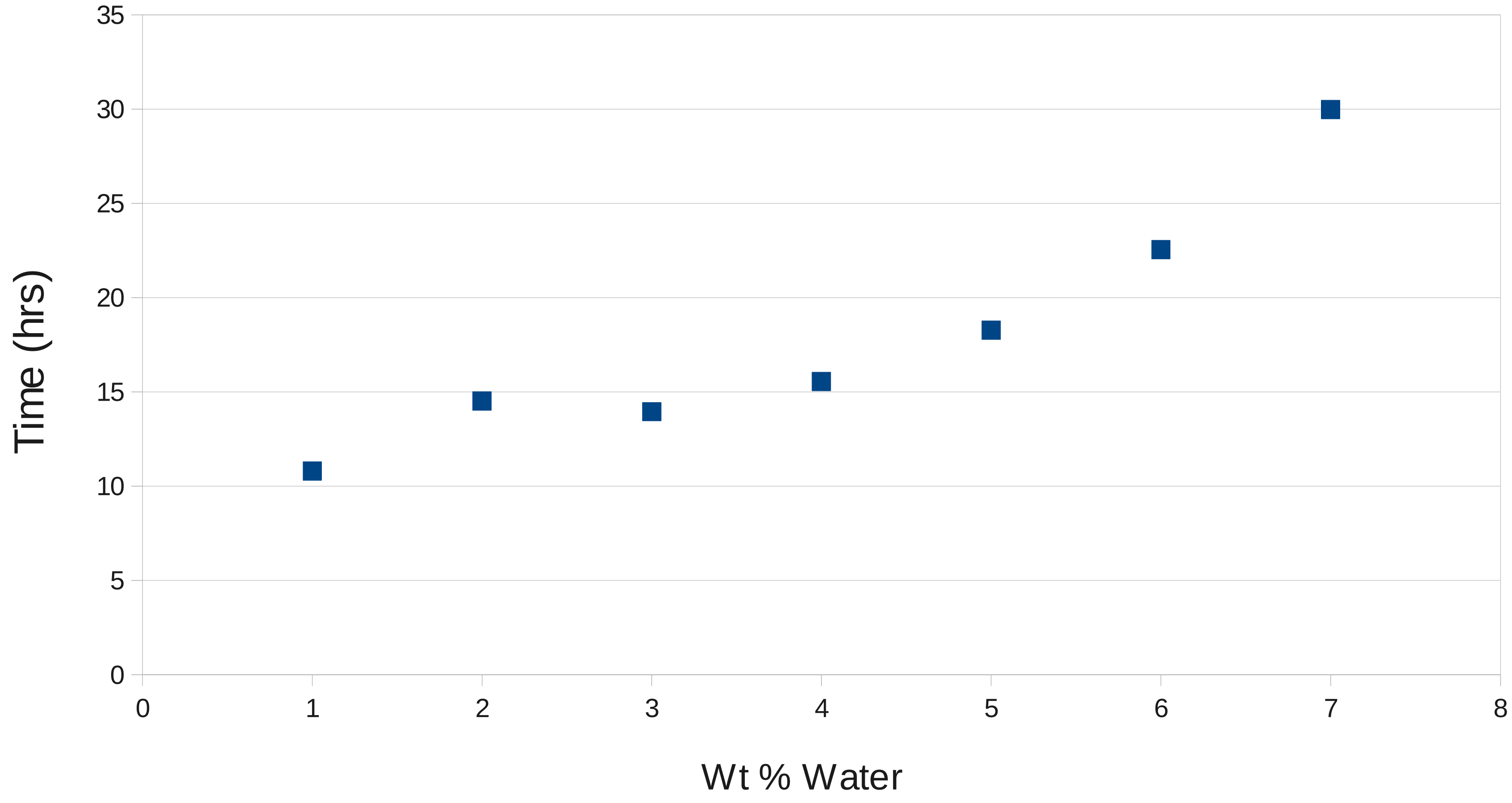
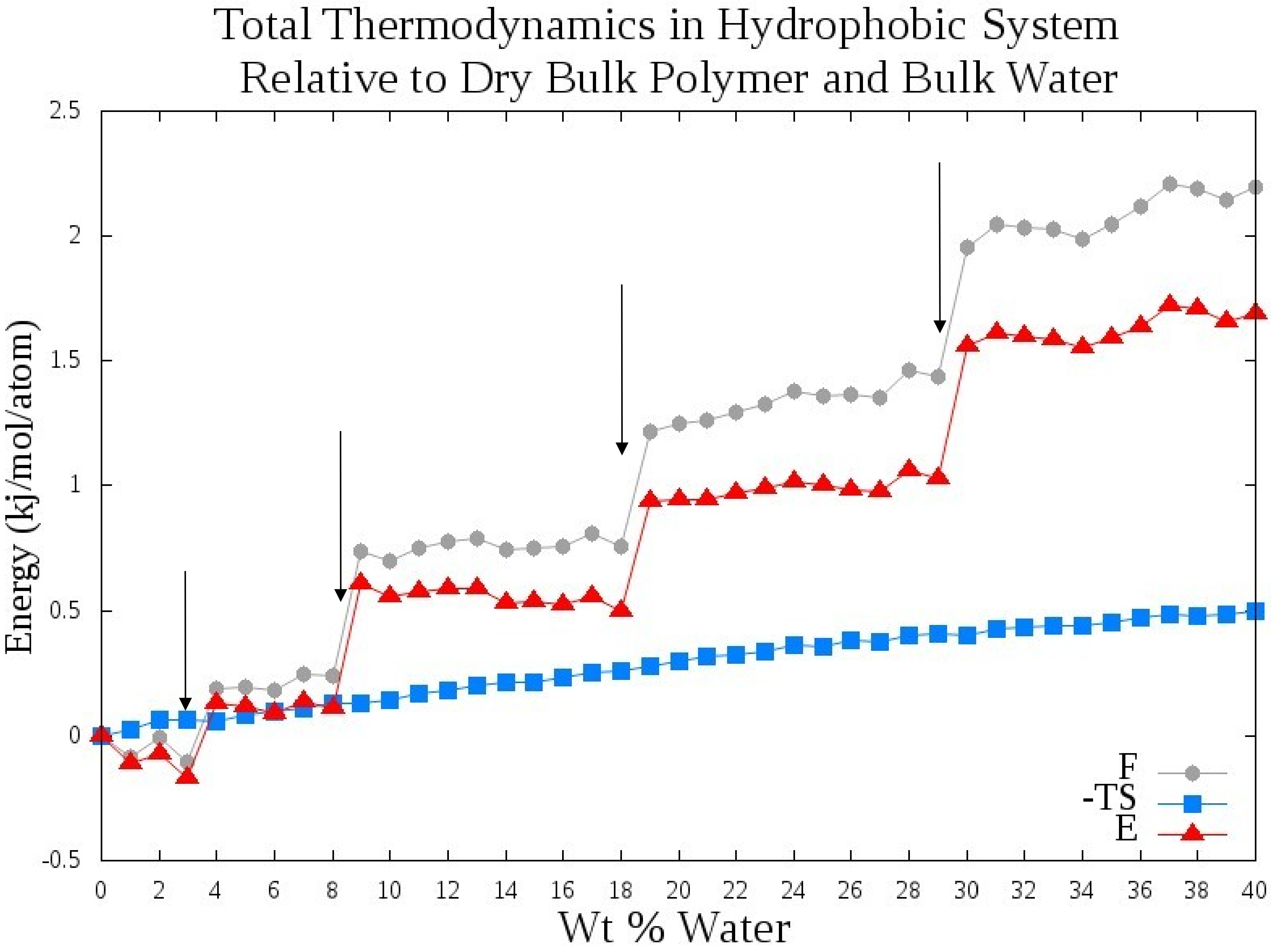
Estimations of Wallclock Simulation Times for Some Representative Hydrophobic Structures

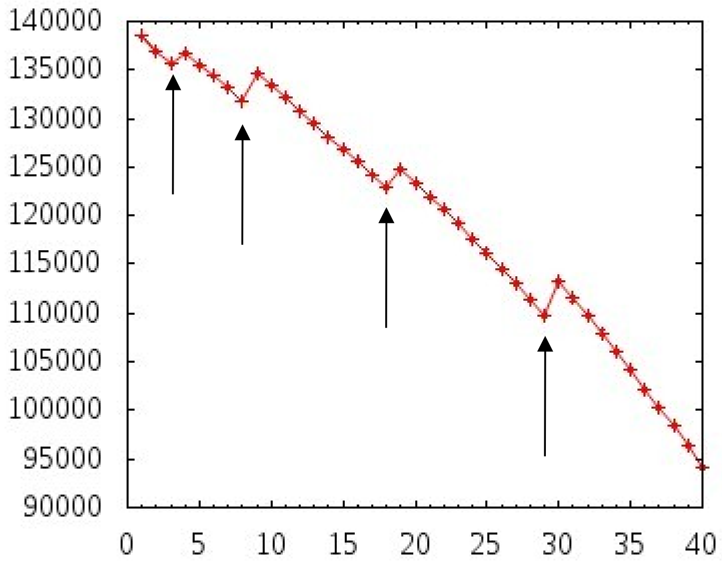


Atomistic calculations are quite expensive. Each data point is an estimate of the amount of wallclock time (time in the real world) to complete the dynamics calculations on the corresponding water content. Notice that for the most part each percent requires about a day of simulation time

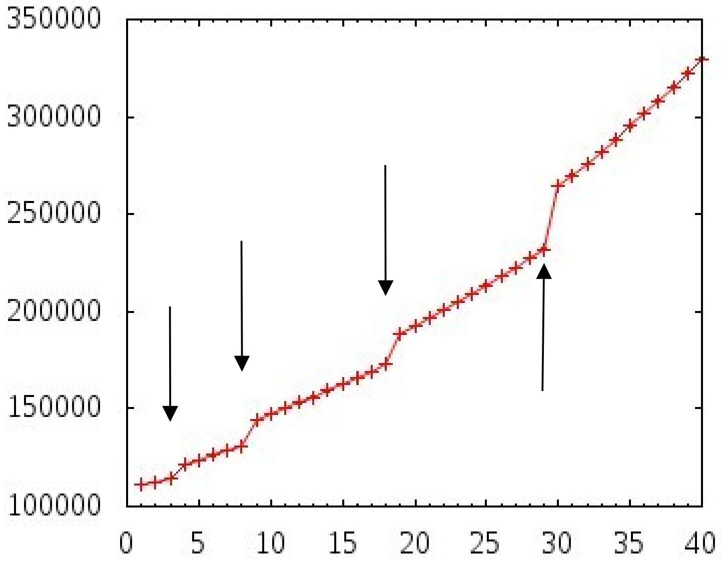


Jumps in energy: 3-4%, 8-9%, 18-19%, 29-30%

Hydrophobic system: Energies (kcal/mol) vs wt % water

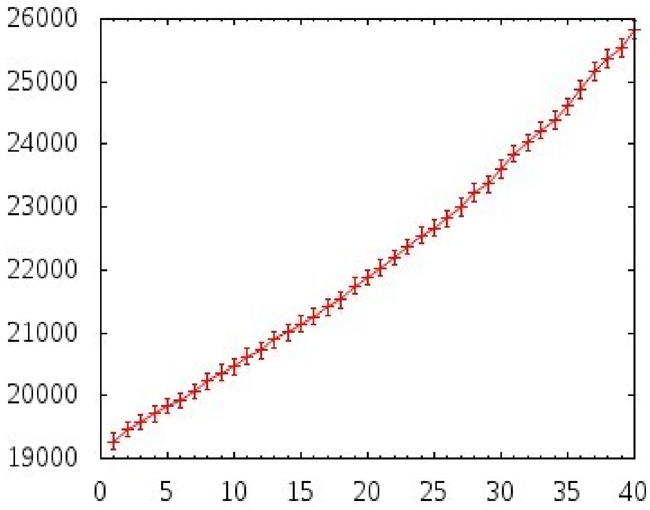


Total MD energy

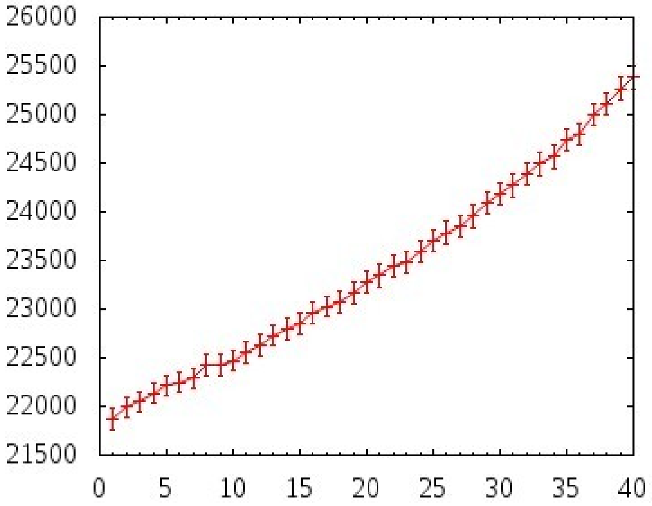


Coulomb energy

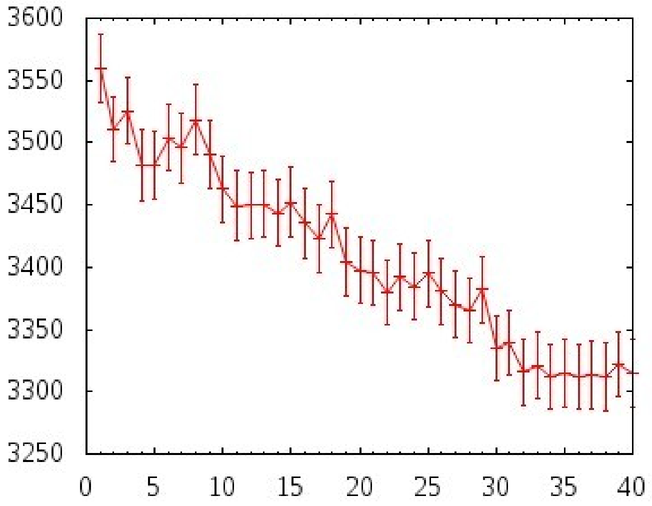
Jumps in Coulomb energy correspond to jumps in total energy



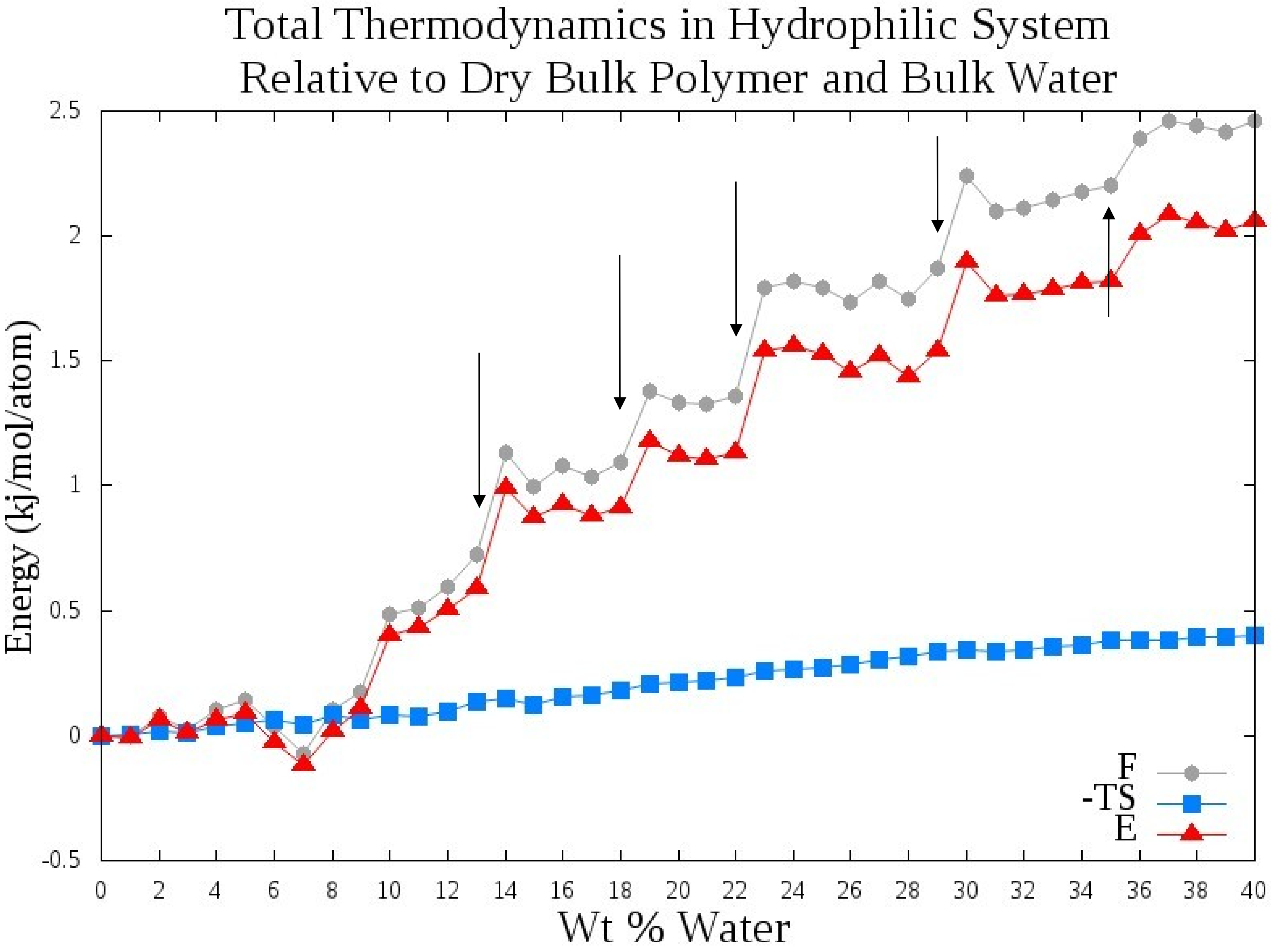
Bond energy



Angle energy

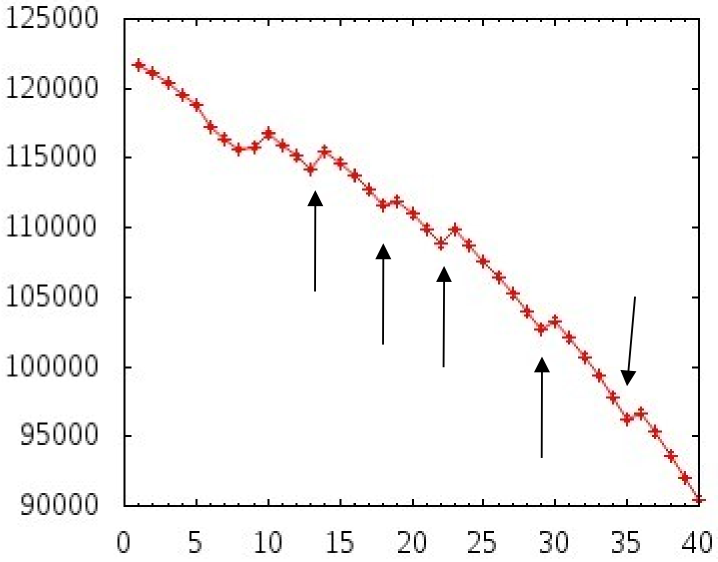


Dihedral energy

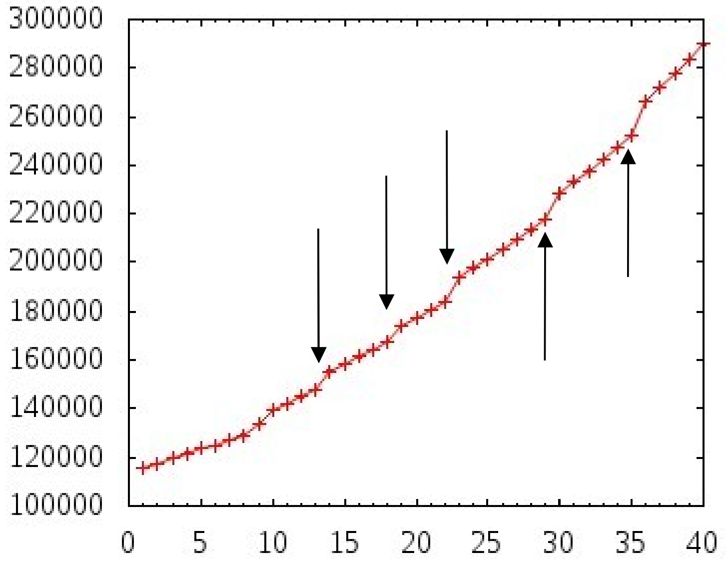


Jumps in energy: 13-14%, 18-19%, 22-23%, 29-30%, 35-36%

Hydrophilic system: MD Energies (kcal/mol) vs wt % water

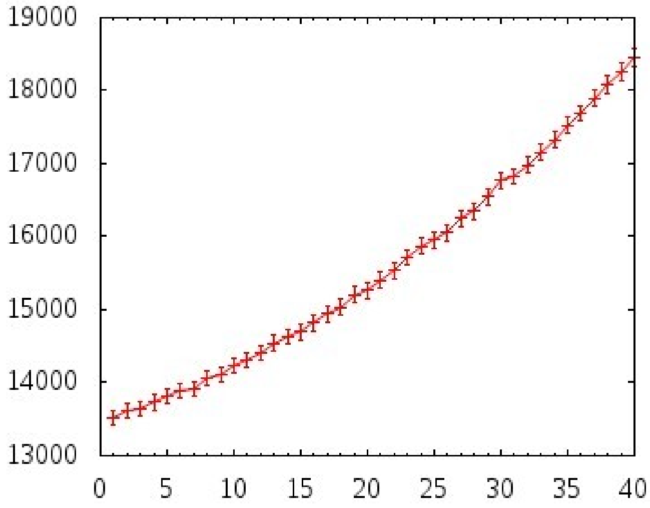


Total MD energy

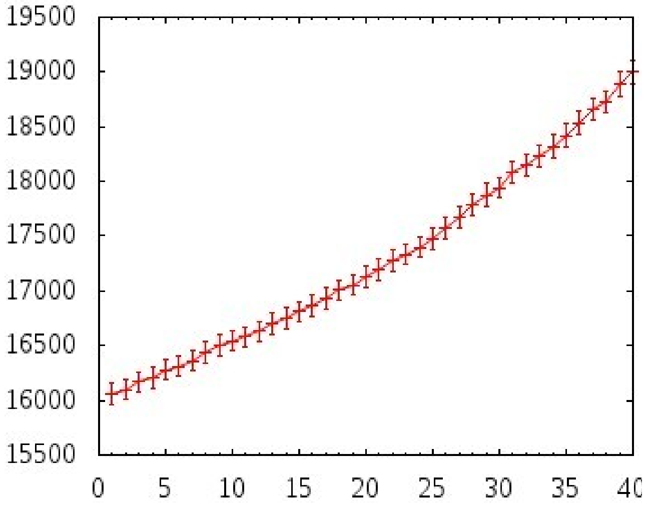


Coulomb energy

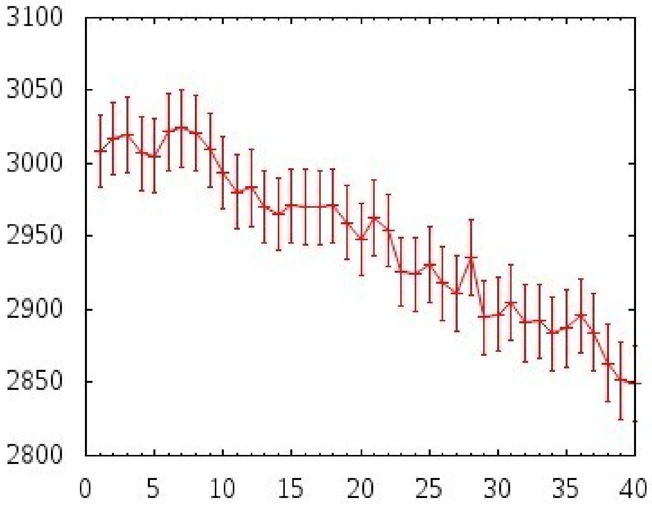
Jumps again reflected in Coulomb energy



Bond energy



Angle energy



Dihedral energy

Changes in Potential Energy

Phobic

% Water	Δ(polymer)	Δ(water)	Δ(total)	% of total from water
9	7700.34	5606.08	13306.42	42.13
19	6187.21	9390.48	15577.69	60.28
30	10348.72	22046.91	32395.63	68.06

Philic

% Water	Δ(polymer)	Δ(water)	Δ(total)	% of total from water
14	-224.16	3690.92	3465.73	106.50
19	-427.46	3768.61	3341.13	112.79
23	-450.20	4020.19	3569.34	112.63
30	-252.84	4853.57	4604.08	105.42

- The previous slide shows the changes in potential energy broken into components. The “% Water” column gives the final water content; the initial is 1% less. So, for the first row in the Phobic section, we have the change in potential energy from the 8% structure to the 9% structure (PE[9%] - PE[8%]).

- We have the potential energy contribution of each individual atom, so we can break up the total potential energy change into the change in potential energy of the polymer atoms (2nd column) and the change in potential energy of the water atoms (3rd column). Comparing each of these individual changes with the total change in potential energy should give us some idea as to whether the changes in potential energy of the polymer or water drive the jumps.

- Notice that for the hydrophilic structure, the polymer potential energy *decreases* at each jump. Thus, the total increase in potential energy is largely the result of changes in the potential energy of the water.

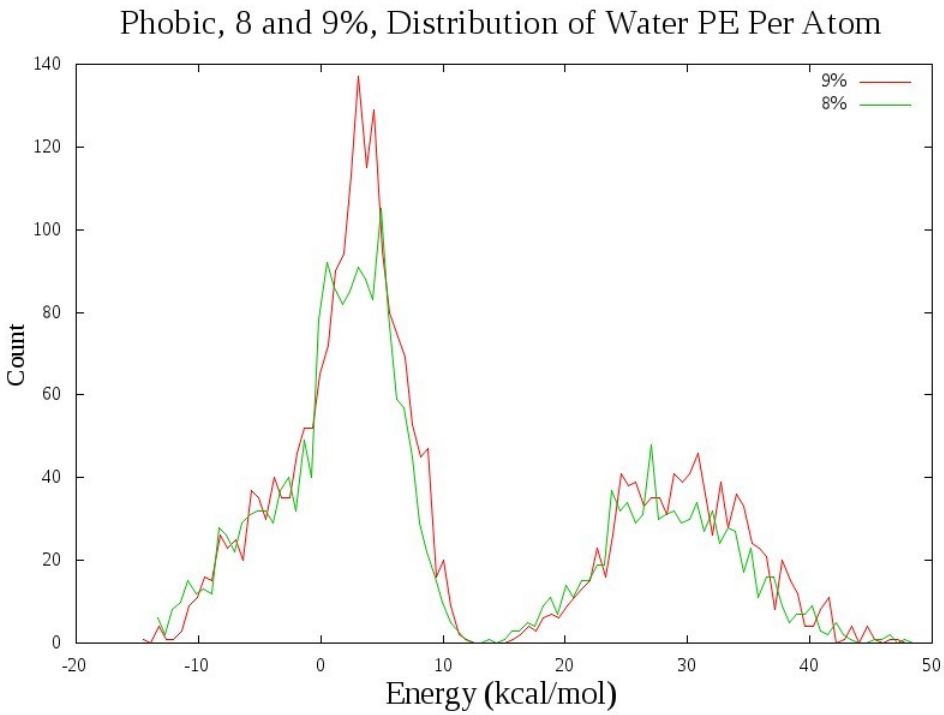
- For the hydrophobic structure, the polymer potential energy *increases* at each jump. The total increase in potential energy is more evenly distributed between the polymer and water parts, although at higher water contents the water potential energy contributes a larger fraction of the total difference.

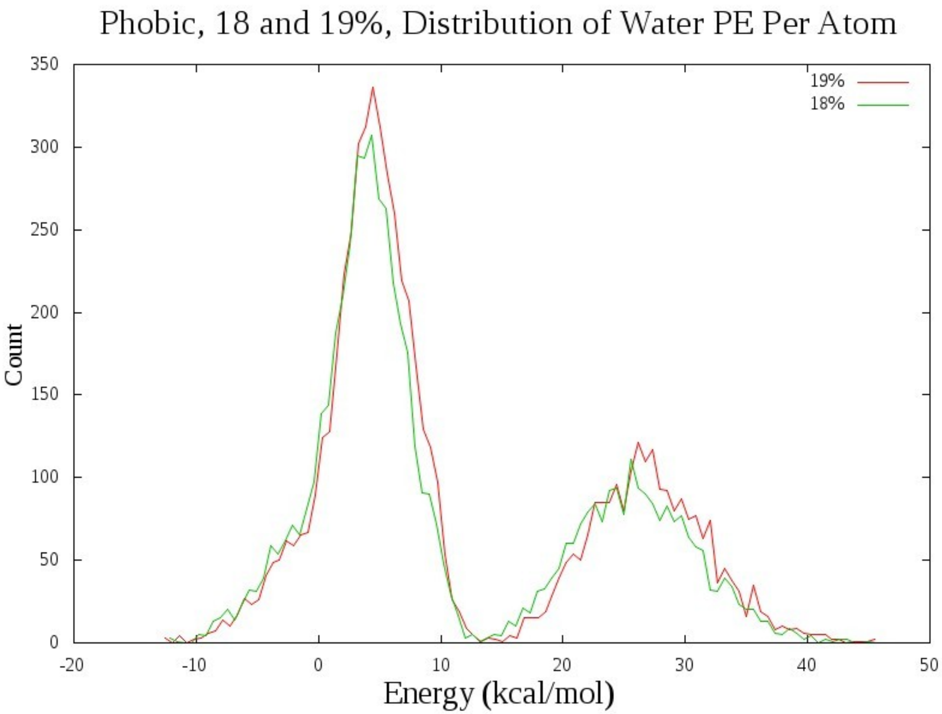
- Since the water seems to be more important in driving the jumps in potential energy, we should look more closely at the water potential energy. First we will consider the hydrophobic case. Could it be that our insertion routine is running out of places to put waters and we're left with some very bad interactions from a few waters?

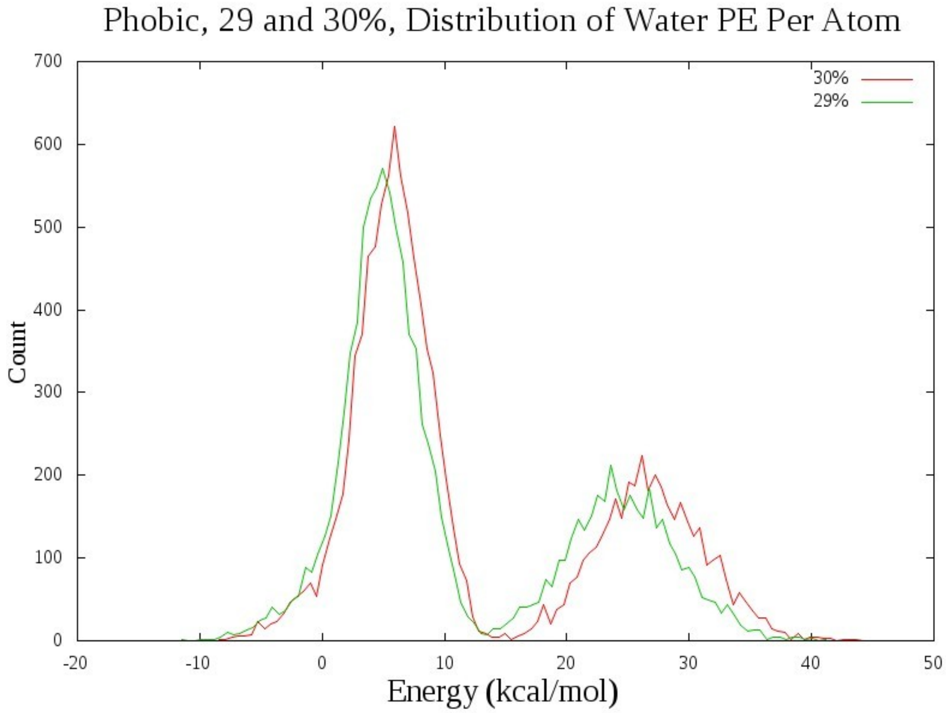
- To find out, we looked at the distribution of the potential energies of each water atom (remember that we calculate the potential energy of each atom, so all we've done here is group together all the atoms that are in water molecules and make a histogram of their potential energies). The x axis is the potential energy in kcal/mol, and the y axis is the number of atoms in water molecules that have that potential energy.

- The following slides shows these distributions before (in green) and after (in red) each jump for the hydrophobic system. Each graph shows the distributions before and after one jump (eg, the first figure shows the distribution of potential energies of water atoms at 8% [green] and 9% [red]).

- Notice that the distributions are quite similar. There seems not to be any large spikes at high potential energy.
- Since we looked at potential energy per atom, we end up with a bimodal distribution (the oxygens all have similar potential energies, and the hydrogens all have similar potential energies as well)


Phobic, 8 and 9%, Distribution of Water PE Per Atom


Phobic, 18 and 19%, Distribution of Water PE Per Atom


Phobic, 29 and 30%, Distribution of Water PE Per Atom

- Could it be that by making a distribution over all the water atoms that we're missing the worst interactions? Could we still have the new waters with very bad potential energies?

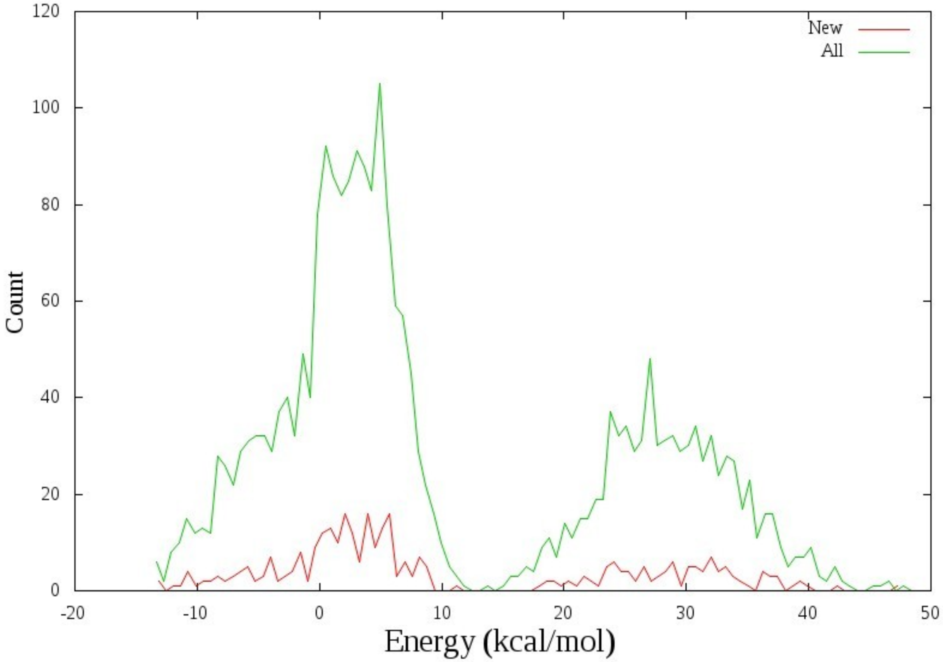
- To check, we looked at the distribution of potential energies of the *new* waters at each water content. That is, instead of grouping all the water atoms together, we group just the water atoms that have been added since the previous water content. Thus, at 9%, we look at the atoms in water molecules that were added to the 8% structure.

- The distribution of new water potential energies is shown in red. For comparison, the total distribution (the distribution of potential energy for *all* waters in the system) is shown in green.

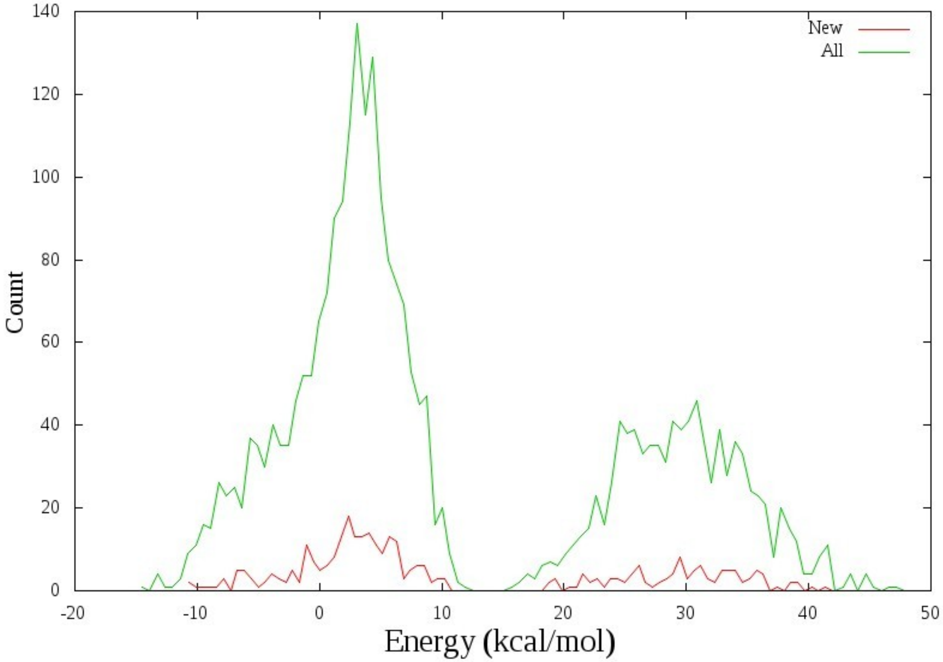
- Each figure now corresponds to a single structure. The water content is noted in the title to each graph.

- If the new waters had particularly bad potential energies, we would expect the distribution of new water potential energies (red) to be shifted to the right (remember the x axis is potential energy) relative to the total distribution (green).

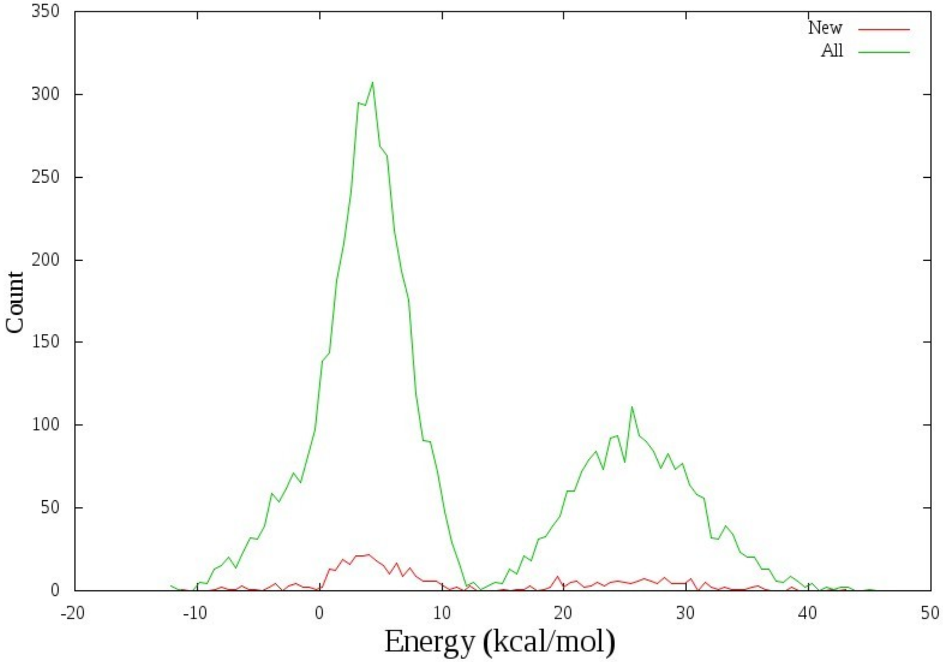
- This does not appear to be the case. The distribution of PE's in the new waters is very similar to that of all the waters.



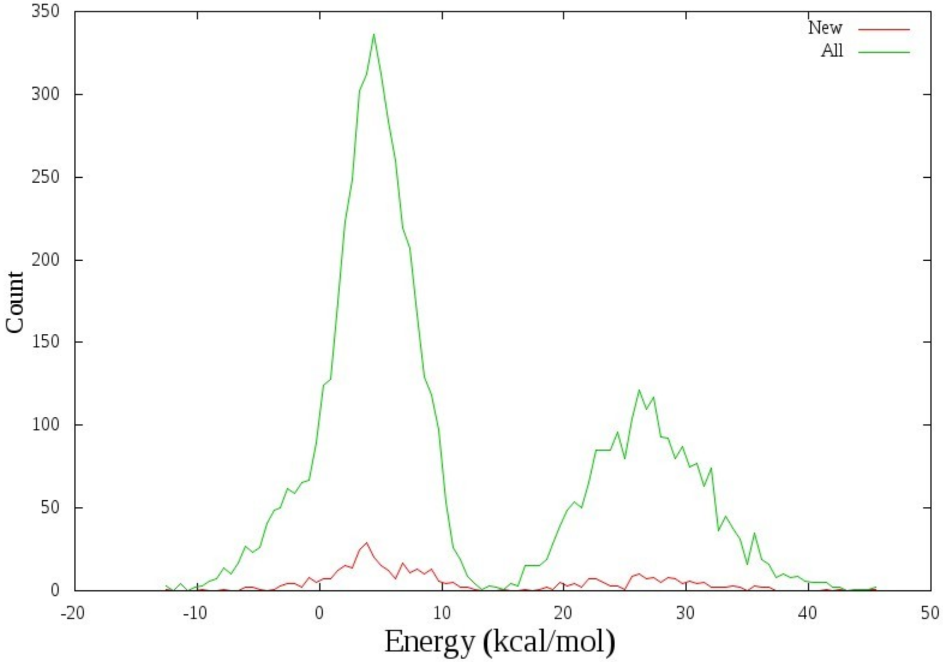
Phobic, 8%, Distribution of Water PE



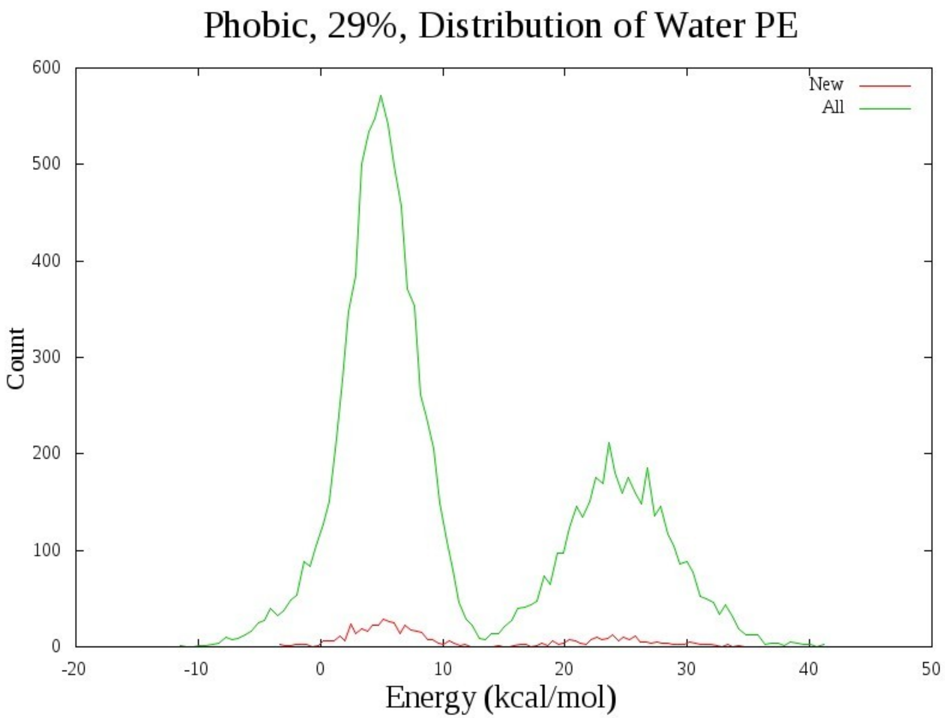
Phobic, 9%, Distribution of Water PE

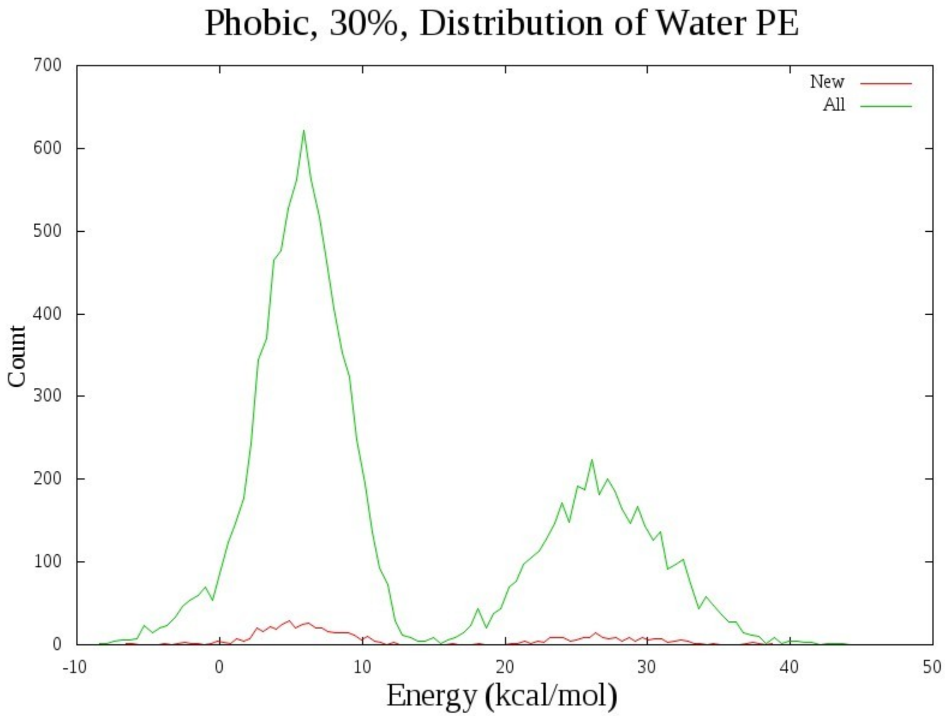


Phobic, 18%, Distribution of Water PE



Phobic, 19%, Distribution of Water PE





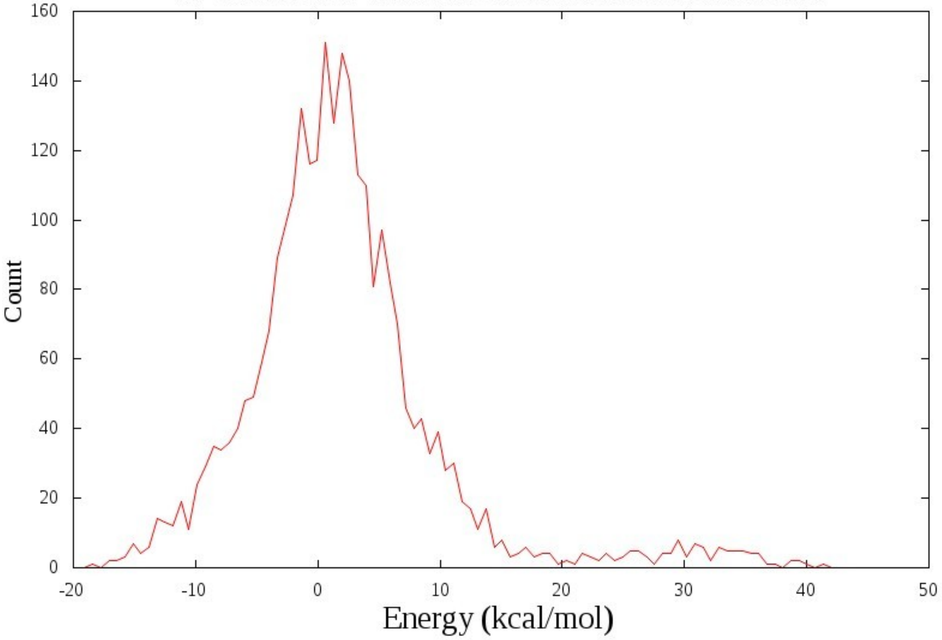
New waters (shown in red) have very similar PE distributions. Notice that the new waters are not the high-lying waters, suggesting that the jumps are not caused by bad insertions

- What about the old waters? Could some of them be suffering large increases in potential energy at the jumps?

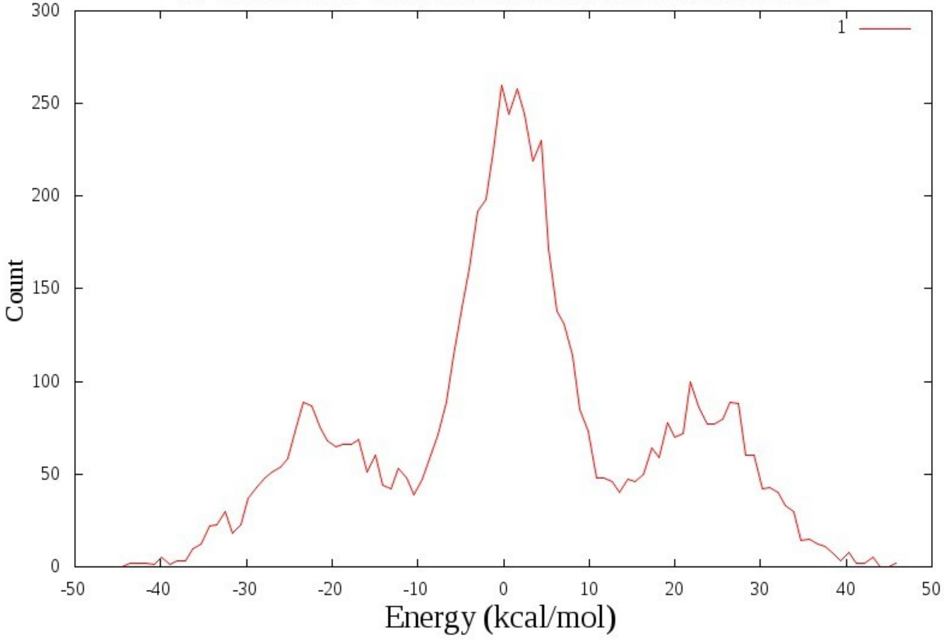
- To check this, we looked at a distribution of *changes* in the potential energy of the water atoms. So, we grouped together all the atoms that were in water molecules and present in a structure on both sides of a jump (for instance 8 and 9%). Then, for each atom we looked at the difference in PE across the jump (so for each atom, PE[9%] - PE[8%] for example).

- We then made a distribution of these differences. So, on the next slide we see *change* in potential energy on the x axis, while on the y axis we have the number of atoms in water molecules present before and after a jump that suffered that change in PE. So the first figure on the next slide shows us a histogram of changes in potential energy of the water atoms that were in both the 8 and 9% structures.

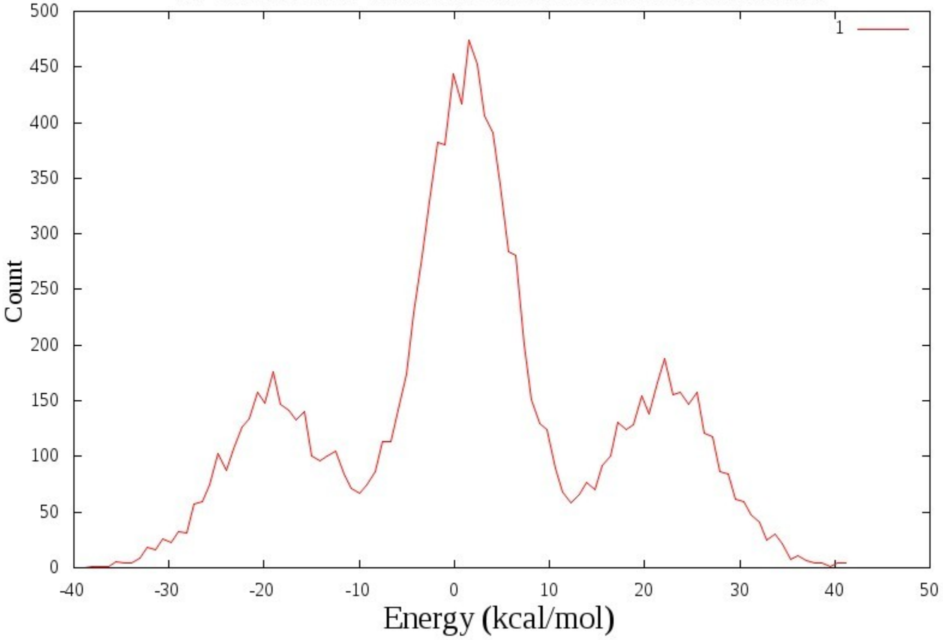
- If some of the old waters were suffering large increases, we would expect to see a spike at high change in PE (to the right on the figures on the next slide). The distributions are centered around zero. Some of the atoms increase in PE, some decrease. The increases outweigh the decreases to give a net increase in water PE (as we saw on slide 1). However, it again seems that no especially bad waters drive the change.



Phobic, 9%, Distribution of Differences in Water PE Relative to Previous Structure



Phobic, 19%, Distribution of Differences in Water PE Relative to Previous Structure



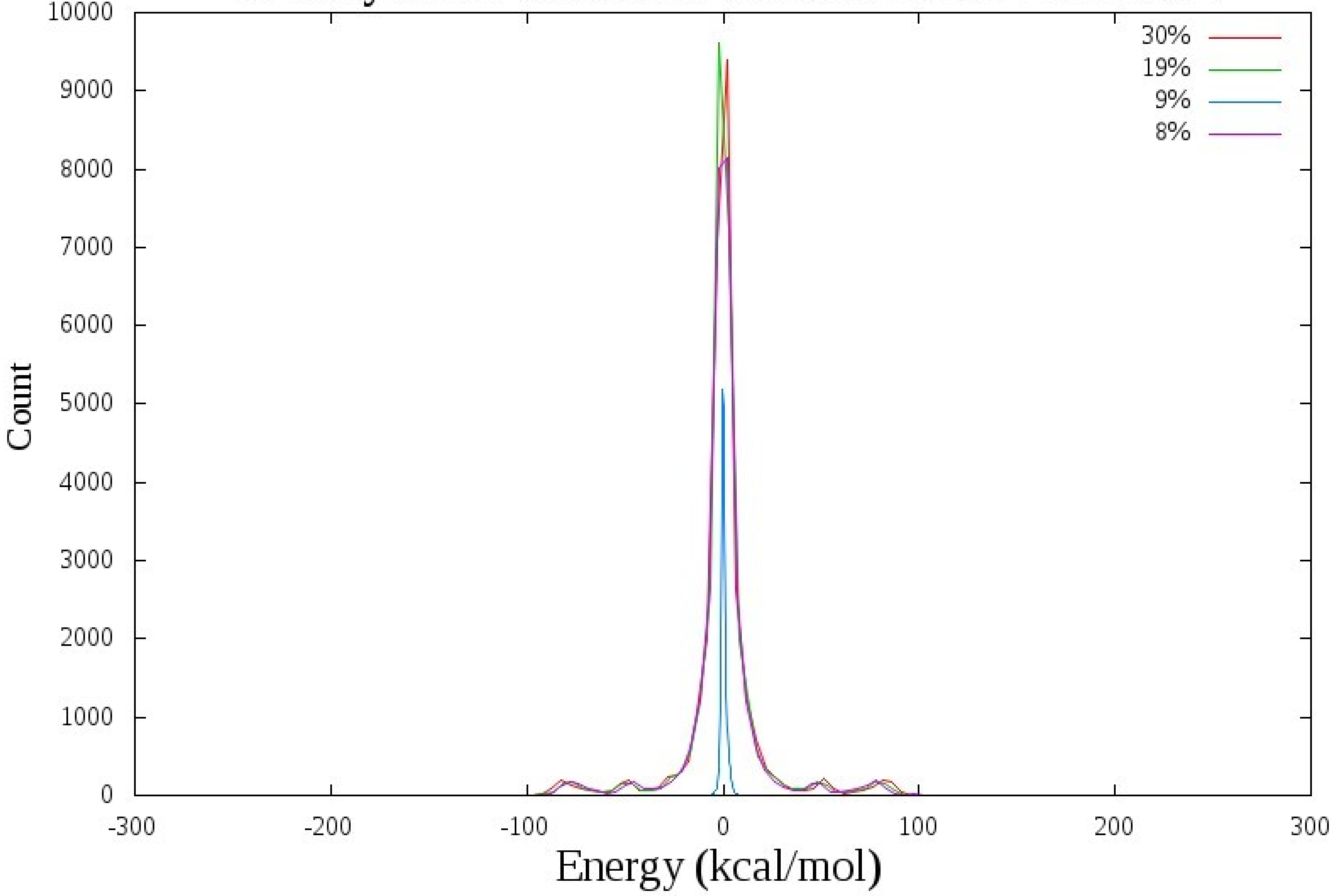
Phobic, 30%, Distribution of Differences in Water PE Relative to Previous Structure

Distribution of differences in PE by atom for waters (this only considers the “old” waters, ie, the ones that are present in both the 18 and 19% structures)

- What about the polymer atoms? Do any of them suffer large changes in PE that cause the jumps?

- Check distribution of changes in polymer atom PE to find out. This is exactly the same idea as the previous slide, except now instead of grouping together the atoms in water molecules, we're grouping together polymer atoms.

- No obvious large spike to account for change in polymer PE. Overall change in polymer PE comes from summing many small changes rather than few large ones.

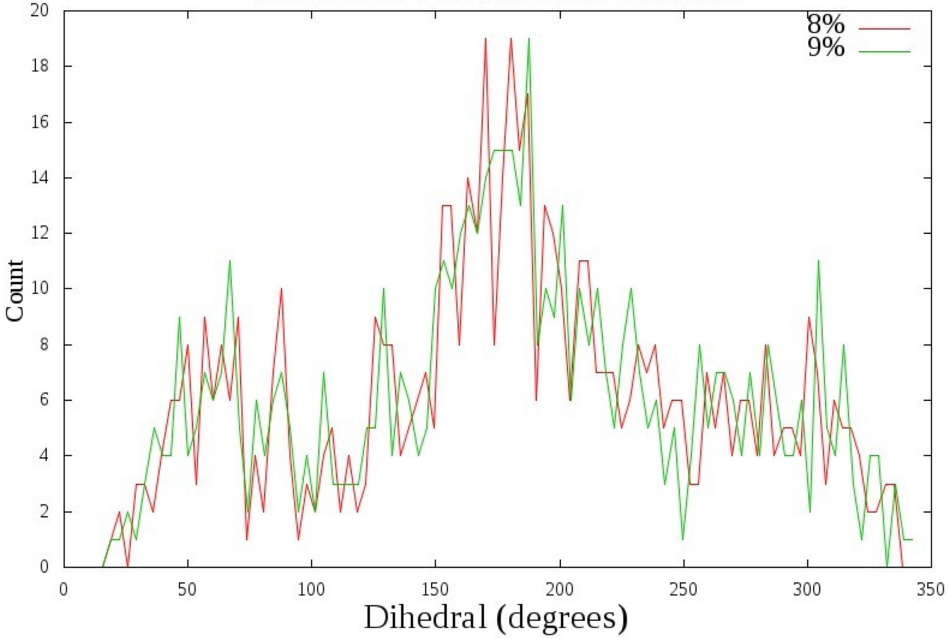


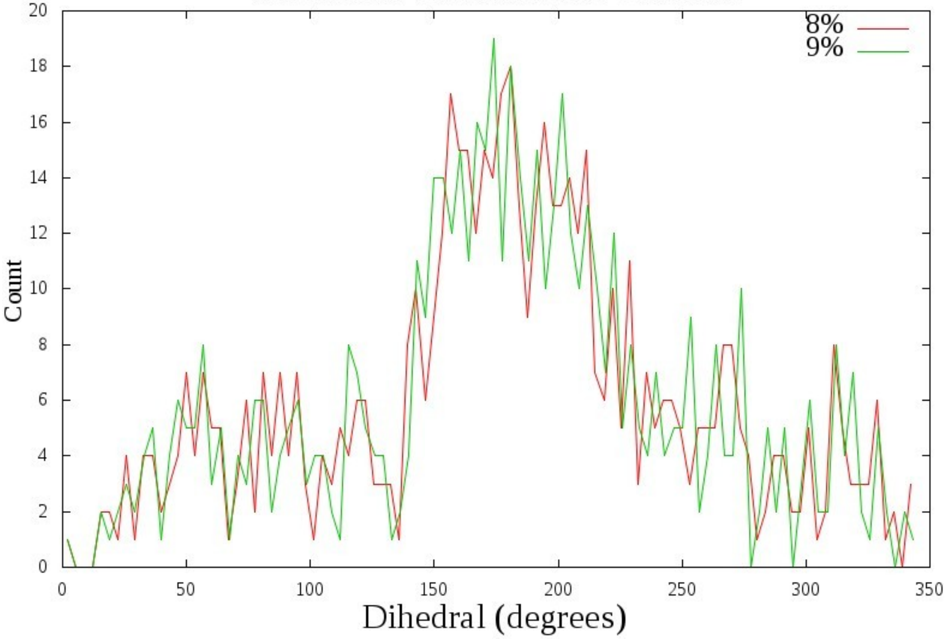
Phobic, Distribution of Differences in Polymer PE Relative to Previous Structure

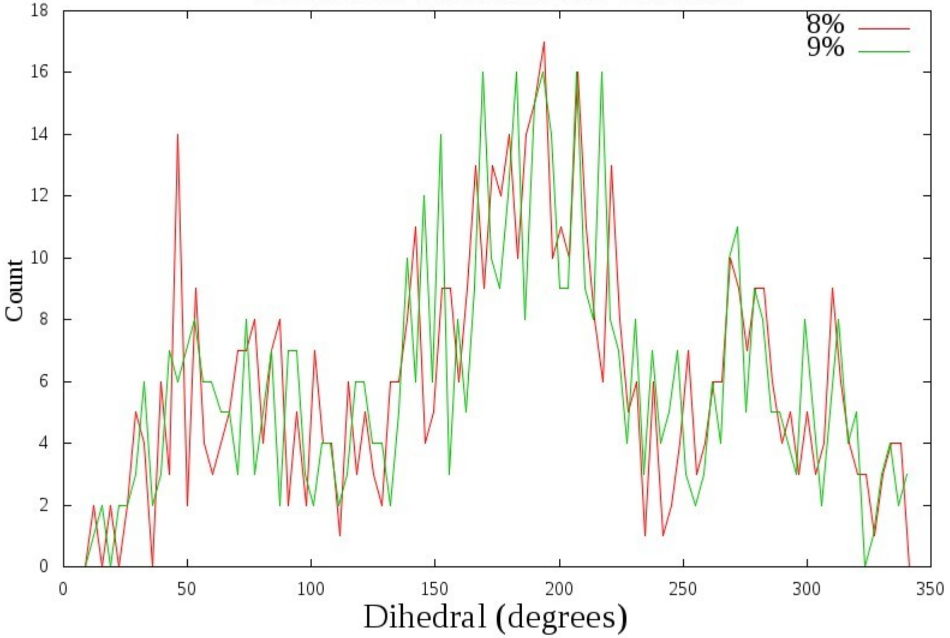
- Nothing has jumped out as the cause of the energy jumps from our analysis of potential energy changes so far. Maybe we can find something out by examining the structure of the polymer. We'll do that by looking at distributions of backbone dihedrals. We start at one end of a polymer chain and look at the dihedral of the first 4 (atoms 1,2,3, and 4, say). Then we shift up one atom and find the dihedral for atoms 2,3,4,5 and so on until the end of the chain. We can then make a histogram of these backbone dihedrals for each chain.

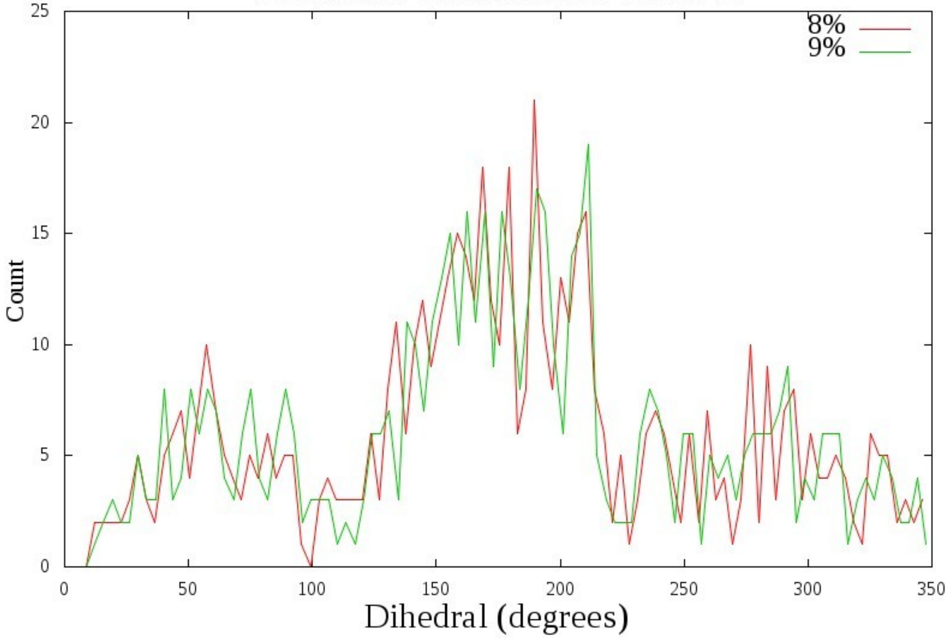
- The next 3 slides show these distributions. Each figure shows the distribution of backbone dihedrals before a jump (red) and after (green) for one of the four chains in our simulation. Each slide has 4 such figures (one for each chain). Each slide considers one of the jumps. (So the first slide looks at 8-9%, the second 18-19, and so on. Recall these were the water contents where we saw jumps in the energy for the hydrophobic system).

- We expect structural changes in the polymer to be reflected in changes in the distribution of backbone dihedrals. If at a jump many polymer torsions change, this could help us get a handle on what's happening.

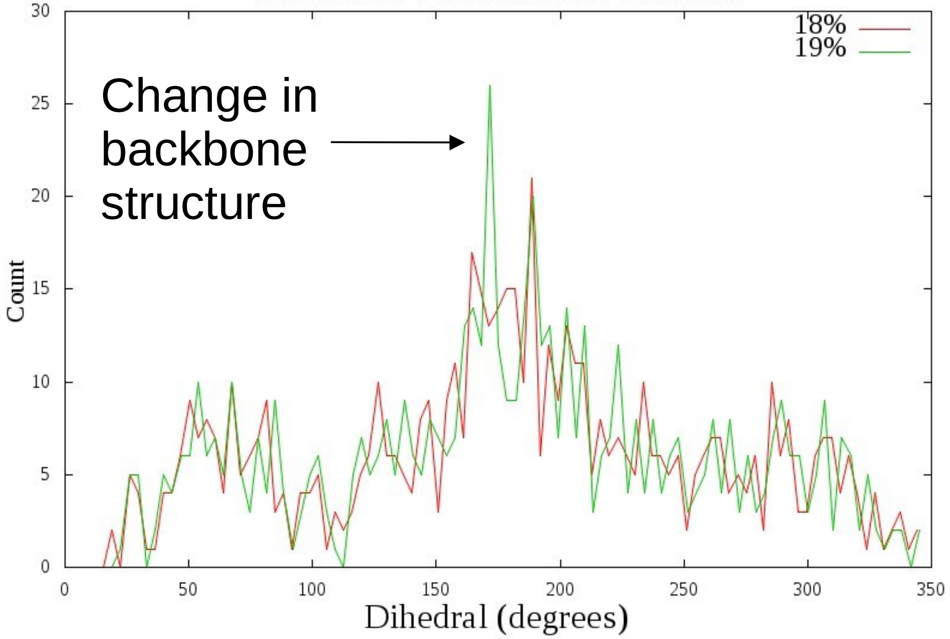

Phobic, 8 and 9%, Distribution of Backbone Dihedrals in Chain A


Phobic, 8 and 9%, Distribution of Backbone Dihedrals in Chain B


Phobic, 8 and 9%, Distribution of Backbone Dihedrals in Chain C

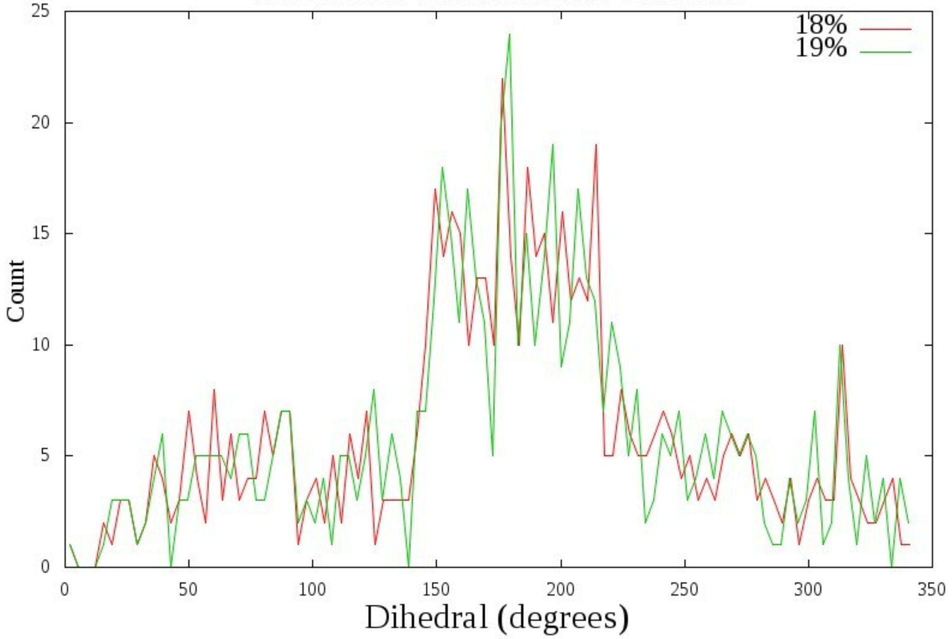

Phobic, 8 and 9%, Distribution of Backbone Dihedrals in Chain D

Phobic, 18 and 19%, Distribution of Backbone Dihedrals in Chain A

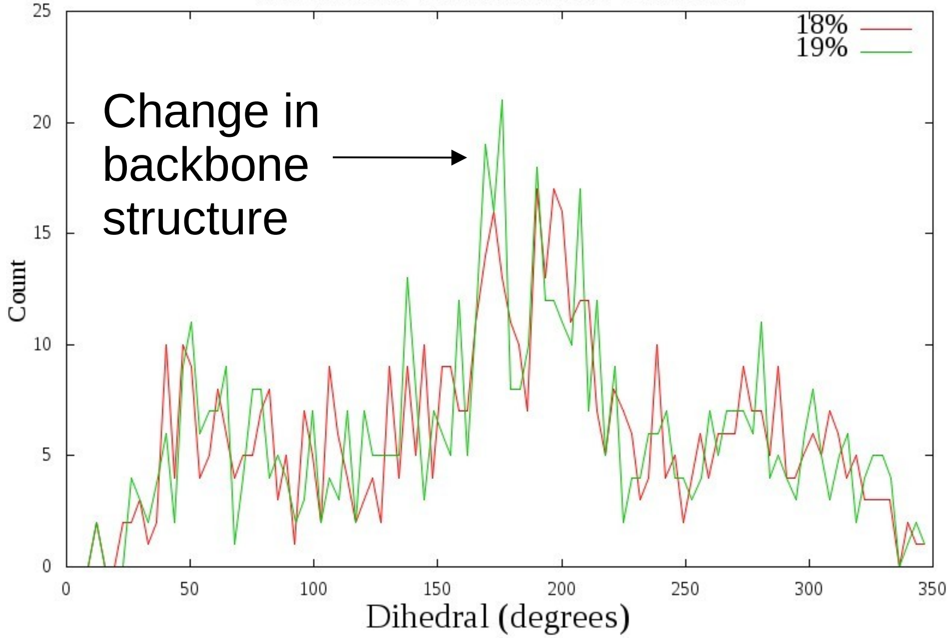


Change in backbone structure

Phobic, 18 and 19%, Distribution of Backbone Dihedrals in Chain B

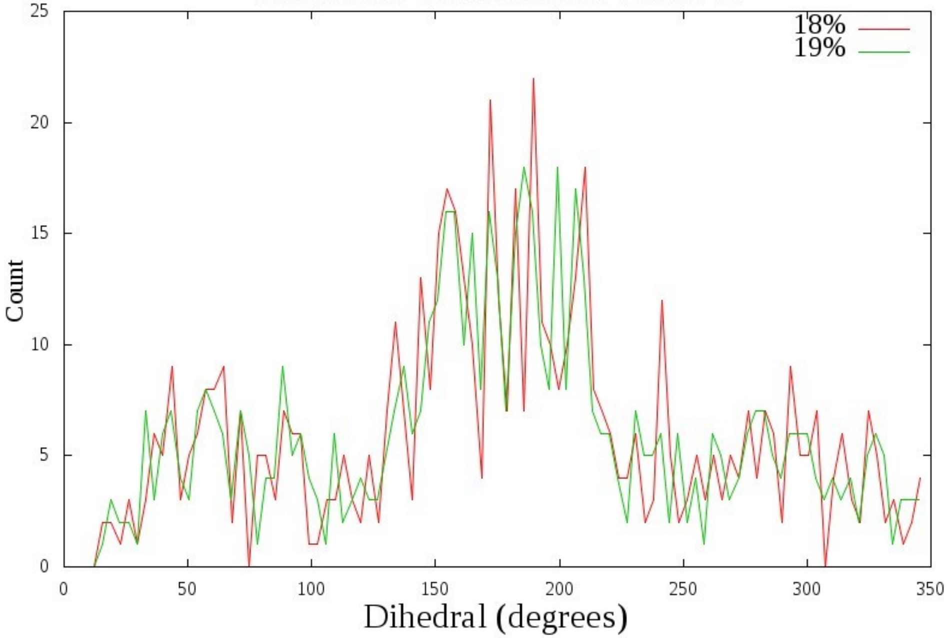


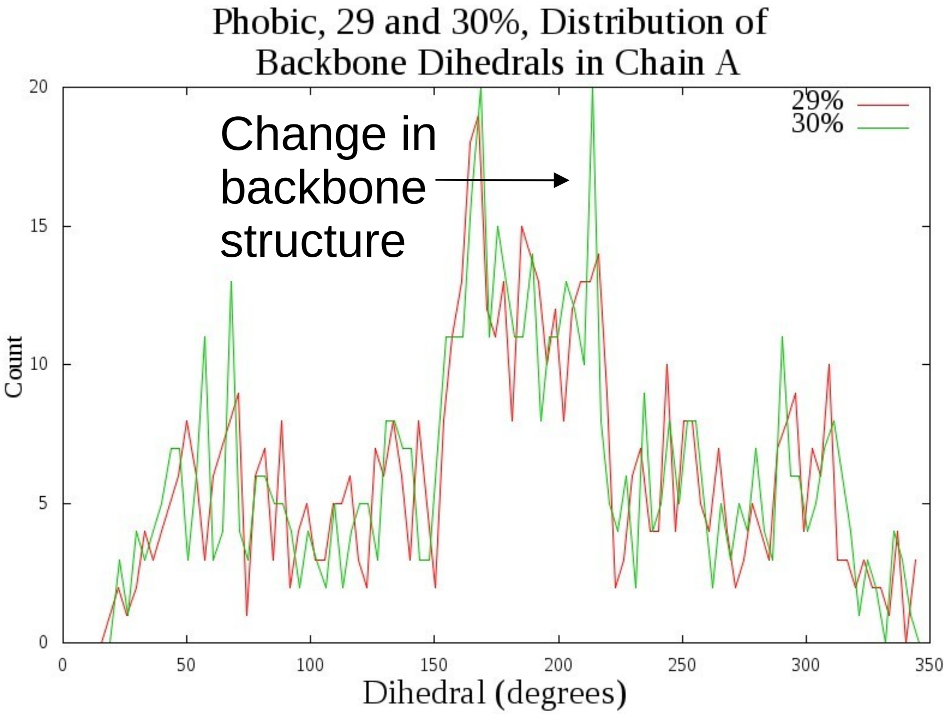
Phobic, 18 and 19%, Distribution of Backbone Dihedrals in Chain C



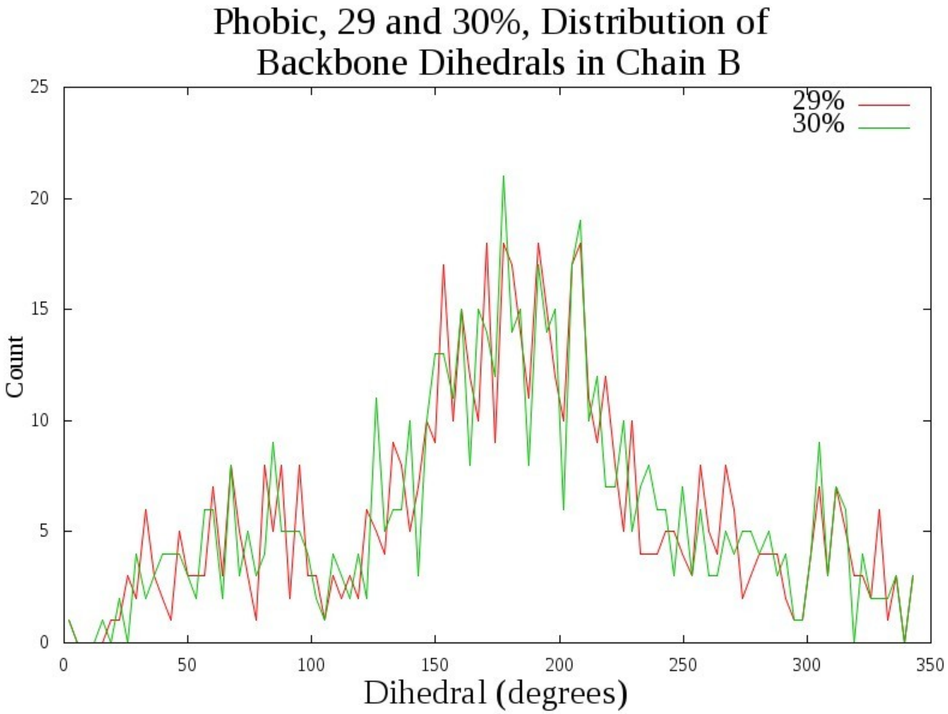
Change in backbone structure

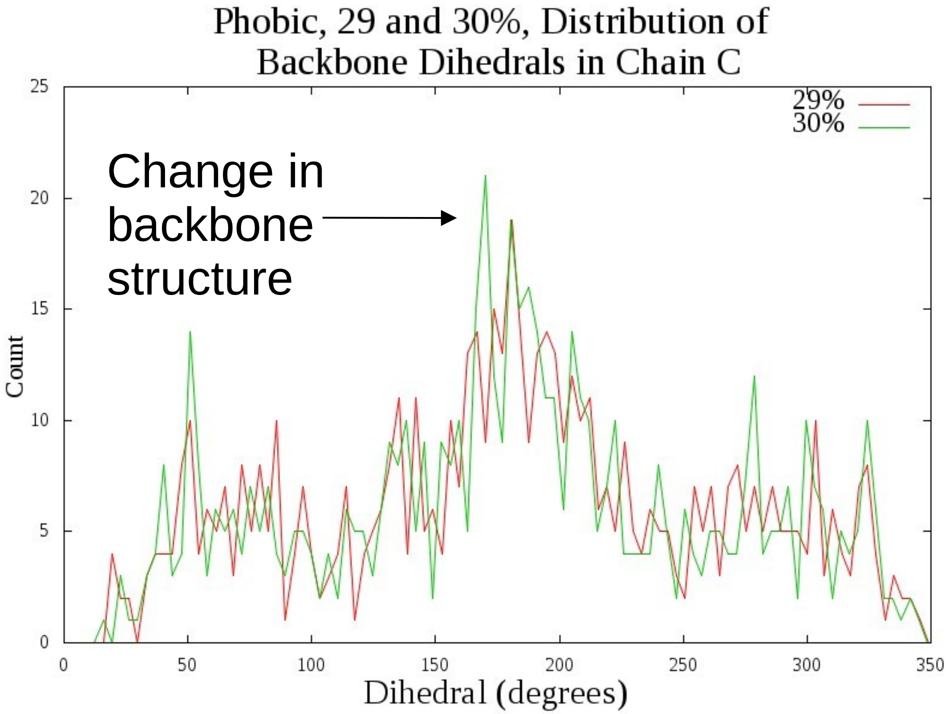
Phobic, 18 and 19%, Distribution of Backbone Dihedrals in Chain D



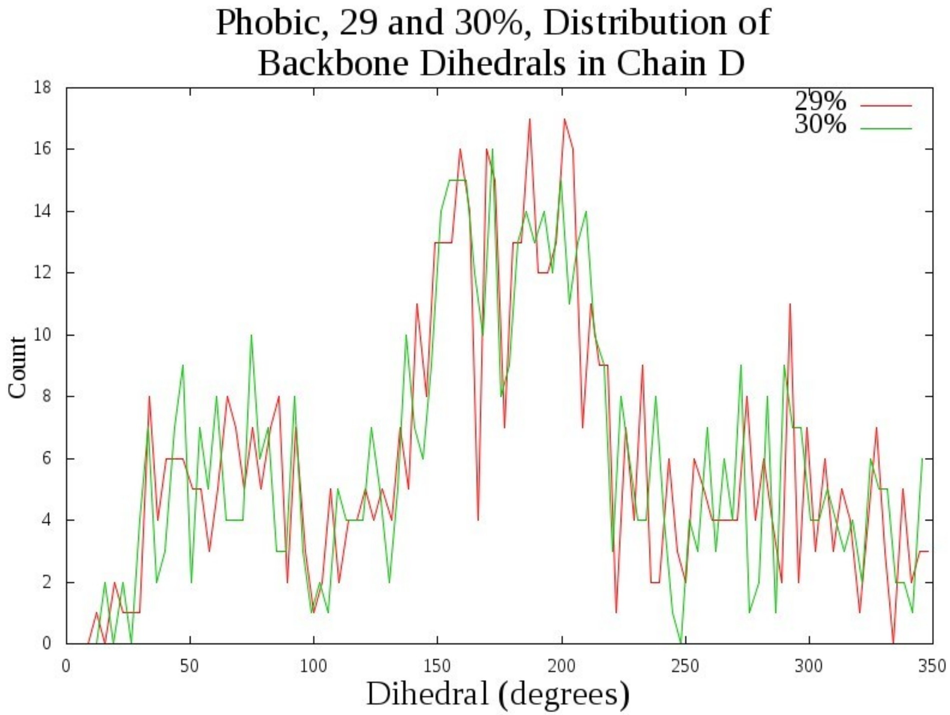

Phobic, 29 and 30%, Distribution of Backbone Dihedrals in Chain A

Change in backbone structure


Phobic, 29 and 30%, Distribution of Backbone Dihedrals in Chain B


Phobic, 29 and 30%, Distribution of Backbone Dihedrals in Chain C

Change in backbone structure

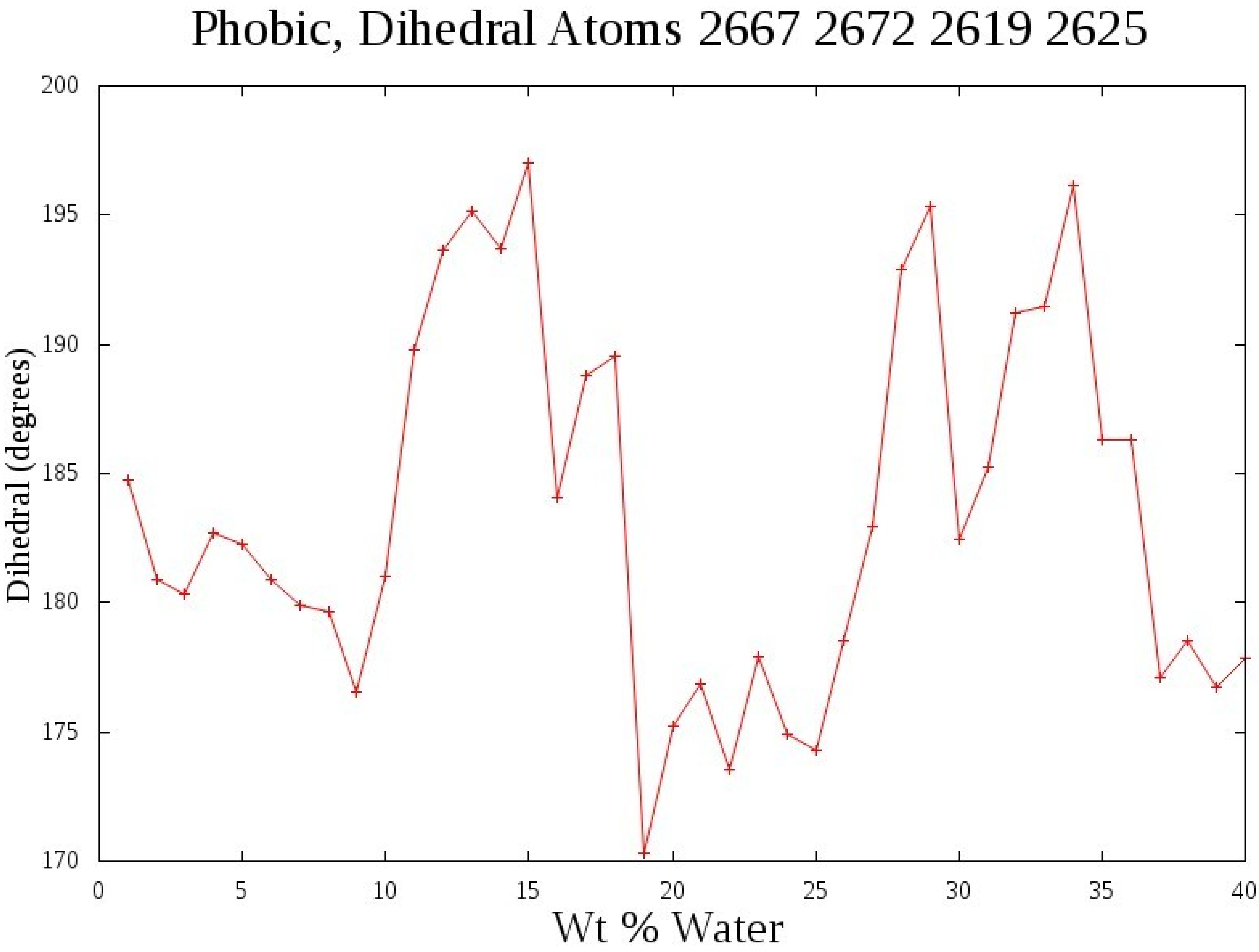

Phobic, 29 and 30%, Distribution of Backbone Dihedrals in Chain D

Backbone Structure – Strategy

- Look for differences in backbone dihedral distribution
- E.g., the 19% chain A structure has more backbone dihedrals at ~170 than the 18% (there are plenty of others, but we'll focus on this one somewhat arbitrarily for the moment)
- Find backbone dihedrals that “scatter into” this state (the ones that are ~170 in the 19% structure, but are different in the 18%)
- Look at the dihedrals that change by more than a few degrees
- The next slide shows these dihedrals. The first 4 columns give us the IDs of the atoms in the dihedral. The next column gives the dihedral in the 19% structure. The following gives the same for the 18%. The last column gives the change in dihedral.
- The dihedral with the largest change is highlighted in red. The dihedrals with the next 6 largest changes are highlighted in yellow.

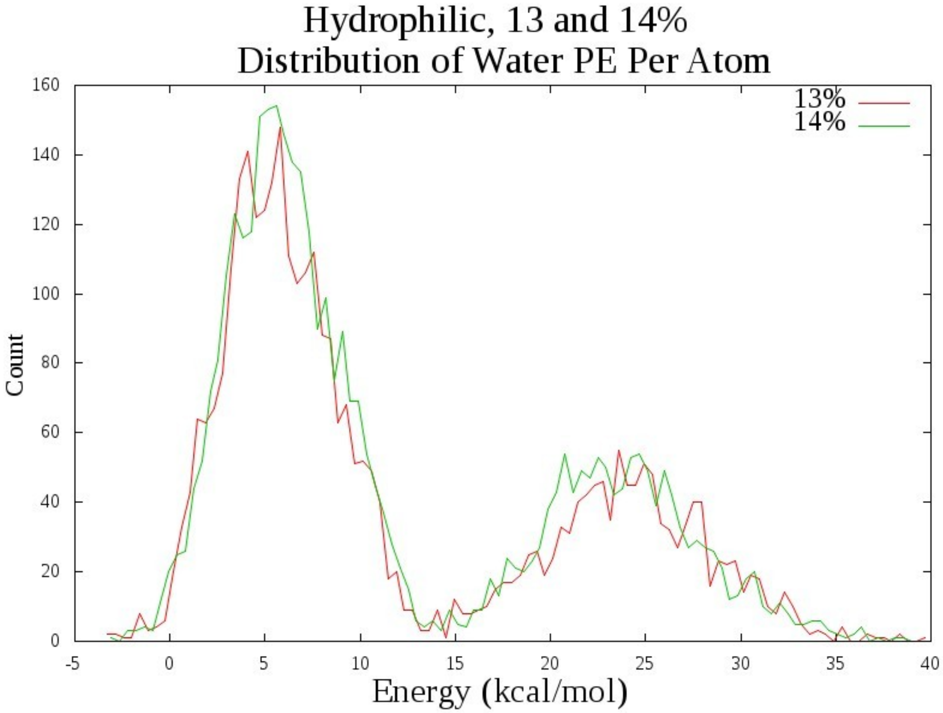
Dihedral Changes in Backbone of Phobic Chain A: 18-19%

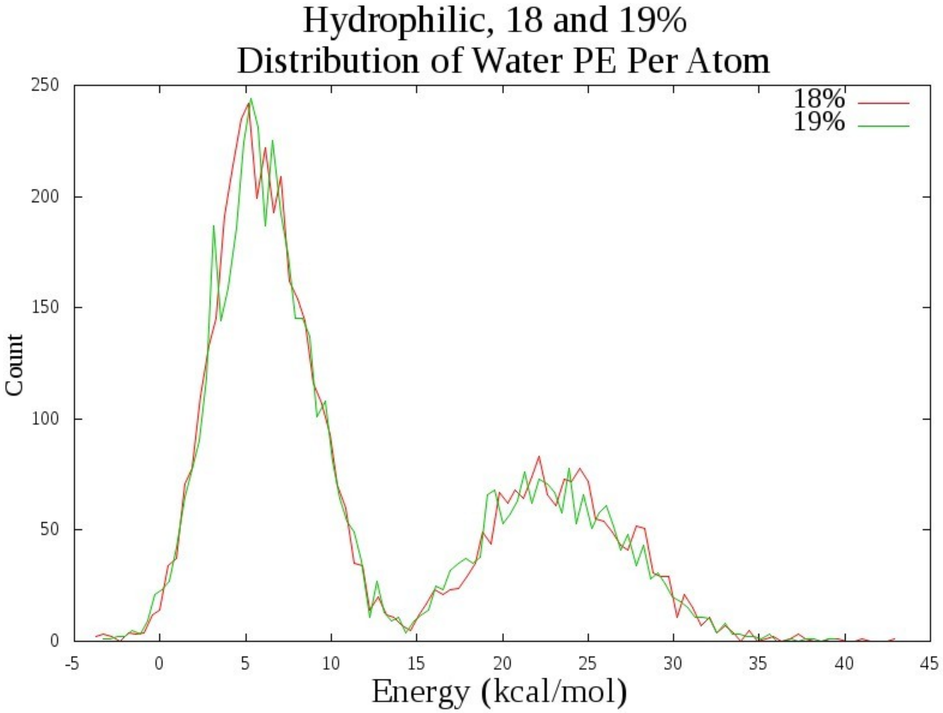
ATOM1	ATOM2	ATOM3	ATOM4	Dihed-19	Dihed-18	Delta
6918	6924	6903	6909	170.489645	174.747461	-4.257816
6924	6903	6909	6888	172.59909	169.458823	3.140267
6462	6467	6414	6419	172.112157	169.576894	2.535263
4095	4100	4047	4052	170.555102	174.182604	-3.627502
2807	2774	2786	2760	170.572745	169.892551	0.680194
2745	2751	2730	2735	172.398691	177.990447	-5.591756
2667	2672	2619	2625	170.289306	189.548023	-19.258717
2553	2559	2531	2543	170.309511	178.048591	-7.73908
2559	2531	2543	2517	170.844134	177.258973	-6.414839
2133	2139	2118	2124	172.874981	179.086613	-6.211632
1625	1637	1604	1616	172.861208	179.816854	-6.955646
1515	1487	1499	1473	171.421053	178.075268	-6.654215
1074	1080	1052	1064	170.431548	162.936488	7.49506
276	281	228	234	172.681185	173.848535	-1.16735
54	60	39	45	170.013422	169.196422	0.817

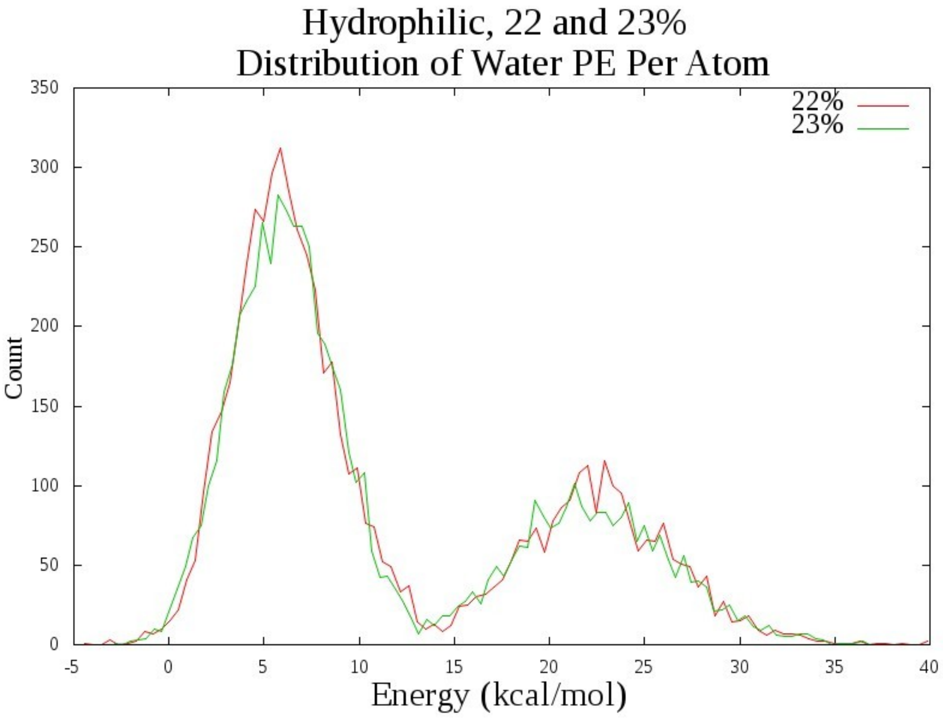


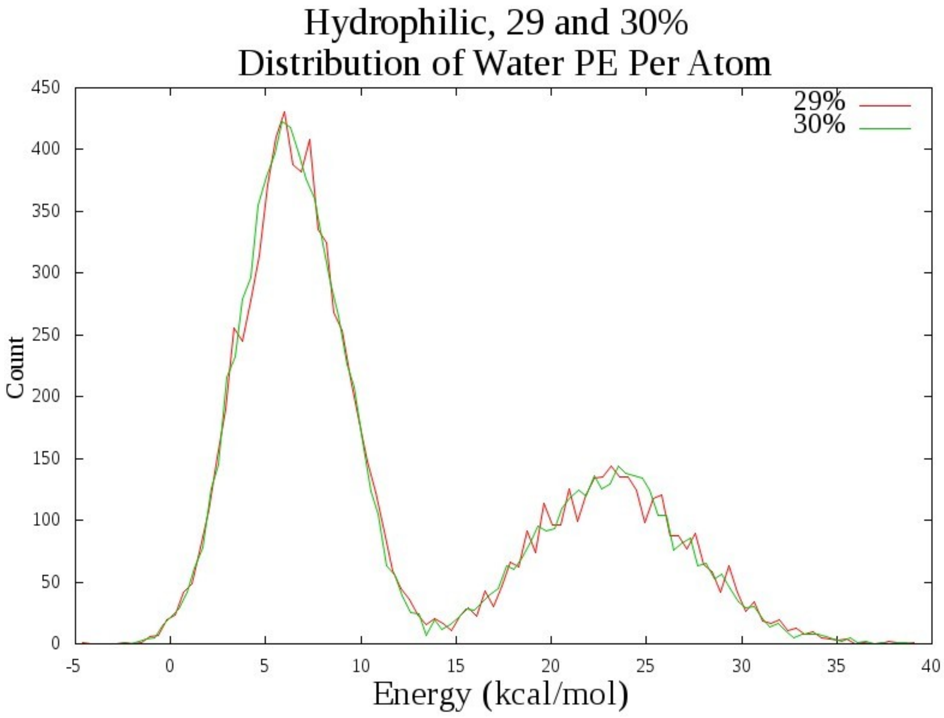
This particular backbone dihedral changes sharply at every jump in energy

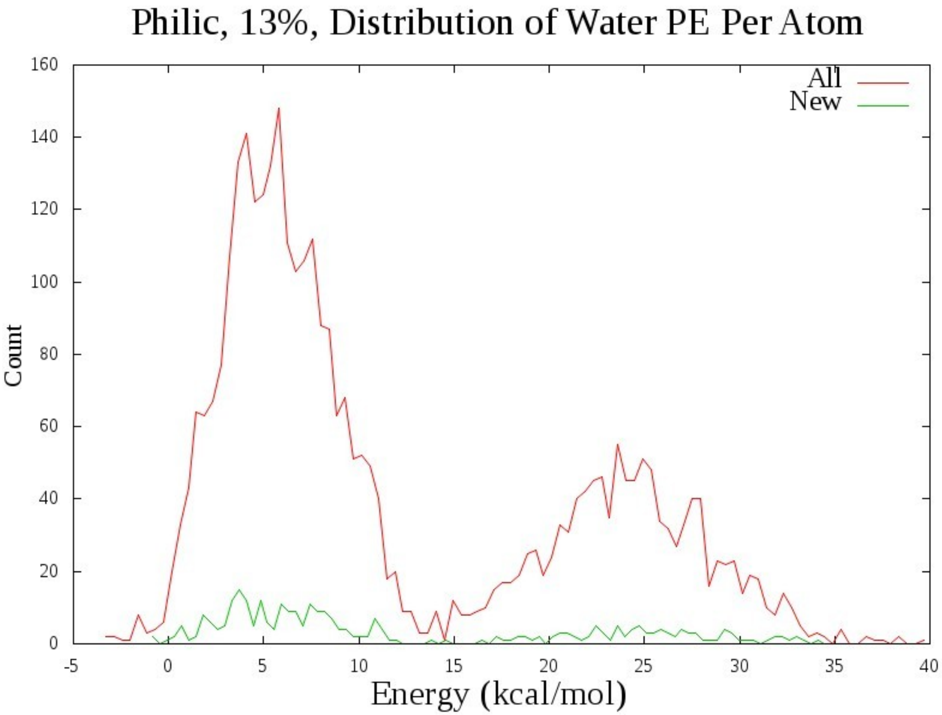
We next performed a similar analysis for the hydrophilic system


Hydrophilic, 13 and 14%
Distribution of Water PE Per Atom

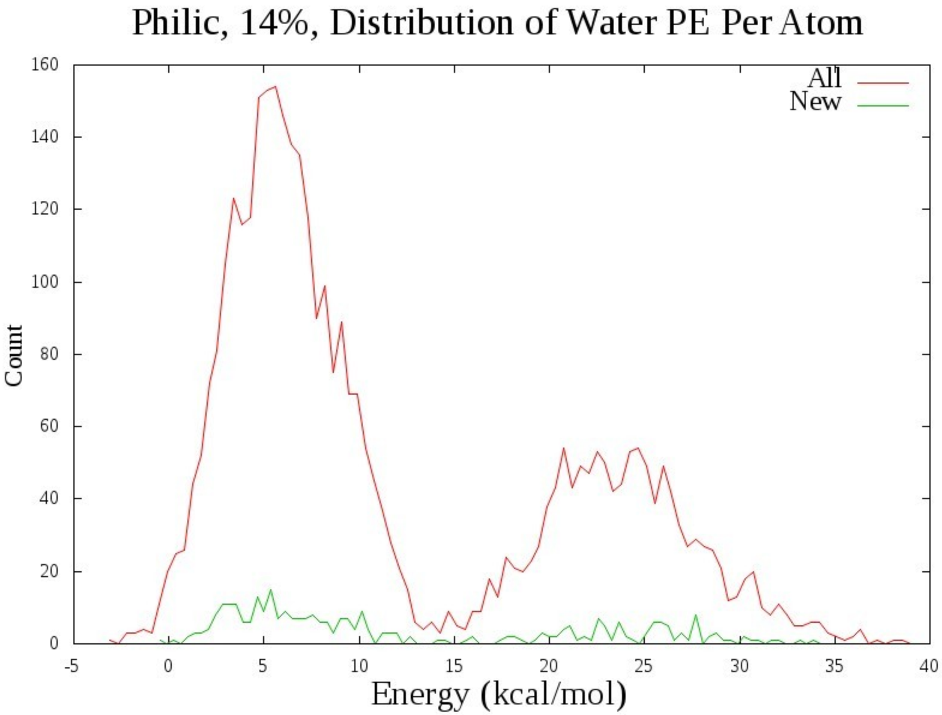

Hydrophilic, 18 and 19%
Distribution of Water PE Per Atom


Hydrophilic, 22 and 23%
Distribution of Water PE Per Atom

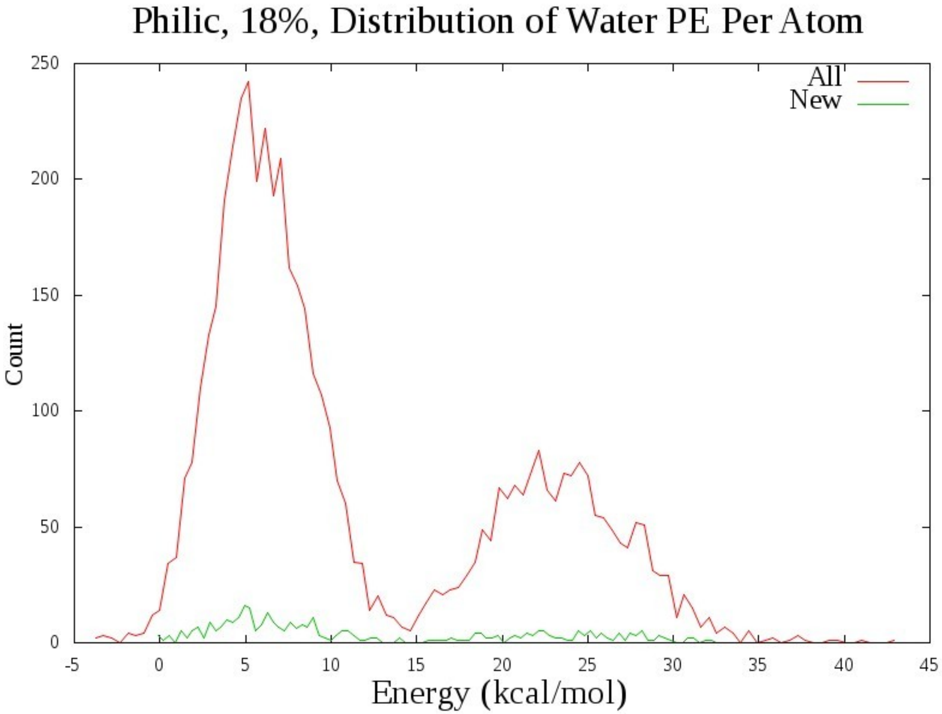

Hydrophilic, 29 and 30%
Distribution of Water PE Per Atom



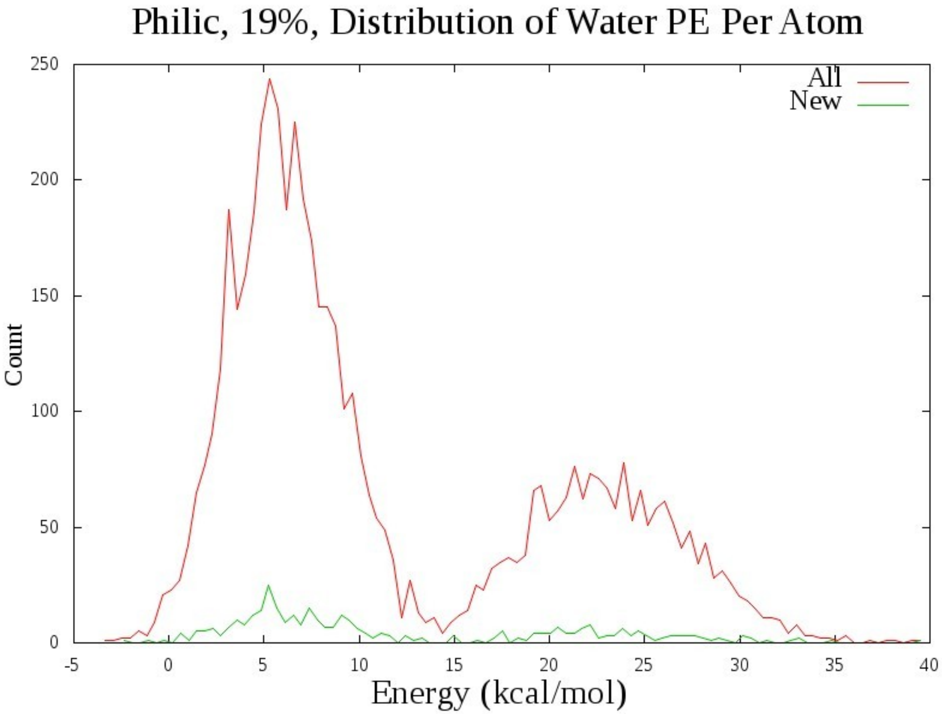
Philic, 13%, Distribution of Water PE Per Atom



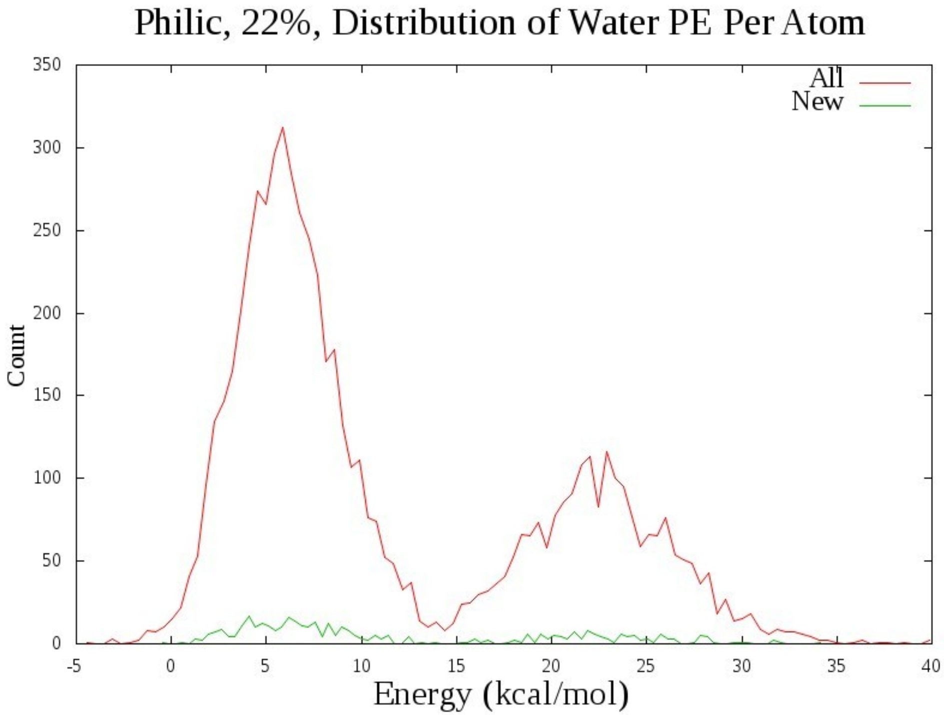
Philic, 14%, Distribution of Water PE Per Atom

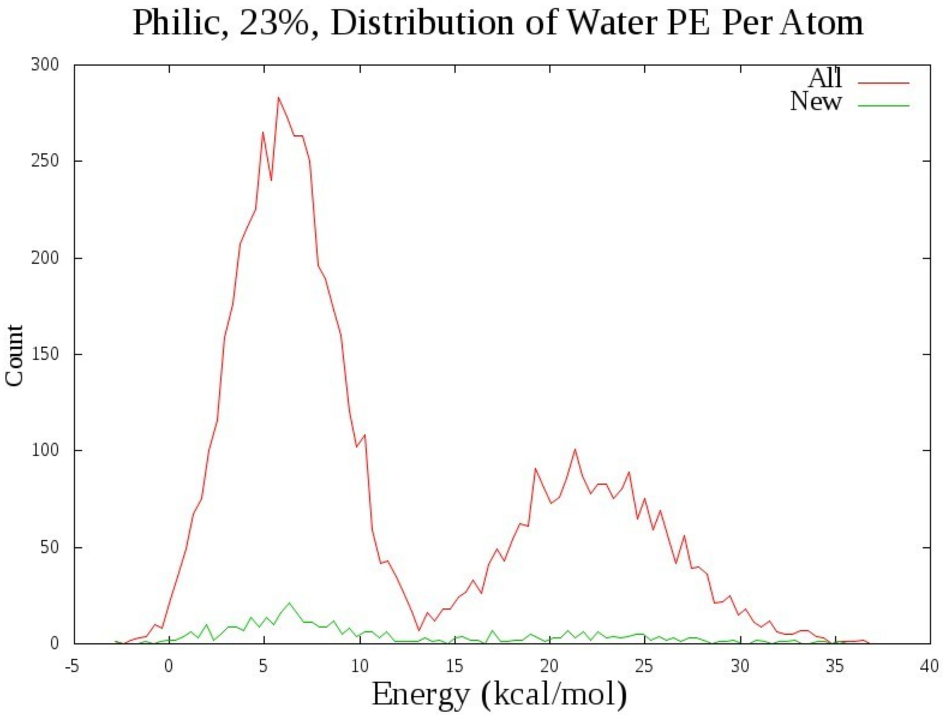


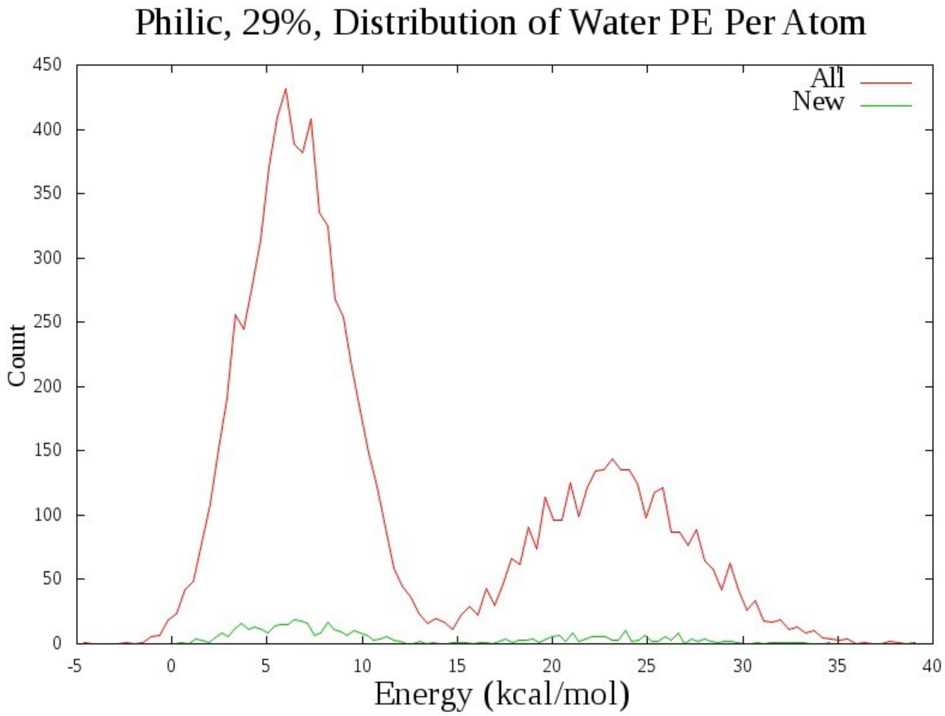
Philic, 18%, Distribution of Water PE Per Atom

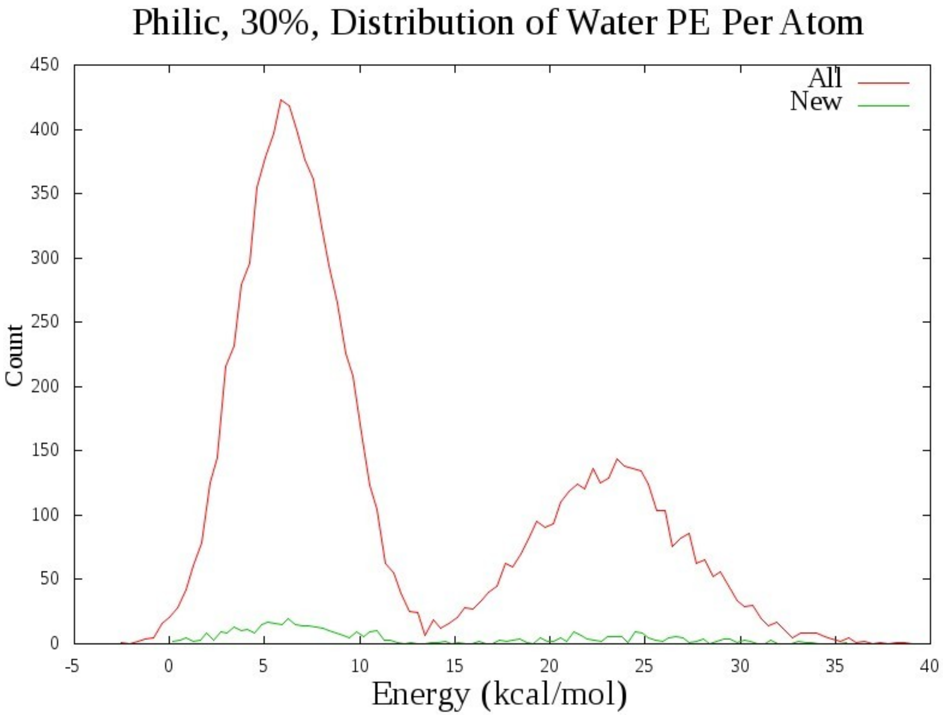


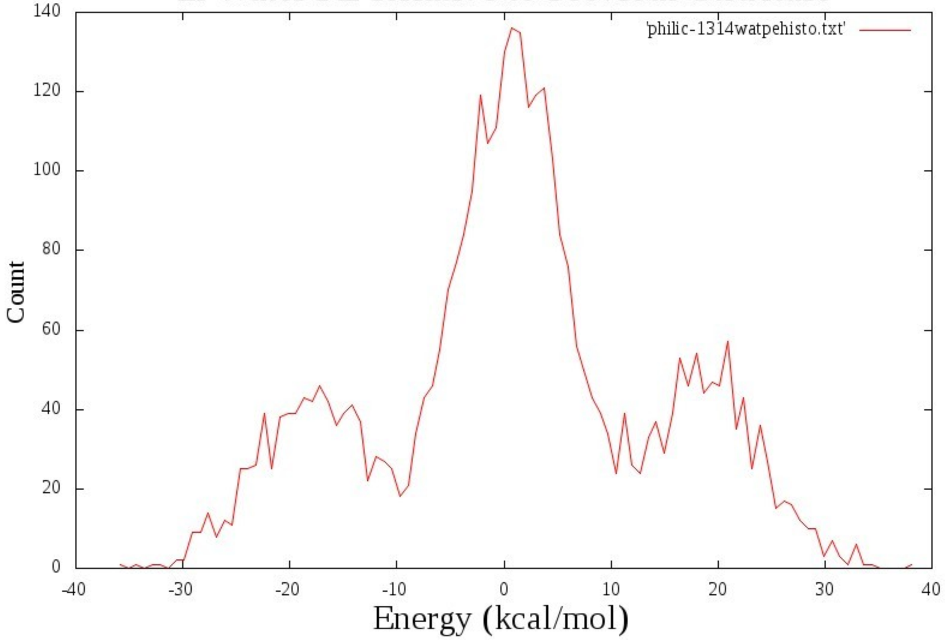
Philic, 19%, Distribution of Water PE Per Atom


Philic, 22%, Distribution of Water PE Per Atom

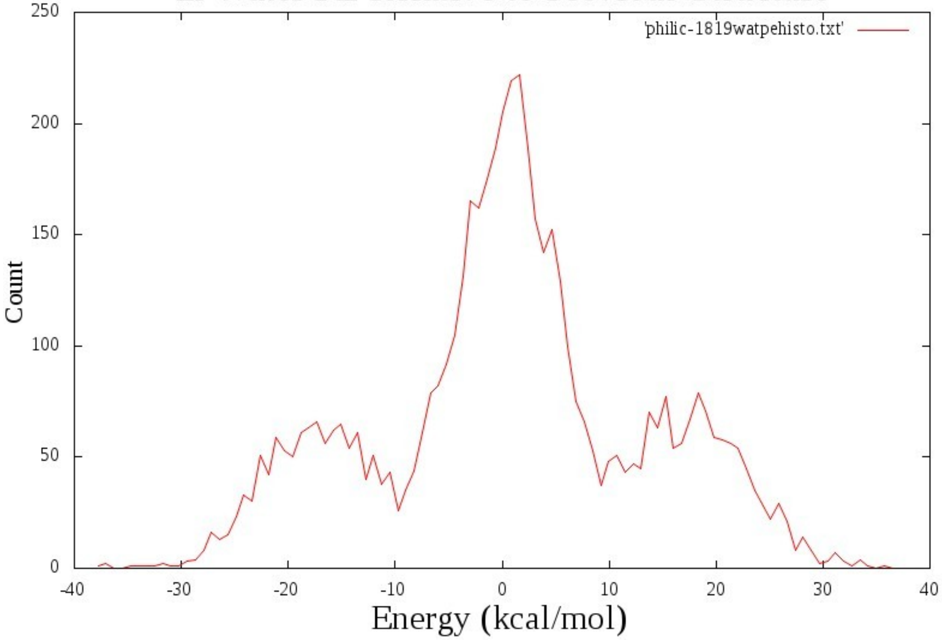

Philic, 23%, Distribution of Water PE Per Atom


Philic, 29%, Distribution of Water PE Per Atom

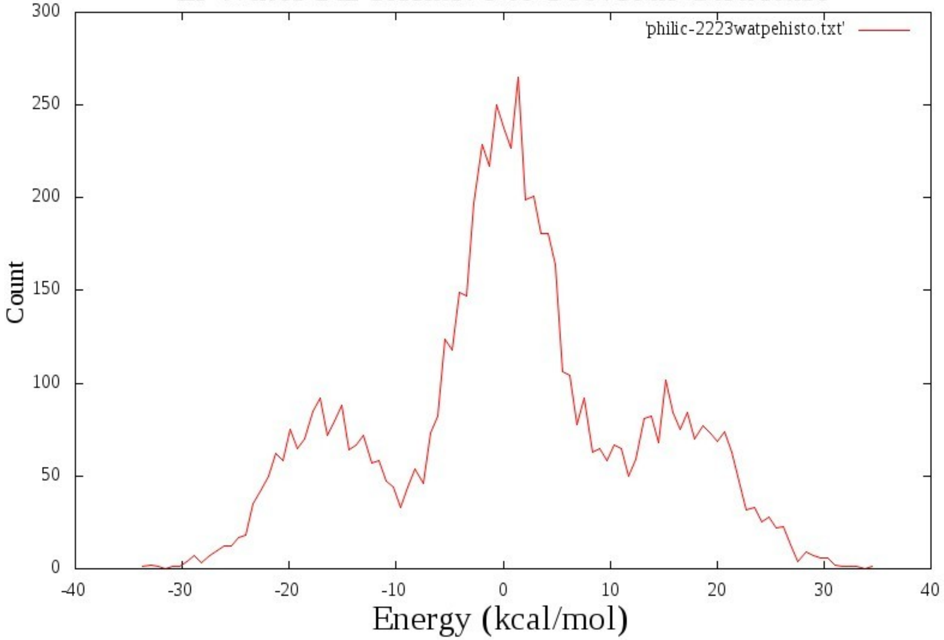

Philic, 30%, Distribution of Water PE Per Atom



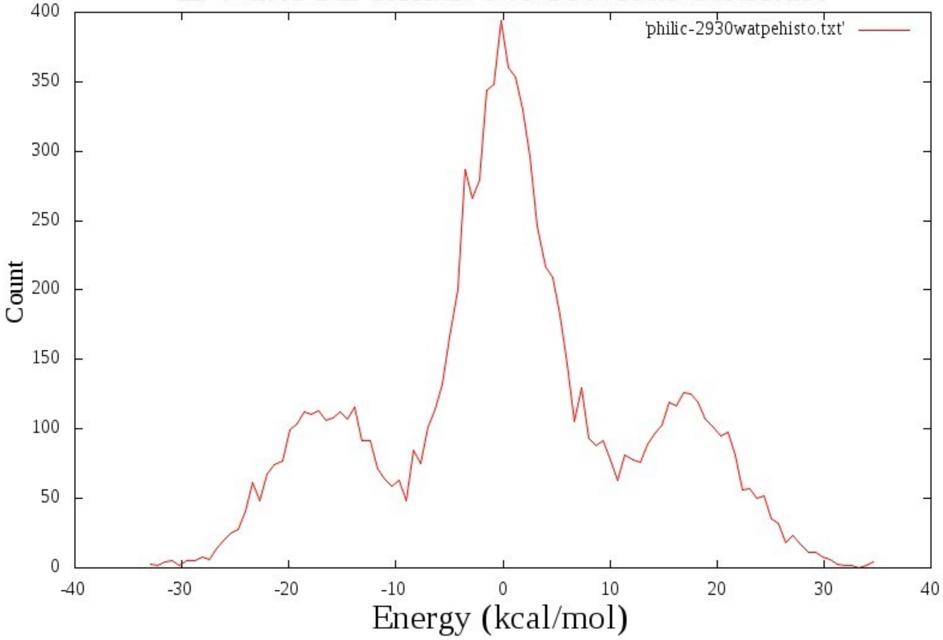
Philic, 14%, Distribution of Differences in Water PE Relative to Previous Structure



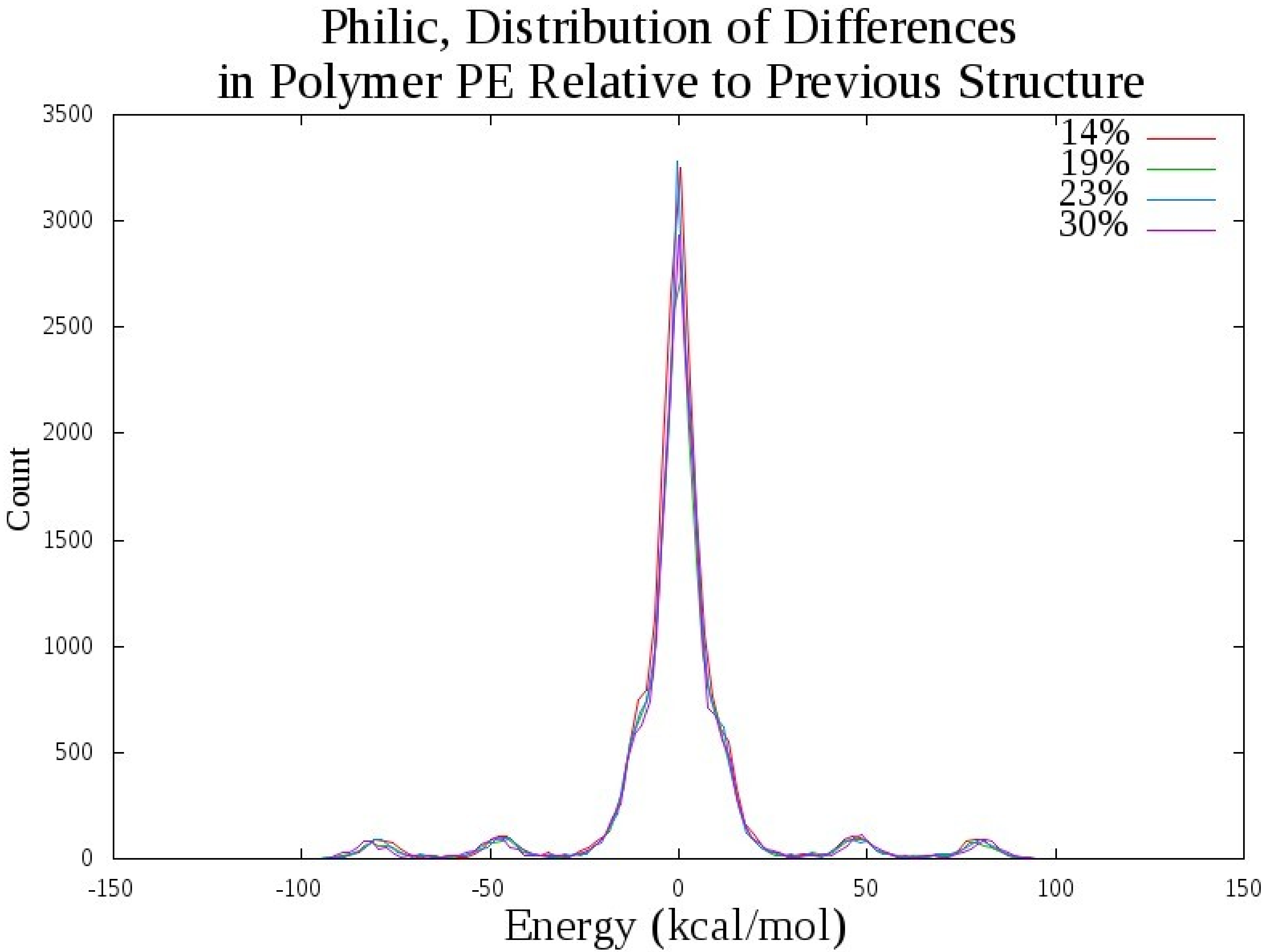
Philic, 19%, Distribution of Differences in Water PE Relative to Previous Structure

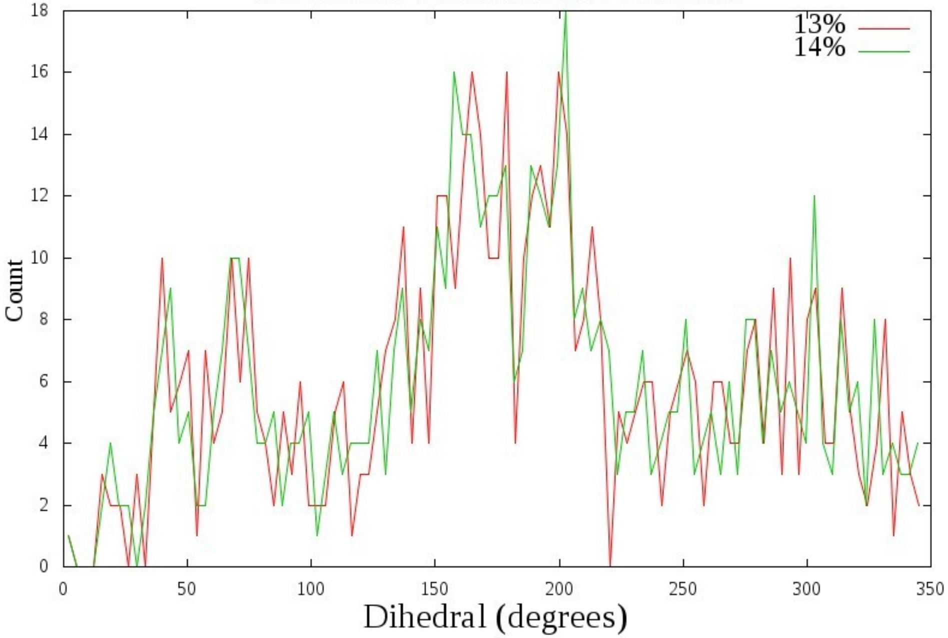


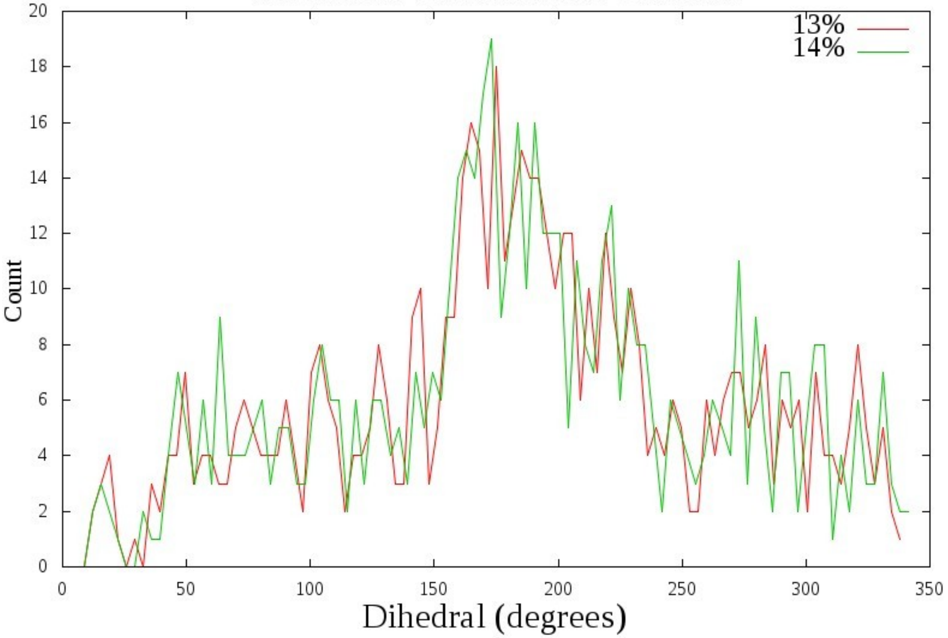
Philic, 23%, Distribution of Differences in Water PE Relative to Previous Structure

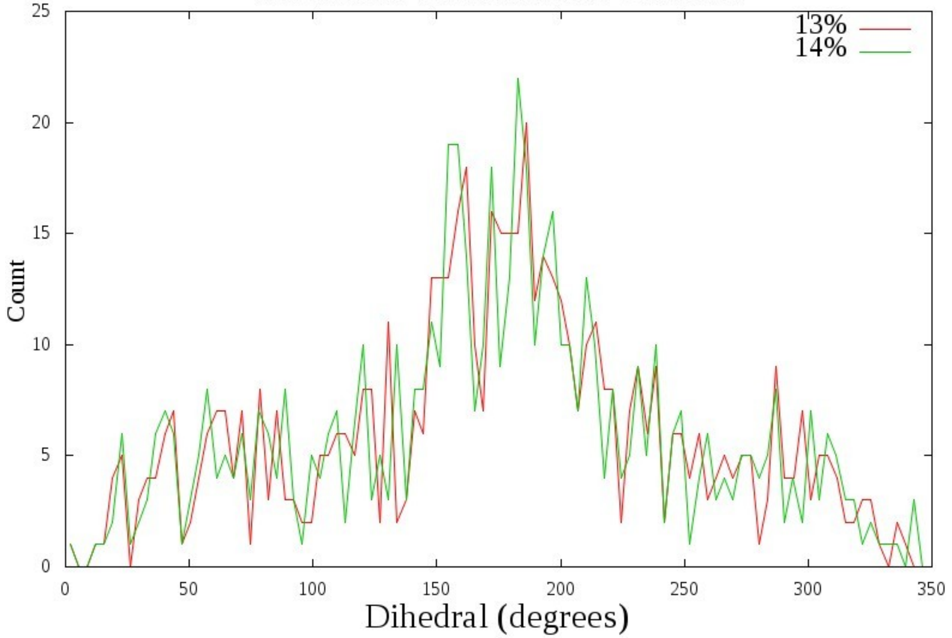


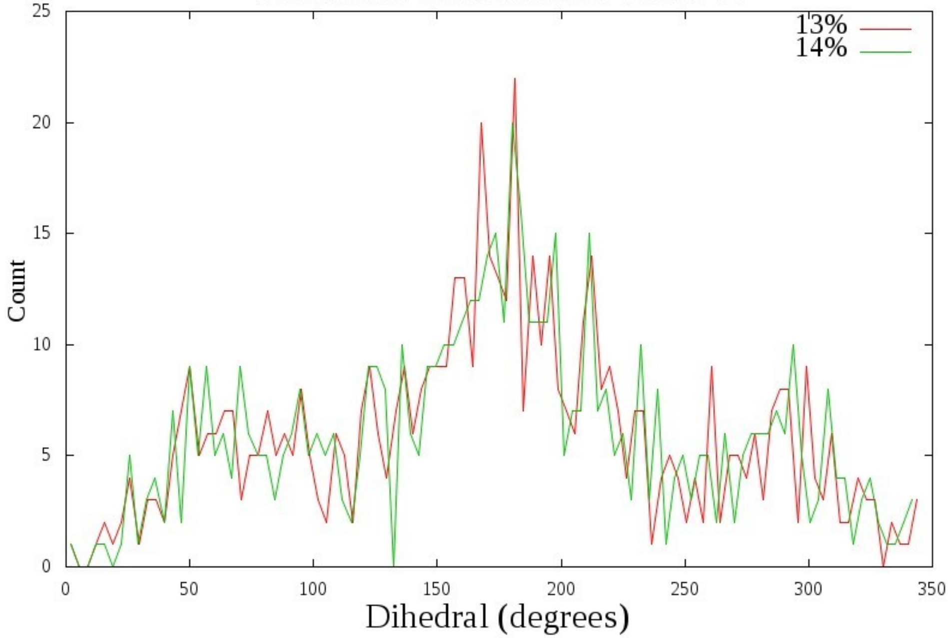
Philic, 30%, Distribution of Differences in Water PE Relative to Previous Structure


Philic, Distribution of Differences
in Polymer PE Relative to Previous Structure
Count
Energy (kcal/mol)
3500
3000
2500
2000
1500
1000
500
0
-150
-100
-50
0
50
100
150
14%
19%
23%
30%

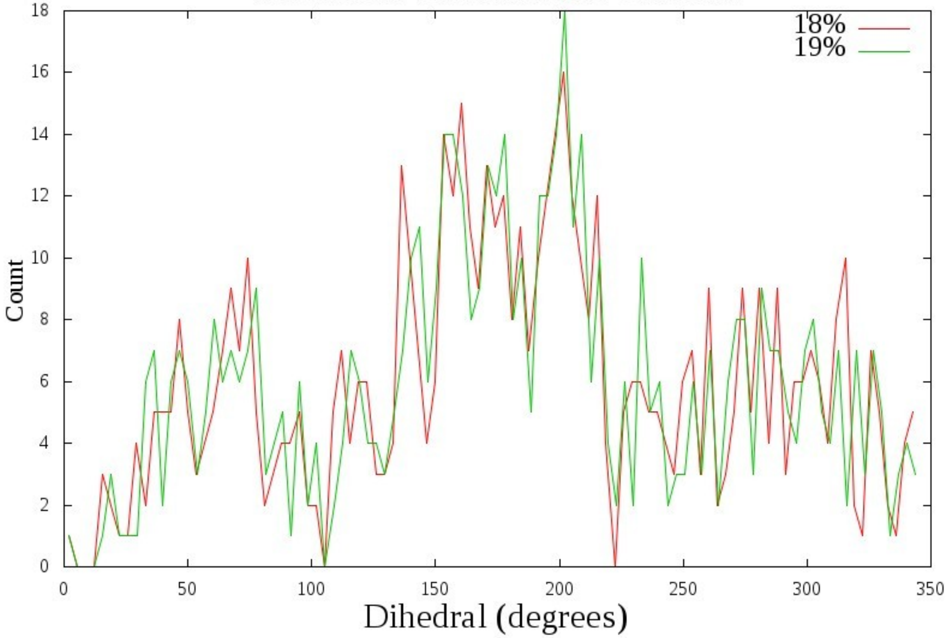

Philic, 13 and 14%, Distribution of Backbone Dihedrals in Chain A


Philic, 13 and 14%, Distribution of Backbone Dihedrals in Chain B

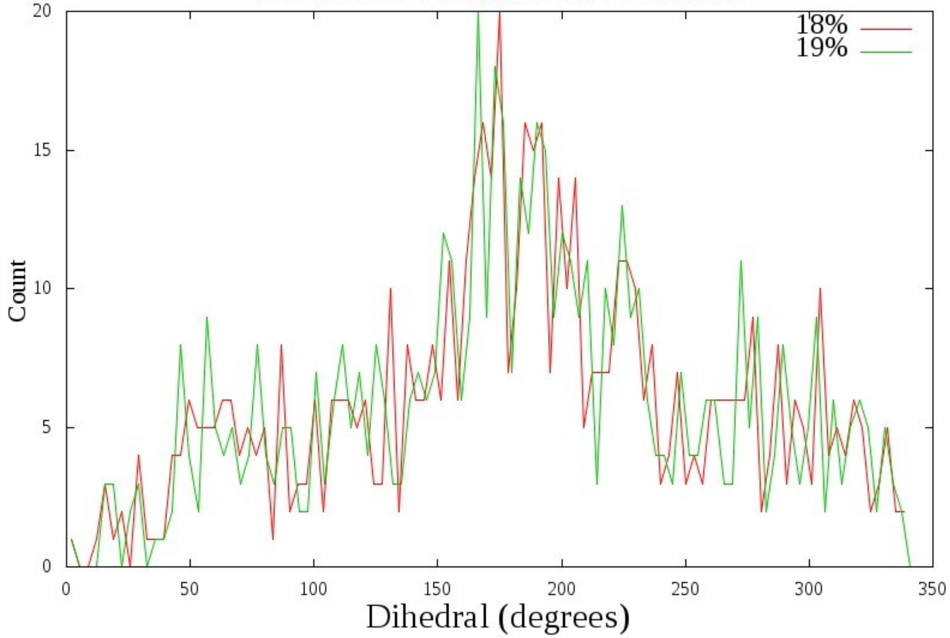

Philic, 13 and 14%, Distribution of Backbone Dihedrals in Chain C


Philic, 13 and 14%, Distribution of Backbone Dihedrals in Chain D

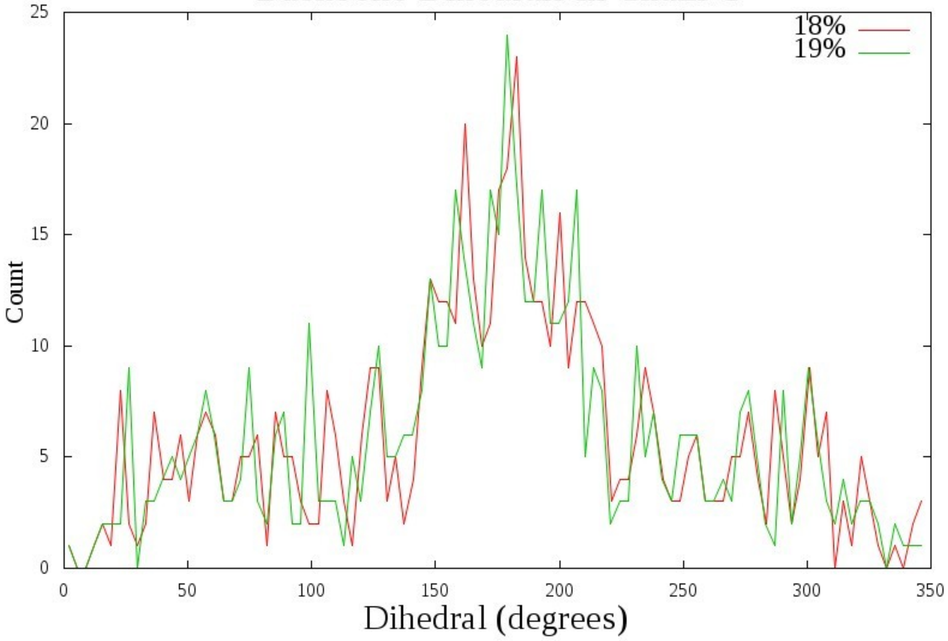
Philic, 18 and 19%, Distribution of Backbone Dihedrals in Chain A



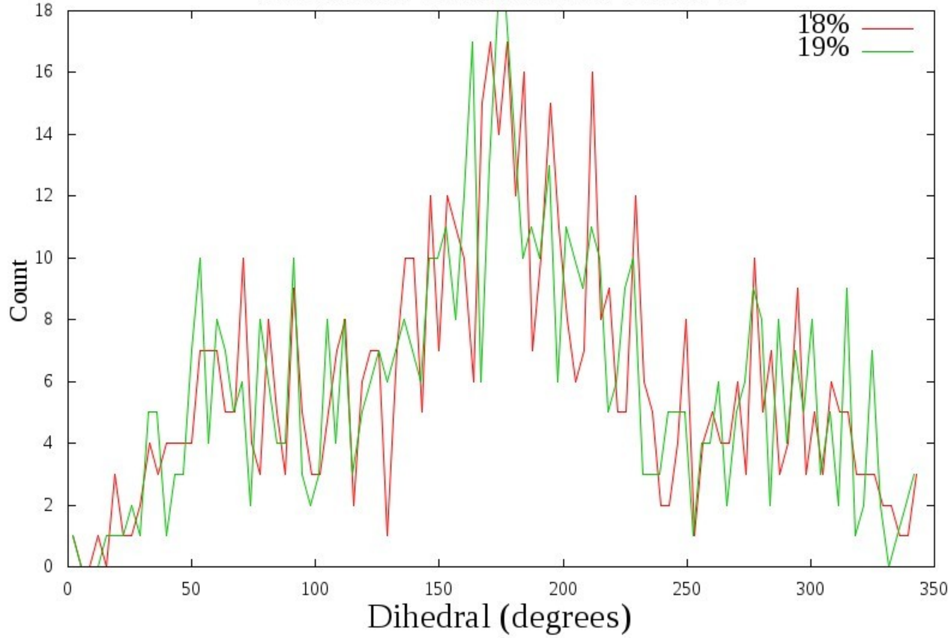
Philic, 18 and 19%, Distribution of Backbone Dihedrals in Chain B

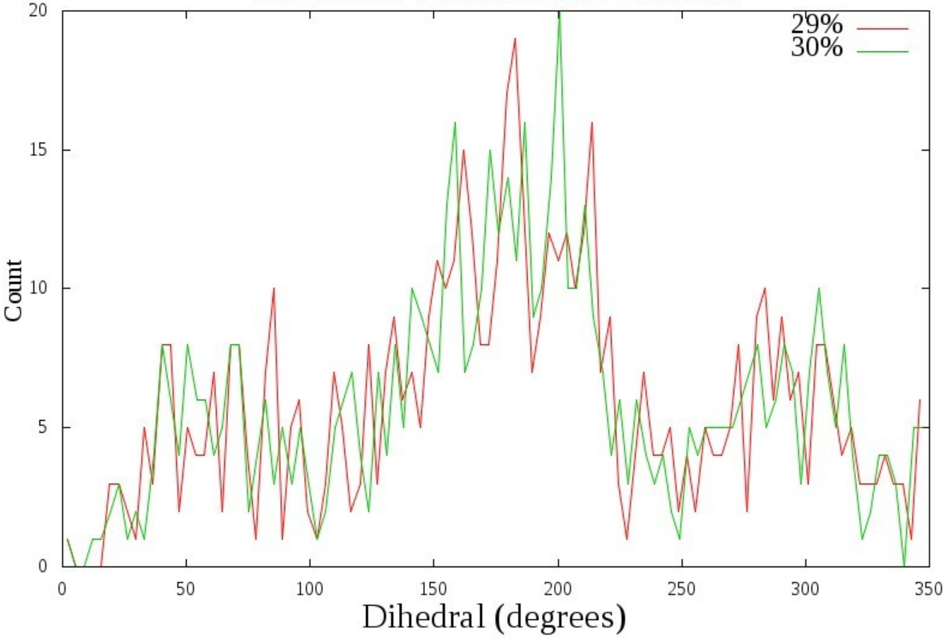


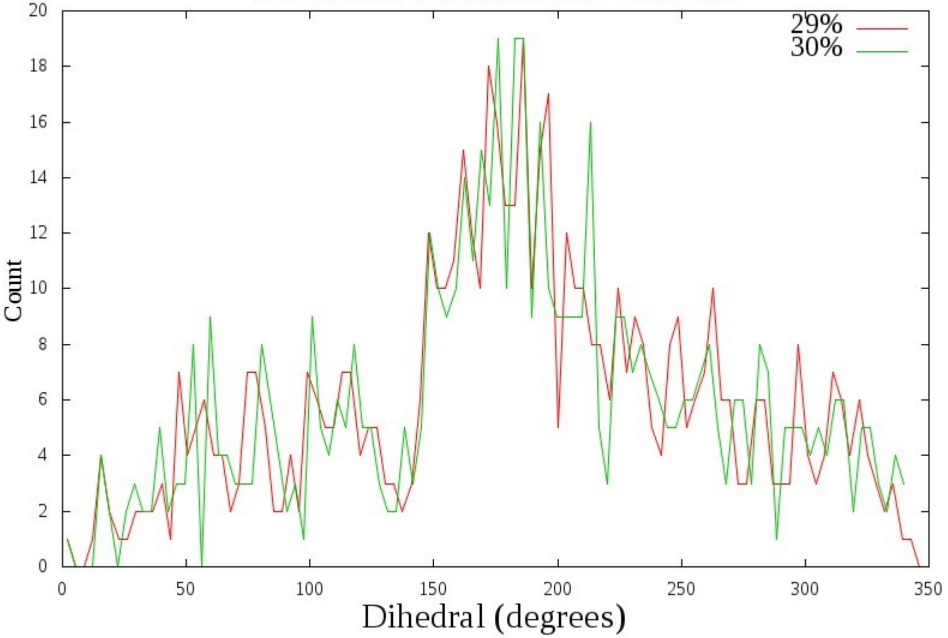
Philic, 18 and 19%, Distribution of Backbone Dihedrals in Chain C

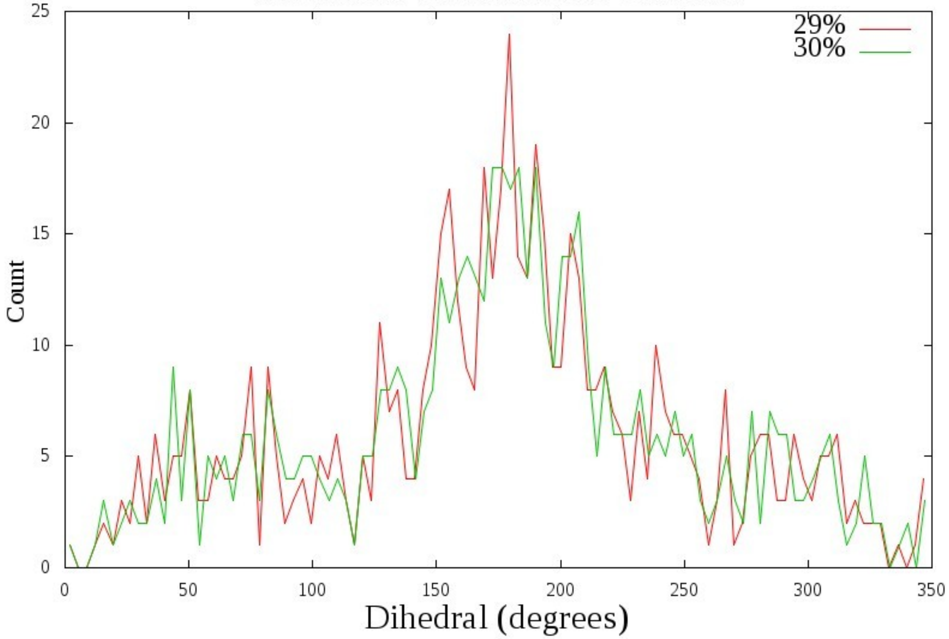


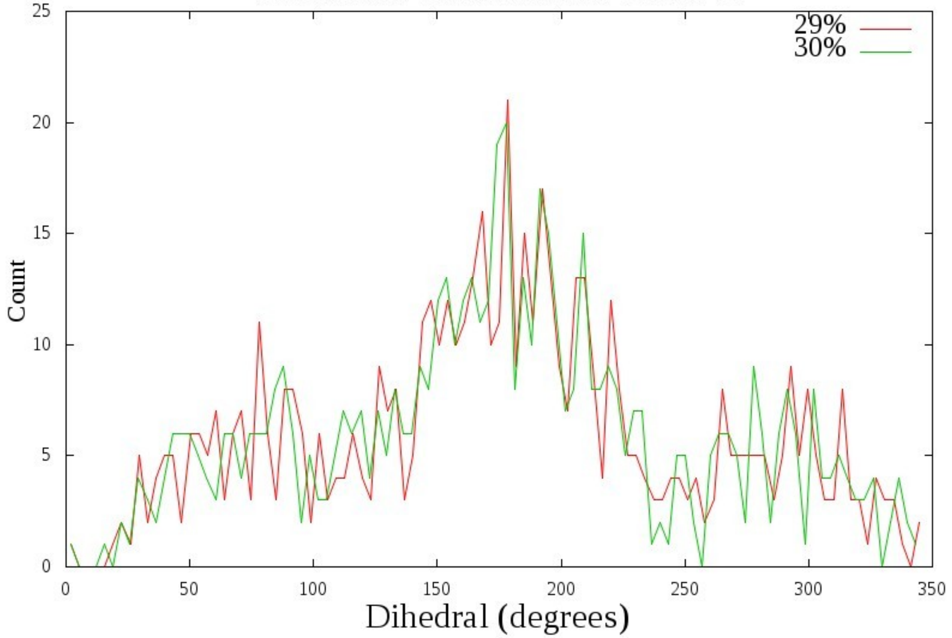
Philic, 18 and 19%, Distribution of Backbone Dihedrals in Chain D




Philic, 29 and 30%, Distribution of Backbone Dihedrals in Chain A


Philic, 29 and 30%, Distribution of Backbone Dihedrals in Chain B


Philic, 29 and 30%, Distribution of Backbone Dihedrals in Chain C


Philic, 29 and 30%, Distribution of Backbone Dihedrals in Chain D

ATOM 2	ATOM 2	ATOM 3	ATOM 4	Dihed-30	Dihed-29	Delta
5441	5408	5420	5387	200.243092	210.875189	-10.632097
5022	5028	5000	5012	199.225653	183.078573	16.14708
4898	4865	4877	4851	199.791198	220.003348	-20.21215
4820	4787	4799	4766	199.964223	207.092808	-7.128585
3995	3962	3974	3948	200.150224	195.82752	4.322704
3461	3473	3447	3453	198.872474	204.427388	-5.554914
3453	3432	3438	3410	200.970181	210.873309	-9.903128
3410	3422	3396	3402	200.917877	195.447808	5.470069
3314	3326	3300	3306	199.982706	193.286798	6.695908
1991	2003	1970	1982	201.134844	198.341946	2.792898
1935	1941	1920	1926	199.674325	202.848026	-3.173701
1308	1314	1286	1298	202.254371	197.876006	4.378365
1277	1244	1256	1230	201.224884	205.260716	-4.035832
1244	1256	1230	1236	198.941505	198.241882	0.699623
1011	990	996	968	201.037362	188.003755	13.033607
338	350	324	330	201.337608	209.931218	-8.59361
77	44	56	30	199.917589	185.061889	14.8557