Resolving Ambiguous Side-chain Orientations of Asparagine and Glutamine

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The electron densities obtained from proteins are sometimes insufficient to distinguish certain atom types. Prominent examples are the oxygen and nitrogen atoms in the side chains of Glutamine (GLN) and Asparagine (ASN) and the nitrogens in the imidazole ring of Histidine (HIS). Assignments of these atom types is often achieved indirectly by using information in the neighborhood of such atoms. This is often unreliable and it is known [1] that approximately 15% of these assignments are incorrect.

We derive a mean force heavy atom potential [2] from a set of highly resolved PDB [3] protein chains. Ambiguous residues in this set are evaluated using the potential and in case of an unfavorably high interaction energy the reverse orientation is taken. This procedure is iterated till convergence. The final potential function is then used for assigning the correct side-chain orientation of ambiguous amino acids in an arbitrary PDB file. A comparison to expert curated assignments [4] shows sensitivity and selectivity values higher than 90% for ASN and GLN. A web service is available athttp://services.came.sbg.ac.at/flipper.

[1] Hooft R.W.W, et al., *Proteins*, 1996, **26**, 363. [2] Sippl M.J., *Proteins*, 1993, **17**, 355. [3] Berman H.M., et al, *Nucleic Acids Res*., 2000, **28**, 235. [4] Word J.M., et al, *J. Mol. Biol.*, 1999, **285**, 1735.

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