\text{CH}_3\text{-O})_4\text{Si}$  and  $(\text{C}_2\text{H}_5\text{-O})_4\text{Si}$

No peptides → Amorphous



Presence of a peptide (Pep1=KSLSRHDHIHHH)



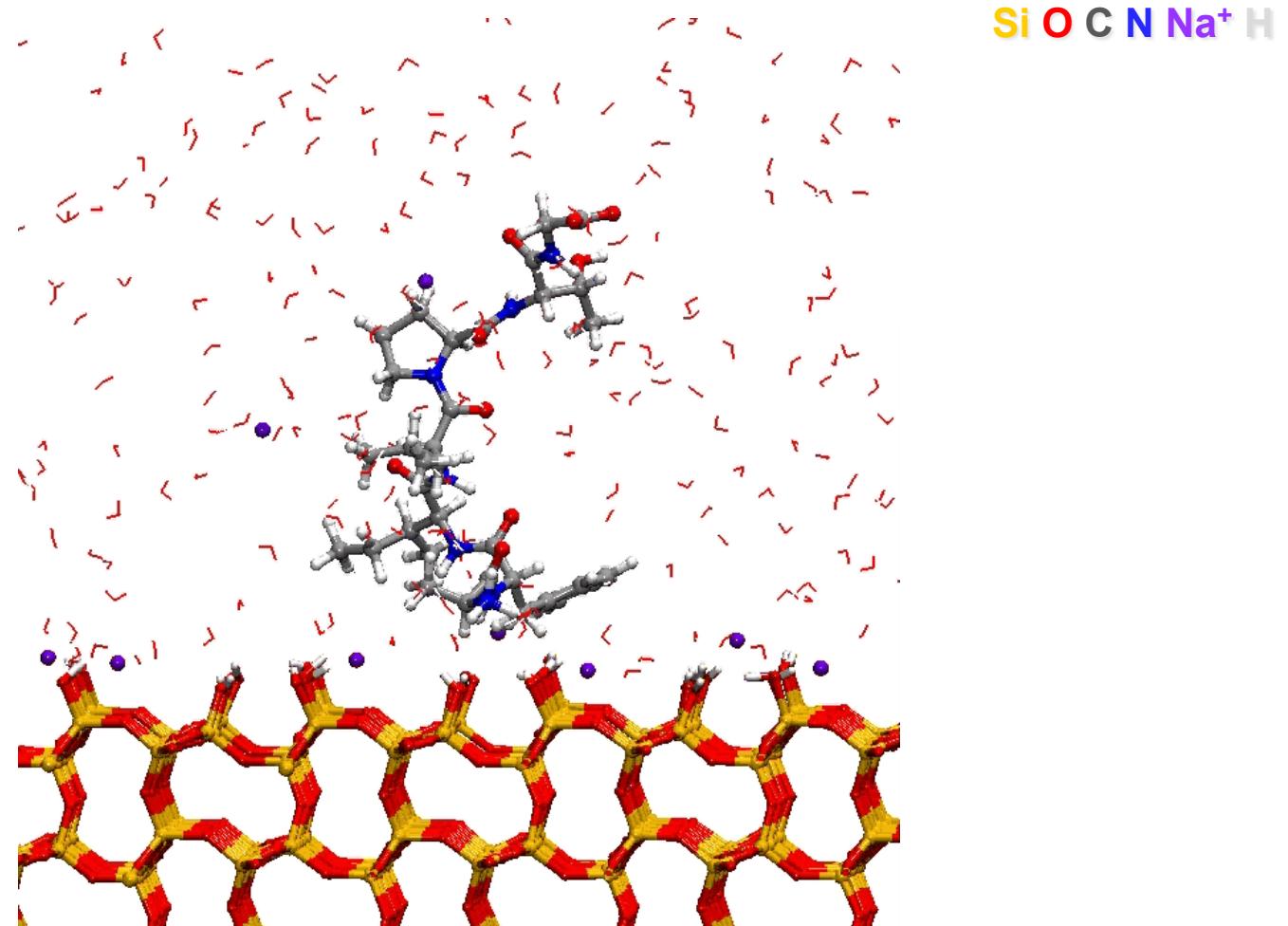
C. C. Perry (Nottingham)

**Collection of NPs**

- Peptides inhibit uniform growth and support formation of nanoparticles (size control possible by tuning pH)
  - Buried nanoscale interfaces difficult to monitor by imaging/measurements
- Need to understand molecular interactions



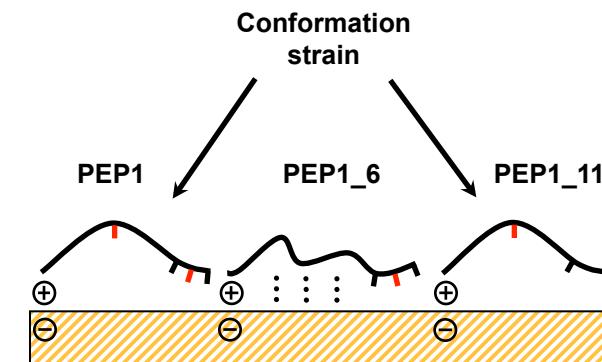
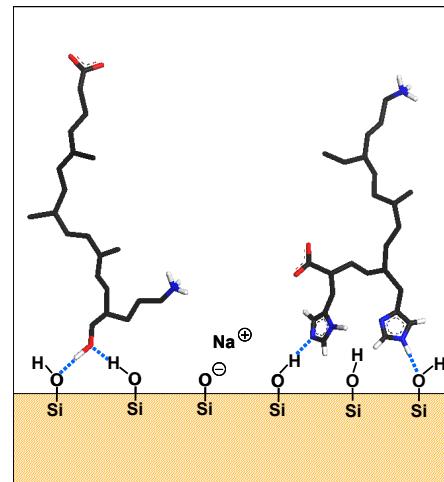
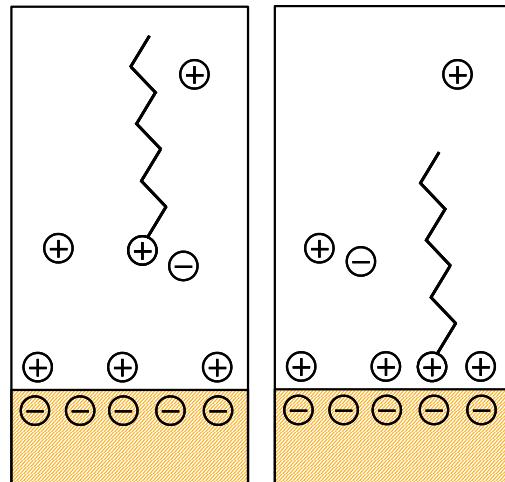
# Molecular Simulation Helps Rationalize Specific Interactions and Experimental Observations



Simulation of a peptide AFILPTG on a Q<sup>3</sup> silica surface in water at pH ~7;  
5 ns simulation time



# Peptide Recognition of the Silica Surface by Ion Pairing and Hydrogen Bonds



- Ion pairing/exchange

Typical density of  $\text{SiO}^- \text{Na}^+$  groups ( $\text{pH} = 7.5$ ):

0.2 .. 1.0 per  $\text{nm}^2$

Total density of  $\text{SiO}^- \text{Na}^+ + \text{SiOH}$  on a Q<sup>3</sup> surface:  
4.7 per  $\text{nm}^2$

- Hydrogen bonds

- Sequence-adsorption relationships

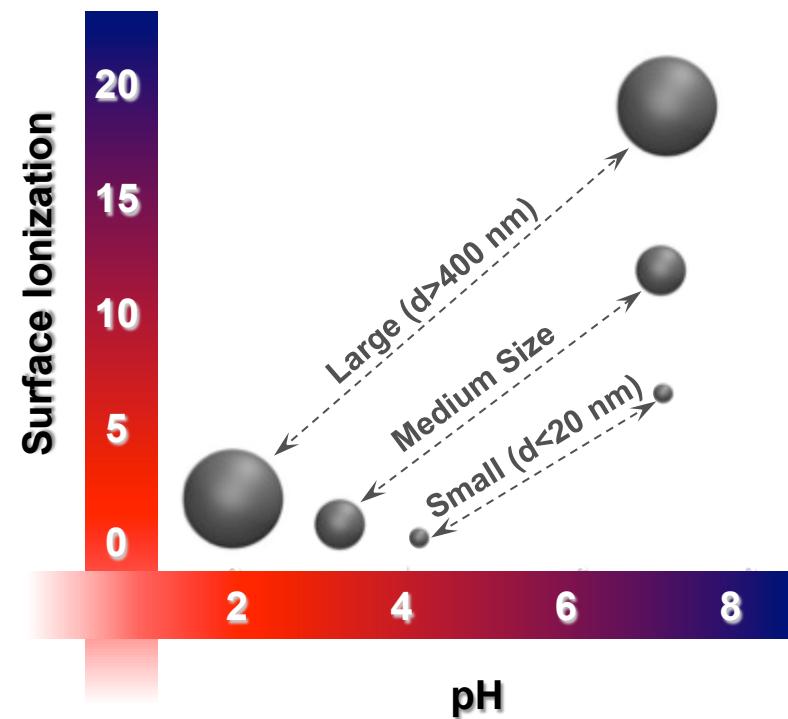
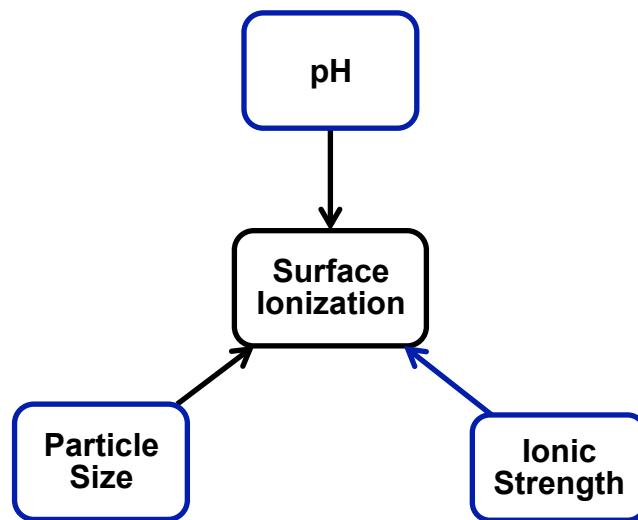
I: conf. restraint

II: flexible and better fit

III: missing H bonds



# Determinants of Surface Ionization and Acidity



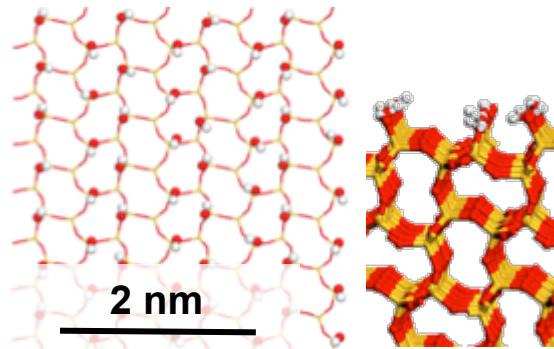
Sequence similarity of peptides attracted to “silica” often less than 20%

==> need for much more detailed understanding

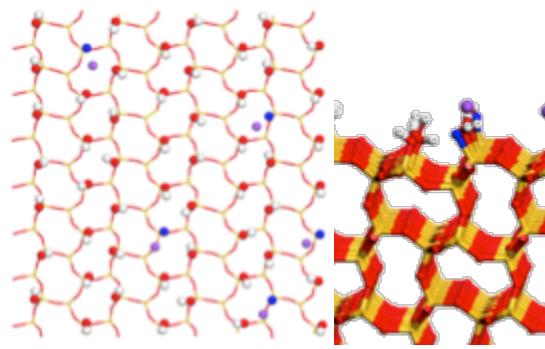


# Differences in Surface Structure by Realistic Silica Models

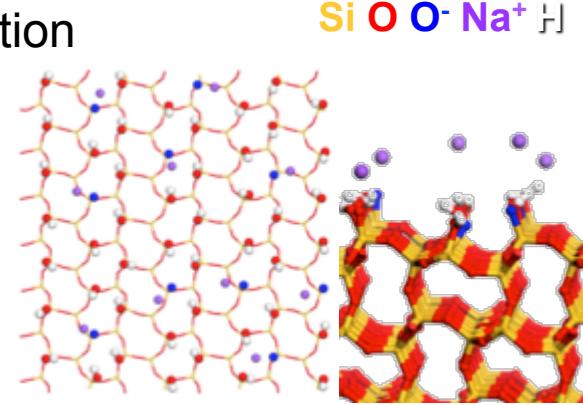
Q3 surfaces, 4.7 SiO(H,Na) per nm<sup>2</sup>, with 0-18% ionization



0% ionized – 4.7 OH/nm<sup>2</sup> (pzc)  
pH~4 for 20 nm particle  
pH~2.5 for 400 nm particle\*

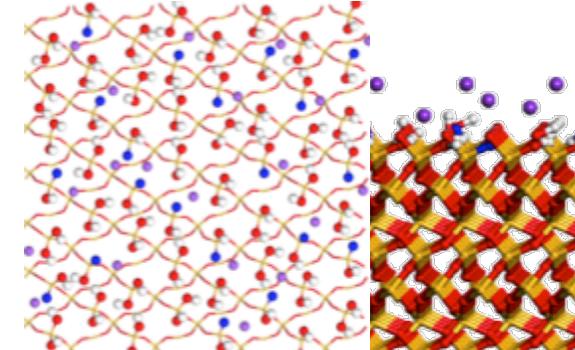
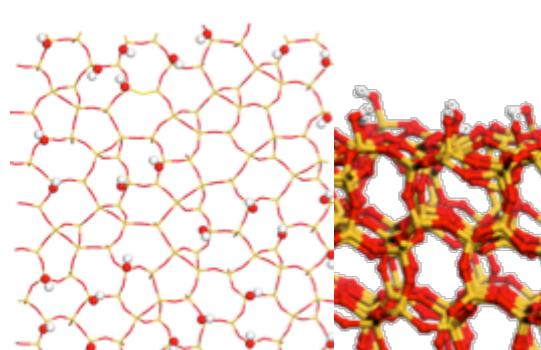
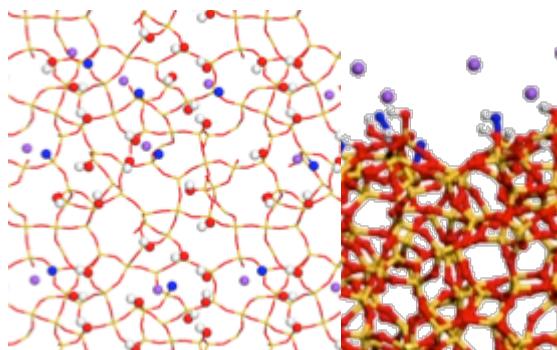


9% ionized –  
pH~7 for 20 nm particle  
pH~5 for 400 nm particle



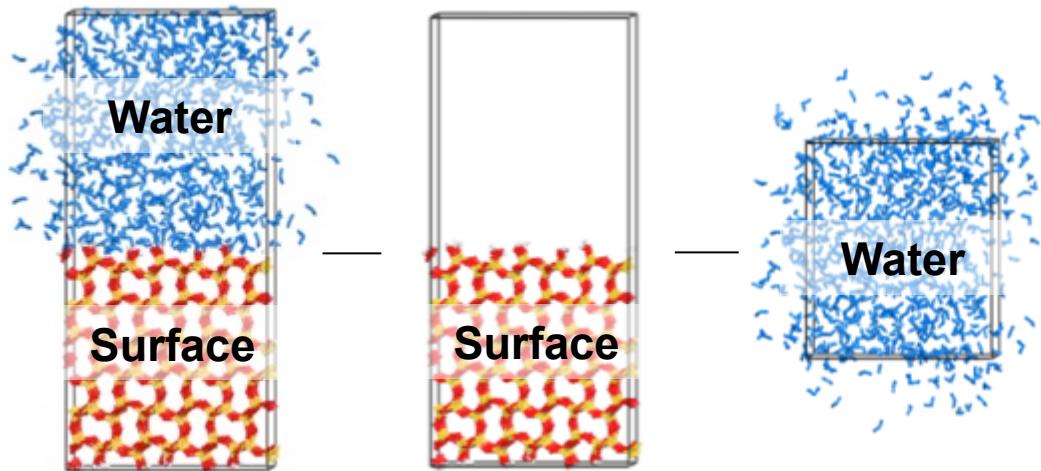
18% ionized –  
pH~9 for 20 nm particle  
pH~7 for 400 nm particle

Amorphous Q3, Q3/Q4, Q2 surfaces with 0-18% ionization



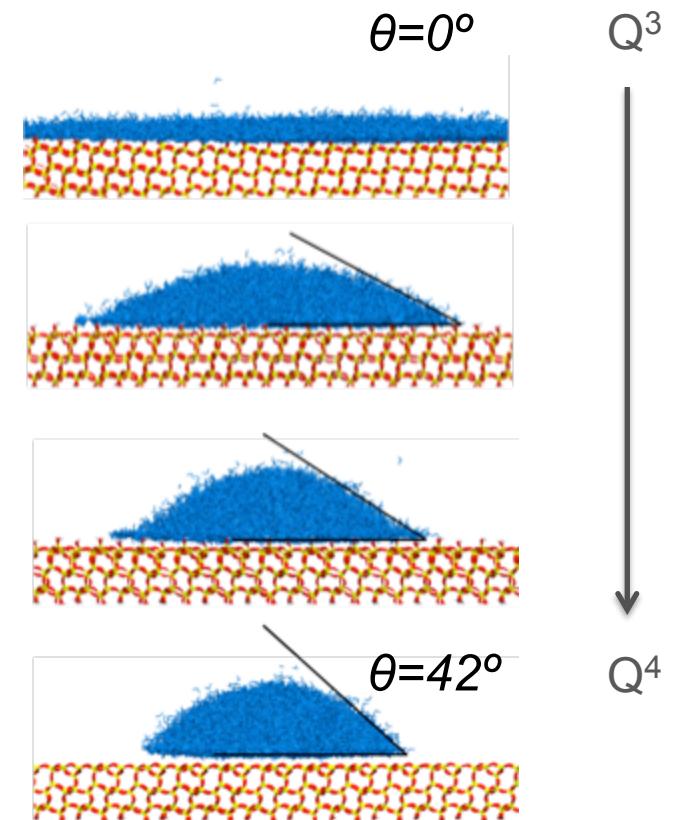


# Energy of Immersion in Water and Contact Angles for Transitional Q<sup>3</sup>/Q<sup>4</sup> Environments



$$\Delta H_{imm} = \frac{E_{water-surface} - E_{surface-vacuum} - E_{water}}{2A}$$

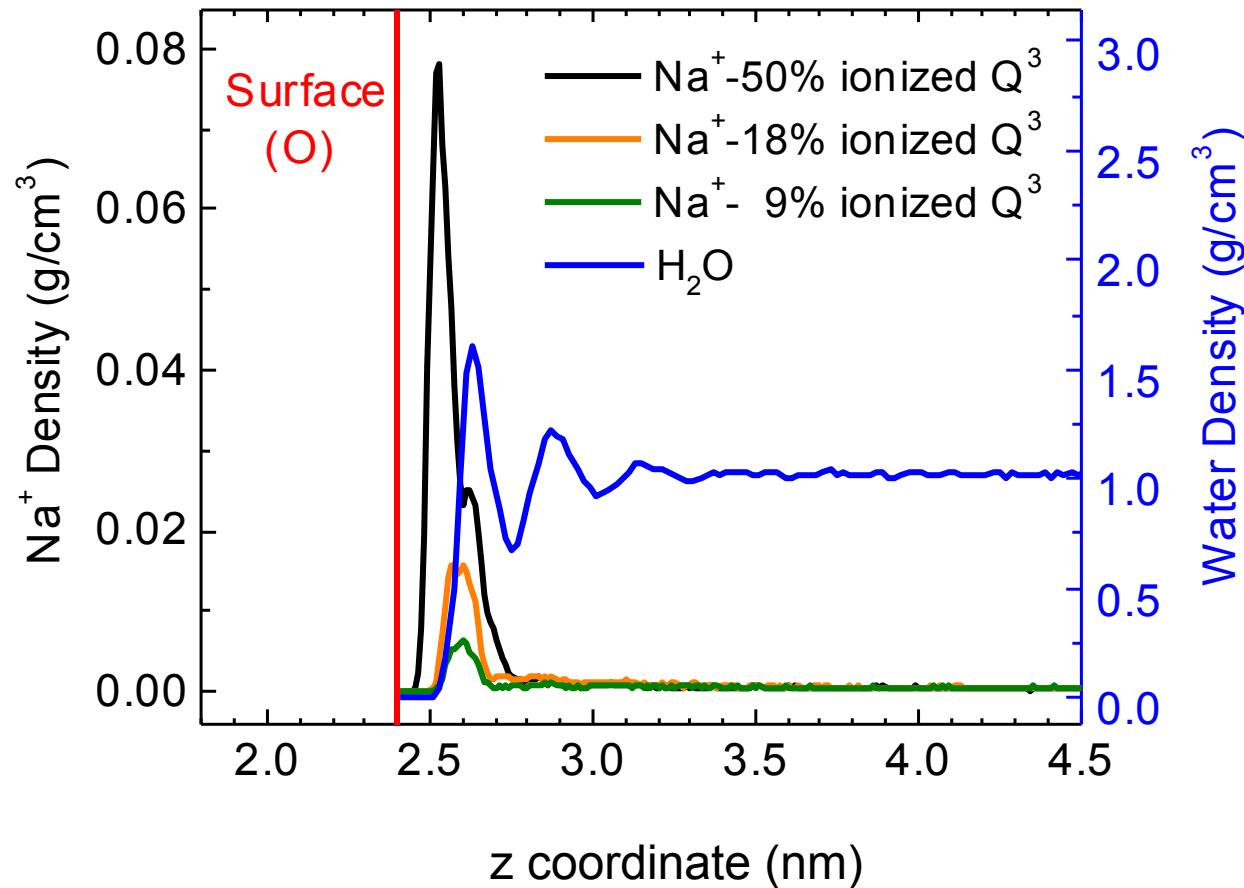
Experiment: 160±5 (Q<sup>3</sup> pyrogenic silica)  
Simulation: 167±2 (SPC), 160±2 (TIP3P),  
157±2 (PCFF)  
(in mJ/m<sup>2</sup>)



- At pzc (deionized H<sub>2</sub>O)
- Deviation sim vs expt < 3°

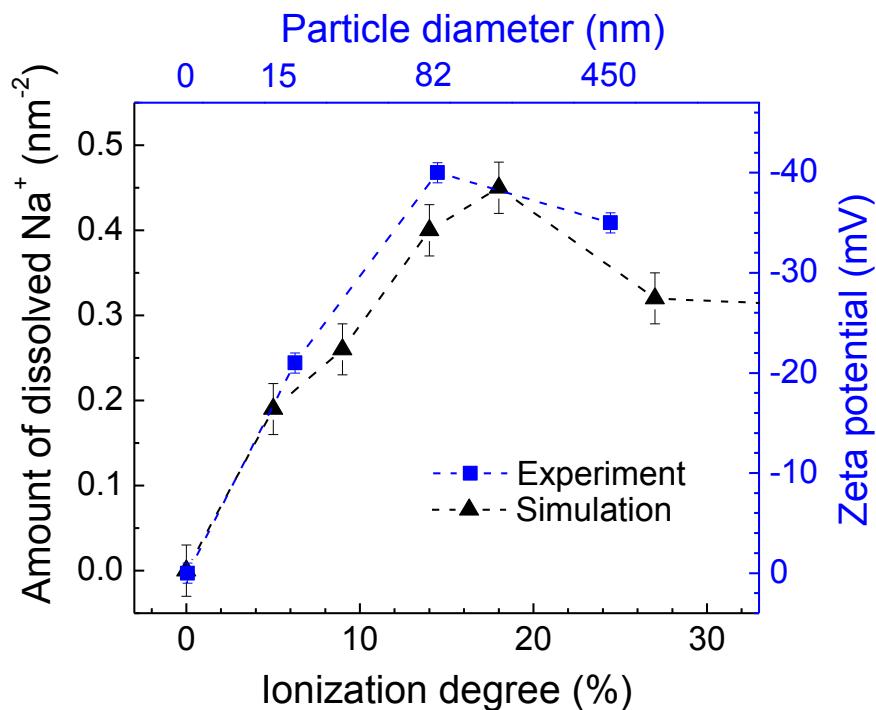
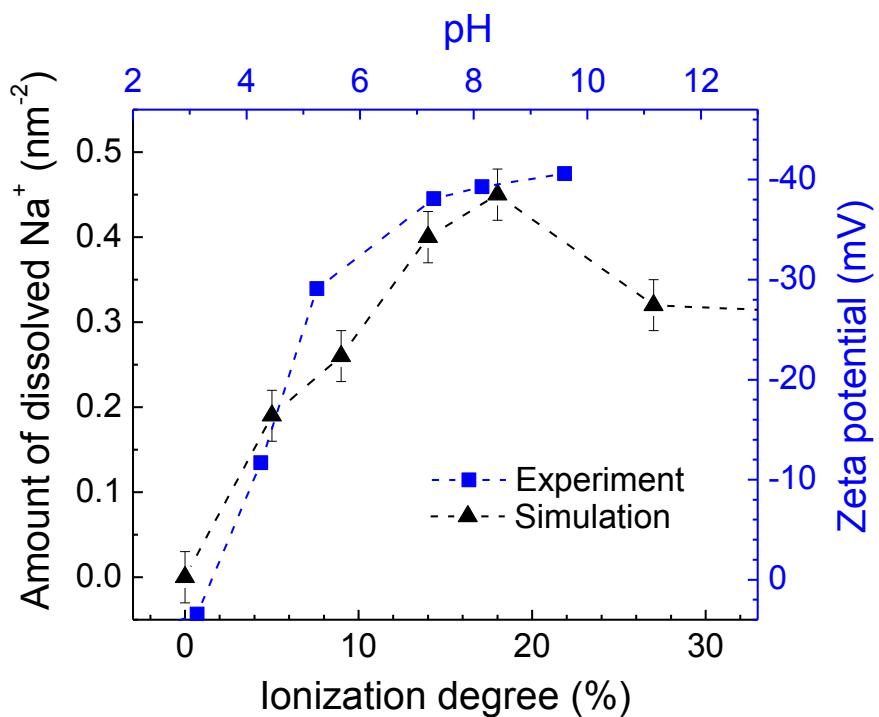


# Density Profile for Ionized Q<sup>3</sup> Surfaces





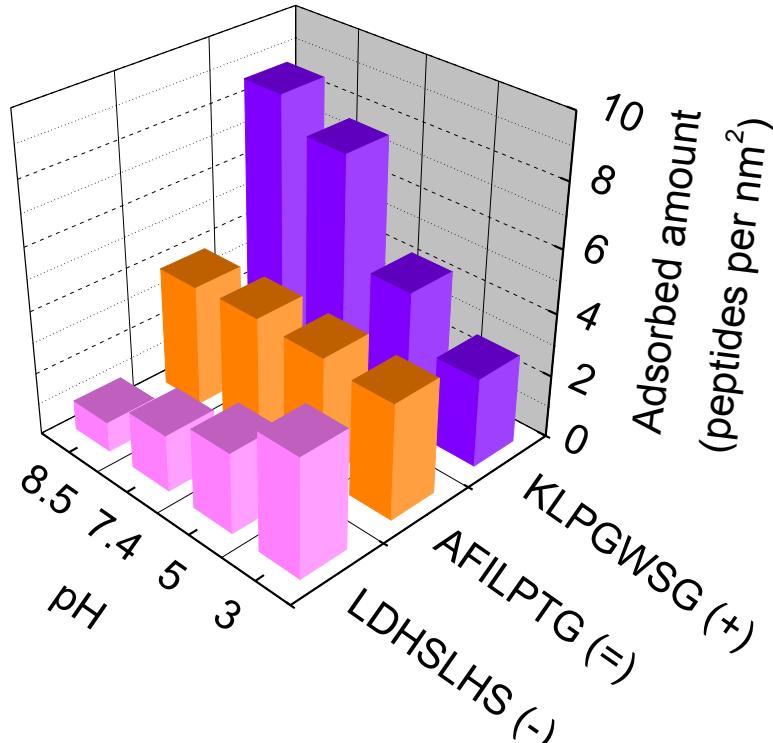
# Different Penetration Depth of Cations Into Solution Versus Zeta Potential



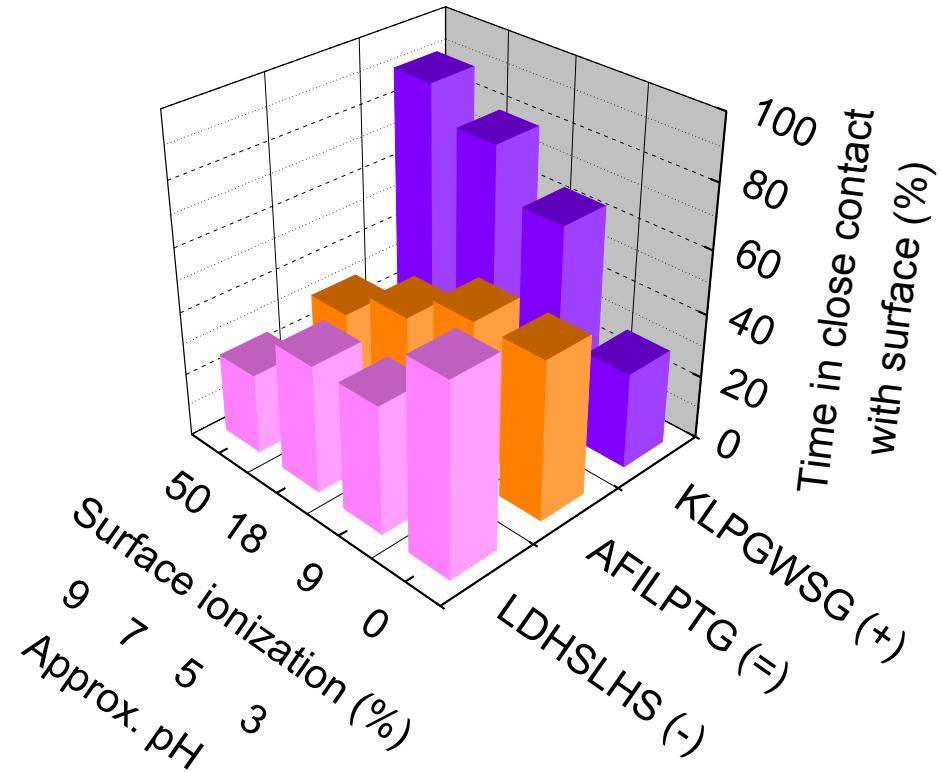
Amount of dissolved  $\text{Na}^+$  from density profile in the simulation ( $>3 \text{ \AA}$ )



# Predictions of Peptide Binding Across a Range of pH



Measurements



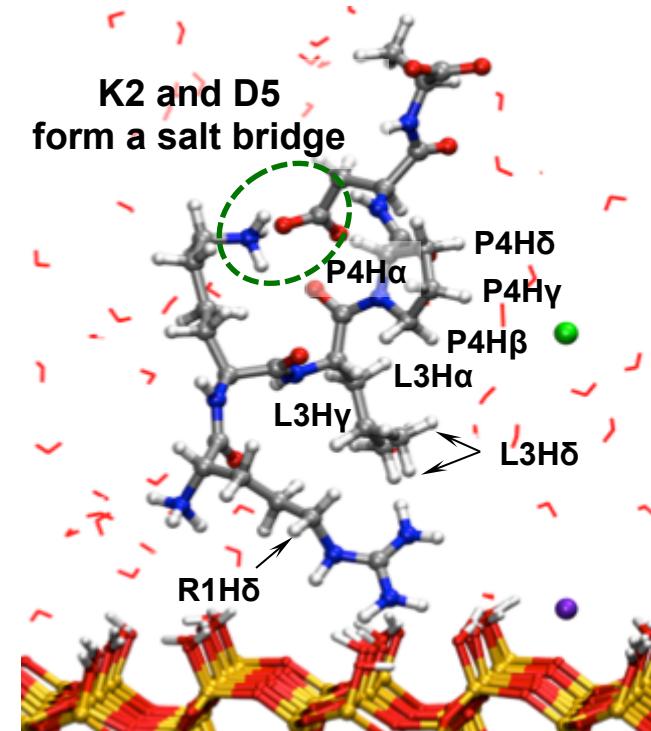
Simulation



# Visualization in Atomic-level Agreement with NOESY

Hydrogen Label	Cross-Peak Intensity from NOESY	Ave. Inter-Nuclear Dist. from Simulation (Å)
L3 H $\delta$ – L3 H $\alpha$	S	2.4 ± 0.1
L3 H $\delta$ – L3 H $\gamma$	S	2.4 ± 0.1
L3 H $\delta$ – P4 H $\alpha$	M	5.6 ± 0.5
L3 H $\delta$ – P4 H $\beta$	W	6.0 ± 0.5
L3 H $\delta$ – P4 H $\gamma$	M	5.3 ± 0.3
L3 H $\delta$ – P4 H $\delta$	S	3.7 ± 0.5
L3 H $\delta$ – R1 H $\delta$	W	7.7 ± 0.7

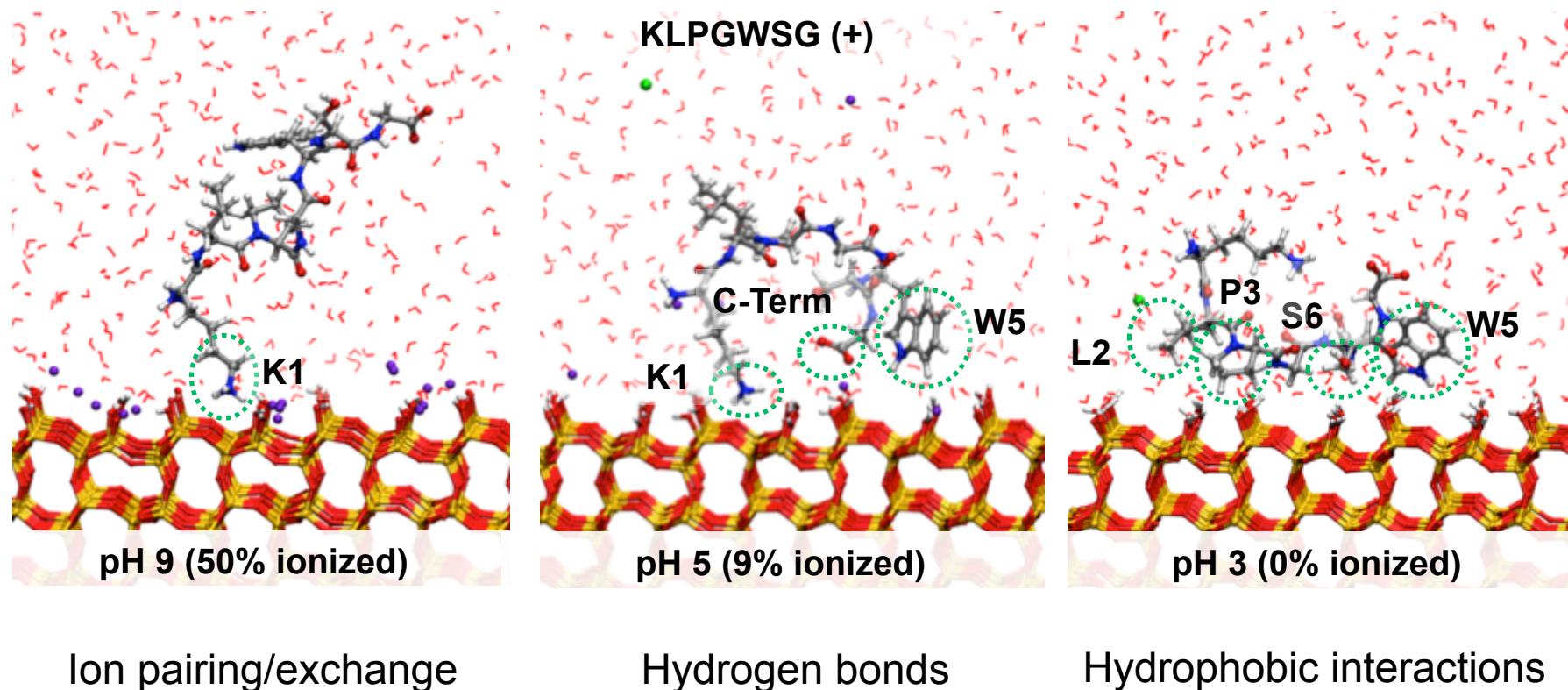
S=strong, M=medium, W= weak



RKLPA on Q<sup>3</sup> silica (4% ionized)



# Changes in Mechanism as a Function of pH



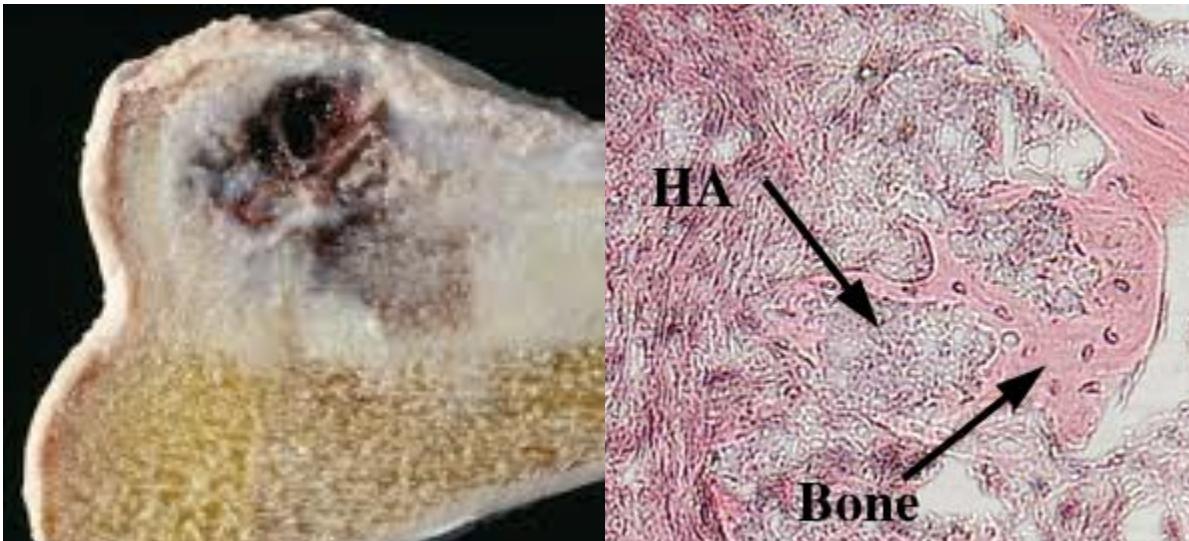
Ion pairing/exchange

Hydrogen bonds

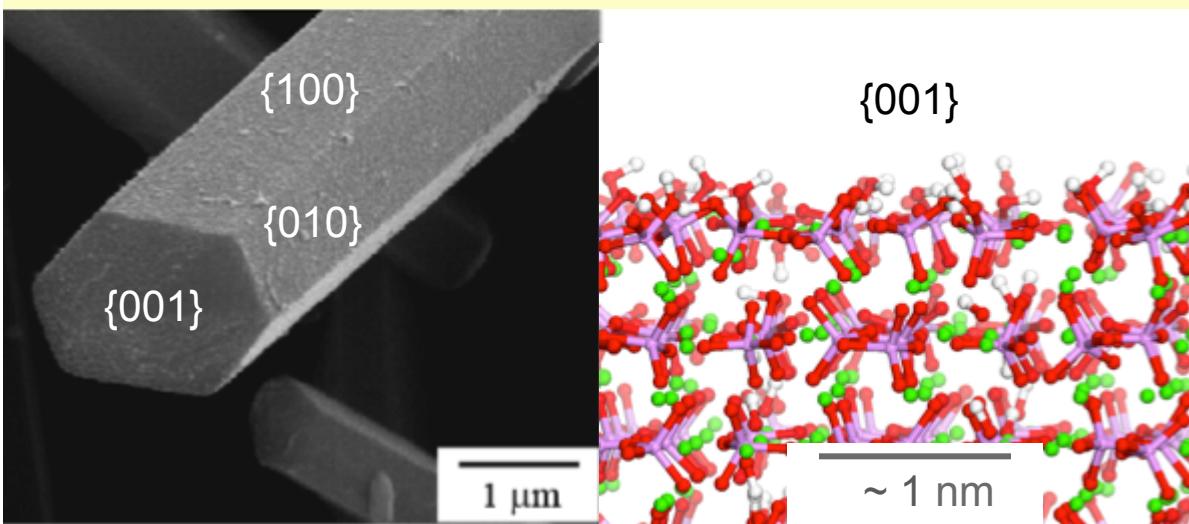
Hydrophobic interactions



# Apatites: Molecular Understanding of Bone, Dentin, and Related Diseases



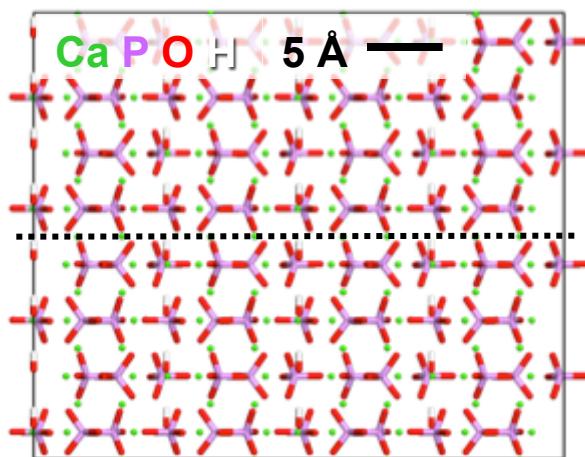
Interface Engineering: surface tension, pH, protein adhesion  
Simulation  $\Leftrightarrow$  Experiment  $\Leftrightarrow$  Clinical guidance



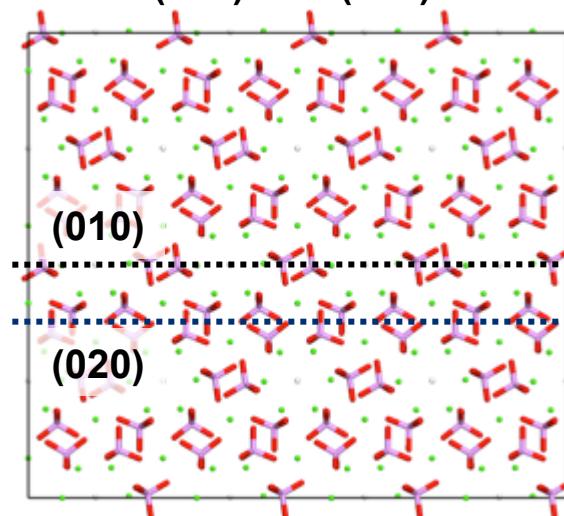


# Crystal Shape and Cleavage Planes (Side View)

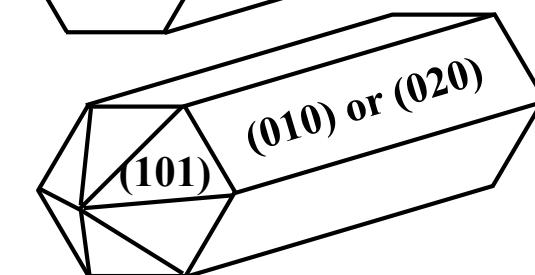
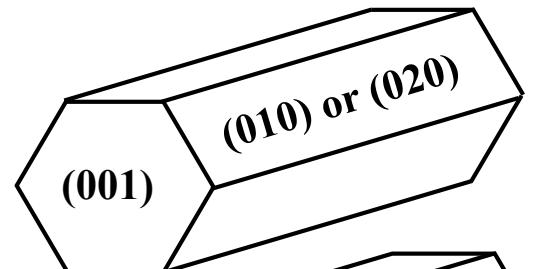
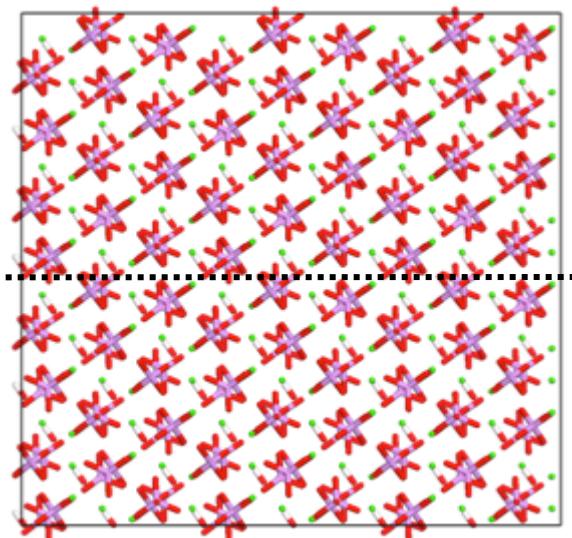
(001)



(010) and (020)

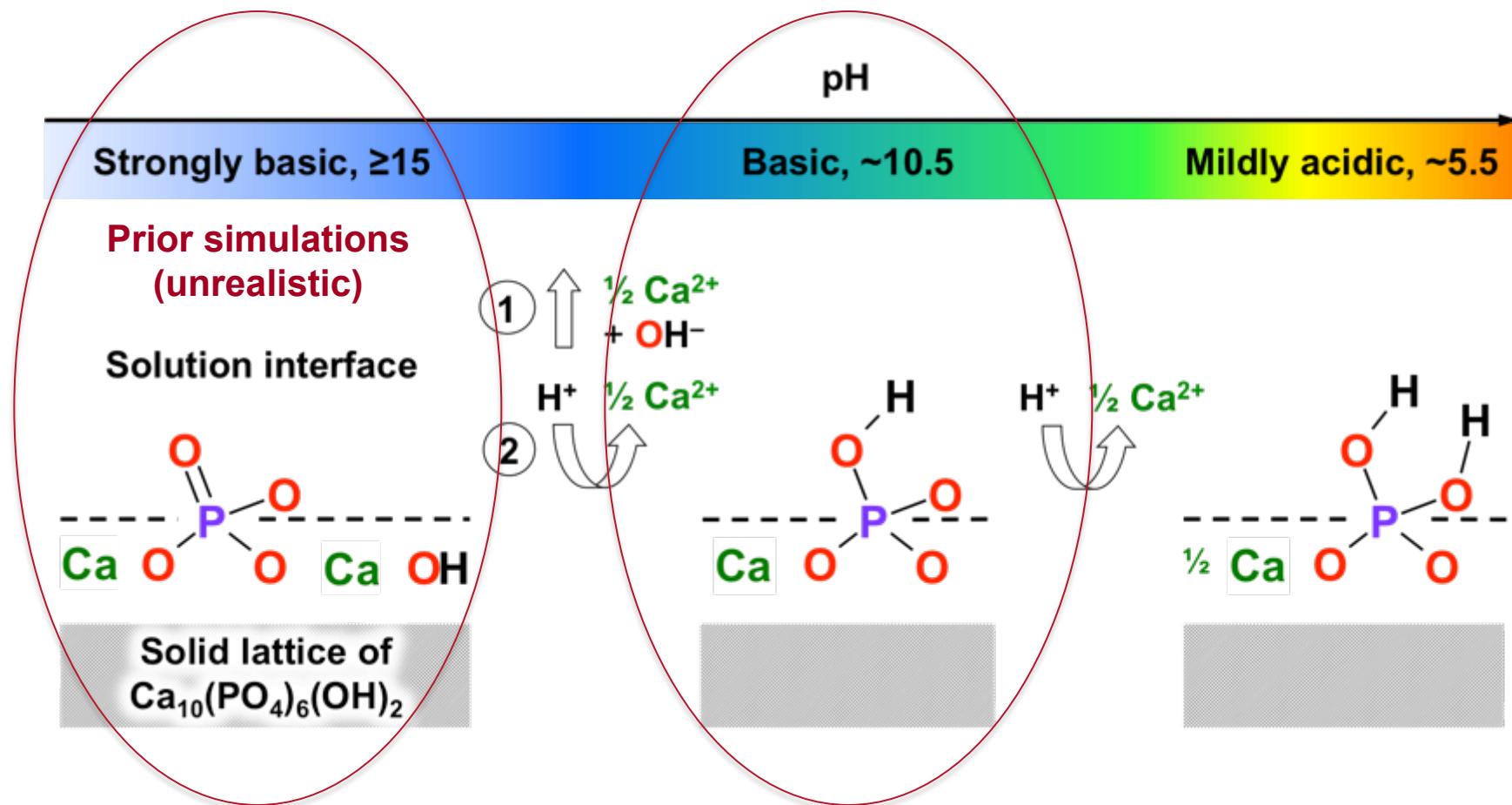


(101)





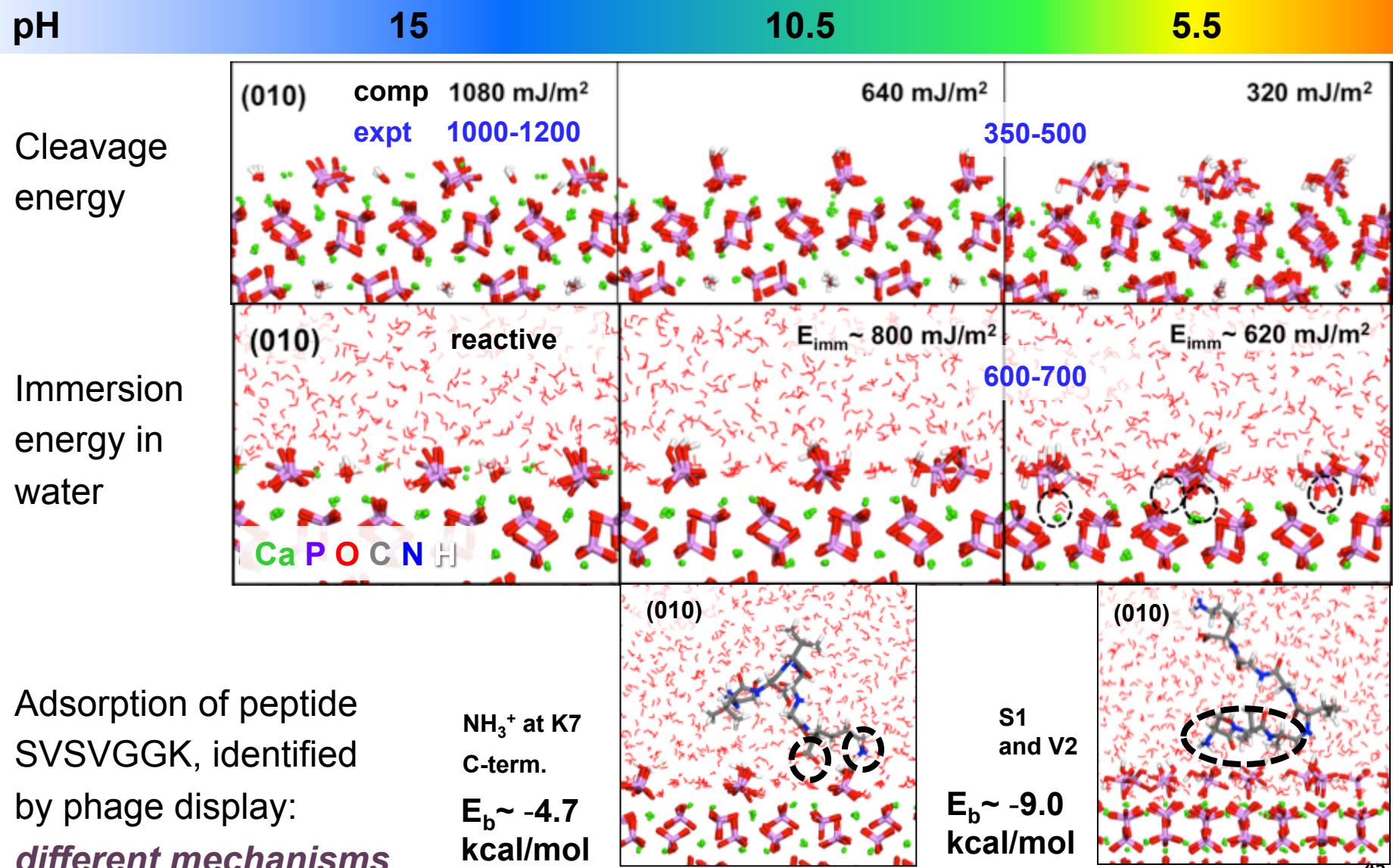
# pH Dependence of Surface Structure of Apatite



- Major dependence of cleavage energy, immersion energy, and specific adsorption of peptides on protonation state



# Surface Properties as a Function of pH





# Hydroxyapatite Structural and Elastic Properties – Experiment and Simulation

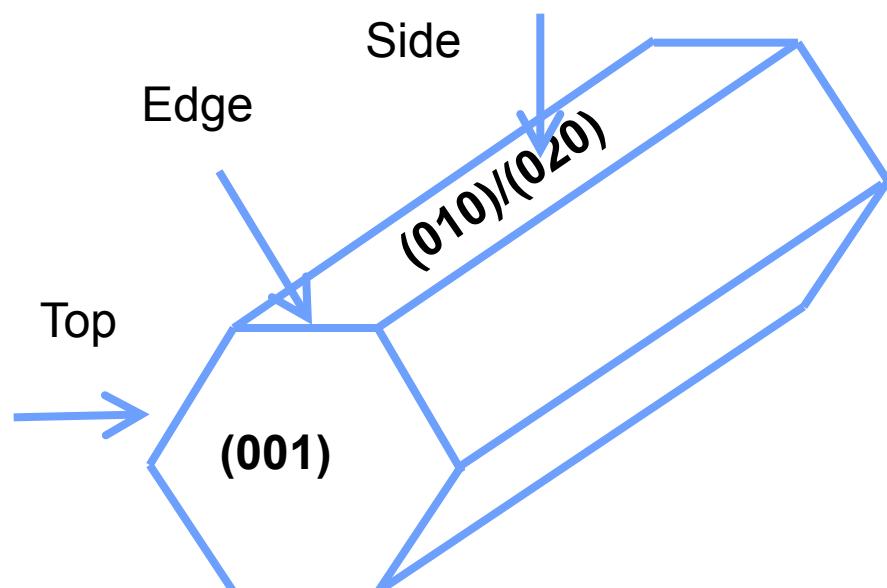
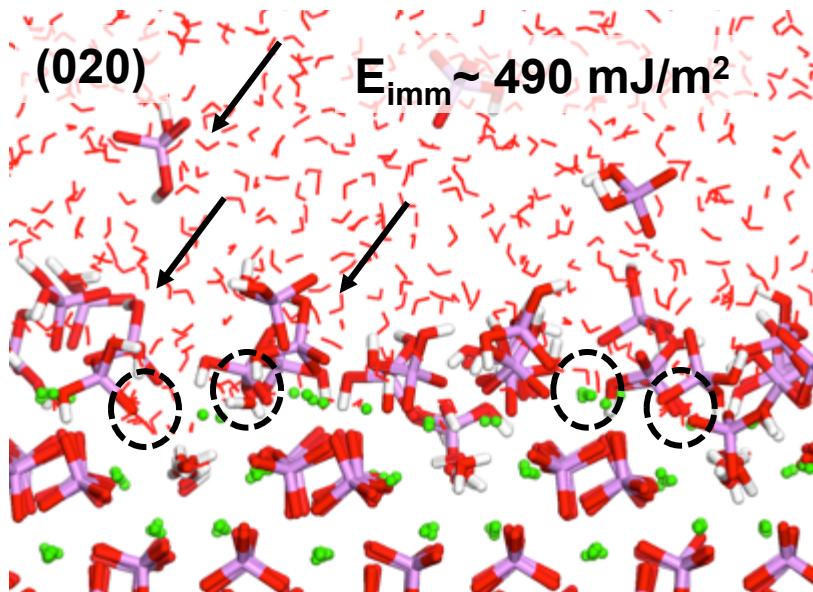
Lattice Parameters								
	cell dim.	a (Å)	b (Å)	c (Å)	α (deg)	β (deg)	γ (deg)	Density (g/cm³)
Exp <sup>a</sup>		18.83	18.83	13.75	90	90	120	3.160
9-6	$2 \times 2 \times 1$	18.82	18.81	13.75	90.00	90.00	120.02	3.167
12-6	$2 \times 2 \times 1$	18.78	18.77	13.95	90.00	90.00	119.99	3.135
Elastic Constants and Modulus								
	C <sub>11</sub>	C <sub>33</sub>	C <sub>44</sub>	C <sub>12</sub>	C <sub>13</sub>	E <sub>iso</sub> <sup>h</sup>	K	G <sub>iso</sub> <sup>h</sup>
Exp <sup>b</sup>	137	172	39.6	42.5	54.9	114	89.0	44.5
9-6 <sup>c</sup>	129.9	156.6	44.8	35.6	45.8	111.8	72.9	45.7
12-6 <sup>c</sup>	147.3	185.4	47.5	47.3	43.1	121.2	81.3	48.5
FF-Buckingham (de Leeuw)	134.4	184.7	51.4	48.9	68.5	118.8	90	46.6
DFT 1	140.0	174.8	47.5	42.4	58.3	120.6	84.5	47.7
DFT 2	145.2	191.4	37.6	47.8	73.6	106.6	90.7	46.6
DFT 3	117.1	231.8	56.4	26.2	55.6	132.1	82	51.7



# Dissolution/Crystal Growth Equilibria

- First model with validated surface and interface properties

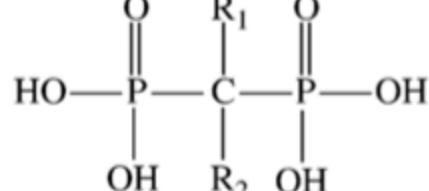
→ Can the models aid to understand nucleation and growth of crystallites in physiological environments (bone ~pH 6)?



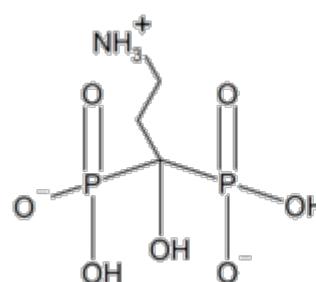


# Action of Osteoporosis Drugs on Different Crystallite Surfaces

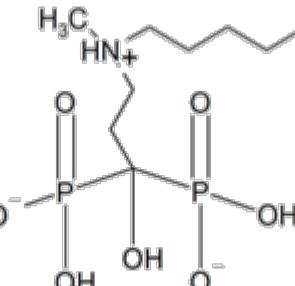
How might the molecules slow down bone dissolution?



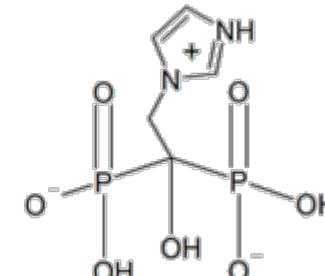
Generic Bisphosphonate



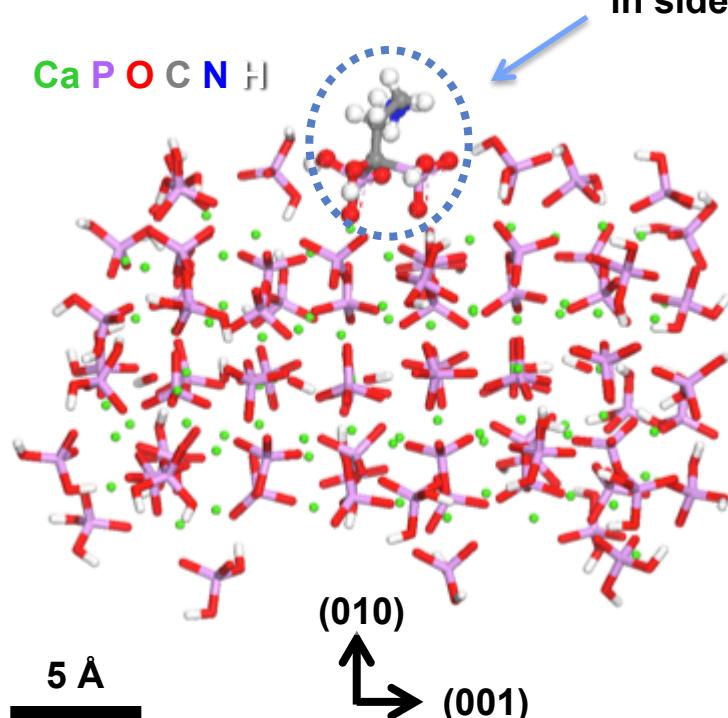
Pamidronate  
in side view



Ibandronate



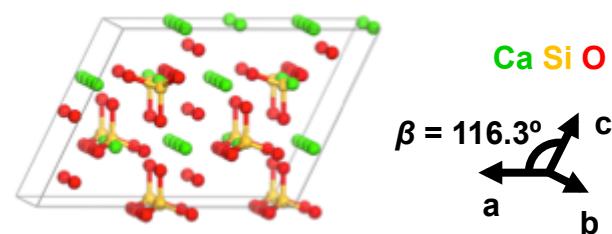
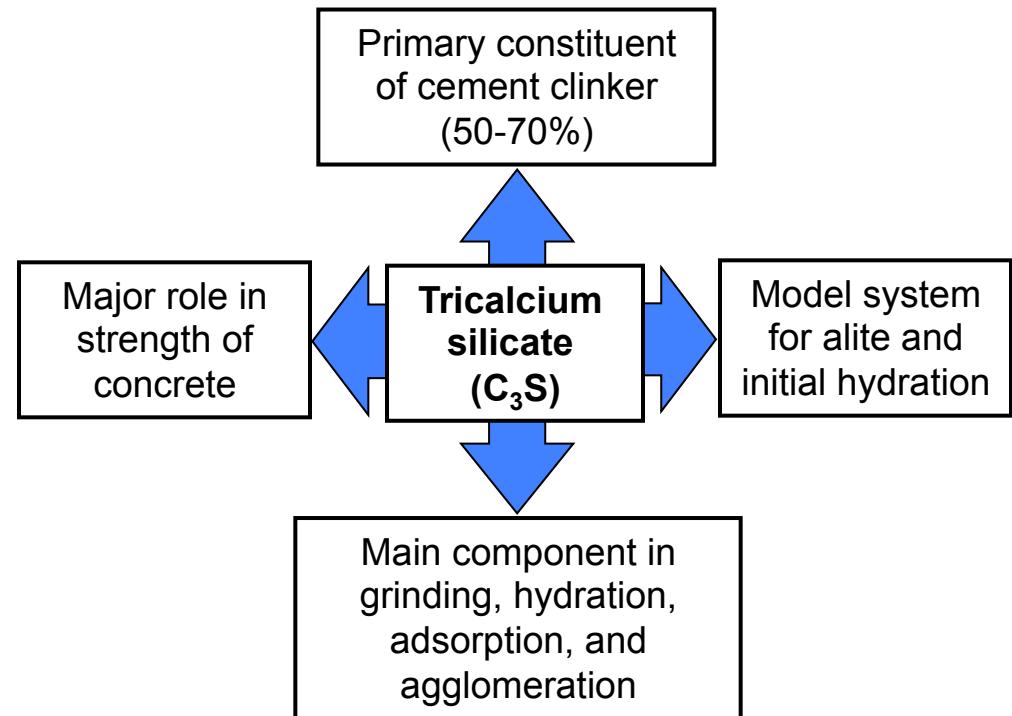
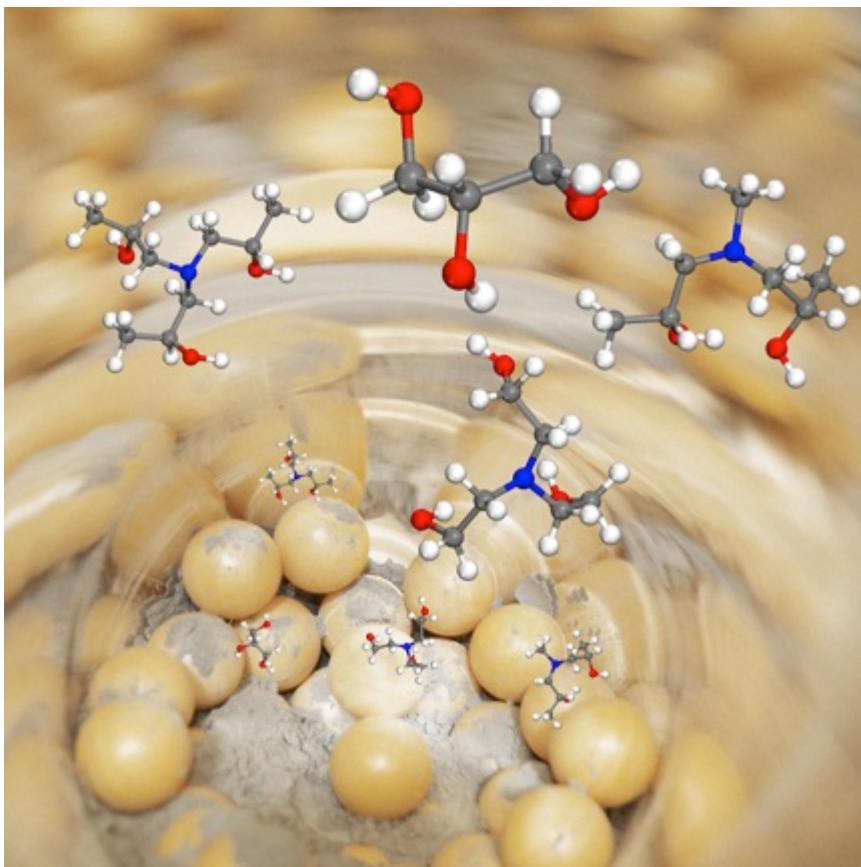
Zoledronate



- Nanocrystallites (~3 nm) are structurally flexible at pH 6
- Extended (hkl) facets are structurally stable and indicate different adsorption strength – facet preferences among various molecules can be quantified

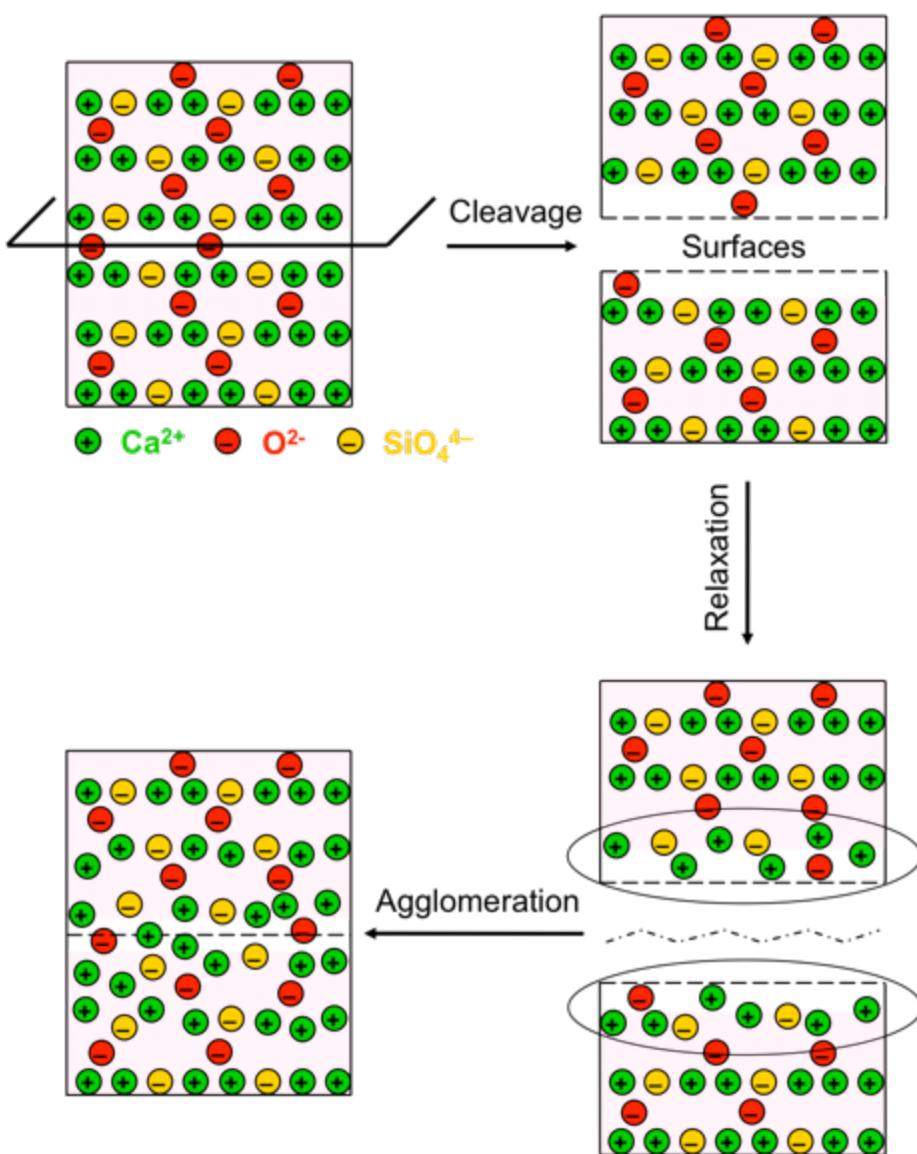


# Cement Minerals: Tricalcium Silicate $\text{Ca}_3\text{SiO}_5$





# Cleavage Properties of Tricalcium Silicate



Miller Indices	Cleavage Energy <sup>a</sup> (mJ/m <sup>2</sup> )
(1 0 0), (2 0 0)	$1534 \pm 56$
(0 1 0), (0 2 0)	$2157 \pm 120$
(0 4 0), (0 -4 0)	$1324 \pm 25$
(0 0 1) ~ (0 0 3)	$1335 \pm 25$
... (10+ more)	... (10+ more)

Surface-averaged cleavage energies (mJ/m <sup>2</sup> )		
$\text{Ca}_3\text{SiO}_5$	Computed	<b><math>1340 \pm 40</math></b>
$\text{Ca}_3\text{SiO}_5$	Expt	<b>N.A.</b>
$\text{CaO}$	Expt	<b><math>1310 \pm 200^b</math></b>
$\text{Ca}(\text{OH})_2$	Expt	<b><math>1180 \pm 100^b</math></b>

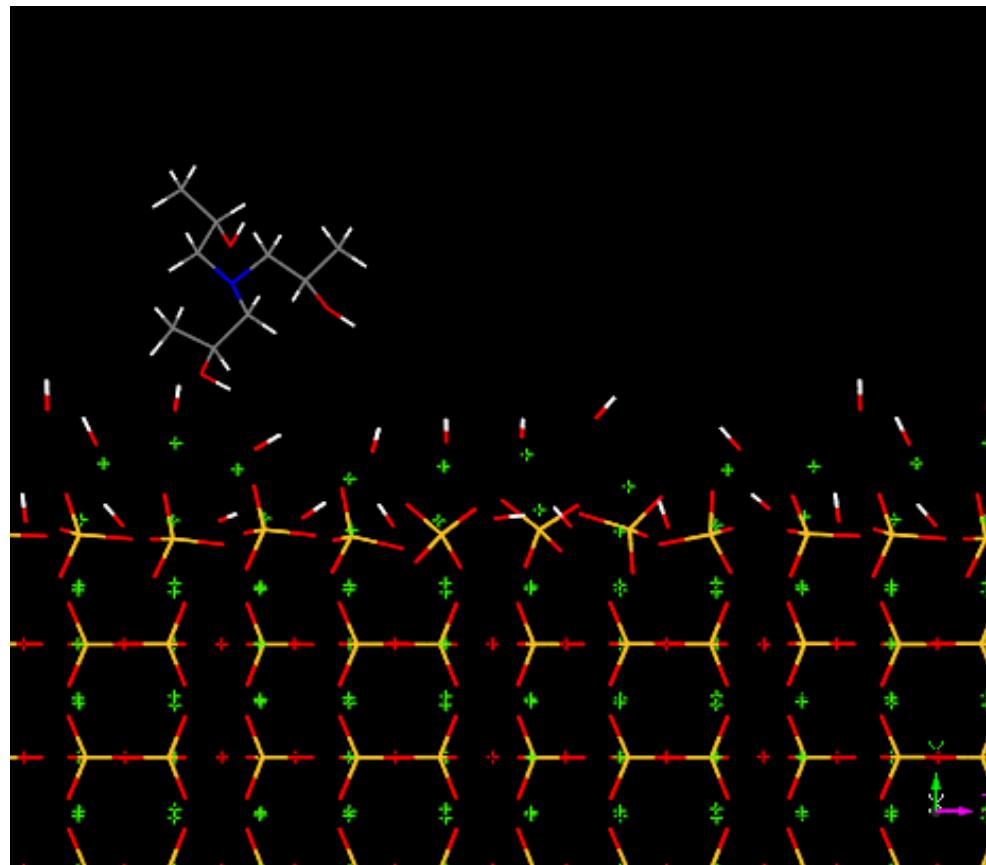


# Mechanical Properties of Tricalcium Silicate

<b>Bulk Modulus</b>	<b>Computed</b>	<b>Experiment</b>
$K$	$105 \pm 5$	105.2 <sup>a</sup>
<b>Young's Moduli</b>	<b>Computed</b>	<b>Experiment</b>
$E_x$	$152 \pm 6$	$135 \pm 7, 147 \pm 5^b$
$E_y$	$176 \pm 3$	and 117.6 <sup>a</sup> (direction unknown)
$E_z$	$103 \pm 11$	
<b>Poisson Ratios</b>	<b>Computed</b>	<b>Experiment</b>
$\nu_{xy}$	$0.303 \pm 0.042$	
$\nu_{xz}$	$0.273 \pm 0.043$	
$\nu_{yx}$	$0.225 \pm 0.021$	0.314 <sup>a</sup>
$\nu_{yz}$	$0.197 \pm 0.027$	(direction unknown)
$\nu_{zx}$	$0.372 \pm 0.041$	
$\nu_{zy}$	$0.299 \pm 0.058$	



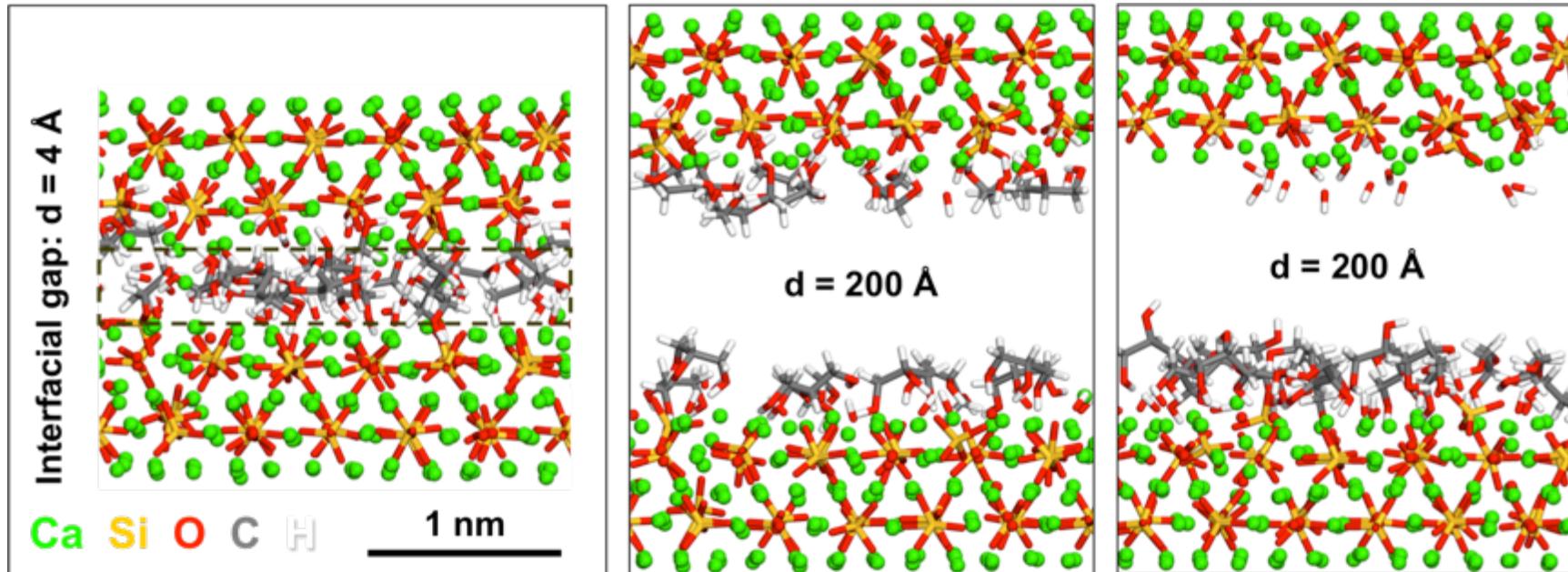
# Adsorption of Organic Molecules



- Ca coordination and hydrogen bonds to the surface determine adsorption energy
- Temperature-dependent disorder of the C3S surface
- Agglomeration reduction depends on thickness of organic layer and mitigation of local dipoles



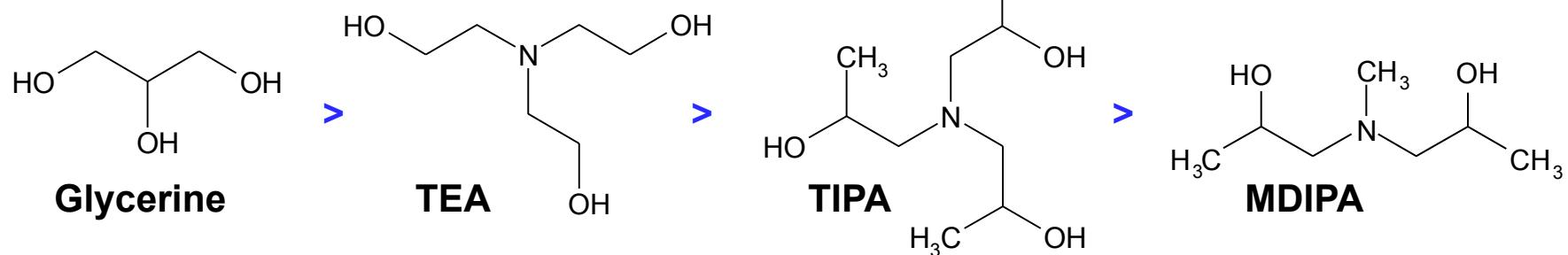
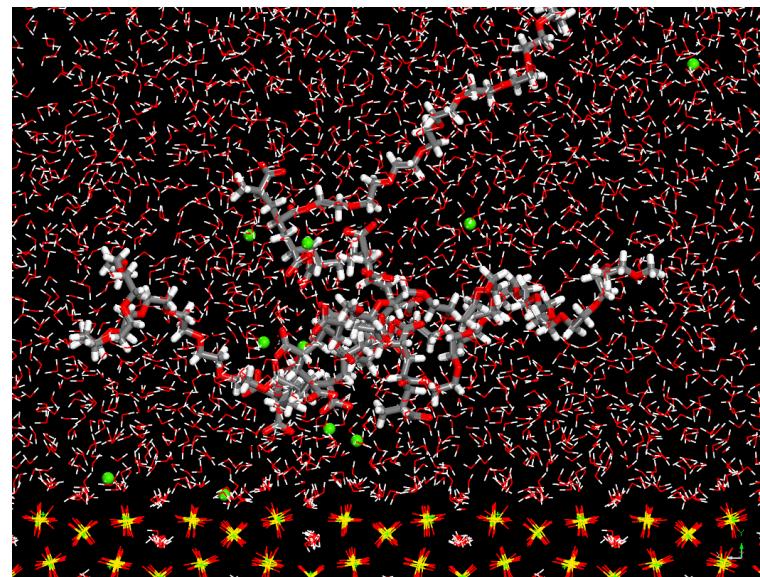
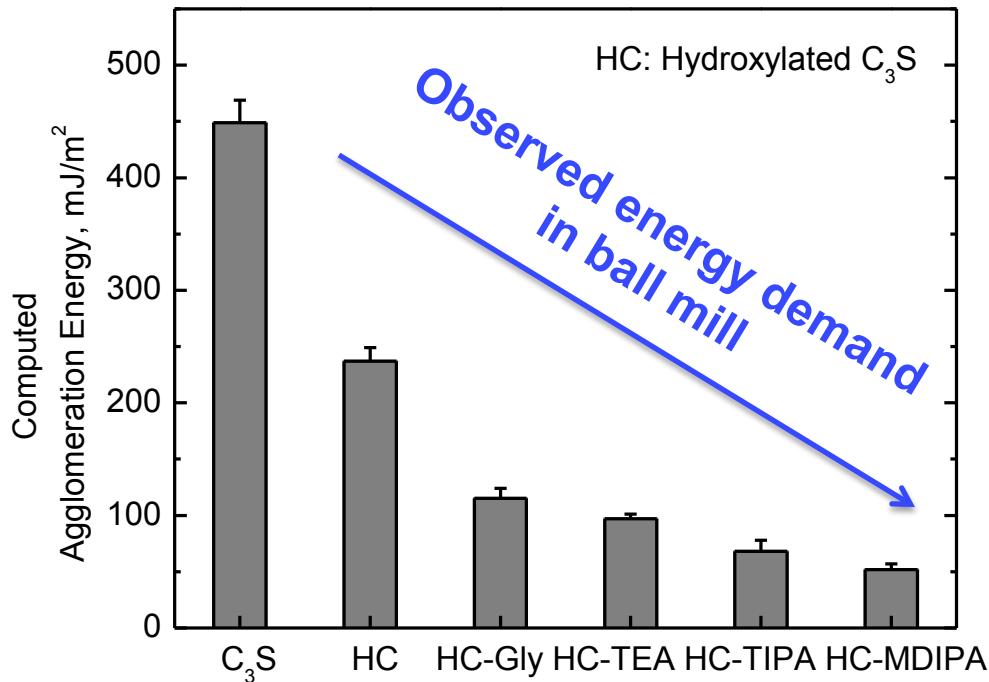
# Agglomeration of Tricalcium Silicate: Dry, Hydrated, and Organically Modified



- Ca coordination and hydrogen bonds to the surface determine adsorption energy
- Temperature-dependent disorder of the C3S surface
- Agglomeration reduction depends on thickness of organic layer and mitigation of local dipoles



# Agglomeration of Tricalcium Silicate: Dry, Hydrated, and Organically Modified

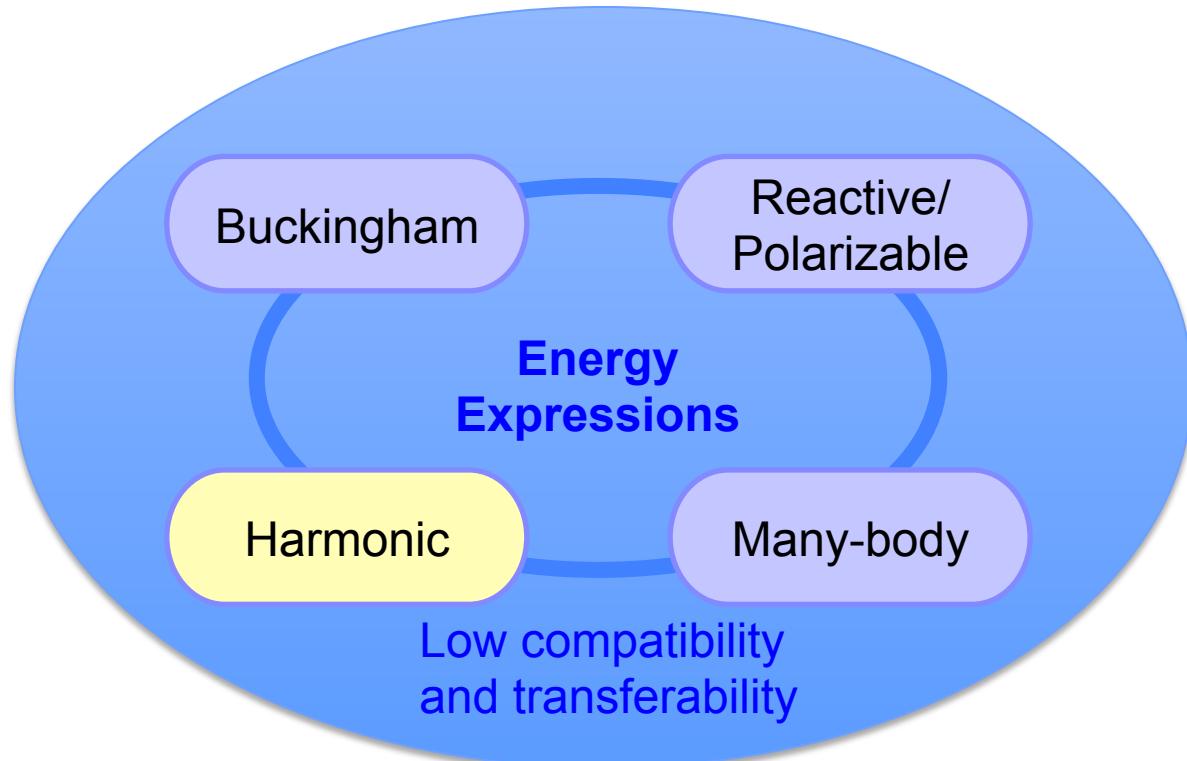


Design of grinding aids and prediction of polymer effects feasible (e.g. PCEs)

*Approach to Chemically Accurate,  
Thermodynamically Consistent Force Field  
Parameterizations*



# Choice of Energy Expression



Harmonic

=

Bonded  
terms

+

Atomic  
charges

+

Lennard-Jones  
parameters

CHARMM, AMBER,  
PCFF, COMPASS,  
GROMACS, OPLS-AA

Equivalent

Moderate differences

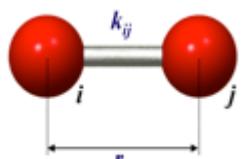


# Potential Energy Function of a Structure (PCFF)

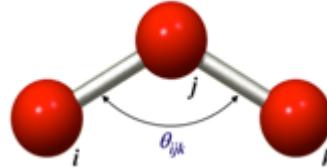
$$E_{pot}(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) = \underbrace{E_{bonds} + E_{angles} + E_{torsions} (+ E_{out-of-plane})}_{\text{bond}} + \underbrace{E_{Coulomb} + E_{vdW}}_{\text{non-bond}}$$

- Bonded terms describe the energy contained in the internal degrees of freedom, and non-bonded terms the interactions between molecules

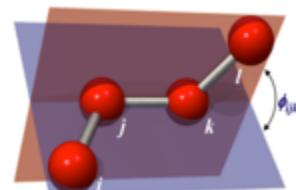
## Bonded Interactions:



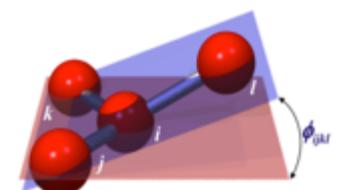
**Bond potential**



**Angle potential**



**Proper dihedral**



**Improper**

$$E_{bonds}(r_{ij}) = \sum_{ij} \frac{k_{ij}}{2} (r_{ij} - r_0)^2$$

$$E_{angles}(\theta_{ijk}) = \sum_{ijk} \frac{k_{ijk}}{2} (\theta_{ijk} - \theta_0)^2$$

$$E_{torsions}(\phi_{ijkl}) = \sum_{ijkl} \frac{k_\phi}{2} (1 + \cos 3\phi_{ijkl})$$

## Non-bonded Interactions:

$$E_{vdW} = \sum_{ij} \epsilon_{ij} \left[ 2 \left( \frac{r_0}{r_{ij}} \right)^9 - 3 \left( \frac{r_0}{r_{ij}} \right)^6 \right]$$

LJ 9-6 potential for van der Waals interaction

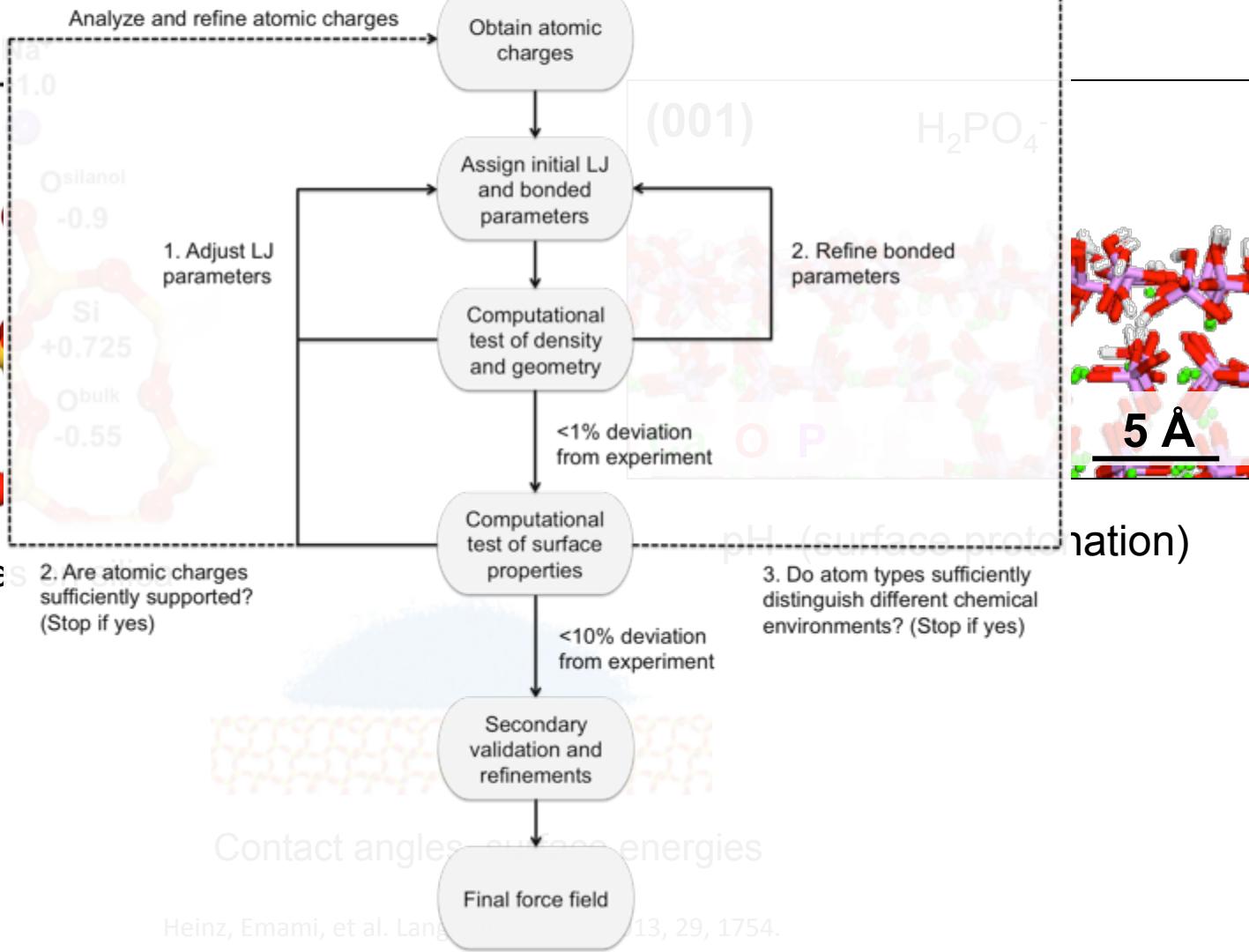
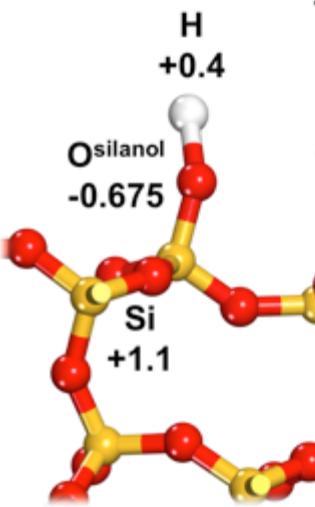
$$E_{Coulomb} = \sum_{ij} \frac{q_i q_j}{4\pi\epsilon_0 r_{ij}}$$

Electrostatic interactions (polarity)



# Key Elements of parameterization

- Parameters in agreement with measured properties at the atomic and macroscopic scale: polarity ( $q, \mu$ ), structure (XRD), and surface energy





# Interpretation of Parameters

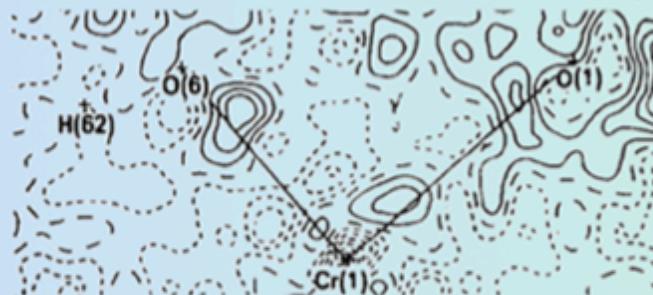
Parameter	Impact in simulation
Compatibility of parameters with existing force fields for (bio)organic compounds	Scope of application
Atomic charges	Surface and interface properties, adsorption, conformation of polar molecules
Lennard-Jones well depth	Surface and interface properties, adsorption, cohesion, conformation of molecules
Surface chemistry (hydration, protonation, charge defects)	Interfacial properties and dynamics
Torsion potential	Molecular conformation, chain folding
Lennard-Jones diameter (knowledge-based)	Density (atom size)
Vibration constants	IR/Raman spectra, elastic properties
Bond and angle constants (X-ray)	Geometry of covalent bonds and angles



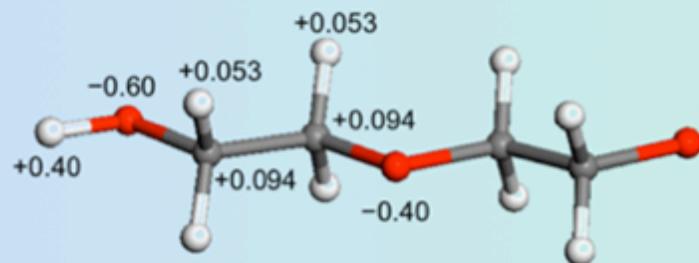
# Validation of Atomic Charges

Atomic charges  $q_i$  in agreement with

## 1. Deformation electron density (XRD, ND)



## 2. Dipole moments (MW, IR)



## 3. Extended Born cycle (ref. 58)

- Atomization energies
- Ionization energies/electron affinities
- Coordination number
- Trends across periodic table for similar compounds
- Melting points, boiling points, solubility

## 4. Other methods

- Force field assigned charges
- QM/Hirshfeld, Qeq, MP2/CHELPG, Gasteiger, Löwdin, Bader, Mulliken  
(high uncertainties common)



# Atomic Charges from X-Ray Deformation Densities

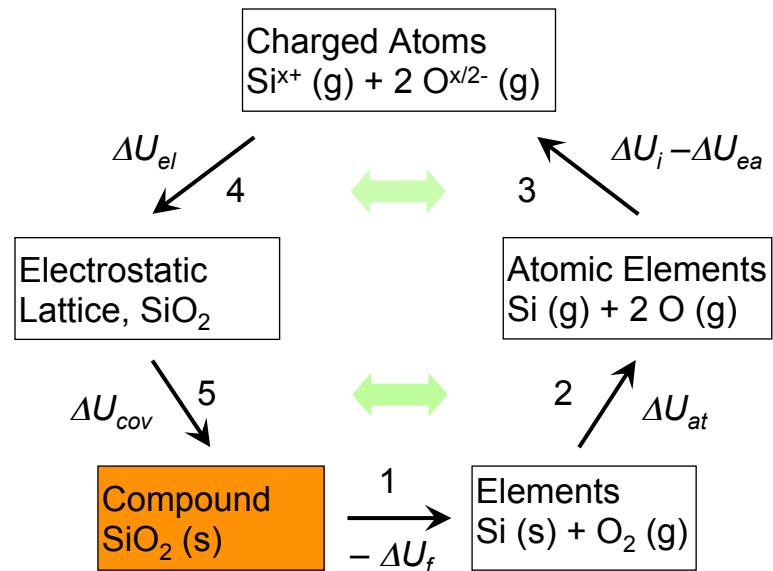
Compound	Atom	Charge in units of e
LiF	Li	0.95 (3)
LiI	Li	0.67 (5)
LiNO <sub>2</sub> · H <sub>2</sub> O	Li(H <sub>2</sub> O)	0.83
	N	0.51
	O (nitrite)	-0.67
NaCl	Na	1.00 (0)
NaNO <sub>3</sub> <sup>a</sup>	Na	0.95 (5)
	N	-0.20 (10)
	O	-0.25 (10)
KBr	K	0.8 (1)
CaF <sub>2</sub>	Ca	2.00 (0)
MgO	Mg	1.6 (2)
Al <sub>2</sub> O <sub>3</sub>	Al	1.32 (5)
AlO(OH)	Al	1.47 (27)
	H	0.20 (5)
AlPO <sub>4</sub> <sup>b</sup>	Al	1.4 (1)
	P	1.0 (1)
CrSO <sub>4</sub> · 5 H <sub>2</sub> O <sup>c</sup>	Cr(H <sub>2</sub> O) <sub>5</sub>	0.96 (20)
	S	0.24 (6)
	O (sulfate)	-0.30 (6)
Co[O(NC <sub>5</sub> H <sub>5</sub> ) <sub>6</sub> (ClO <sub>4</sub> ) <sub>2</sub>	Co	1.74 (4)
	Cl	-0.12 (1)
	O (perchlorate)	-0.15 (4)
	Pyridine-N-oxide ligand	-0.05 (5) [individual: O -0.83, N 0.27, C ~ -0.2, H ~ 0.3]
CuSO <sub>4</sub> · 5 H <sub>2</sub> O <sup>c</sup>	Cu(H <sub>2</sub> O) <sub>5</sub>	1.18 (10)
	S	0.06 (2)
	O (sulphate)	-0.31 (6)
Cu <sub>6</sub> Si <sub>6</sub> O <sub>18</sub> · 6 H <sub>2</sub> O	Cu	1.23 (6)
	Si	1.17 (15)
	O (water)	-0.74 (6)



# Atomic Charges from the Extended Born Model

- Atomization energies  $\Delta U_{at}$  reflect the ability for covalent bonding (purely covalent bonding is possible only in the elements)

H 218													He 0				
Li 159	Be 324									B 565	C 717	N 473	O 249	F 79	Ne 0		
Na 108	Mg 147									Al 330	Si 450	P 317	S 277	Cl 121	Ar 0		
K 89	Ca 178	Se 378	Ti 473	V 514	Cr 397	Mn 281	Fe 416	Co 425	Ni 430	Cu 337	Zn 130	Ga 272	Ge 372	As 302	Se 227	Br 112	Kr 0
Cs 81	Sr 164	Y 421	Zr 609	Nb 726	Mo 658	Tc 678	Ru 643	Rh 557	Pd 378	Ag 285	Cd 112	In 243	Sn 301	Sb 262	Te 197	I 107	Xe 0
Rb 77	Ba 180	La 431	Hf 619	Ta 782	W 849	Re 770	Os 791	Ir 665	Pt 565	Au 366	Hg 61	Tl 182	Pb 195	Bi 207			



- Ionization energies  $\Delta U$ /electron affinities  $\Delta U_{ea}$  reflect the ability for ionic bonding

- Extended Born Model describes relationship between these properties of the elements and resulting properties in a compound, including atomic charges



# Validation of Interfacial Properties

(b) 2<sup>nd</sup> CONDITION FOR THERMODYNAMIC CONSISTENCY:  $\gamma_{AB}$  (expt)  $\Rightarrow \gamma_{AB}$  (sim)

Well depths  $\epsilon_{0,ii}$  and nonbond diameters  $\sigma_{0,ii}$  in agreement with

## 1. Cell parameters and density (XRD)

## 2. Surface properties (at least one)

- Surface tension and components
- Cleavage energy
- Interface tension with water
- Hydration/immersion energy
- Contact angle
- Adsorption energy of test molecules

## 3. Interpretation of parameters

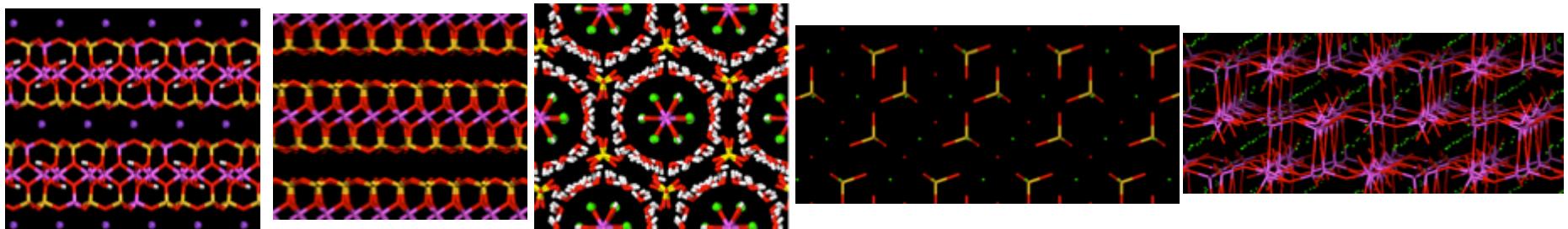
- Rationalize all atomic charges  $q_i$ , nonbond diameters  $\sigma_{0,ii}$ , and well depths  $\epsilon_{0,ii}$  chosen
  - Identify limitations
  - Correlate surface chemistry of model with experiment: crystal shape, Miller facets  $\{h k l\}$ , hydration state, acidity
- Thermodynamic consistency reduces common errors in surface, adsorption, and elastic properties from <500% to <10%



# Examples of Cell Parameters

- Computed unit cell parameters (NPT dynamics) agree  $\pm 0.5\%$  with experimental X-Ray crystal structures (previously  $\pm 3\text{-}5\%$ <sup>1</sup>)

Example Minerals	cell dim.	a (nm)	b (nm)	c (nm)	$\alpha$ (°)	$\beta$ (°)	$\gamma$ (°)	V (nm <sup>3</sup> )	rms dev (pm/atom)	
<b>Mica</b> $K_2Si_6Al_6O_{20}(OH)_4$	exp	5×3×1	2.596	2.705	2.005	90	95.73	90	14.00	0
	sim		2.585	2.691	2.006	89.54	95.36	90.01	13.89	15
<b>Pyrophyllite</b> $Si_8Al_4O_{20}(OH)_4$	exp	5×3×1	2.580	2.690	1.869	91.18	100.46	89.64	12.76	0
	sim		2.589	2.696	1.878	90.62	101.50	90.00	12.84	20
<b>Kaolinite</b> $Si_2Al_2O_5(OH)_4$	exp	3×2×2	1.546	1.788	1.478	91.92	105.04	89.80	3.945	0
	sim		1.552	1.796	1.464	91.8	104.7	90.06	3.942	26
<b>Tobermorite</b> $Ca_4Si_6O_{15}(OH)_2 \cdot 5 H_2O$	exp	2×2×1	1.347	1.477	2.249	90	90	123.25	3.741	0
	sim		1.348	1.467	2.247	89.55	90.15	123.13	3.721	23



- Bond lengths, angles according to exptl crystal structures

<sup>1</sup> E. g., Rutledge 2004; Cygan and Kalinichev 2004; Catlow 2003; Sposito 2003; Manias 2002; Van Santen 1990



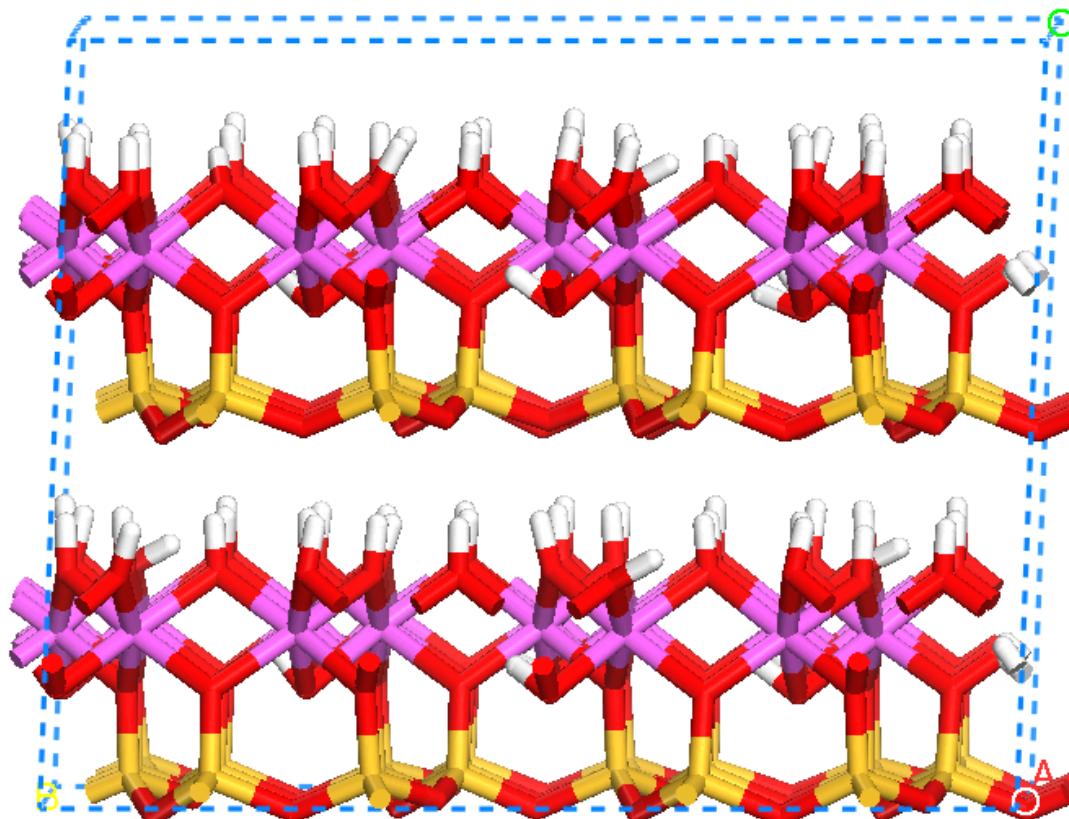
# Clay Minerals: Surface Tensions and Cleavage Energies Vs Experiment (mJ/m<sup>2</sup>)

- Quantitative agreement (refs. 13-25 = other force fields)

Ref.	Pyrophyllite			Montmorillonite		Mica		Principal charges (e)		Principal well depths (kcal/mol)		
	$\gamma^{\text{tot}}$	$\gamma^{\text{el}}$	$\gamma^{\text{vdW}}$	$\Delta E_{\text{cleav}}$	$\Delta E_{\text{cleav}}$	$\text{Si}^{\text{tet}}$	$\text{Al}^{\text{oct}}$	$\text{Si}$	$\text{Al}$	$\text{O}$		
Exptl	39.7 <sup>b</sup>	5.8 <sup>b</sup>	33.9 <sup>b</sup>	50-200 <sup>c</sup>	375 <sup>d</sup>	1.2 <sup>e</sup>	1.45 <sup>e</sup>					
This work	40	8	32	140	380	1.1	1.45	0.03	0.03	0.015		
13, 15	[155]					4	3	0 <sup>f</sup>	0 <sup>f</sup>	49 <sup>f</sup>		
16	[>30]			[>300]	[>500]	2.4				0.47 <sup>g</sup>		
17	-515	2	-517	-3000	-433	0.52	1.33	0	0	0		
18	-1094	13	-1107	-433	-162	1.4	1.68	0	0	6.86		
19	[>15]					1.2	3	0 <sup>h</sup>	0 <sup>h</sup>	<sup>h</sup>		
20	[>15]					1.2	2.8	i	i	i		
22 CLAYFF	81	30	51	167	484	2.1	1.58	$10^{-6}$	$10^{-6}$	0.155		
23	265	155	110	251	683	4	3	0.04	9.04	0.228		
25	260	8	252	340	631	1.1	1.45	0.40	0.50	0.06		



# Kaolinite Dynamics (100 ps)



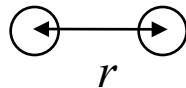
- Note stable relative position of layers

IINTERFACE FF V1.3, see [www.poly-eng.uakron.edu/heinz.php](http://www.poly-eng.uakron.edu/heinz.php)



# Lennard-Jones Models for FCC Metals

- Eliminates earlier errors in surface energies (<=500%)
- Fitted to experimental density ( $r_0$ ) and surface energy ( $\epsilon_0$ ) at 298 K
- Reproduces rel. surface energies {100}/{111}, {110}/{111} and elastic constants within 20%

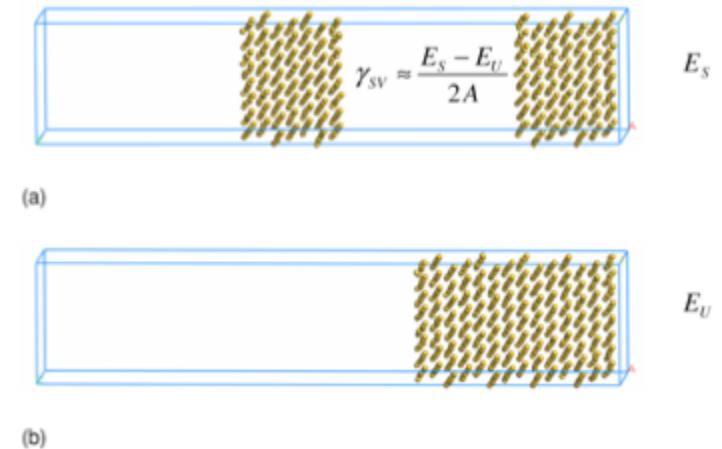


$$E = \epsilon_0 \left[ \left( \frac{r_0}{r} \right)^{12} - 2 \left( \frac{r_0}{r} \right)^6 \right] = \frac{A}{r^{12}} - \frac{B}{r^6} \quad \text{or} \quad E = \epsilon_0 \left[ 2 \left( \frac{r_0}{r} \right)^9 - 3 \left( \frac{r_0}{r} \right)^6 \right]$$

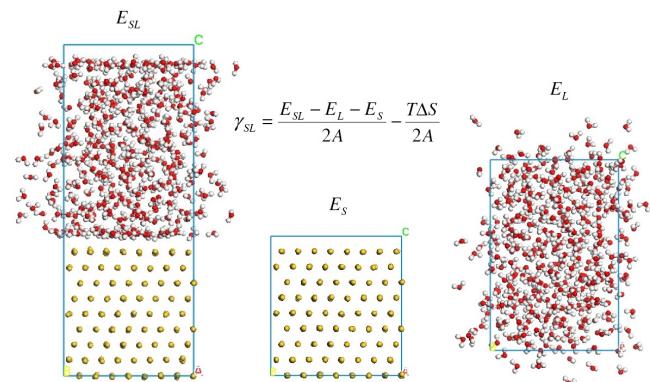
Full compatibility with biomolecular force fields

→ Metal-organic/water/bio interfaces

Currently: Ag, Al, Au, Cu, Ni, Pb, Pd, Pt  
(CHARMM-METAL, CVFF-METAL)



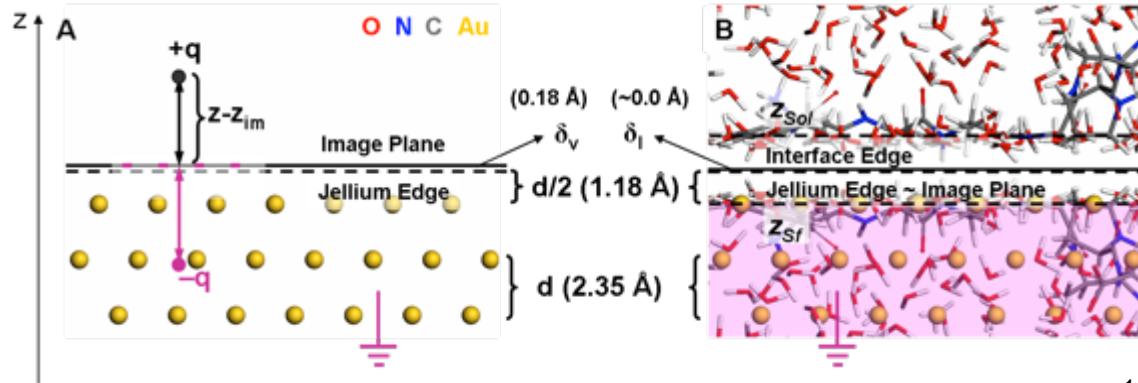
Interface energy with water  
agrees ~10%





# Induced Charges at the Metal-Peptide Interface Fine-Tune Adsorption

- Similar on Au {111} and {100} surfaces



$$E_{im} = \sum_{original}^N \sum_{image (multiple)}^N \frac{q_i q_j}{4\pi\epsilon_0} \frac{1}{2d_{ij}} \left[ \pi/2 - \tan^{-1} \frac{z_{ij}}{d_{ij}} \right]$$

Total attraction per surface area -50 to -70 mJ/m<sup>2</sup>

- Per water molecule: -0.6 kcal/mol (1<sup>st</sup> layer)
- Per amino acid: 0 to -10 kcal/mol

Net contribution by polarization to adsorption:

- 5 kcal/mol for A3 peptide on {111} (-20 for peptide and +15 for replaced water)
- 16 kcal/mol** for Flg-Na<sub>3</sub> peptide on {100} (-20 for peptide and +4 for replaced water)

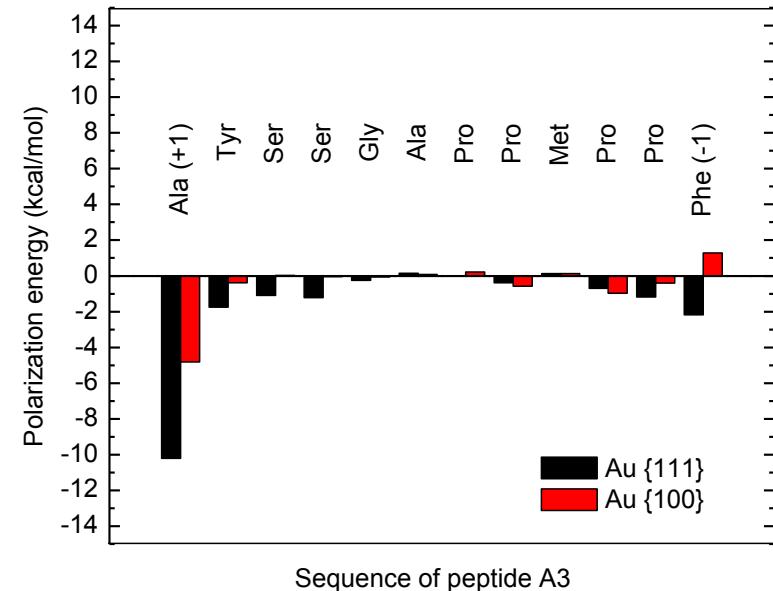


Image potential only significant for charged peptides on surfaces of weak epitaxy

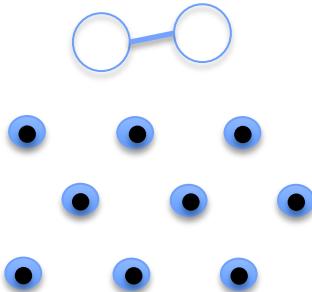


# Inclusion of Induced Charges for Metals: A Polarizable LJ Model

Induced charges can be the dominant contribution to adsorption for

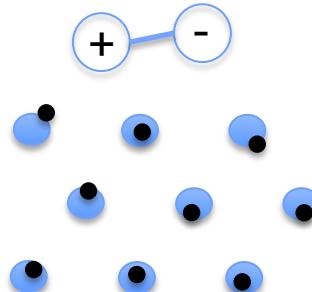
- 1) nonpolar polymers/molecules in a polar solvent
- 2) ionic polymers/molecules in lowly polar solvent/nonpolar solvent  
(no contribution if polarity of solvent and solute is about the same)

## Inclusion of image potential



Non-polar molecule adsorbed:

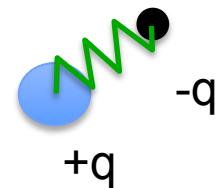
Neat LJ potential/  
no image potential



Polar molecule adsorbed:

Neat LJ potential +  
attractive image potential

- Metal atom
- Dummy charge



Parameters to be added

- 1) Polarity  $+q/-q$
- 2) Force constant  $k$

Advantages:

- 1) Could be (nearly) same for different metals
- 2) Applicable to any metal surface shape and  $\{hkl\}$  facet
- 3) Integrates smoothly in MD or MC<sup>69</sup>

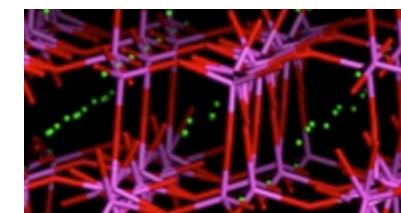


# Influence of Chosen Energy Expression is Small

Similar performance of various energy expression, e.g., for tricalcium aluminate

Property	Expt	PCFF	CHARMM	CVFF	AMBER	OPLS-AA
Lattice parameter	1.5263 <sup>b</sup>	1.5265	1.5280	1.5240	1.5267	1.5258
$a$ (nm)						
Al–O <sup>ring</sup> bond length (pm)	175.5 <sup>b</sup>	174.5	174.0	173.5	176.0	175.5
Al–O <sup>apical</sup> bond length (pm)	175.0 <sup>b</sup>	174.5	172.5	172.0	174.5	174.5
Cleavage energy (mJ/m <sup>2</sup> )	1250 ±150 (±12%) <sup>c</sup>	1260	1325	1321	1341	1380
Bulk modulus (GPa) at 0-1 GPa	106 ±8 <sup>d</sup>	98 ±3	107 ±3	108 ±3	107 ±3	108 ±3

Typically 5-10% lower modulus and cleavage energy using 9-6 LJ potential (PCFF) vs 12-6 LJ potential (others)



# ***Tutorial: How to Use the INTERFACE Force Field, Connect with Laboratory Tests and Multi-Scale Simulation Methods***



# How to Use the INTERFACE Force Field

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## 1) Download from Web (Heinz webpage)

<http://www2.uakron.edu/cpspe/dpe/web/nsi/interface-force-field.php>

Content:

- Force field files
- Surface model database
- Utility programs (to help file conversion in CHARMM)
- Documentation

## 2) Prepare structure for simulations

(using atom types and charges provided in models)

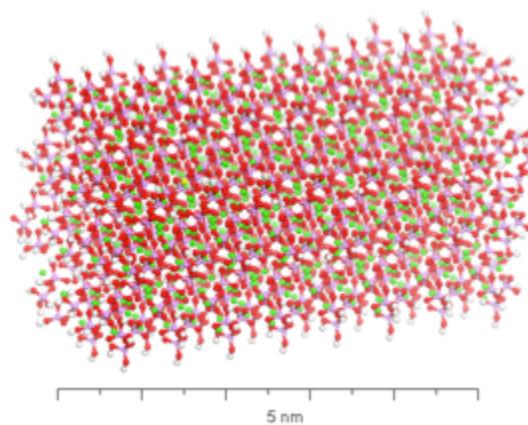
## 3) Perform MD/MC simulations

LAMMPS, NAMD, Towhee, GROMACS, **Materials Studio Discover/Forcite (easiest)**, ...



# Structure Preparation for Simulations

- Verify chemical identity, defects, pH (if applicable) of surfaces and the representation in models; consult surface model database
- Utilize atomic charges and force field types  
*Materials Studio recommended for viewing  
(other viewers are fine, may not easily visualize charges and force field types)*
- Customize surfaces for specific conditions, create new structures  
(observe charges and atom types)



Hydroxyapatite nanorod



# Structure Preparation for Simulations: Silica as an Example

Choose among typical models or create own structure (porous, amorphous, zeolite)

Type of silica substrate	1. Area density of silanol groups	2. Ionization to $(\text{SiO}^- \text{M}^+)^a$	3. Surface topography
Quartz surfaces, silica nanoparticles >200 nm size, silica at pH > 9	$Q^2$ and $Q^2/Q^3$ (9.4 to 4.7 per $\text{nm}^2$ )	pH 2: ~0 per $\text{nm}^2$ pH 5: ~0.5 per $\text{nm}^2$ pH 7: ~1.0 per $\text{nm}^2$ pH $\geq 9$ : ~1.5 per $\text{nm}^2$	Substrate-specific: smooth, rough, porous
Most silica glasses, porous silica, silica nanoparticles <200 nm size	$Q^3$ (4.7 per $\text{nm}^2$ )	pH 3: ~0 per $\text{nm}^2$ (0%) pH 5: ~0.3 per $\text{nm}^2$ (6%) pH 7: ~0.6 per $\text{nm}^2$ (13%) pH $\geq 9$ : ~0.9 per $\text{nm}^2$ (20%)	
Silica surfaces and nanoparticles annealed at 200-1000 °C	$Q^3/Q^4$ and $Q^4$ (4.7 to 0 per $\text{nm}^2$ )	pH 4: ~0 per $\text{nm}^2$ pH 7: 0-0.6 per $\text{nm}^2$ depending on $Q^3$ content	

Source: INTERFACE documentation; published in F. S. Emami, H. Heinz et al. Chem. Mater. 2014, 26, 2647.



# Perform an MD/MC Simulation

## Choose a force field:

- PCFF-INTERFACE
  - CVFF-INTERFACE
  - CHARMM-INTERFACE
  - Implementation in OPLS-AA, AMBER, GROMOS (fcc metals, apatite, silica etc feasible)
- 1) Ready-to-run in Materials Studio (Accelrys, Inc.) using PCFF-INTERFACE and CVFF-INTERFACE with **Forcite** and **Discover** programs  
(keep atomic charges and force field types from model database, automatic charges and force field typing for polymers, water etc acceptable)
  - 2) Ready-to-run in **LAMMPS** after msi2lmp conversion  
(included in LAMMPS package), or similarly in **TOWHEE**
  - 3) Run in **NAMD** using CHARMM-INTERFACE after conversion into .pdb/.psf format  
**Need to use utility programs (or scripts) to prepare simulation input**



# Usage Specifics for CHARMM-INTERFACE

Input preparation requires a few steps, similar to native CHARMM:

- Build complete start structure in Materials Studio or other builder program, for example, mineral/nanoparticle-biopolymers-water
- Export coordinates of surface/nanoparticle, water, biopolymers in .car/.mdf format or .pdb format
- Build .pdb/.psf files for each biomolecular/water part using psfgen (in CHARMM package) and surface/nanoparticle part using car\_Imp\_to\_pdb\_psf (Utility program in INTERFACE package)
- Merge .pdb/psf files of all components using merge\_pdb\_psf\_files (Utility program in INTERFACE package)

→ Ready to run with **NAMD, CHARMM**

Automated generation of surface models and simulation input files in planning to improve user-friendliness



# Multi-Scale Opportunities

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- Quantum mechanical/classical atomistic simulations are feasible using QM/MM and ONIOM approaches – no difference in techniques to native force fields such as CHARMM, PCFF, CVFF, AMBER, OPLS-AA
- Classical atomistic/coarse grain simulations in dual-resolution are feasible at the same time, by using the same energy expression; reversible mapping between the two levels of description is feasible; the coarse grain model should reproduce density and surface energies of the chosen compounds consistent with the INTERFACE approach
- Mapping between atomistic and continuum approaches is feasible, for example, continuum field parameters (continuum DFT) can be derived from time-averaged molecular density maps and concentration profiles in atomic resolution; vice versa, atomistic models can be built using continuum information
- Comparison to experimental measurements are always important since the INTERFACE force field derives from and improves by validation of structural, thermodynamic, and mechanical properties



# Team

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# Thank You