**Introduction**

We present the Hotspots API, a Python toolkit for the detection of small molecule binding hotspots and application of results to structure-based drug discovery (SBDD) methods.

**Motivations**
- Programmatic access to algorithm and integration
- Platform for collaboration
- Pathway for productisation.

**SuperStar**
Using IsoStar data, interaction propensities are mapped to functional groups on the target molecule highlighting likely interactions.

**Fragment Hotspot Maps**
Predicts the location of small molecule binding hotspots in proteins. Weighs SuperStar by pocket burial and samples with pseudomolecular probes.

**Use Cases**

**Tractability Assessment**
1. Calculate Maps
2. Restrict to “Drug” Volume ~500 Å
3. Sort by median score value
4. Plot scores distributions

**Improving Docking with GOLD**
- Supports application of results to GOLD docking.
- Previous work has shown improved early enrichment when using hotspot H-bond constraints for VS.

**Pharmacophore Modelling**
- Pharmacophores can be created from:
  - overlaid ligands
  - a hotspot result
- Generated pharmacophore can be used to:
  - search CSD & PDB with CSD-CrossMiner
  - search ZINC with Pharmit

**Global Pharmacophoric Analysis**
- The work on the Hotspot API supports futures objectives.
- Using PD8 data, this project aims to map “global” pharmacophoric space of protein hotspots.
- Then, design a virtual small molecule screening library covering it.
- We aim to increase the biological relevance of screening libraries to improve HTS efficiency.

**Future**
- [github.com/prcurran](http://github.com/prcurran)
- pcurran@ccdc.cam.ac.uk