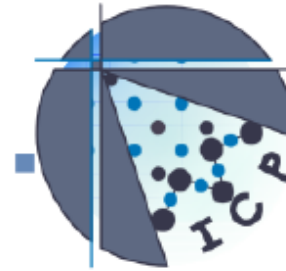**University of Stuttgart**
Germany

INSTITUTE FOR COMPUTATIONAL PHYSICS

Water models in classical simulations

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Water

- transparent, odorless, tasteless and ubiquitous

- really simple: two H atoms attached to single O atom

- extraordinary substance:
  - importance as a solvent, a solute, a reactant and a biomolecule, structuring proteins, nucleic acids and cells
  - about 2/3 of human body, 93.3% of blood

- hundred times as many water molecules in our bodies as the sum of all the other molecules put together
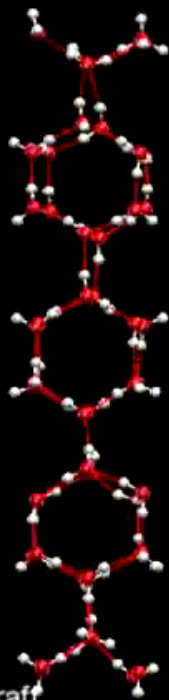
life cannot evolve or continue without liquid water (solvation of biomolecules (DNA), ions, proteins)

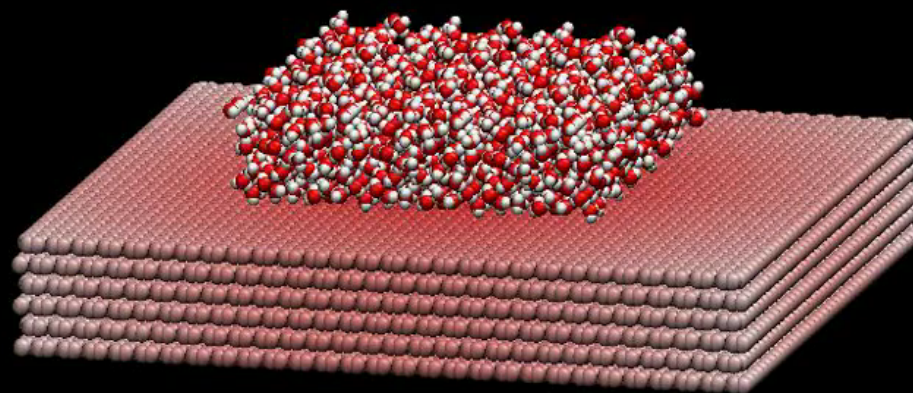- **but** poorly understood: small size but complex with enormous capabilities
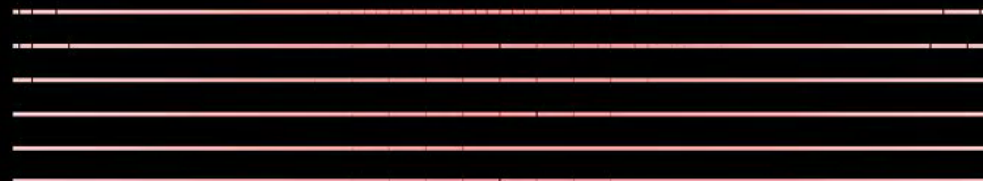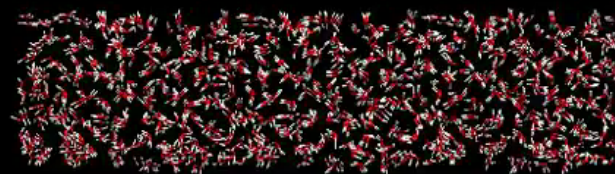
Material: http://www.lsbu.ac.uk/water/

Water models in computer simulations, C. Caleman (2007)

Melting of ice, ice structure

Jindřich Soukup, William Pfalzgraff
Schola ludus 2010, Nové Hrady

Water droplet at a graphitic
surface
by M. Sega

History

✓**1932** - Spectroscopic proofs of the V-shaped water molecule

✓**1933** - Bernal and Fowler [J.Chem. Phys. 1, 515 (1933)] propose 1st realistic interaction potential for water

✓**1953** - Metropolis et al [J. Chem. Phys. 21, 1087 (1953)] presents the 1st Monte Carlo sampling scheme

✓**1957** - Adler and Wainwright [J.Chem. Phys. 27, 1208 (1957)] performed 1st MD simulation

✓**1969** - Baker and Watts [J.Chem. Phys. Lett. 3, 144 (1969)] 1st computer simulations of water

✓**1976** – Lie *et al,* [J. Chem. Phys. 64, 2314 (1976)] 1st pair potential from ab initio calculations for water

✓**1981** - Berendsen et al [ntermolecular Forces, Reidel Publ.] construct the 1st "accurate" and simple pair potential for liquid water

✓**1993** - Laasonen *et al* [J. Chem. Phys. 99, 9080 (1993)] 1st ab initio calculations for liquid water

Water molecule: H₂O

tiny and V-shaped; molecular diameter about 2.75 Å.
liquid state, in spite of 80% of the electrons involved in bonding,
the three atoms do not stay together as the hydrogen atoms are
constantly exchanging between water molecules due to (de)protonation.

0.9584 Å
95.84 pm

104.45°
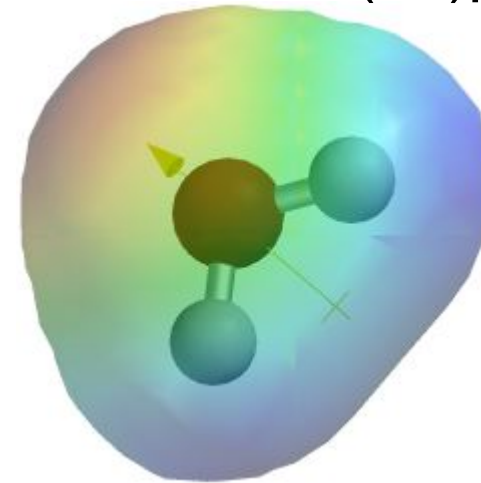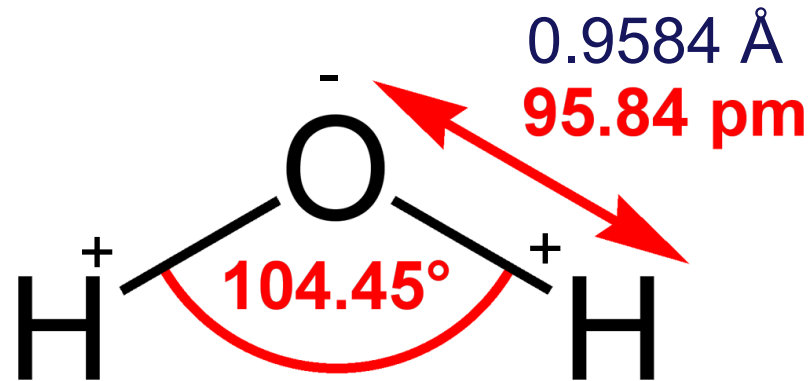
electron density
distribution of H₂O

Many different classical water models

modelling parameters:
- number of charges
- interactions
- dipole moment

Why is water such a good solvent?
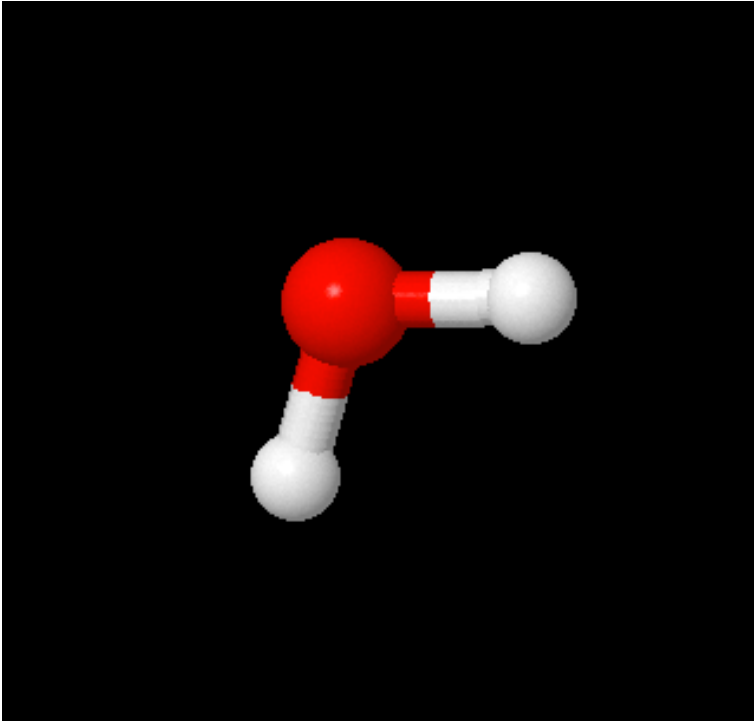
http://www.edinformatics.com/
interactive_molecules/water.htm

- Polar substance
  - good for dissolving salts, ions...
  - Large relative dielectric constant (≈80)
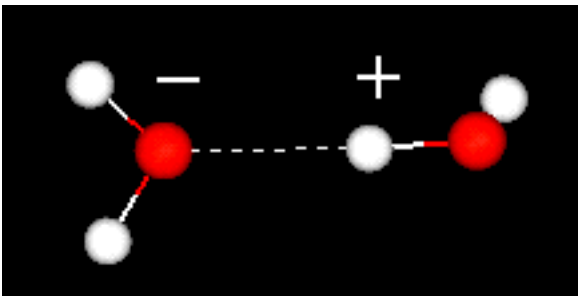
- Hydrogen bonds
  - network former, liquid water has structure
  - an atom of hydrogen is attracted by rather strong forces to two atoms instead of only one,
  - a high cohesiveness and, thus, surface tension

Hydrogen Bonds

In water, the strength of hydrogen bonds are about 5 kcal/mol ≈ 8.4 k_BT

What do we get, if we calculate the electrostatic energy of an H-O pair?

$$E / k_B T = l_B \frac{q_1 \cdot q_2}{r} = 7.1 \frac{0.8 \cdot 0.4}{1.8}$$

≈ 1.25 k_BT

Question : Why so low ?
Answer: In this model, van der Waals contribution need to be taken into account! **Effective interactions**...

Water parameterization

● each model developed to fit well with one particular physical structure or parameter (e.g., the density anomaly, radial distribution function, critical parameters

● the more fitting parameters that are required by the model (and some require over 50), the better the fit

● some models show a lack of robustness due to their sensitivity to the precise model parameters, system size or simulation method

● some are polarizable, others reproduce 'average' structures

● Note: Water molecules in liquid water are all non-equivalent (differ in molecular orbitals, precise geometry ,molecular vibrations) due to hydrogen bonding status (influenced by arrangements of surrounding water molecules

Water models: mainly 4 structures, 3-5 interaction points

a, b, c:planar
d:tetrahedral

q_2: mid-point in c
    lone-pairs in d
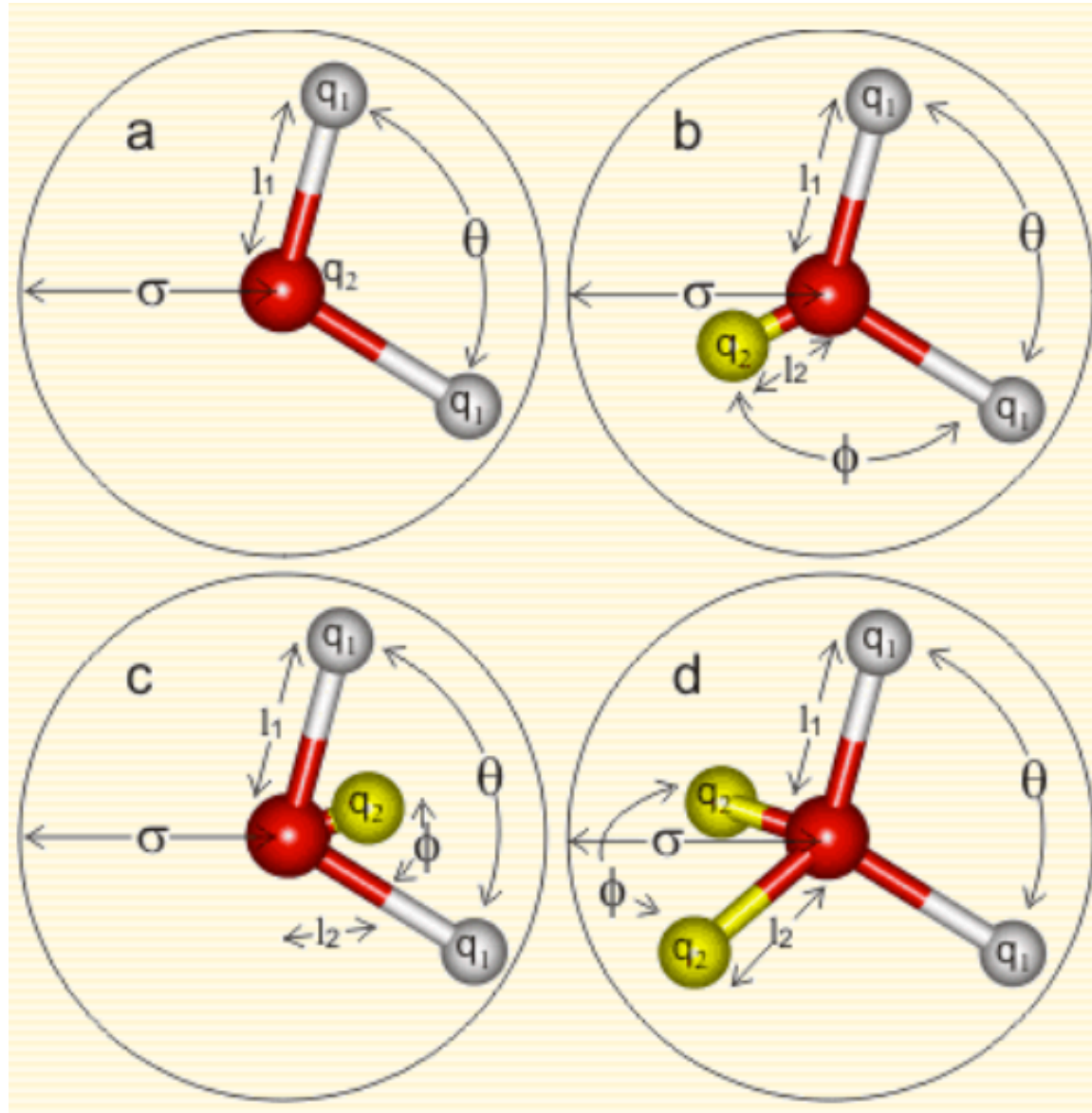
Water models - parameters

Model	Type	σ Å [6]	ε kJ mol⁻¹ [6]	l_1 Å	l_2 Å	q_1 (e)	q_2 (e)	θ°	φ°
SSD [511]	-[8]	3.016	15.319	-	-	-	-	109.47	109.47
SPC [94]	a	3.166	0.650	1.0000	-	+0.410	-0.8200	109.47	-
SPC/E [3]	a	3.166	0.650	1.0000	-	+0.4238	-0.8476	109.47	-
SPC/HW (D$_2$O) [220]	a	3.166	0.650	1.0000	-	+0.4350	-0.8700	109.47	-
SPC/Fw [2] [994]	a	3.166	0.650	1.0120	-	+0.410	-0.8200	113.24	-
TIP3P [180]	a	3.15061	0.6364	0.9572	-	+0.4170	-0.8340	104.52	-
TIP3P/Fw[2] [994]	a	3.1506	0.6368	0.9600	-	+0.4170	-0.8340	104.5	-
PPC [1, 2] [3]	b	3.23400	0.6000	0.9430	0.06	+0.5170	-1.0340	106.00	127.00
TIP4P [180]	c	3.15365	0.6480	0.9572	0.15	+0.5200	-1.0400	104.52	52.26
TIP4P-Ew [649]	c	3.16435	0.680946	0.9572	0.125	+0.52422	-1.04844	104.52	52.26
TIP4P-FQ [197]	c	3.15365	0.6480	0.9572	0.15	+0.63[1]	-1.26[1]	104.52	52.26
TIP4P/Ice [838]	c	3.1668	0.8822	0.9572	0.1577	+0.5897	-1.1794	104.52	52.26
TIP4P/2005 [984]	c	3.1589	0.7749	0.9572	0.1546	+0.5564	-1.1128	104.52	52.26
TIP4P/2005f [1765]	c	3.1644	0.7749	0.9664	0.15555	+0.5564	-1.1128	104.75	52.375
SWFLEX-AI [2] [201]	c	four terms used		0.968[1]	0.14[1,3]	+0.6213	-1.2459	102.7[1]	51.35[1]
COS/G3 [704] [9]	c	3.17459	0.9445	1.0000	0.15	+0.450672	-0.901344	109.47	-
COS/D [1617] [9] [16]	c	3.4365	0.5119	0.9572	0.257	+0.5863	-1.1726	104.52	-
GCPM[2] [859] [10]	c	3.69 [4,11]	0.9146 [4]	0.9572	0.27	+0.6113	-1.2226	104.52	52.26
SWM4-NDP[2] [13] [933]	c	3.18395	0.88257	0.9572	0.24034	0.55733	-1.11466	104.52	52.26
ST2 [872] [12]	d	3.10000	0.31694	1.0000	0.80	+0.24357	-0.24357	109.47	109.47
TIP5P [180]	d	3.12000	0.6694	0.9572	0.70	+0.2410	-0.2410	104.52	109.47
TIP5P-Ew [619]	d	3.097	0.7448	0.9572	0.70	+0.2410	-0.2410	104.52	109.47
TTM2-F [1027] [14]	c	five parameters used		0.9572	0.70	+0.574	-1.148	104.52	52.26
POL5/TZ [2] [256]	d	2.9837 [4]	[4]	0.9572	0.5	varies [5]	-0.42188	104.52	109.47
Six-site [491]	c/d[7]	3.115$_{OO}$ 0.673$_{HH}$	0.715$_{OO}$ 0.115$_{HH}$	0.980	0.8892$_L$ 0.230$_M$	+0.477	-0.044$_L$ -0.866$_M$	108.00	111.00
QCT [1251]	a[15]	3.140	0.753	0.9614	-	+0.6064	-1.2128	104.067	-

Water model types

- Rigid models:
  - fixed atom positions (match known geometry of water)
  - only non-bonded interactions
- Flexible models:
  - Atoms on "springs"
  - include bond stretching and angle bending
  - Reproduce vibration spectra
- Polarizable models:
  - include explicit polarization term (enhances ability to reproduce water in different phases and interaction between them)
  - first attempt (Barnes *et al*, Nature (1979)
  - examples: SPC/FQ, Tip4p/FQ (computationally only 1.1 times the corresponding rigid model.

Potentials:
        ab initio determined from calculations of dimers, trimers or higher order clusters
        empirical (e.g. Lennard-Jones) developed to reproduce experimental data in gas or liquid phase

Most common water models

● SPC (Berendsen *et al, Interaction Models for Water in Relation to Protein Hydration*, in Intermolecular Forces, edt. B. Pullman, p. 331, D. Reidel Publishing Company, Dordrecht, 1981)

● SPC/E (Berendsen *et al*, J. Phys. Chem. **91**, 6269 (1987))

● TIP3P (Jorgensen *et al*, J. Am. Chem. Soc. **105**, 1407 (1983))

● TIP4P (Jorgensen *et* al, J. Am. Chem. Soc. **105**, 1407 (1983))

● TIP5P (Mahoney & Jorgensen, J. Chem. Phys. **112**, 8910 (2000))

Force fields: some water models developes in a specific force field and often adopted to other force field

e.g. SPC, SPC/E – GROMOS
Tip3p – AMBER (modified Tip3p for CHARMM)
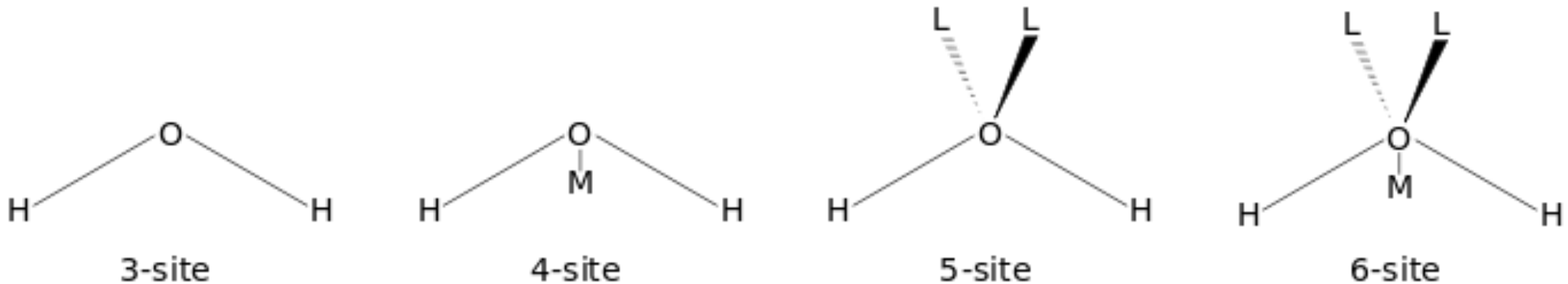Tip4p, Tip5p – OPLS

Simple water models

Rigid molecule interacting via non-bonded interactions
with other molecules:

partial charges

$$E_{ab} = \sum\sum \frac{k_c q_i q_j}{r_{ij}} + A\frac{1}{r_{00}^{12}} - B\frac{1}{r_{00}^{6}}$$

K_c is electrostatic constant
332.1 Å kcal/mol ≈ 1/4πε$_0$

Coulomb

LJ for O-O

One varies the location and size of partial charges:

3-site   4-site   5-site   6-site

differ in physical properties like diffusion constant,
dielectric constant, density, heat of vaporization, ...

3-site: Each atom gets a point charge assigned and Oxygen atom also has ist own Lennard-Jones parameters. Popular in MD(simple & efficient)

4-site: The negative charge sits on a dummy atom M instead of on the position of the O. This improves the electrostatic distribution around the water molecule.

5-site: The negative charges are split and sit on the L-L (lone pairs) of oxygen with a tetrahedral-like geometry.
a **lone pair** is a valence electron pair without bonding or sharing with other atoms

6-site: combines all sites of 4-site and 5-site

3-site   4-site   5-site   6-site
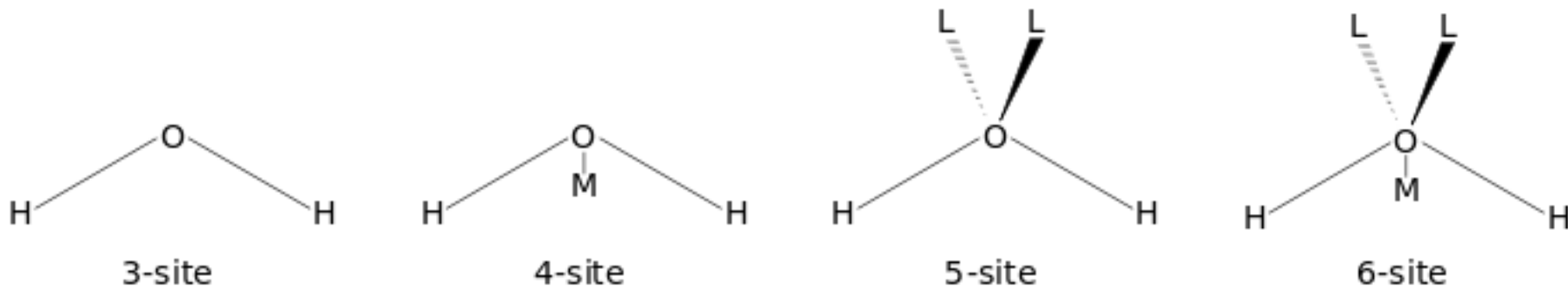
Water computational cost

Number of interatomic distances

$$T_{CPU} \propto N$$

3-site: 3 x 3 = 9   distances for each pair of water molecules

4-site: 3 x 3 charge – charge

      + 1 x   LJ (O-O) = 10 distances

5-site: 4 x 4 charge – charge

      + 1 x   LJ (O-O) = 17 distances

6-site: 5 x 5 charge – charge

      + 1 x   LJ (O-O) = 26 distances

In MD simulations most molecules are rigid → need constraint algorithms

→ can use larger time steps

Some models also exist in flexible variants:

- flex.SPC
- TIP4PF
- ...

Different models reproduce different properties correct, but never all:
Diffusion, dielectric const., density, phase behavior, etc....

Common 3-site modells

Model	TIPS	SPC	TIP3P	SPC/E
r (OH) [Å]	0.9572	1.0	0.9572	1.0
α (HOH)	104.52	109.47	104.52	109.47 (tetrahedral)
$A \times 10^{-3}$ [kcal Å^{12} / mol]	580.0	629.4	582.0	629.4
B [kcal Å^6 / mol]	525.0	625.5	595.0	625.5
q (O) [e]	-0.80	-0.82	-0.834	-0.8476
q (H) [e]	+0.40	+0.41	+0.417	+0.4238

- model known geometry of water molecule
- SPC uses ideal tetraeder shape of 109.47° (Simple Point Charge)
- TIP3P uses slightly modified CHARMM force field (tranferable intermolecular potential functions, see W.L. Jorgensen, *JACS* **103,** 33 (1981)

Water models - efficiency

Model	Type	μ_{gas} (D)	μ_{liq} (D)	ε	E_{conf} (kJ/mol)
SPC	R	2.27	2.27	65	–41
SPC/E	R	2.35	2.35	71	–41.5
TIP3P	R	2.35	2.35	82	–41.1
TIP4P	R	2.18	2.18	53	–41.8
TIP5P	R	2.29	2.29	81.5	–41.3
SPC/FQ	P	1.85	2.83	115	
TIP4P/FQ	P	1.85	2.62	79	–41.4
Exp.		1.855	2.95 (25°C)	78.4	–41.5

μ: dipole moment
ε: dielectric constant
E_{conf}: average configurational energy

SPC/E water model

add average polarization energy:

α is the isotropic polarizability const. $\approx 1.608 \times 10^{-40}$ F m.

$$E_{pol} = \frac{1}{2} \frac{\sum (\mu - \mu_0)^2}{\alpha_i}$$

$\mu = 2.35$ D   effective dipole moment of polarized water in the SPC/E model

$\mu_0 = 1.85$ D   dipole moment of isolated water (1.85 D from exp.)
Since the charges are constant this results in a constant correction of 1.25 kcal/mol in total interaction energy

$$E_{ab} = E_{Coulomb} + E_{LJ} + E_{pol}$$

$\Longrightarrow$ better density and diffusion constant than the SPC model

Water models - efficiency

Model	% of experimental value		
	Specific heat, C_P	Shear viscosity	Thermal conductivity
SPC	102	31	144
SPC/E	108	37	153
TIP3P	107	36	146
TIP4P	118	47	135
TIP4P-Ew	115	64	147
TIP4P/2005	120	65	149
TIP5P	120	88	111
TIP5P-Ew	141	91	102

In reality: water flexible and polarizable ➔ models without these are not expected to have high predictability
Predictability becomes worse as temperature is lowered

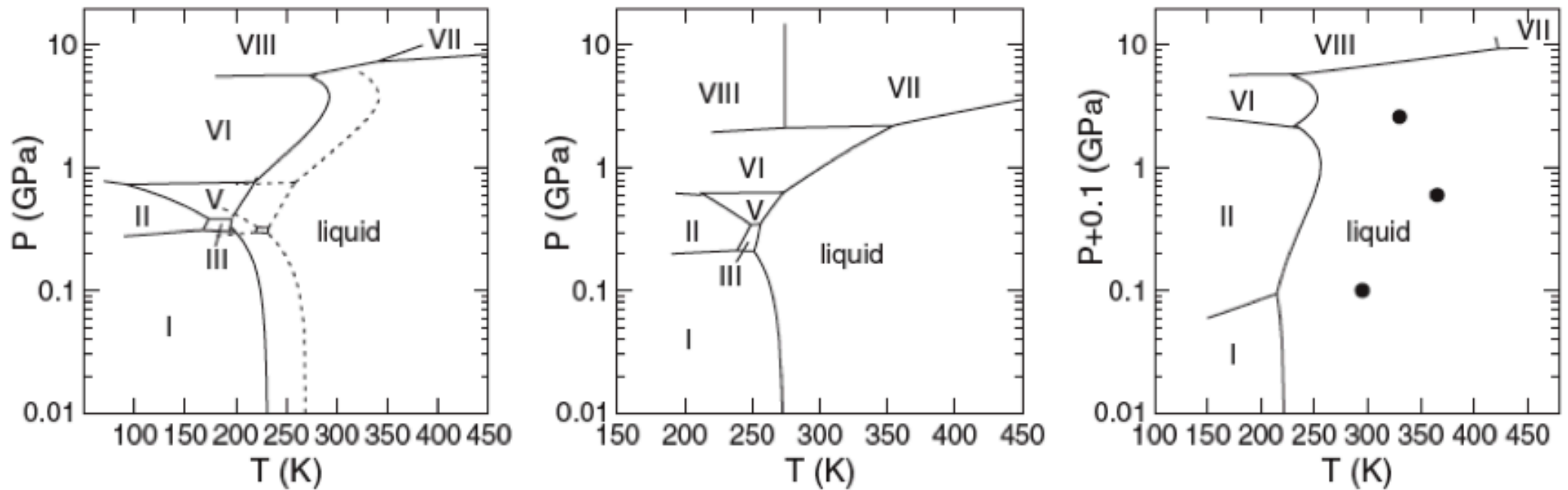http://www.lsbu.ac.uk/water/models.html

Phase diagram of water

Figure 1. Phase diagram of water as obtained from experiment (centre), for the SPC/E model (right) and for the TIP4P and TIP4P/ice models (left). Left side, solid lines (TIP4P), dashed lines (TIP4P/ice). Right side, lines: coexistence line of SPC/E; symbols: stability limit of the ice phases (note the shift of 0.1 GPa in p for this model).

C. Vega *et al*, J. Phys.: Condens. Matter **17**, S3284 (2005).

Solid phase: water exhibits one of the most complex phase diagrams with 13 different (known) solid structures; from the simple water models (SPC, SPC/E, TIP3P, TIP4P and TIP5P) only TIP4P provides a qualitatively correct phase diagram on water.

Physical properties of water: complexities

Density

Many potentials are fitted to reproduce the experimental liquid density, which is the case for most of the models that show good agreement. When the density is not used as a fitting parameter,as in the case with ab initio potentials (for example MCY, MCYL and NEMO) the results are rather poor.
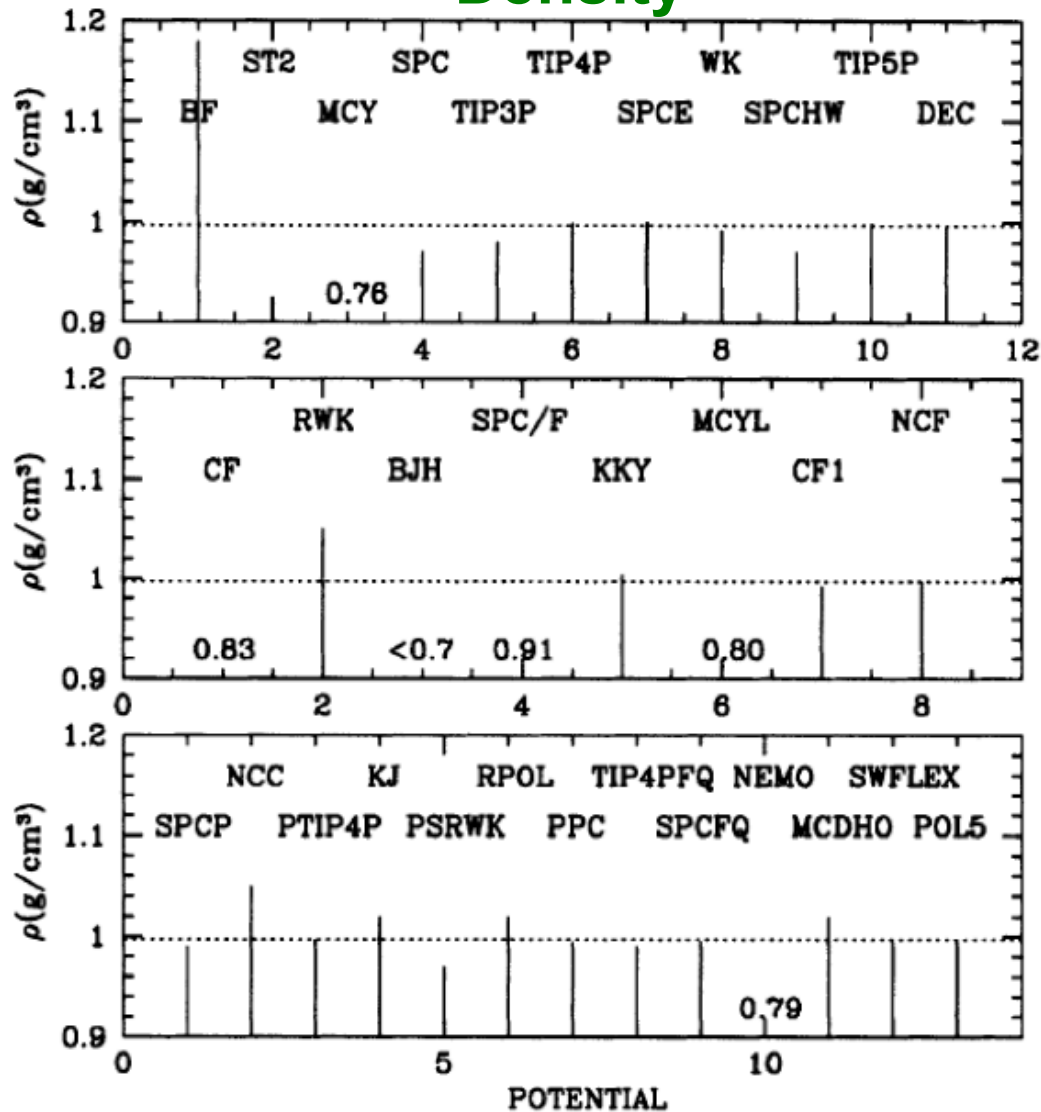
Diffusion coefficient

Water mobility is an indicator of the influence of the hydrogen bonds on the molecular motion.
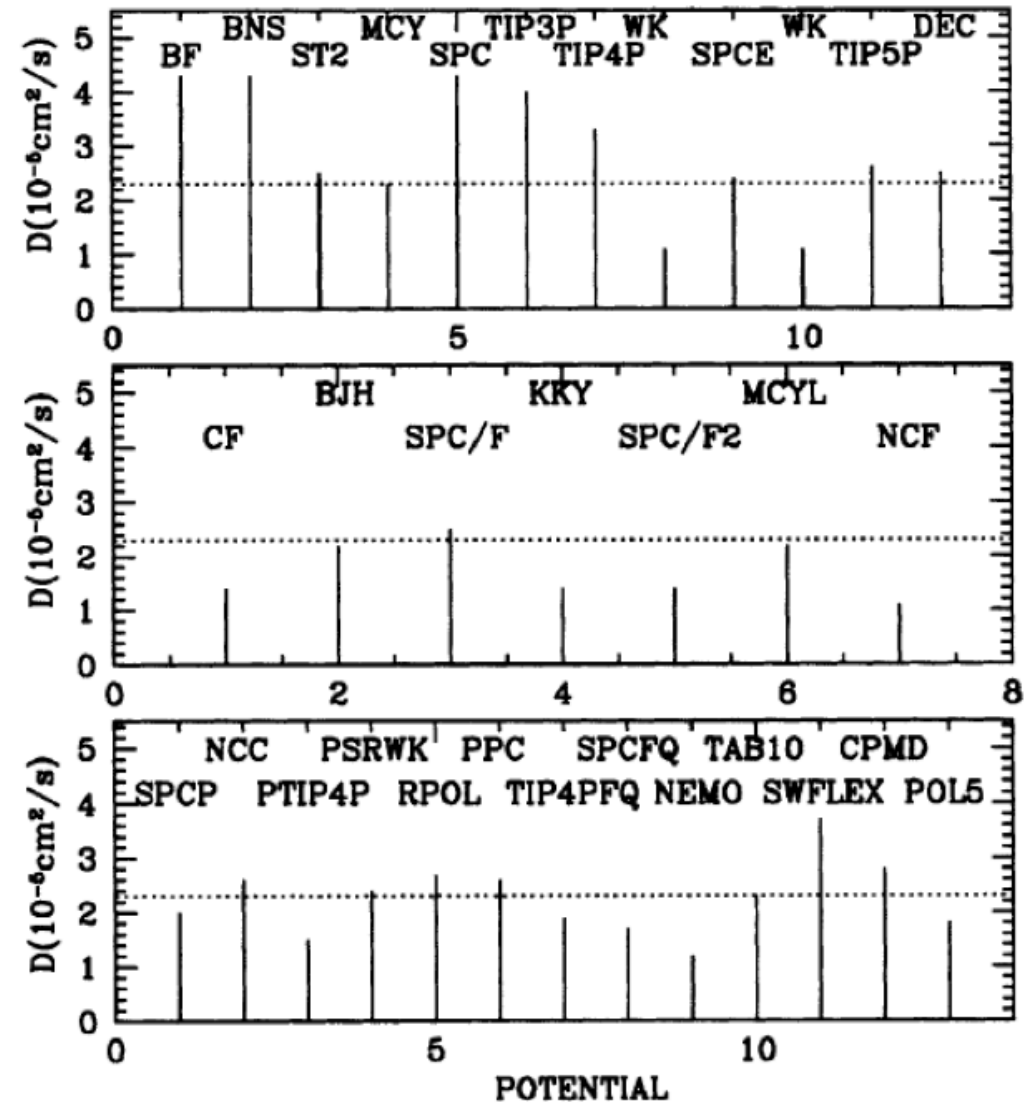Diffusivity is overestimated by many of the common water rigid models.

Comparison of physical properties

top panel: rigid models
middle panel: flexible models
lower panel: polarizable models

Water models in computer simulations, C. Caleman (2007)

# Beyond the most common water models

F3C - Levitt et al . A water model calibrated for simulation of molecular dynamics of proteins and nucleic acids in solution..

DEC - Guillot & Guissani [J. Chem. Phys. **114**, 6720 (2001)]. A water model that employs diffuse charges, in addition to the usual point charges, on the oxygen and hydrogen atoms, to account for charge penetration effects.

TIP4P/FLEX - Lawrence & Skinner [Chem. Phys. Lett. **369**, 472 (2003)]. Model that well describes the absorption spectra for liquid water.

MB model – Silverstein, Haymet & Dill [JACS **120**, 3166 (1998)] (resembles Mercedes-Benz logo). Reproduces features of water in 2-D systems (better for educational purposes than for real simulations.
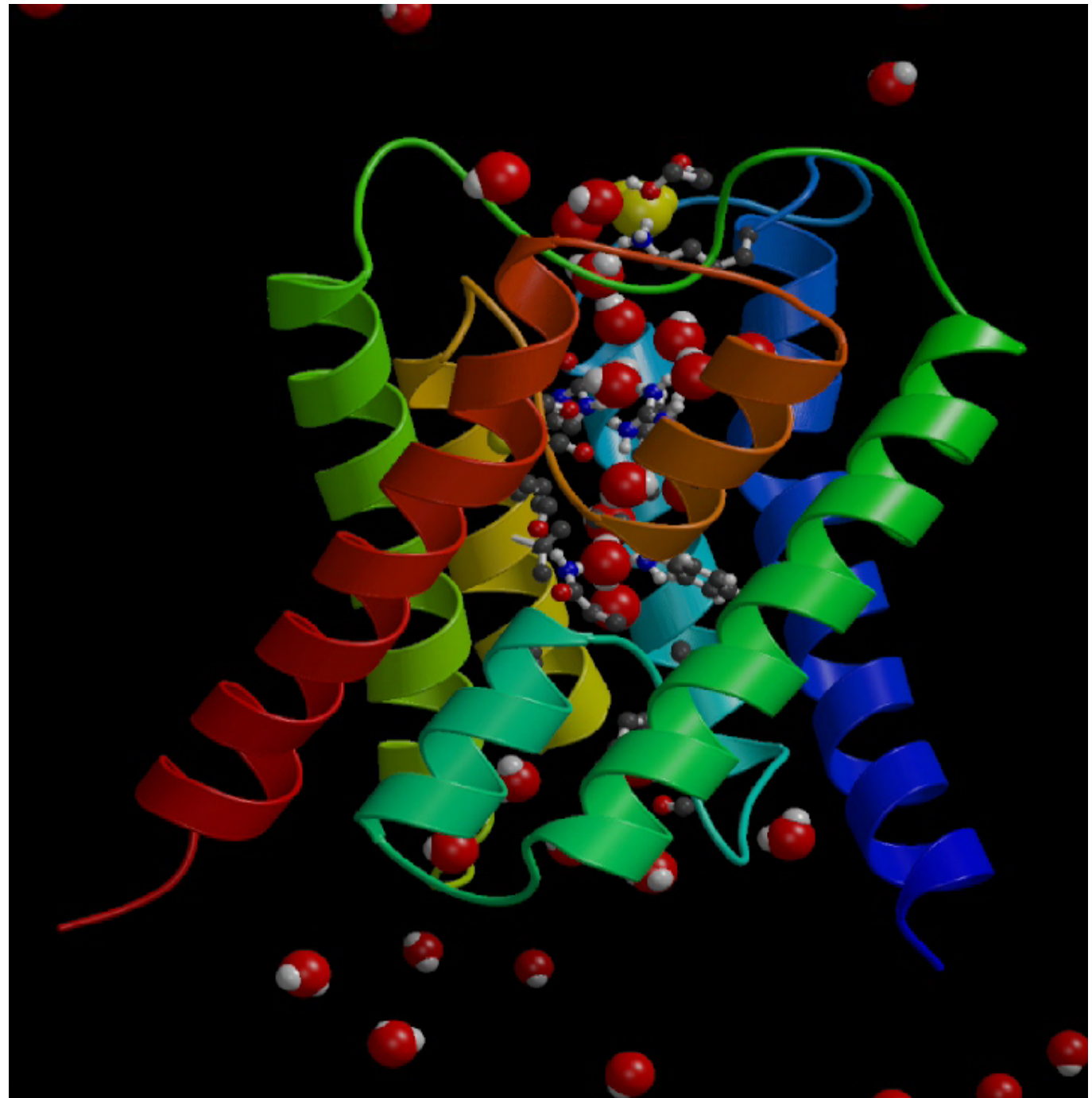
Coarse-grained models: one- and two-site models, where each site represents a number of water molecules [e.g. Izvekov & Voth. *J. Chem. Phys.* **123,** 134105 (2005)].

Aquaporin Channel http://www.mpibpc.mpg.de/groups/de_groot/gallery.html
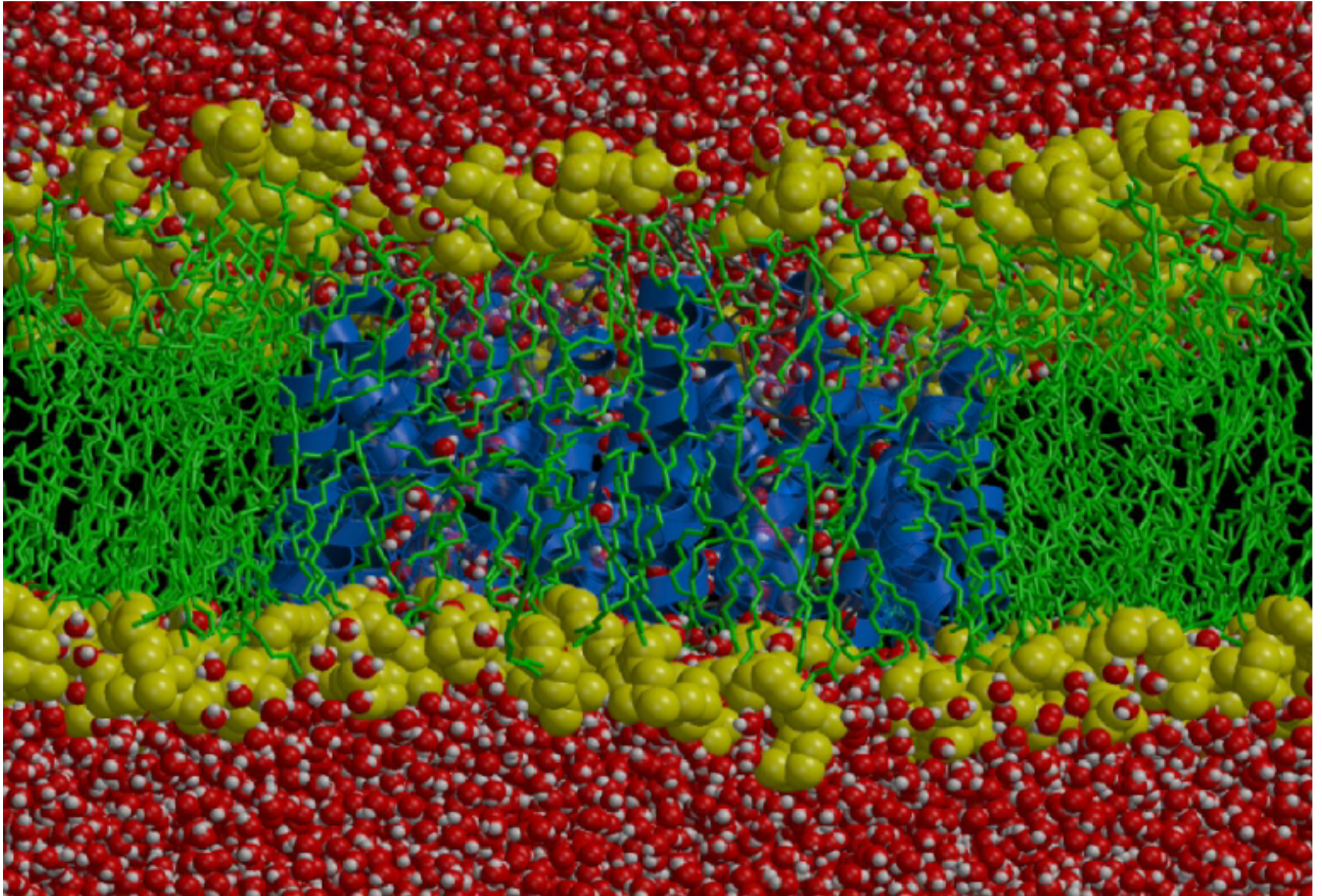
Aquaporin Channel

Simplified view:

· excess water left out,
· lipids not shown
· channel shown as ribbon

Notes:

o No water model available is able to reproduce all the water properties with good accuracy. All empirical models are parameterized and the *ab* initio models do also not behave well

o But, it is possible to describe the force field of water using simple empirical models, and make predictions

o It is worth considering which models to use when performing any simulation including water. Computional cost vs. accuracy.

References

A. Wallqvist and R. D. Mountain, *Molecular models of water: Derivation and description*, Reviews in Computational Chemistry **13** 183 (1999)**.**

B. Guillot, *A reappraisal of what we have learnt during three decades of computer simulations on water*, J. Mol. Liq. **101** 219 (2002)**.**

Implicit water models

▪represent the solvent and counterions as a continuous medium

▪simulations with implicit water can usually be run more quickly than explicit simulations

▪usually not interested in the distribution of individual water molecules in the solvent-solute interface.

Common implicit water model:
-- **Solvent accessible surface** area models
-- **Poisson-Boltzmann** equation
-- **Generalized Born** models