Accuracy of Vcharge with the VC/2004 Parameterization
A comparative analysis

Vcharge is a new method of generating partial charges that is adjusted to reproduce Hartree-Fock electrostatic potentials (ESPs) computed with GAMESS at the 6-31G* level.

- Runs approximately 22 times faster than AM1-BCC for a set of 19 drug molecules (see data below)
- Does not require a realistic 3D conformation
- Does not require files to include hydrogen atoms, so long as formal charges are specified
- Assigns equal charges to chemically equivalent atoms
- Charges do not depend upon conformation.

Amino Acids and Nucleic Acids

Vcharge gives charges that are highly similar to those of standard force-fields like AMBER and CHARMM, as well as the relatively time-consuming AM1-BCC method, as shown in the following table.

	Correlation Coefficient	**<|Diff|>** (e)
Amino Acids		
VC/2004-AMBER94	0.95	0.08
AM1-BCC-AMBER94	0.95	0.07
VC/2004-CHARMM22	0.96	0.04
AM1-BCC-CHARMM22	0.94	0.08
AMBER94-CHARMM22	0.93	0.08
VC/2004-AM1-BCC	0.97	0.06
dNucleotides		
VC/2004-AMBER94	0.95	0.10
AM1-BCC-AMBER94	0.97	0.09
VC/2004-CHARMM22	0.95	0.10
AM1-BCC-CHARMM22	0.97	0.09
AMBER94-CHARMM22	0.93	0.08
VC/2004-AM1-BCC	0.95	0.13

Table 1: Comparisons of various charge sets and charging models for the 20 common amino acids in both neutral and ionized forms, and for the 5 common nucleic acid bases. Vcharge calculations were done for amino acids with neutral caps and deoxynucleotides with methyl phosphate caps.

Note that AM1-BCC charges are conformation-dependent. For example, AM1/BCC charges vary on average by 0.06 e over 53 low-energy conformations of the deoxythymidine nucleotide, with a maximum deviation of 0.14 e. Here, the AM1-BCC charges were computed with the lowest energy conformation generated by VeraChem's conformational search program Vconf with Vcharge charges.

Drugs and Drug-Like Compounds

Vcharge was compared with AM1-BCC for

> amprenavir, viagra, thyroxine, tenofovir, sotalol, rosuvastatin, pramipexole, pioglitazone, naproxen, lexapro, levonorgestrel, ibuprofen, gleevec, fosamax, depakote, claritin, citalopram, ciprofloxacin, and ceftriaxone

Vcharge matches AM1-BCC closely: the correlation coefficient across all atoms of all compounds is **0.94**, and the mean unsigned difference is only **0.09 e**.

Vcharge is substantially faster, requiring an average of only **0.8 seconds** per compound, compared with **17 seconds** for AM1-BCC.

The following figures compare Vcharge and AM1-BCC charges via a scatter plot (left) and a histogram of differences (right) for all atoms of all compounds.