**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. Weights SuperStar by pocket burial and samples with pseudomolecular probes.


**Hotspots API**

- Programmatic access to hotspots
- Growing support for SBDD applications
- Built on top of the CSD Python API (CSD License required)
- Latest stable package on PyPi and GitHub

**Use Cases**

1. **Tractability Assessment**
   - Calculate Maps
   - Restrict to “Drug” Volume ~500 Å³
   - Sort by median score value
   - Plot scores distributions


2. **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**

- Overlaid ligands
- A hotspot result

Generated pharmacophore can be used to:
- Search CSD & PDB with CSD-CrossMiner
- Search ZINC with Pharmit

**Future**

- 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

**Options:**
- 1. H-Bond Constraint
- 2. Apolar fitting points
- 3. Rescore

**Constraint**

- IF 1%
- No Constraint: 9.8
- 1 constraint (penalty = 10): 12.7
- 1 constraint (penalty = 100): 15.7

**AKT1 (PDB: 3cqw)**

**Global Pharmacophoric Analysis**

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