From Dynamics to Thermodynamics using Molecular Simulation

David van der Spoel

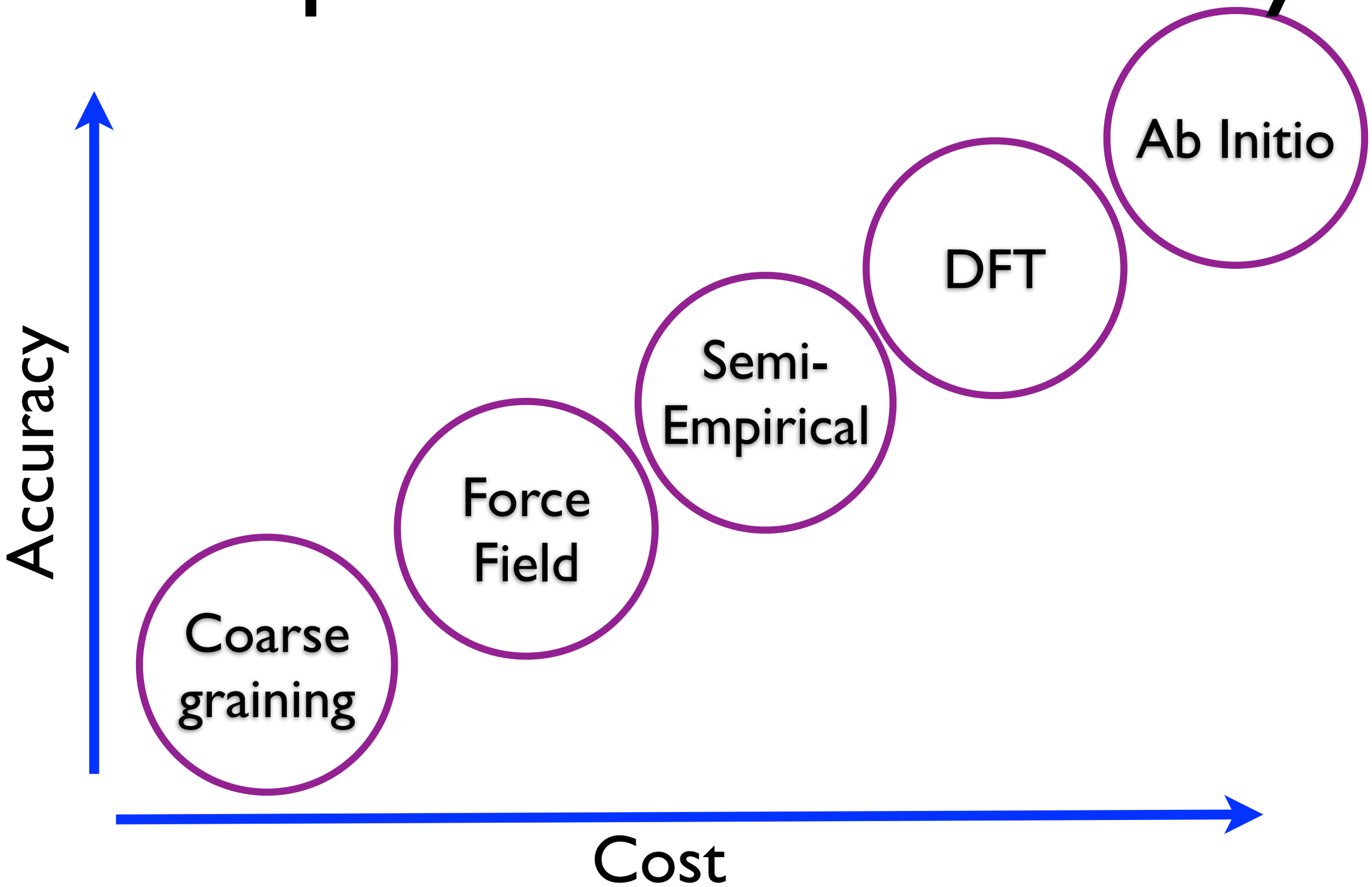
Computational Chemistry

- Physical models to describe molecules
- Software to evaluate models and do predictions - GROMACS
- Model validation and development
- Applications in Chemistry - Water & other liquids
- (Applications in Biology - PitGP, Virus, Malaria)

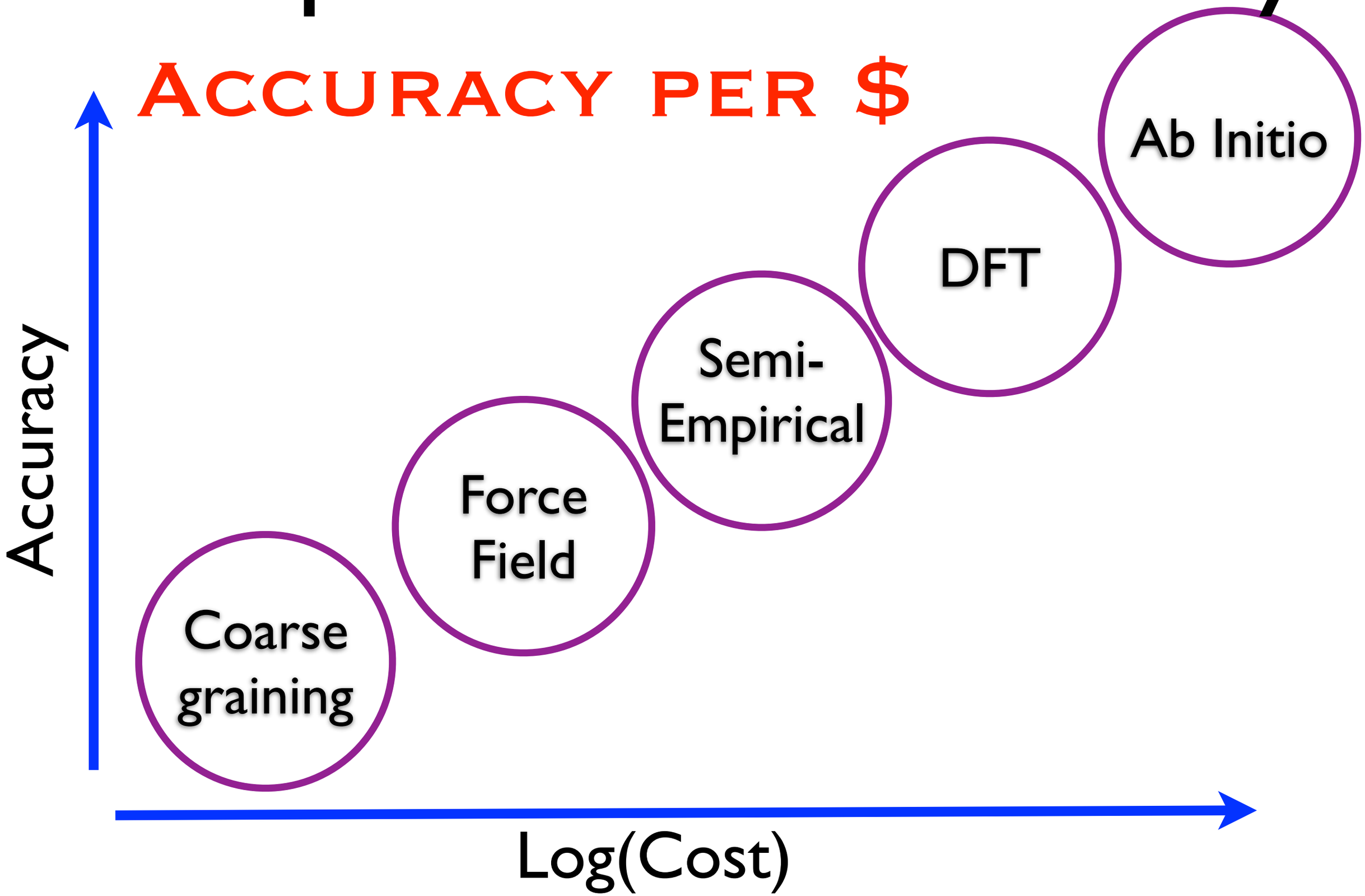
Computational Chemistry

- Ab-initio methods
- Density functional theory
- Semi-empirical
- Atomistic Force field
- Coarse grained FF / QSAR / Continuum descriptions

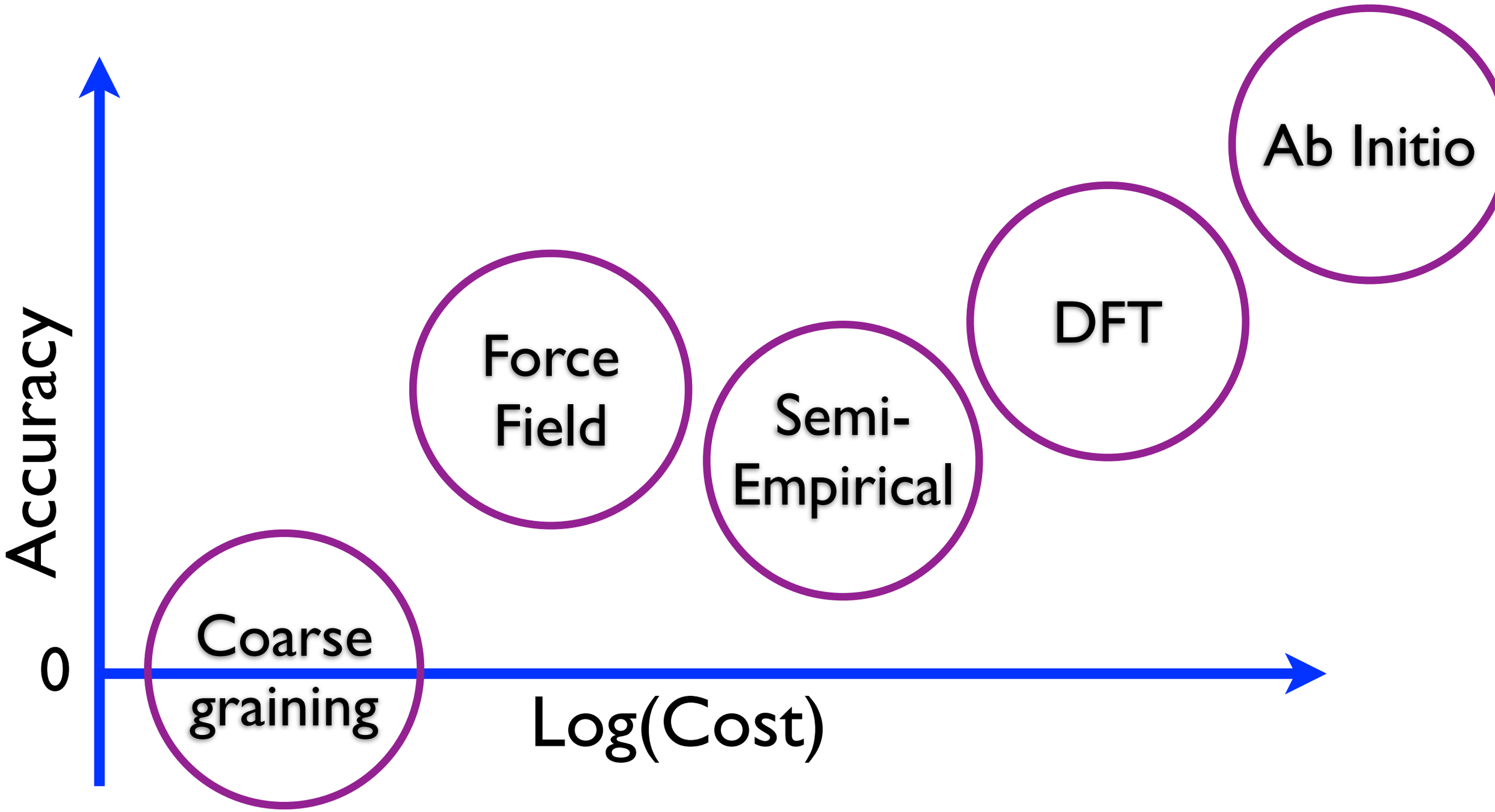
Computational Chemistry



Computational Chemistry



Computational Chemistry



Depends on the problem!

What is Molecular Dynamics

- Coordinates of atoms/particles as a function of time
- Time correlation functions
- Experimental: Nuclear Magnetic Resonance spectroscopy
- Computer simulations at different levels of spatial and temporal accuracy
- Sampling the conformational space - partition function

$$U = \sum_{\text{All Bonds}} \tfrac{1}{2} K_b (b - b_0)^2 + \sum_{\text{All Angles}} \tfrac{1}{2} K_\theta (\theta - \theta_0)^2$$

$$+ \sum_{\text{All Torsion Angles}} K_\phi [1 - \cos(n\phi + \delta)]$$

$$+ \sum_{\text{All nonbonded pairs}} \varepsilon \left[\left(\frac{r_0}{r}\right)^{12} - 2\left(\frac{r_0}{r}\right)^{6} \right]$$

$$+ \sum_{\text{All partial charges}} 332 q_i q_j / r$$

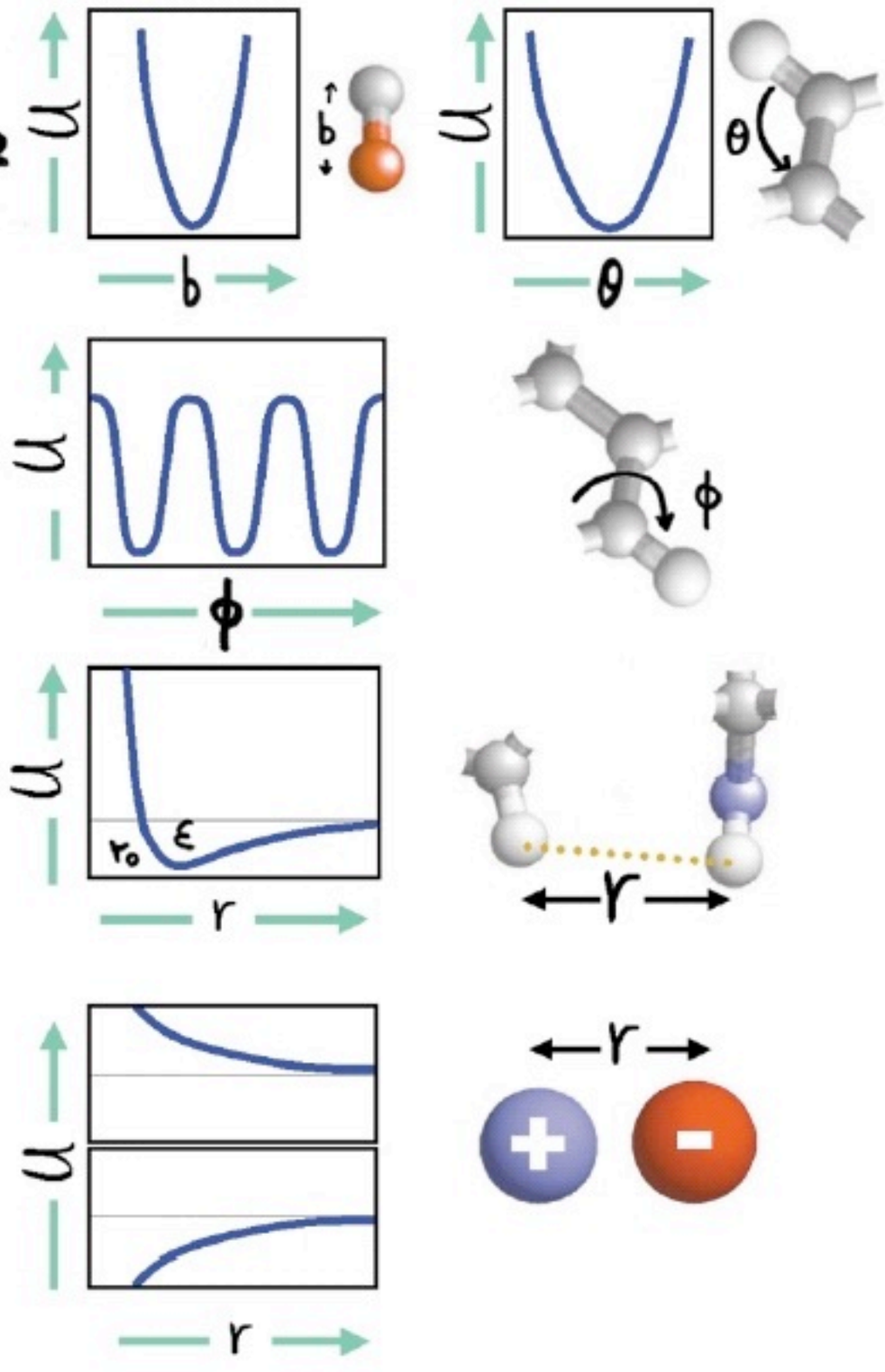


Fig. 1 The total potential energy of any molecule is the sum of terms allowing for bond stretching, bond angle bending, bond twisting, van der Waals interactions and electrostatics. Many properties of a biomolecules can be simulated with such an empirical energy function.

M.Levitt, Nat. Struct. Biol. 8 (**2001**), p. 392-393

How Many Lennard-Jones Parameters for a Protein?

- Two parameters per interaction
- One atom type per element (C,H,N,O,S) : 10 with combination rules, 40 without
- With four atom types per element: 40 with combination rules, 760 without

The Physical Model

- What determines the quality?
- How can we test it?

Our Gr8t Software

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Sök

David van der Spoel | Hitta vänner | Startsida

logg

Dolda inlägg

Information

Vänners aktivitet

Statistik

Foton

REDIGERA

Om verksamheten Redigera

GROMACS is a software package for simulations of molecular dynamics.

481

gillar detta

GROMACS

Redigera sidan

Programvara · Redigera information

logg — GROMACS · Alla (senaste)

Dela: Inlägg | Foto | Länk

Skriv något...

Navid Zolfaghari
I wonder to see if any workshop is going to be held in U.S.
Gilla · Kommentera · den 10 februari kl. 19:14

Santosh Kumar
Can anyone tell that how to add the new residue in the forcefield in gromacs ? is the any tutorial for this???
Gilla · Kommentera · den 8 februari kl. 19:56

Thanos Tequila
Hi gromacs users,
I have some trouble trying to complie gromacs on a GPU. Is there an easy, step by step, guide to help me complete this process? :):)
thanks
Gilla · Kommentera · den 4 februari kl. 18:09

Neshat Haq
Hi gromacs users ,
Can anyone tell, what are the considerations to be kept in mind while going for a metalloprotein simulation, like protein containing Fe3+ and Mn2+ ions.
Or is there any tutorial describing the steps, in your knowledge.
Gilla · Kommentera · den 31 januari kl. 11:00

Donal Murphy
If you're using GPUs in your work and want to share exciting new

Administratörer (2) [?] Visa alla

Använd Facebook som GROMACS

Aviseringar

Marknadsför med en annons

Visa tidigare statistik

Bjud in vänner

Bjud in e-postkontakter

Du och GROMACS

11 vänner gillar detta.

Sponsrade — Skapa en annons

Se Abduction ikväll!
cdon.se

Nu finns actionfilmen Abduction på Blu-ray och DVD! Med Taylor Lautner och Michael Nyqvist.

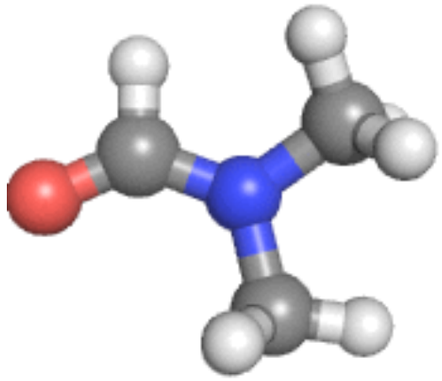
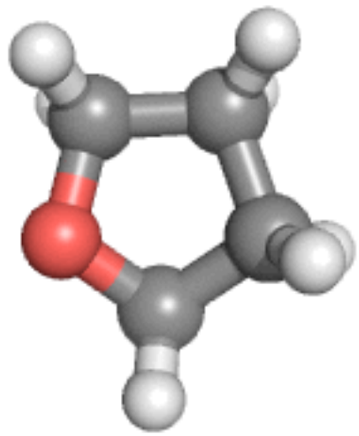
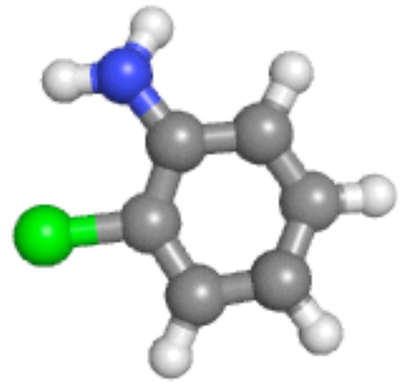
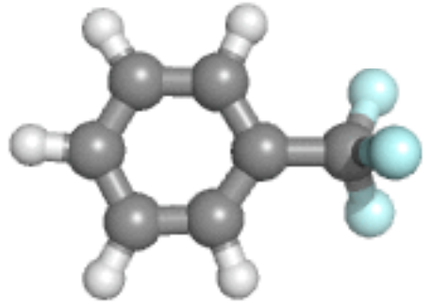
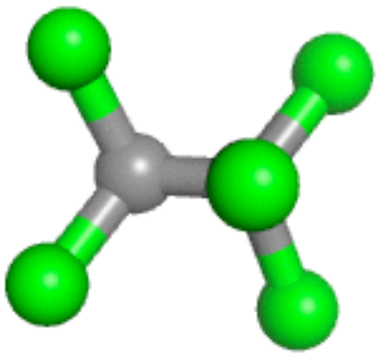
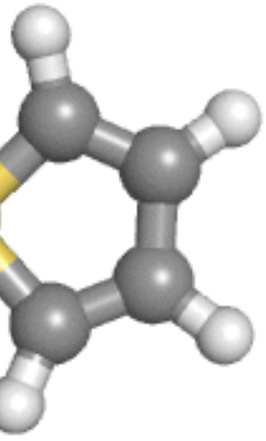
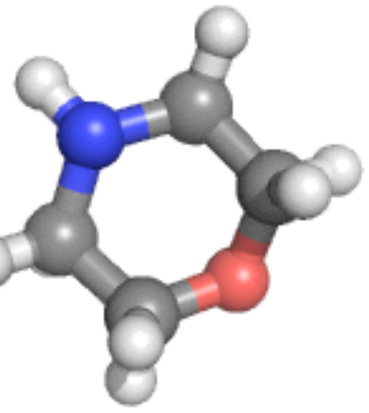
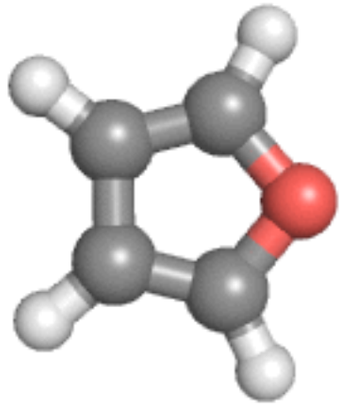
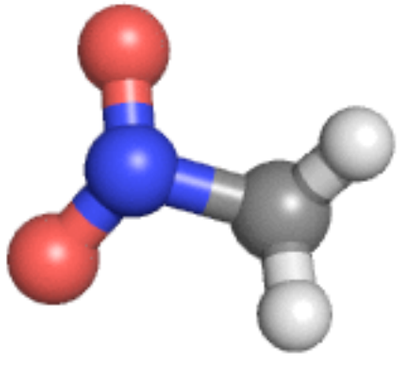
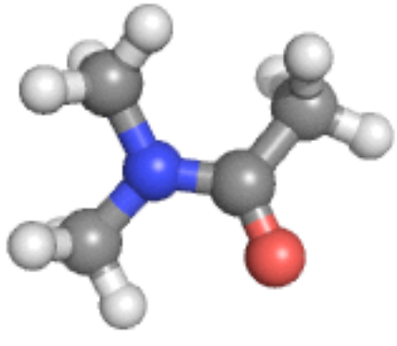
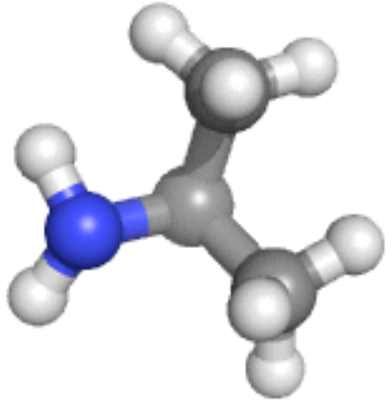
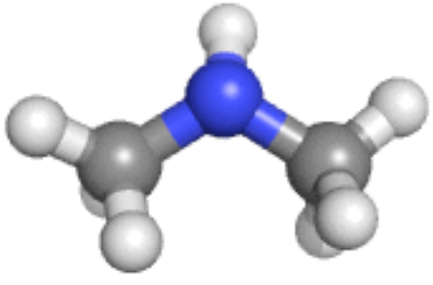
Stockholm!
groupon.se

Upplev de 5 roligaste aktiviteterna i Stockholm.

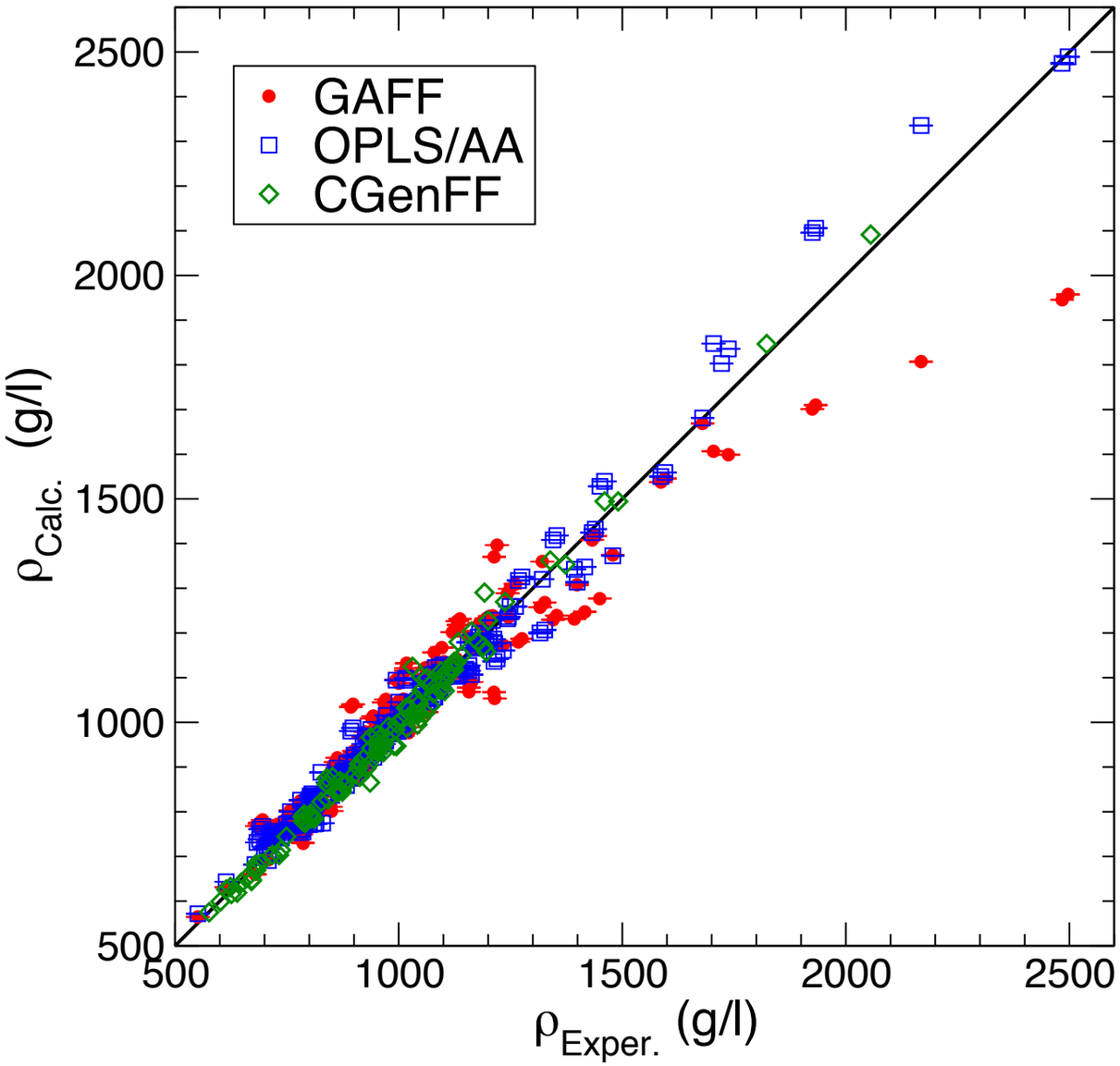
http://www.gromacs.org

Liquid FF Benchmark

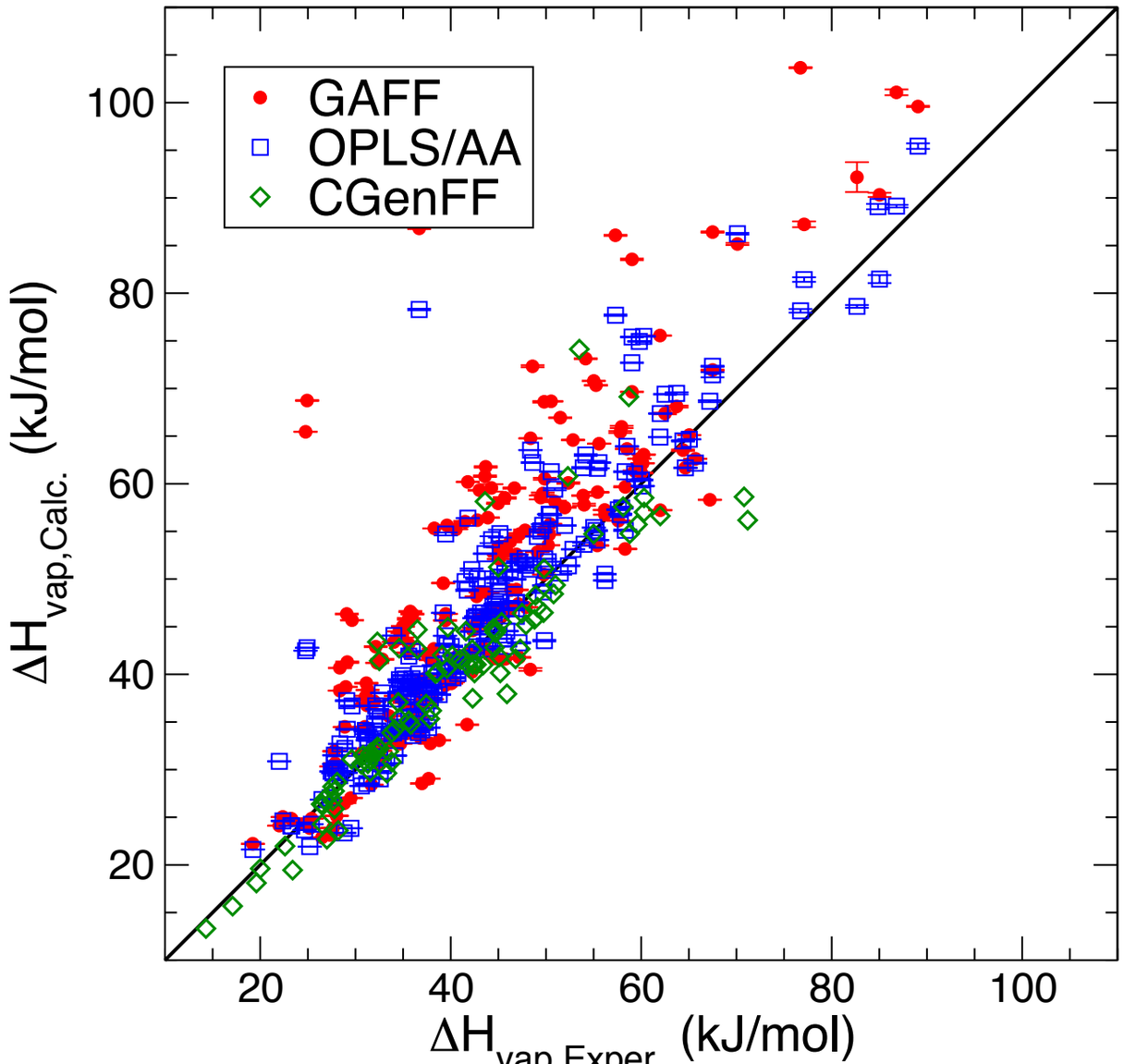
- Test available force field for how good they reproduce properties for ~ 150 organic liquids
- 1000 molecules/box 10 ns production sims
- OPLS/AA, GAFF + CGenFF from literature

Simple props



Density

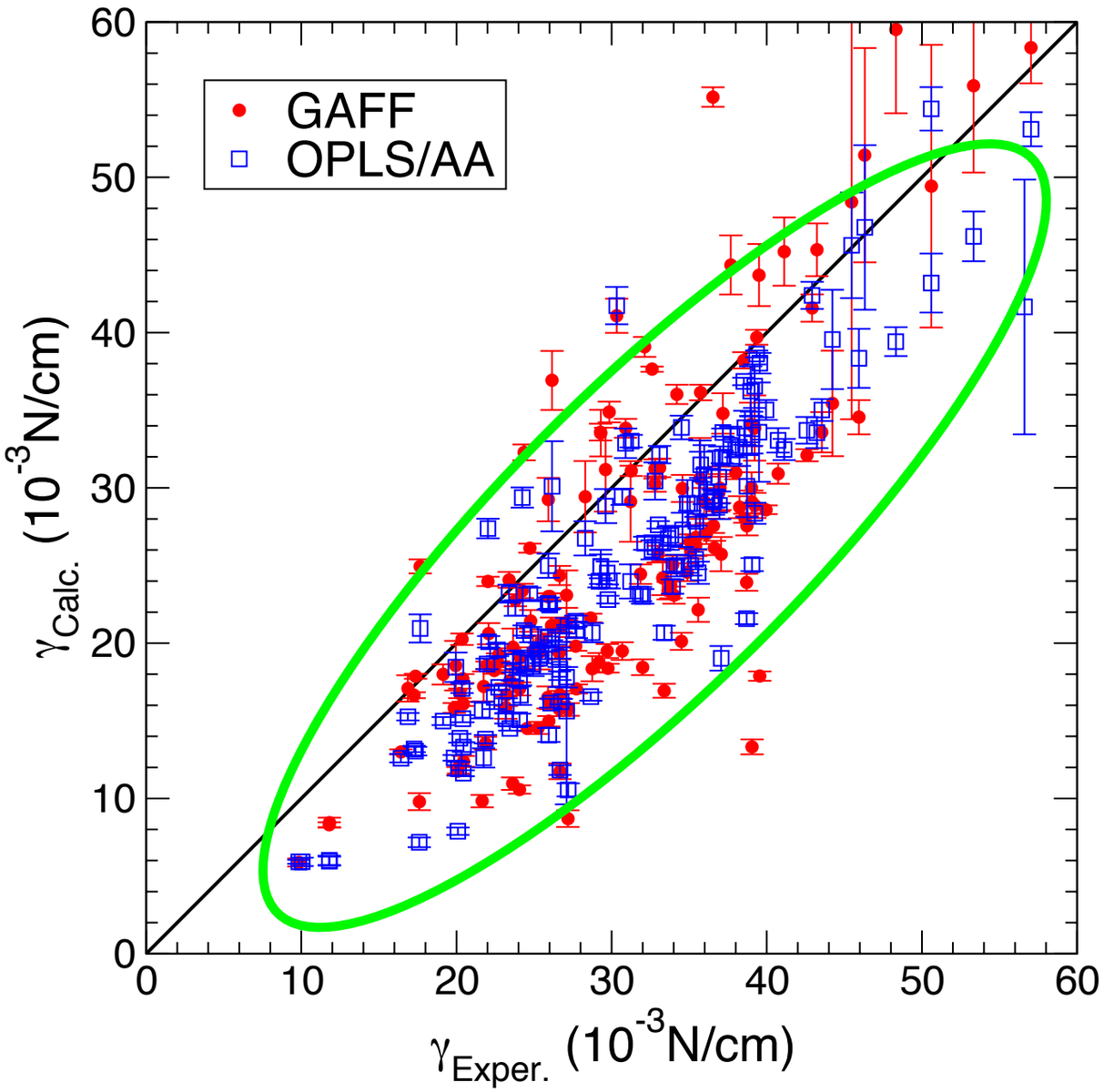


Enthalpy of Vaporization

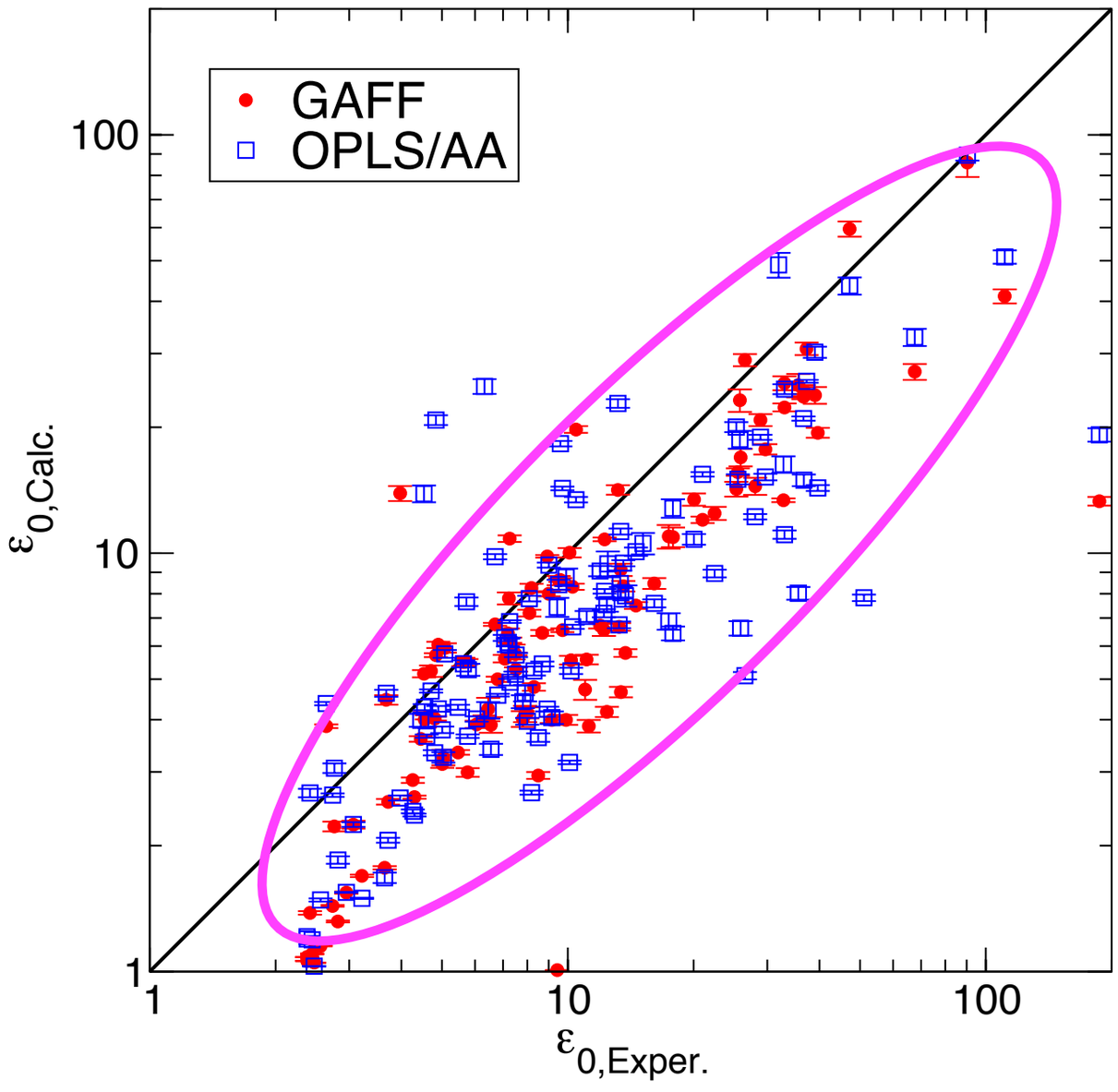
Not so simple props

Due to cut-off of Van der Waals forces?

Polarization?



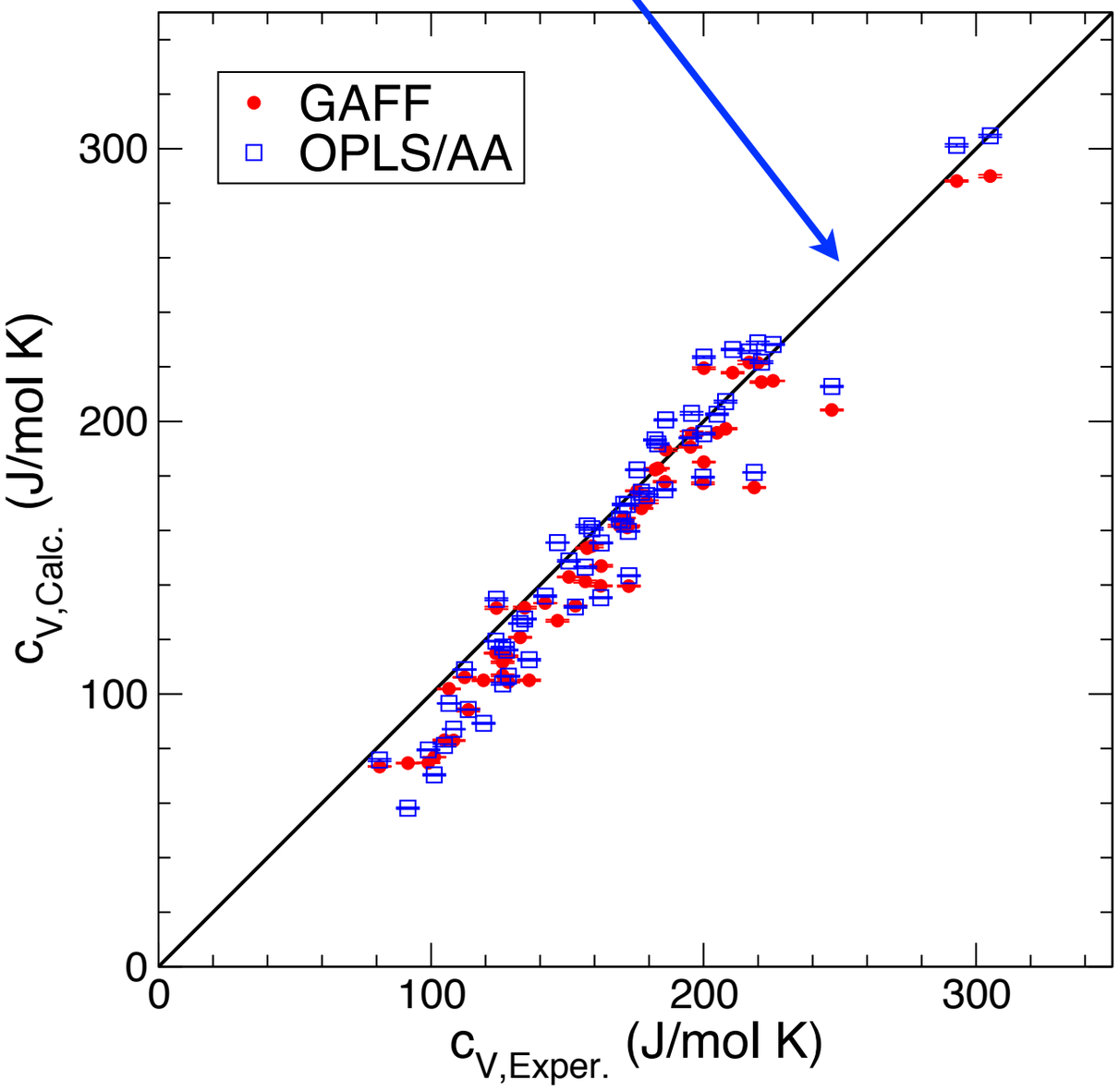
Surface Tension



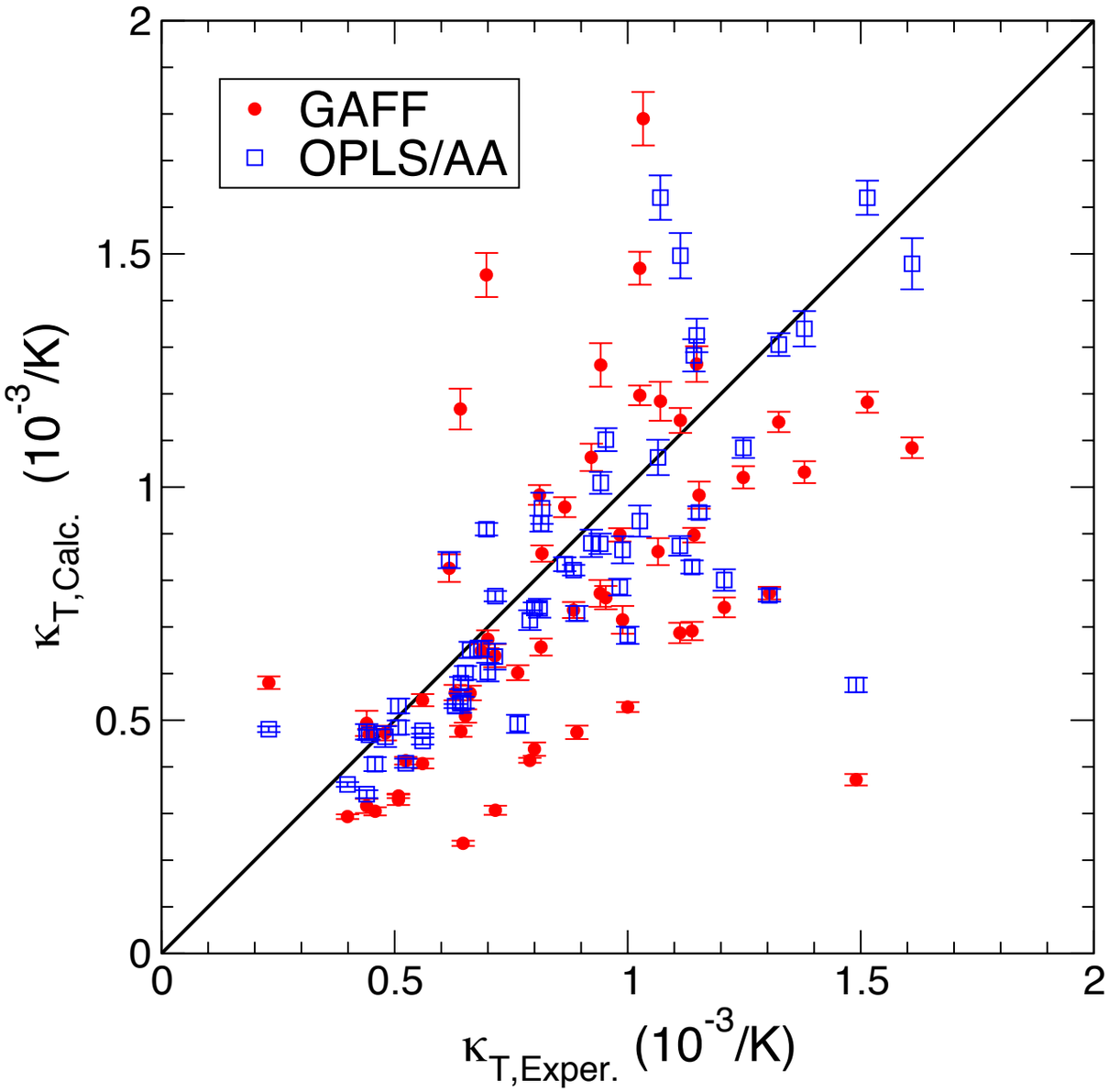
Dielectric Constant

2 Phase Thermodynamics method!

Complex props



Heat capacity



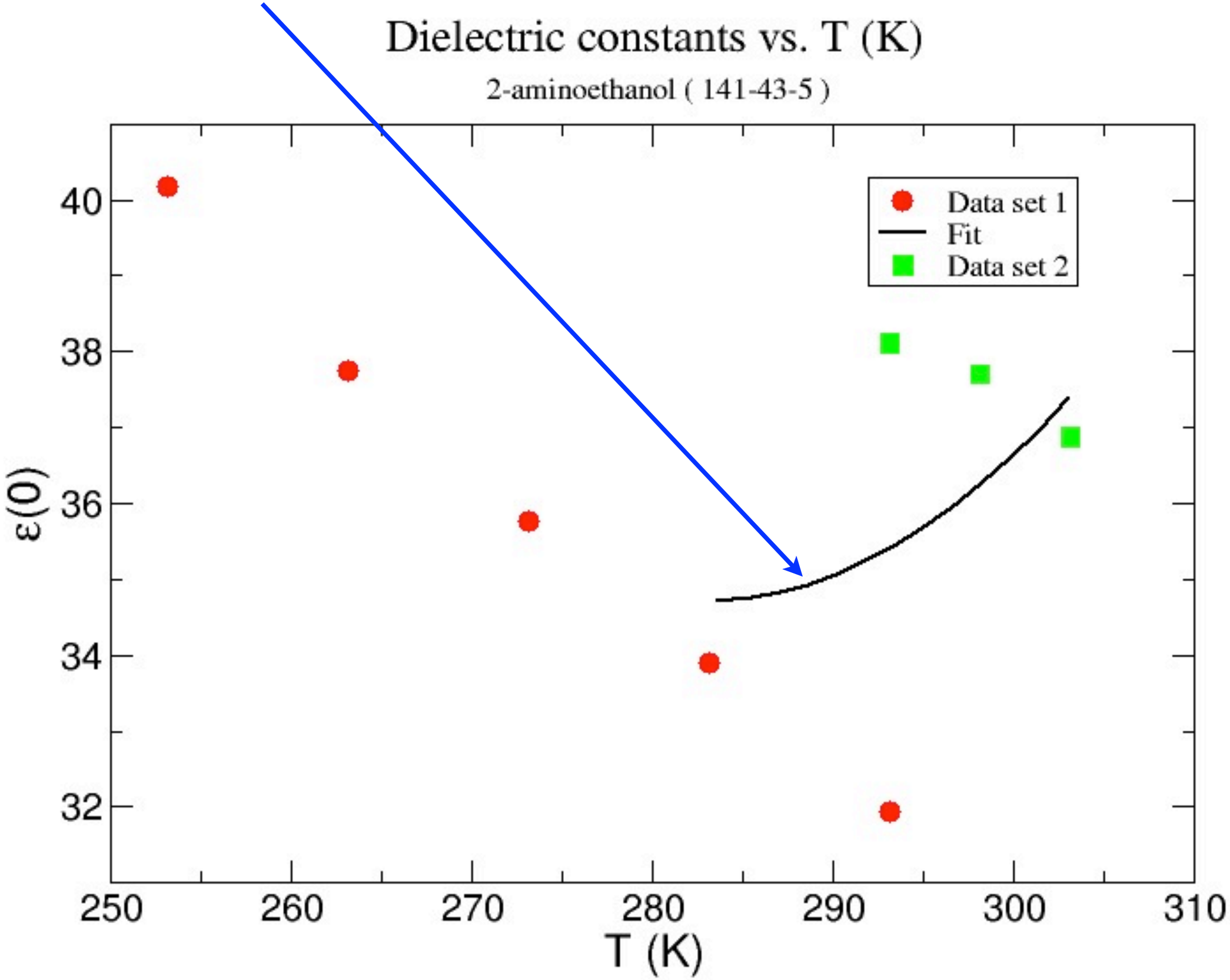
Compressibility

Yihzak Marcus: The Properties of Solvents

Table 3.1 Thermophysical properties of solvents (temperature dependent properties at 25°C, unless otherwise noted)

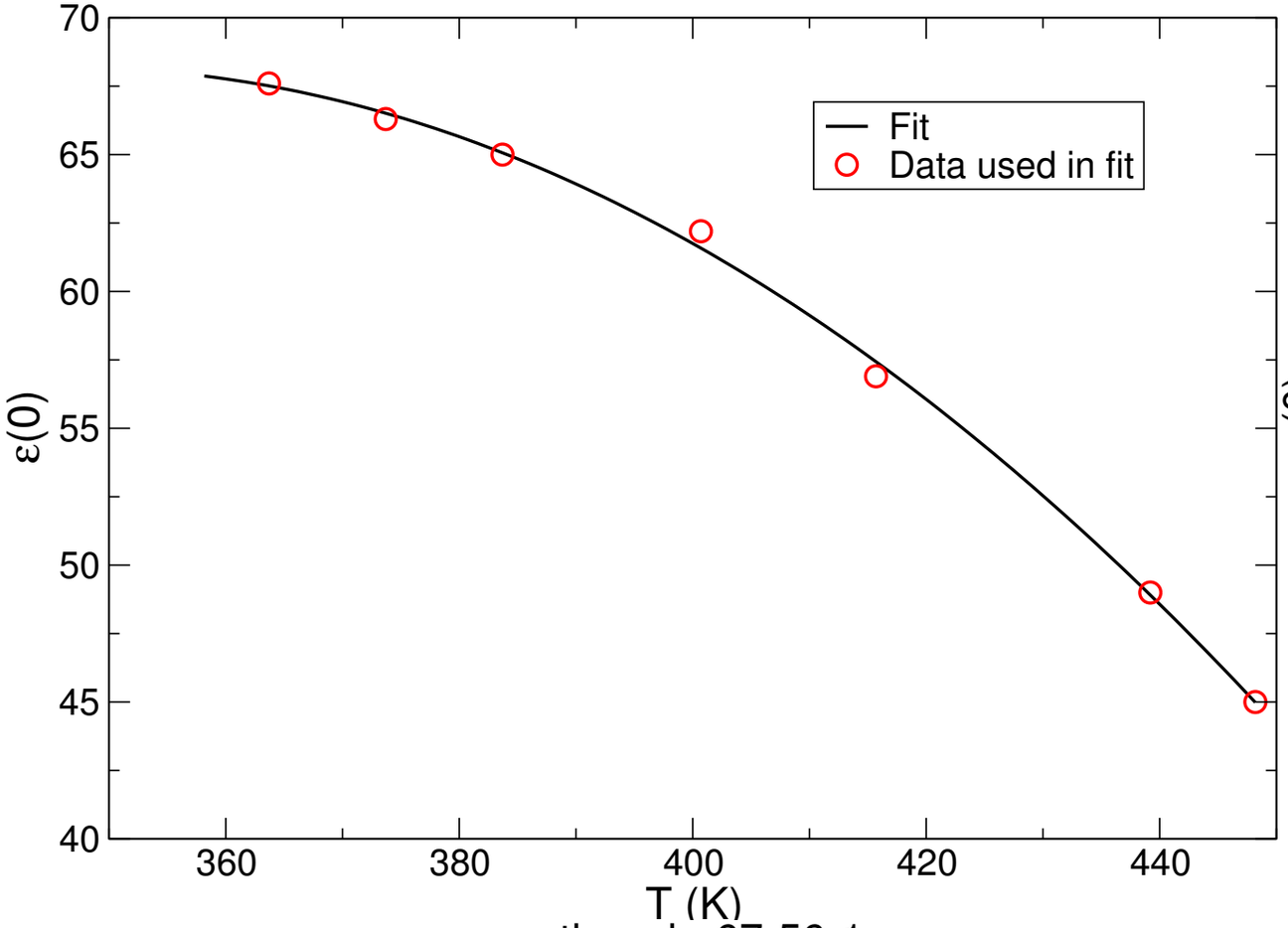
No	Name	M	Tm	Tb	Tc	d	V	α_P	κ_T	p	dHv	δ	Cp
0	vacuum	0.00				0.0000 j	0.0						0.00 j
10	tetramethylsilane	88.23	174.1 [1]	299.8 [1]	450.4 [2]	0.6464 [1]	136.5	1.84 [2]	2.884 [gg]	9.56E+01 [1]	24.20 [1]	12.6	204.1 [1]
20	n-pentane	72.15	143.4 [1]	309.2 [1]	496.7 [1]	0.6214 [1]	116.1	1.58 [1]	2.180 [1]	6.87E+01 [1]	26.41 [1]	14.4	167.1 [1]
30	2-methylbutane	72.15	113.3 [1]	301.0 [1]	460.4 [1]	0.6140 [1]	117.5	1.66 [1]	2.450 [1]	9.17E+01 [1]	24.84 [1]	13.8	165.4 [1]
40	n-hexane	86.18	177.8 [1]	341.9 [1]	507.7 [1]	0.6549 [1]	131.6	1.39 [1]	1.706 [1]	2.02E+01 [1]	31.48 [1]	15.0	195.4 [1]
50	c-hexane	84.16	279.9 [1]	353.9 [1]	553.6 [1]	0.7742 [1]	108.7	1.23 [1]	1.140 [1]	1.30E+01 [1]	32.89 [1]	16.8	156.0 [1]
60	n-heptane	100.2	182.6 [1]	371.6 [1]	540.7 [1]	0.6793 [1]	147.5	1.27 [1]	1.442 [1]	6.10E+00 [1]	36.58 [1]	15.2	224.9 [1]
70	n-octane	114.2	216.4 [1]	398.8 [1]	568.8 [1]	0.6987 [1]	163.5	1.17 [1]	1.282 [1]	1.87E+00 [1]	41.49 [1]	15.5	254.1 [1]
80	2,2,4-trimethyl pentane	114.2	165.8 [1]	372.4 [1]	543.9 [1]	0.7122 [1]	160.4	1.20 [1]		6.50E+00 [1]	35.15 [1]	14.7	238.5 [1]
90	n-decane	142.2	243.5 [1]	447.3 [1]	617.6 [1]	0.7263 [1]	195.9	1.05 [1]	1.093 [1]	1.80E-01 [1]	51.38 [1]	15.8	314.5 [1]
100	n-dodecane	170.3	263.6 [1]	489.5 [1]	658.3 [1]	0.7541 [1]	228.6	0.98 [1]	0.989 [1]	1.50E-01 [1]	61.29 [1]	16.0	375.9 [1]
110	n-hexadecane	226.4	291.0 [3]	560.0 [3]	720.6 [2]	0.7700 [1]	294.1	0.88 [1]	0.867 [3]	2.00E-04 [1]	81.09 [1]	16.3	501.4 [2]
120	benzene	78.12	278.7 [1]	353.2 [1]	562.2 [1]	0.8690 [1]	89.9	1.23 [1]	0.962 [1]	1.27E+01 [1]	33.85 [1]	18.8	135.7 [1]
130	toluene	92.14	178.2 [1]	383.8 [1]	591.8 [1]	0.8619 [1]	106.9	1.07 [1]	0.922 [1]	3.75E+00 [1]	37.99 [1]	18.8	157.2 [1]
140	o-xylene	106.1	248.0 [1]	417.6 [1]	630.3 [1]	0.8760 [1]	121.2	0.95 [1]	0.811 [1]	8.80E-01 [1]	43.43 [1]	18.0	188.0 [1]
150	m-xylene	106.1	225.3 [1]	412.3 [1]	617.1 [1]	0.8604 [1]	123.4	0.99 [1]	0.862 [1]	1.10E+00 [1]	42.66 [1]	18.0	183.4 [1]
160	p-xylene	106.1	286.4 [1]	411.5 [1]	616.2 [1]	0.8569 [1]	123.9	1.00 [1]	0.859 [1]	1.17E+00 [1]	42.38 [1]	18.1	181.6 [1]
170	ethylbenzene	106.1	178.2 [1]	409.3 [1]	617.2 [1]	0.8625 [1]	123.1	1.02 [1]	0.865 [1]	1.30E+00 [1]	42.25 [1]	18.0	185.5 [1]
180	cumene	120.1	177.1 [1]	425.6 [1]	631.1 [1]	0.8573 [1]	140.2	0.98 [1]	0.893 [1]	6.10E-01 [1]	45.14 [1]	17.6	198.9 [1]
190	mesitylene	120.1	228.4 [1]	437.9 [1]	637.3 [1]	0.8610 [1]	139.6	0.94 [1]	0.699 [1]	3.30E-01 [1]	7.48 [1]	18.1	209.1 [1]
200	styrene	104.1	242.5 [1]	418.3 [1]	636.9 [1]	0.9010 [1]	115.6	0.97 [1]		8.40E-01 [1]	43.93 [1]	18.9	182.5 [1]
210	tetralin	132.2	237.4 [1]	480.8 [1]	754.0 [1]	0.9657 [1]	136.9	0.72 [1]		5.30E-02 [1]	55.23 [1]	19.4	217.4 [1]
220	cis-decalin	138.2	230.1 [1]	468.9 [1]	702.2 [1]	0.8931 [1]	154.8	0.85 [1]		1.00E-01 [1]	51.34 [1]	17.8	232.0 [1]
230	water	18.02	273.2 [1]	373.2 [1]	647.1 [1]	0.9974 [1]	18.1	0.26 [1]	0.457 [1]	3.17E+00 [1]	43.91 [1]	47.9	75.30 [1]
240	methanol	32.04	175.5 [1]	337.7 [1]	512.6 [1]	0.7872 [1]	40.7	1.19 [1]	1.248 [1]	1.69E+01 [1]	37.43 [1]	29.3	81.47 [1]
250	ethanol	46.07	158.7 [1]	351.4 [1]	513.9 [1]	0.7848 [1]	58.7	1.09 [1]	1.153 [1]	7.89E+00 [1]	42.32 [1]	26.0	112.3 [1]
260	n-propanol	60.10	147.0 [1]	370.3 [1]	537.3 [1]	0.8003 [1]	75.1	1.01 [1]	1.025 [1]	2.73E+00 [1]	47.45 [1]	24.4	143.8 [1]
270	i-propanol	60.10	185.2 [1]	355.4 [1]	508.3 [1]	0.7815 [1]	76.9	1.08 [1]	1.332 [1]	6.03E+00 [1]	45.39 [1]	23.7	154.6 [1]
280	n-butanol	74.12	184.5 [1]	390.8 [1]	563.0 [1]	0.8057 [1]	92.0	0.93 [1]	0.941 [1]	8.20E-01 [1]	52.35 [1]	23.3	177.0 [1]
290	i-butanol	74.12	165.0 [1]	381.0 [1]	547.8 [1]	0.7978 [1]	92.9	0.98 [1]	1.026 [1]	1.38E+00 [1]	50.82 [1]	22.9	181.0 [1]
300	2-butanol	74.12	158.5 [1]	372.7 [1]	536.0 [1]	0.8030 [1]	92.3	1.06 [1]	0.983 [7]	2.43E+00 [1]	49.72 [1]	22.6	213.8 [1]
310	t-butanol	74.12	298.8 [1]	355.5 [1]	506.2 [1]	0.7810 [1]	94.9	1.26 [1]	0.989 [7]	5.60E+00 [1]	46.69 [1]	21.6	220.3 [1]
320	n-pentanol	88.15	195.0 [1]	411.1 [1]	588.2 [1]	0.8124 [1]	108.5	0.89 [1]	0.884 [1]	3.15E-01 [1]	57.02 [1]	22.4	208.9 [1]

Handbook of Chemistry & Physics

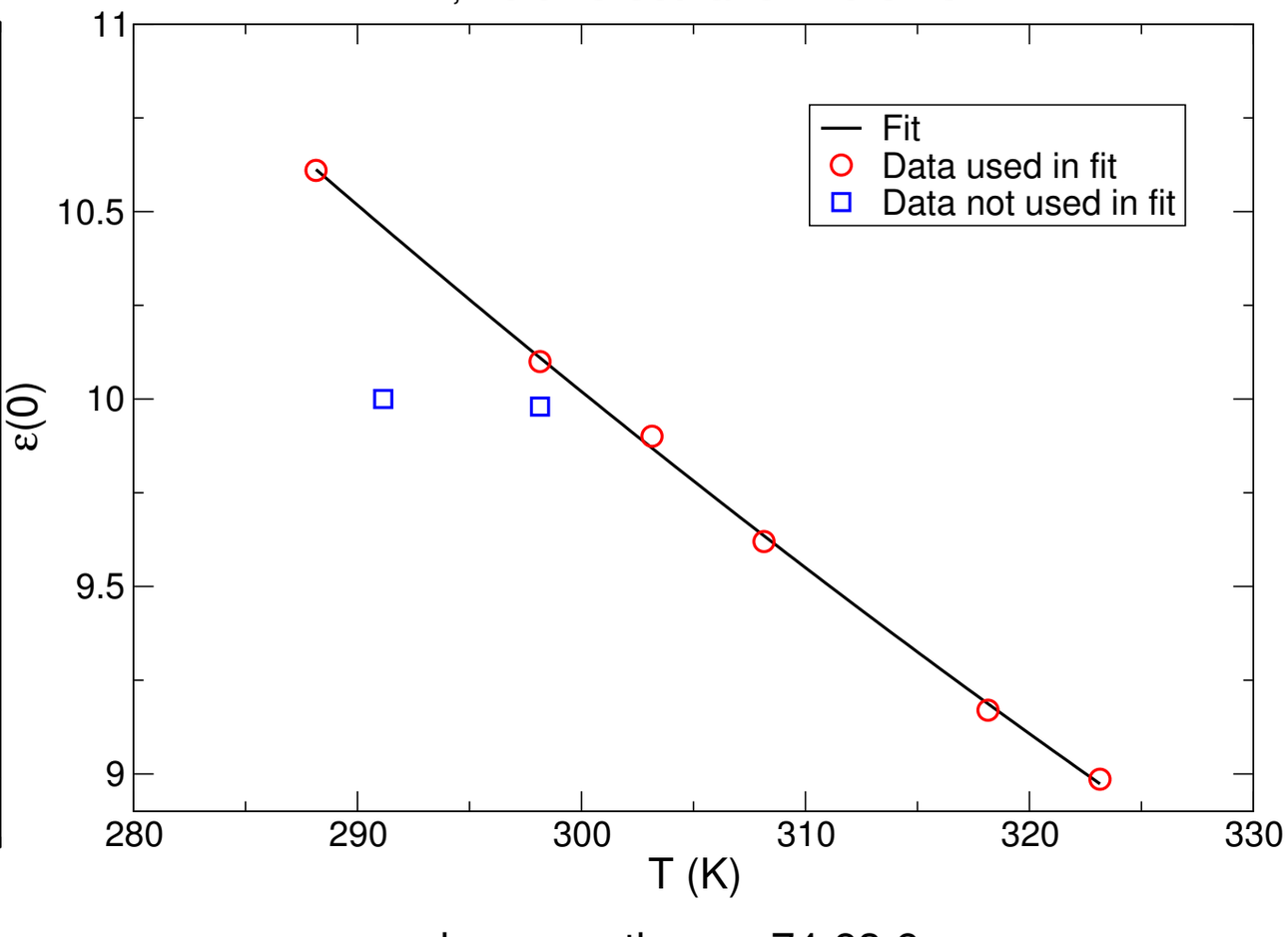


Science in the 21st century...

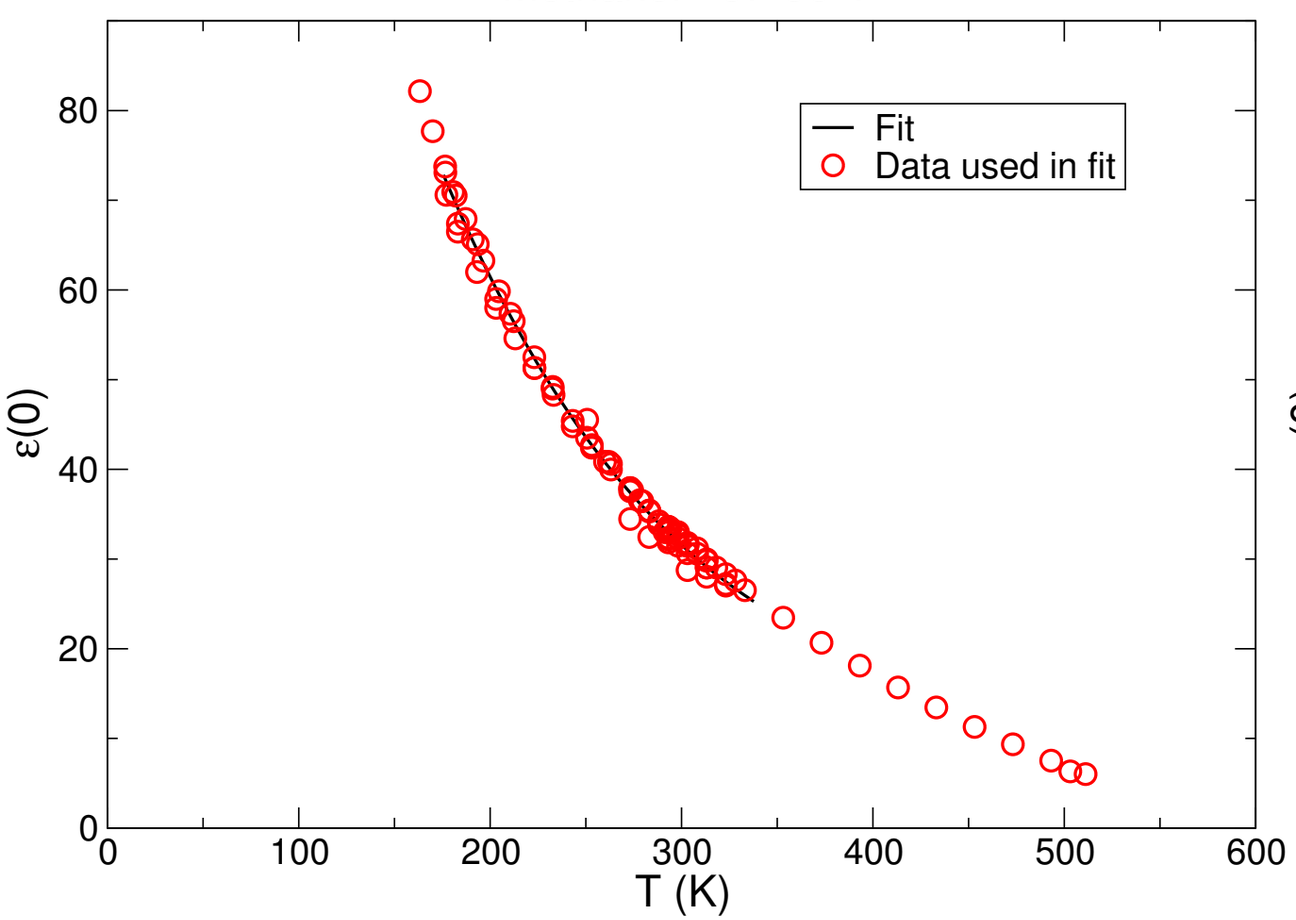
ethanamide - 60-35-5



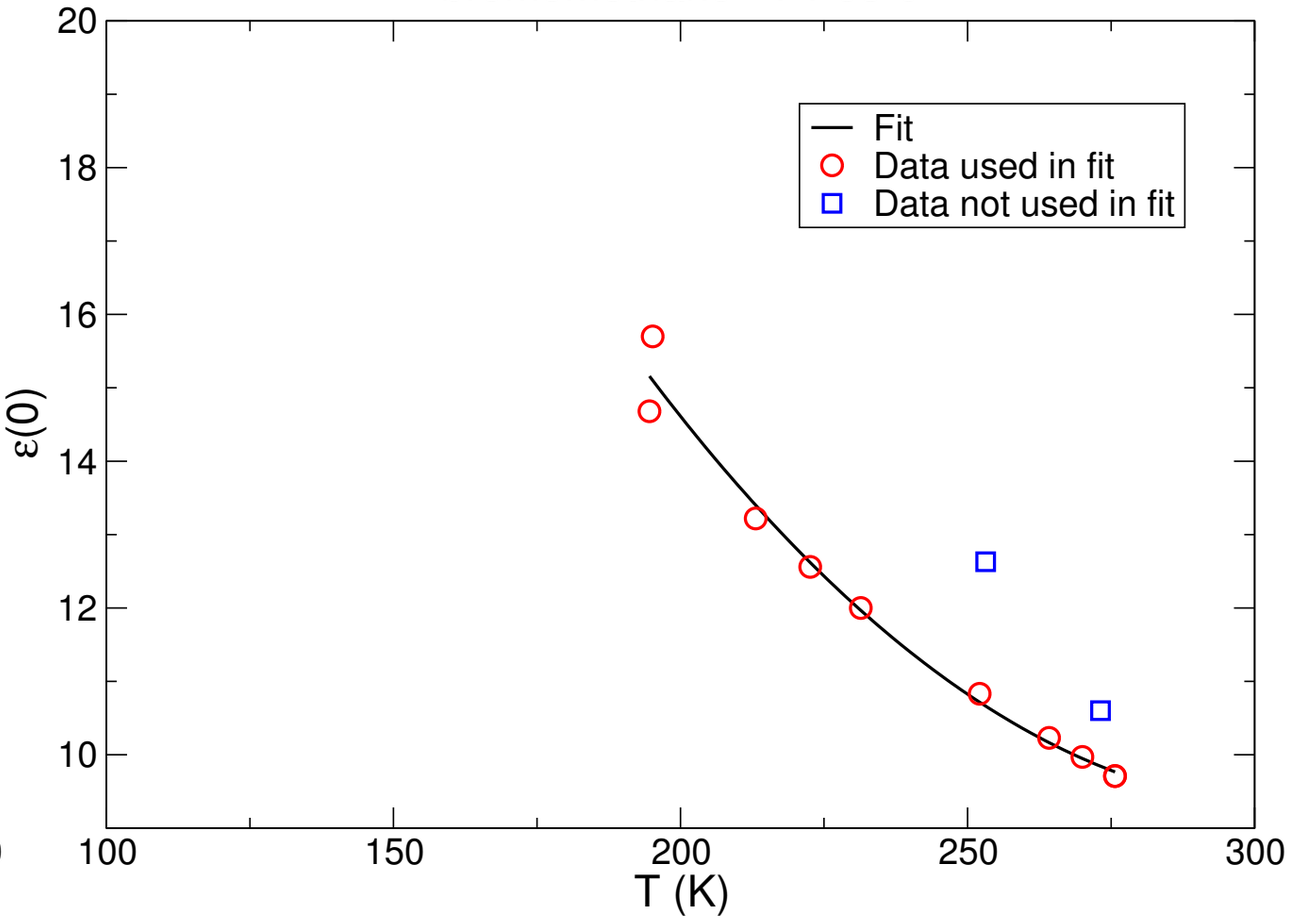
1,1-dichloroethane - 75-34-3



methanol - 67-56-1



bromomethane - 74-83-9



Force field	N	a	b	RMSD	% Dev.	R^2
			ρ (g/l)			
GAFF	235	0.96	58.6	82.9	4	97%
OPLS/AA	235	0.98	21.3	40.3	2	99%
CGenFF[36]	111	1.03	-36.0	26.0	2	99%
OPLS/AA[70]	9	1.01	-24.0	45.3	4	96%
			ΔH_{vap} (kJ/mol)			
GAFF	231	1.07	0.8	10.6	17	83%
OPLS/AA	231	0.96	3.4	6.5	11	89%
CGenFF[36]	95	0.94	2.4	4.7	7	84%
			γ (10^{-3}N/m)			
GAFF	155	0.75	0.9	8.6	23	70%
OPLS/AA	155	0.97	-5.5	7.3	22	89%
			$\varepsilon(0)$			
GAFF	170	0.21	0.6	23.4	52	48%
OPLS/AA	183	0.16	0.7	22.7	57	56%
			α_P (10^{-3}/K)			
GAFF	221	0.90	0.3	0.3	24	67%
OPLS/AA	221	0.91	0.3	0.3	21	75%
OPLS/AA[70]	9	0.53	0.8	0.7	42	39%
			κ_T (1/GPa)			
GAFF	60	0.56	0.1	0.3	31	64%
OPLS/AA	60	0.61	0.2	0.3	21	76%
OPLS/AA[70]	8	0.93	0.0	1.1	59	84%

Statistics

- Quantitative evaluation per property.

Benchmark is Foundation for Future FF

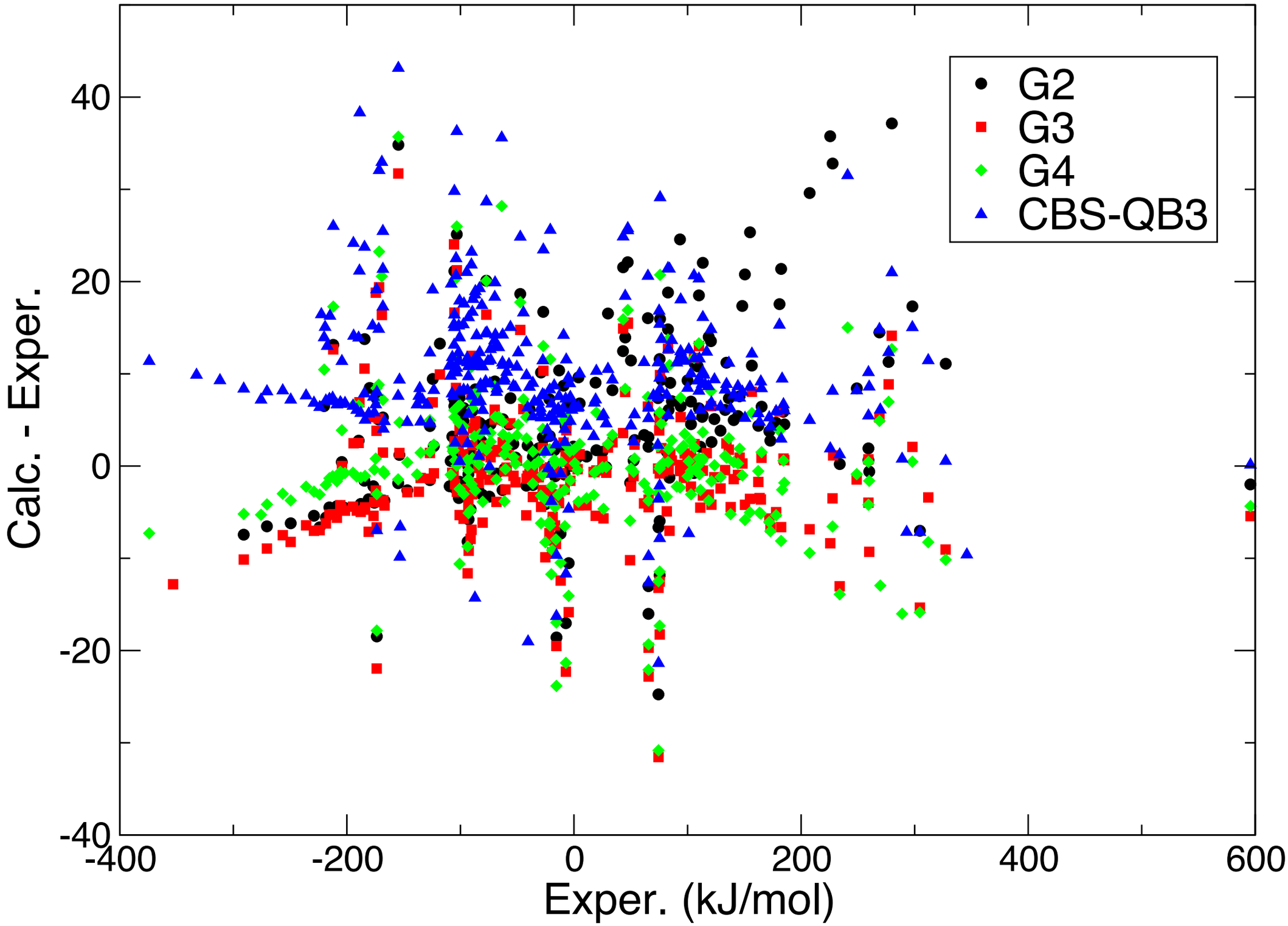
- > 100,000 experimental data points gathered in a SQL database
- Allows rational FF derivation ... at last

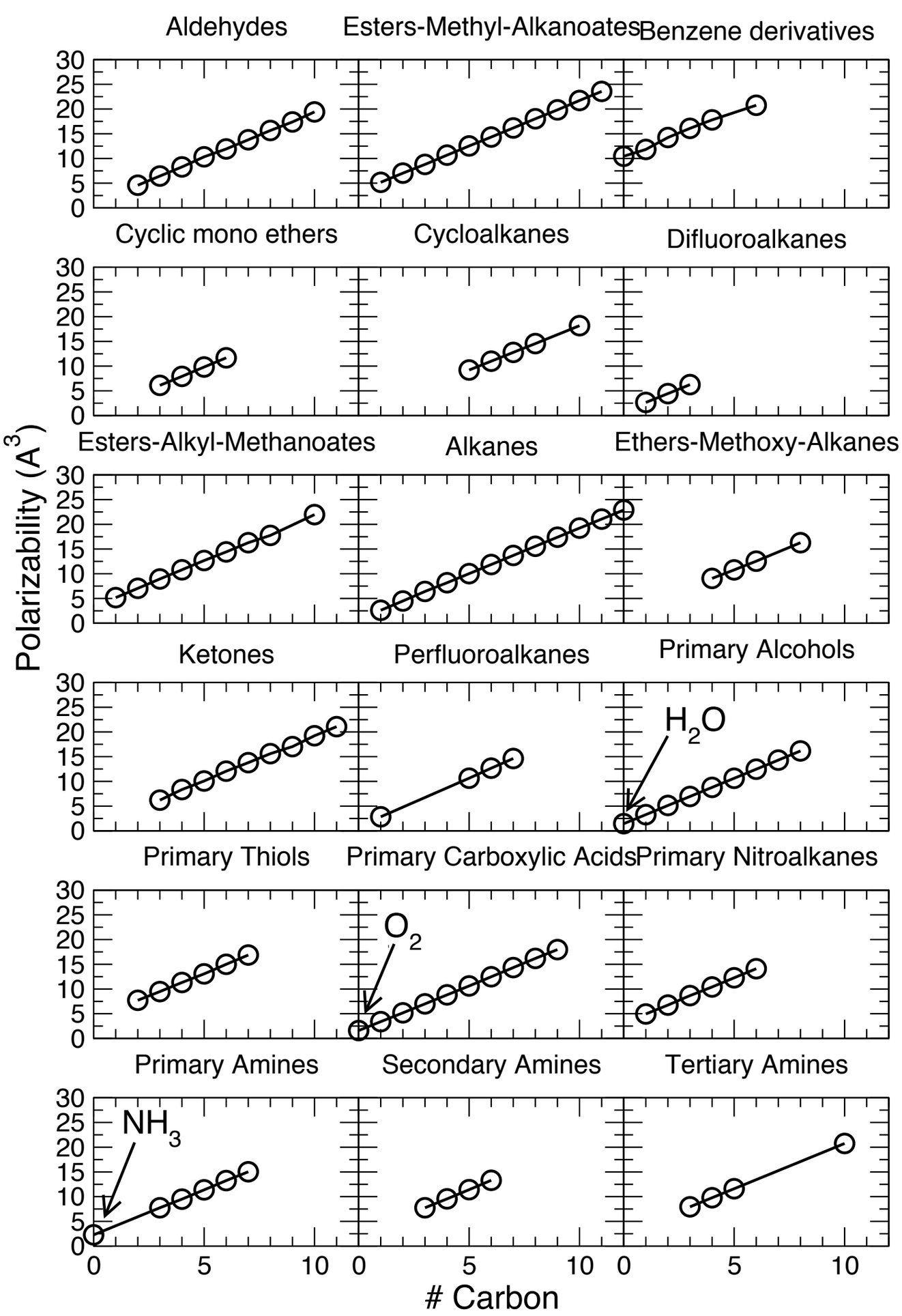
http://virtualchemistry.org/

Can Quantum Chemistry Help?

- Compute properties for which there is no experimental data
- Electric properties (multipole moments) polarizabilities are reproduced well
- Energies ?

Enthalpy of Formation





Fear not

- Nature is linear...

Summary Force Field

- Intermolecular energies within ~ 5-7 kJ/mol in force fields - for supported atom types
- A lot of work going on in force field tuning and development
- Many properties can be computed based on long classical simulations

References

- Carl Caleman, Paul van Maaren, Minyan Hong, Jochen Hub, Luciano Costa, David van der Spoel, J. Chem. Theor. Comput. 8 (2012) 61-74

- David van der Spoel, Paul van Maaren, Carl Caleman, Bioinformatics (2012) doi: 10.1093/bioinformatics/bts020

- Oliver Lange, David van der Spoel, Bert L. de Groot - Biophysical Journal 99 (2010) 647-655

The Two Phase Thermodynamics Method

David van der Spoel, Uppsala University

What's the problem?

- For ideal gases theories exist from which one can derive thermodynamics properties
- For solids another kind of theory exists
- For liquids there is no such thing

I st Ansatz

- Treat Liquid just like a Solid - system of harmonic oscillators

II. CLASSICAL THERMODYNAMICS FROM MOLECULAR DYNAMICS

The standard equations[1] linking the canonical partition function Q and the various thermodynamic variables are

$$E = k_B T^2 \frac{\partial \ln Q}{\partial T} \quad , \tag{2.1}$$

$$C_v = \frac{\partial E}{\partial T} \quad , \tag{2.2}$$

$$A = - k_B T \ln Q \quad , \tag{2.3}$$

$$S = k_B T \frac{\partial \ln Q}{\partial T} + k_B \ln Q \quad , \tag{2.4}$$

in which E is the energy, C_v the constant volume heat capacity, A the Helmholtz free energy, S the entropy, k_B Boltzmann's constant, and T the temperature.

Berens et al. JCP 79 (1983) pp2375

In the harmonic limit, a normal mode analysis allows us to view the system as a set of $3N$ harmonic oscillators. The total canonical partition function Q for the system can then be expressed in terms of the partition functions q_j for the individual modes as

$$Q = \prod_{j=1}^{3N} q_j \tag{3.18}$$

or

$$\ln Q = \sum_{j=1}^{3N} \ln q_j \ . \tag{3.19}$$

If the normal frequencies are continuously distributed we may take the integral

$$\ln Q = \int_0^\infty d\nu\, S(\nu) \ln q(\nu) \ , \tag{3.20}$$

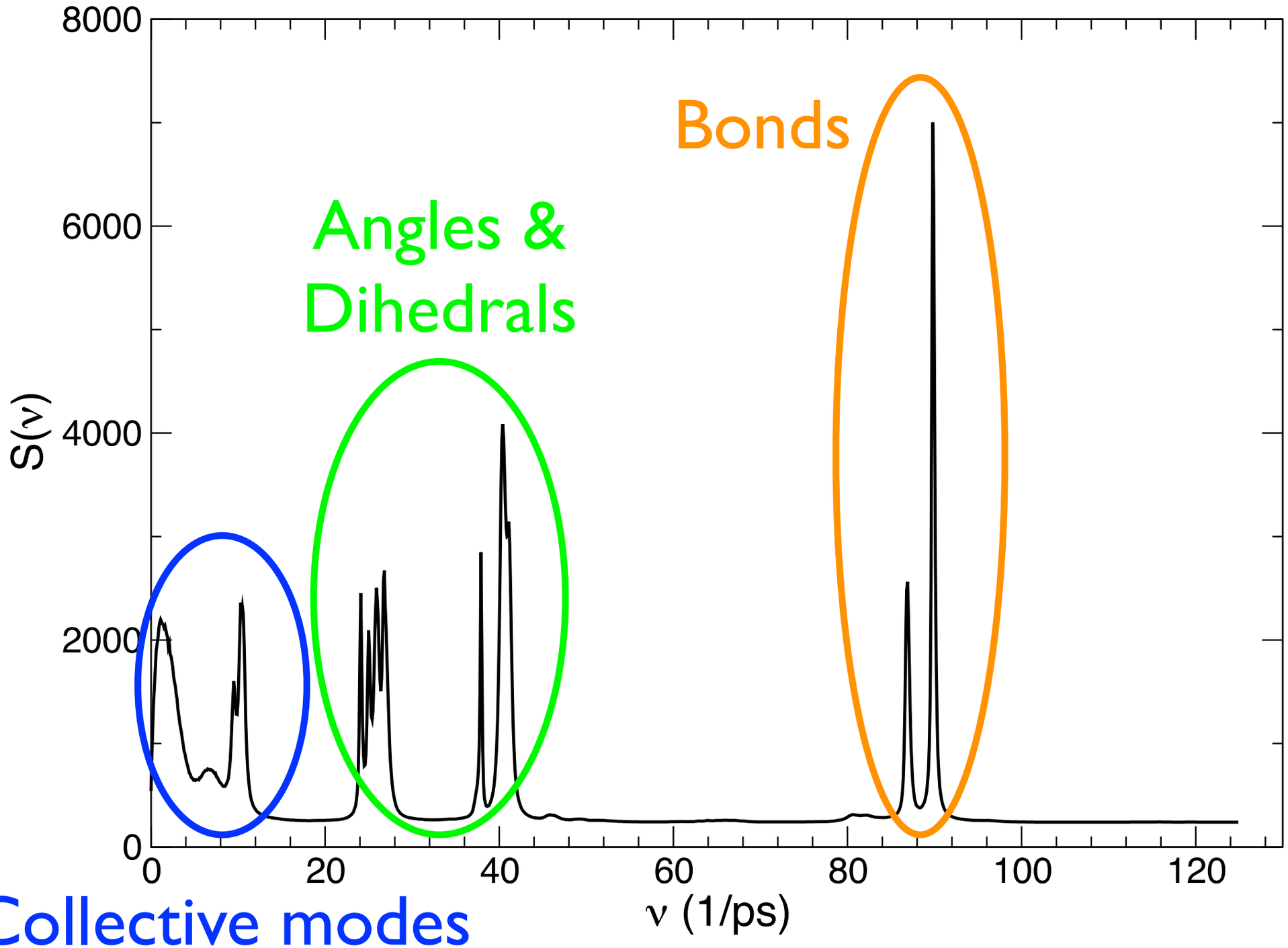
where $S(\nu)$ is the density of normal modes with frequency ν.

Berens et al. JCP 79 (1983) pp2375

The trick

- S(v) can be derived from the velocity auto-correlation function
- Assume the frequencies in the classical simulation are correct (and the amplitudes)
- Reweigh the S(v) to get a corresponding Quantum S(v)

Example - C_2H_6SO



Now we will try to comprehend the solid component of the density of states, $DoS_{\mathrm{solid}}(\nu)$. Here, each mode is considered to be harmonic and we use the partition function for a quantum harmonic oscillator as given by McQuarrie [8]:

$$q^{q}_{\mathrm{HO}}(\nu) = \frac{e^{-\beta h\nu/2}}{1 - e^{-\beta h\nu}} \tag{S9}$$

where h is Planck's constant, $\beta = 1/k_{\mathrm{B}}T$. Since the canonical partion function Q of a system is given by the product of the components (Equations 3.18-3.20, reference [6]):

$$Q = \prod_{i=1}^{N} q_i \tag{S10}$$

and therefore

$$\ln Q = \sum_{i=1}^{N} \ln q_i \tag{S11}$$

Caleman et al. JCTC 8 (2012) 61-74

Final Result I

$$E^{Q} = V_0 + k_B T \int_0^{\infty} d\nu\, S(\nu)\, W_E^{Q}(\nu)\ ; \quad W_E^{Q}(\nu) = \left(\frac{u}{2} + \frac{u}{e^u - 1} \right), \tag{3.40}$$

$$C_v^{Q} = k_B \int_0^{\infty} d\nu\, S(\nu)\, W_{C_v}^{Q}(\nu)\ ; \quad W_{C_v}^{Q}(\nu) = \left(\frac{u^2\, e^u}{(1 - e^u)^2} \right)\ , \tag{3.41}$$

$$A^{Q} = V_0 + k_B T \int_0^{\infty} d\nu\, S(\nu)\, W_A^{Q}(\nu)\ ; \quad W_A^{Q}(\nu) = \left(\ln \frac{1 - e^{-u}}{e^{-u/2}} \right)\ , \tag{3.42}$$

$$S^{Q} = k_B \int_0^{\infty} d\nu\, S(\nu)\, W_S^{Q}(\nu)\ ; \quad W_S^{Q}(\nu) = \left(\frac{u}{e^u - 1} - \ln(1 - e^{-u}) \right). \tag{3.43}$$

Berens et al. JCP 79 (1983) pp2375

2nd Ansatz

- Treat a liquid as a combination of solid and ideal gas - 2 phase thermodynamics
- Gas can be treated as a hard-sphere gas for which analytical thermodynamical results exist

Lin et al. JCP 2003, JPCB 2012, Pascal PCCP 2011

Final Result 2

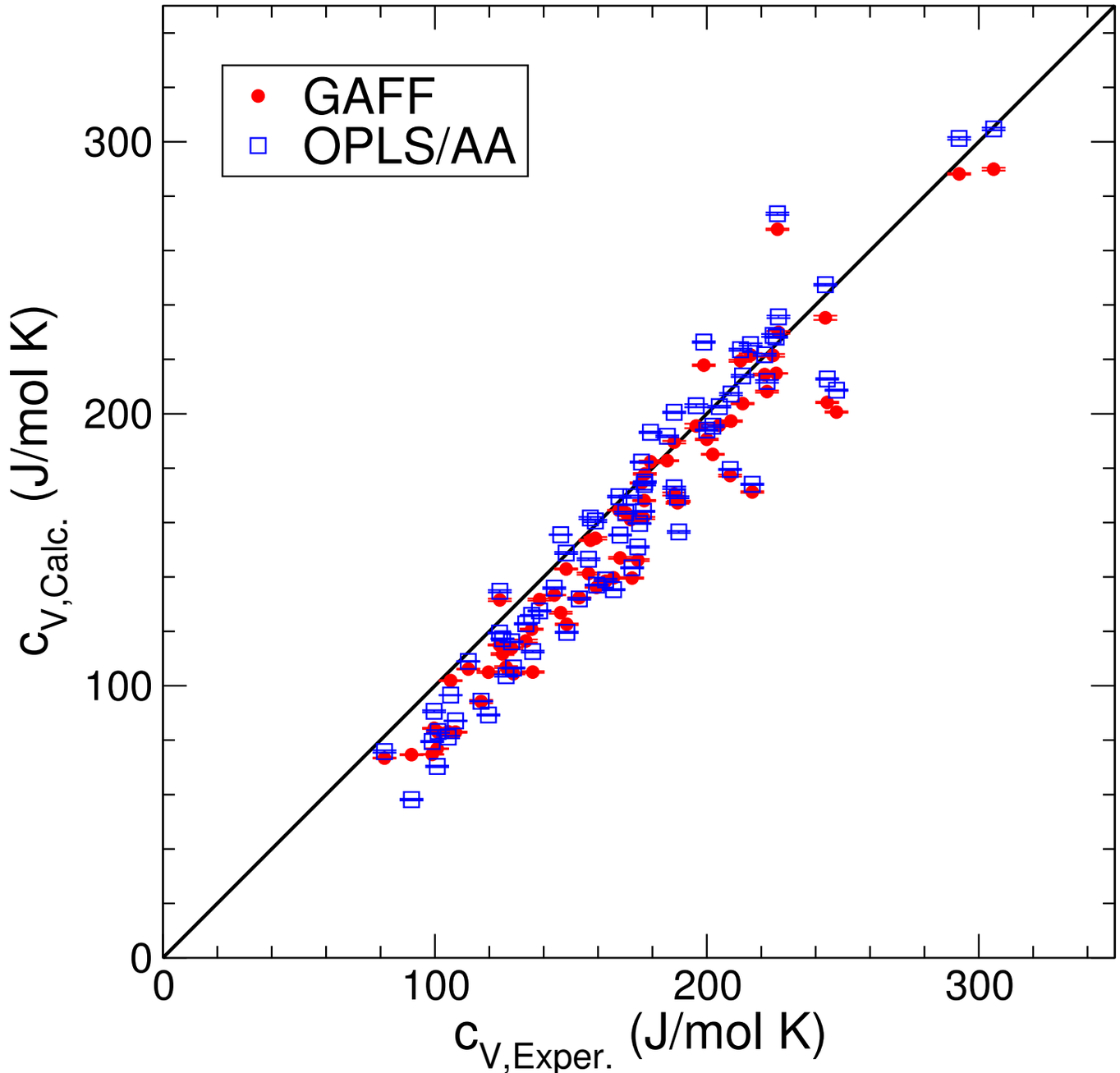
- Determine “fluidicity” - how fluid is the simulation between 0 and 1
- Modified weighting function - same as Berens for the solid part + another for the gas part

Lin et al. JCP 2003, JPCB 2012, Pascal PCCP 2011

How does it work?

- Do MD simulation with flexible bonds, 20-100 ps (time step 0.2 fs)
- Save velocities every 4-5 fs
- Compute mass-weighted velocity ACF and compute properties S, E, A, Cv by weighting the S(v) and integrating!

Heat Capacity Cv

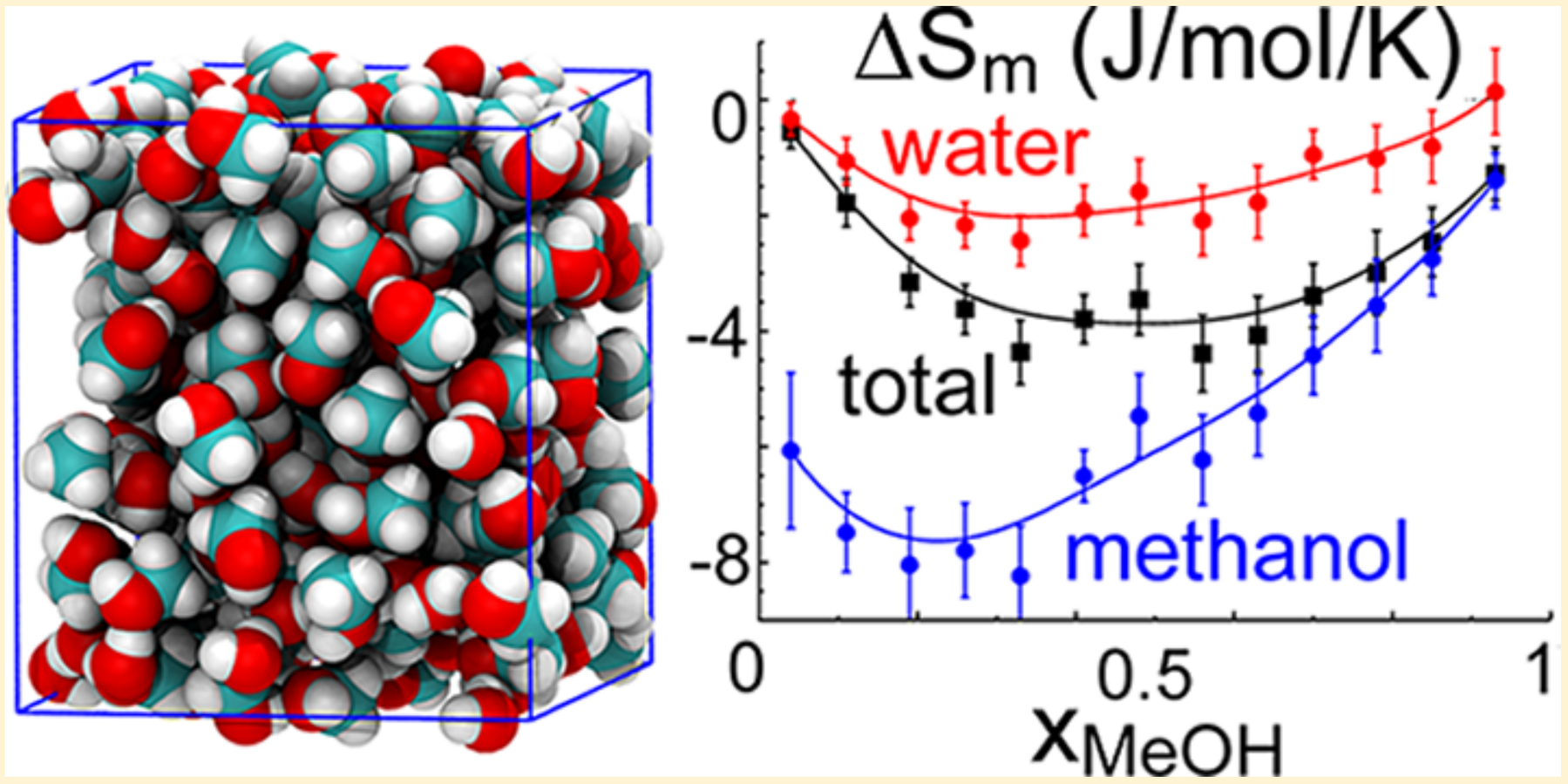


Caleman et al. JCTC 8 (2012) 61-74

Hydrophobic Segregation, Phase Transitions and the Anomalous Thermodynamics of Water/Methanol Mixtures

Tod A. Pascal and William A Goddard, III

J. Phys. Chem. B http://dx.doi.org/10.1021/jp309693d



Summary 2PT

- Promising new method
- Lowest frequencies contribute most - may also work with constraints
- Very recently also for mixtures
- More development and testing needed

References

- Carl Caleman, Paul J. van Maaren, Minyan Hong, Jochen S. Hub, Luciano T. Costa, David van der Spoel: *Force Field Benchmark of Organic Liquids: Density, Enthalpy of Vaporization, Heat Capacities, Surface Tension, Compressibility, Expansion Coefficient and Dielectric Constant* J. Chem. Theor. Comput. **8** pp. 61-74 (**2012**)

- Lin, S. T.; Blanco, M.; Goddard, III, W. A. J. Chem. Phys. 2003, 119, 11792–11805.

- Lin, S.-T.; Maiti, P. K.; Goddard, III, W. A. J. Phys. Chem. B 2010, 114, 8191–8198.

- Pascal, T. A.; Lin, S.-T.; Goddard, III, W. A. Phys. Chem. Chem. Phys. 2011, 13, 169–181.

- Huang, S.-N.; Pascal, T. A.; Goddard, III, W. A.; Maiti, P. K.; Lin, S.-T. J. Chem. Theory Comput. 2011, 7, 1893–1901.

- Berens, P. H.; Mackay, D. H. J.; White, G. M.; Wilson, K. R. J. Chem. Phys. 1983, 79, 2375–2389