BioGPS: the Music for the Chemo- and Bioinformatics Walzer

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Identifying cross-relationships among protein binding sites is becoming increasingly important in the chemo- and bioinformatics field; indeed, protein structural similarity might provide the right answer to a number of questions including *Is a drug repurposable for another target?* W*hat is the molecular mechanism of a drug side-effect? How can we improve the ligand selectivity?* The comparison of protein binding sites in terms of their three-dimensional structure molecular interaction fields can be a useful technique to approach all of these problems. Here, we report a semi-automated method for comparing and clustering protein pockets, called BioGPS, that combines the GRID Molecular Interactions Fields (MIFs) with FLAP pharmacophoric fingerprints. BioGPS identifies and compares protein binding sites by aligning them each other and directly comparing their MIFs. The strengths of this approach are that it is MIF-based, and therefore describes molecular interactions from a ligand perspective, and it is independent of protein superposition or sequence alignment. This approach enables protein-protein virtual screening (drug repurposing, polypharmacology, off-target effects), and also clustering to relate sequence-based similarities to structurebased differences among protein binding sites.