FragMAX

Crystallographic fragment screening at MAX IV

21/10/2021

Structural Biology strategy workshop

FragMAX facility for crystal-based fragment screening

MAX IV Laboratory

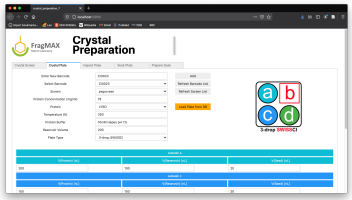
https://www.maxiv.lu.se/fragmax

LP3 - Lund Protein Production Platform

Crystal preparation

Data Collection

Data Analysis



Project management software

SQLite database

WORLDWIDE PDB PROTEIN DATA BANK

Lima *et al.* (2020) Acta Cryst D 76, 771–777.
Lima *et al.* (2021) Acta Cryst D 77, 799-808.

Vetenskapsrådet

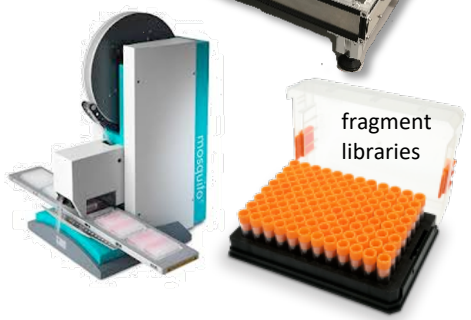
MAX IV

FragMAX facility for crystal-based fragment screening

FragMAX
MAX IV Laboratory

https://www.maxiv.lu.se/fragmax

LP3 - Lund Protein Production Platform



Crystal preparation

Data Collection

Data Analysis

- Access through MAX IV user program for academic and industrial users
- European users can access through iNEXT Discovery
- Available since 2020
- Approx. 50 : 50 interest from academia and industry

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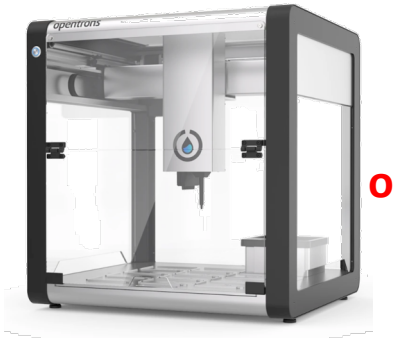
Vetenskapsrådet

MAX IV

Plans for 2022

Workflow:

- Routine preparation of > 300 crystals per day
- Increased automation
- FragMAXapp: from data to PDB in < 1 week
- FragMAXapp for any experiment



or

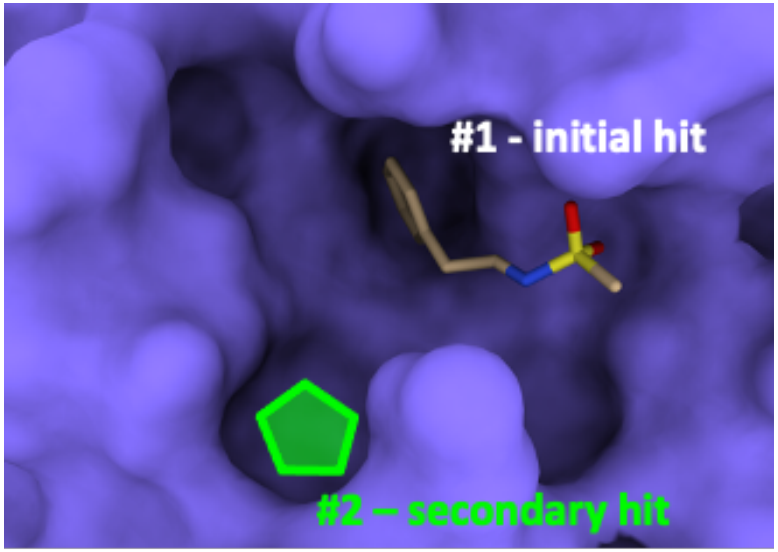
- Cocktail soaks
- Combination soaks
- ”cherrypicking”
- Simplified logistics

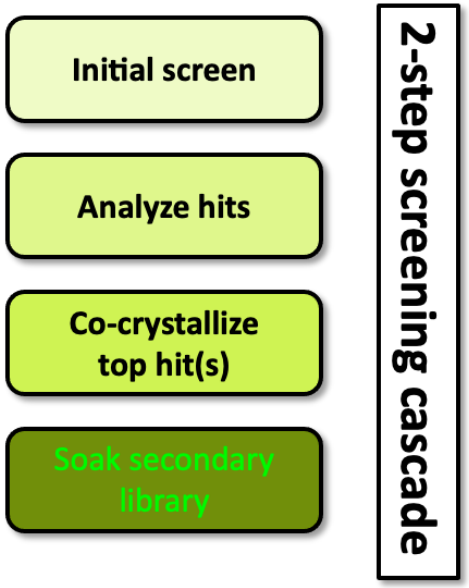
Science:

- New soaking protocols:

  Can we generate a blueprint for compound design by revisiting Fesik’s original idea?

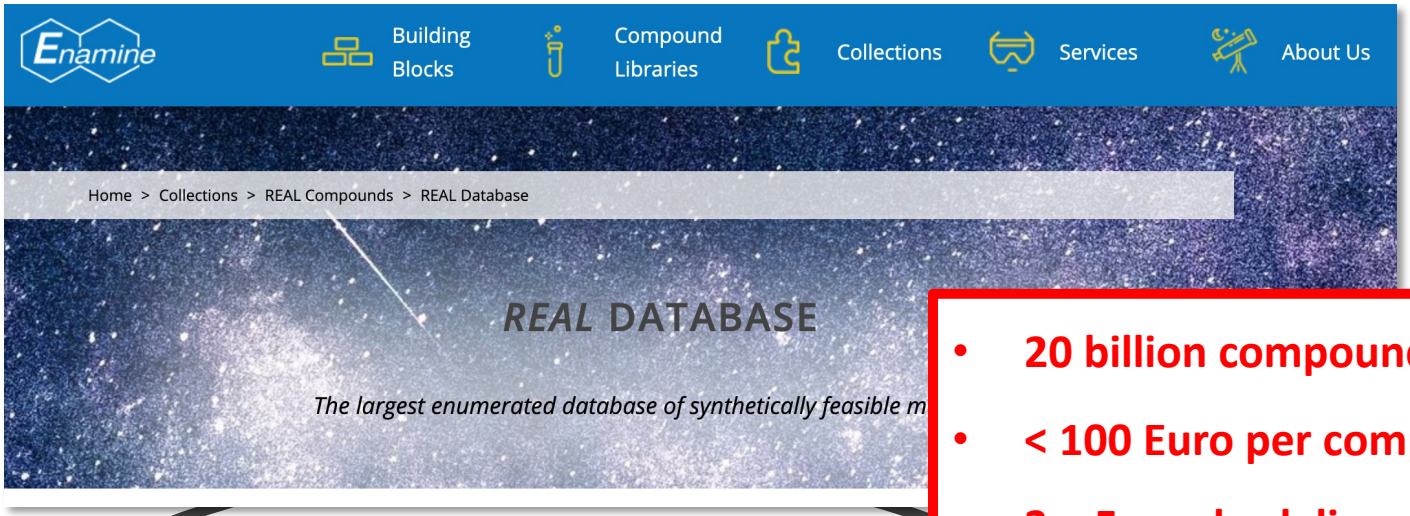
  (Shuker, S. B. et al. Discovering High-Affinity Ligands for Proteins: SAR by NMR. Science 274, 1531–1534 (1996))





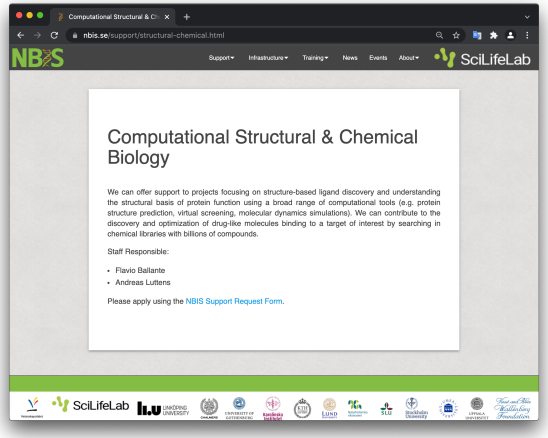
Future plans: accelerated fragment to lead process

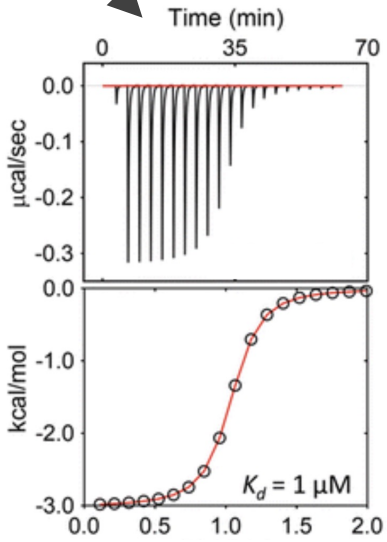
"fragment to µM binder for 1000 Euro…"



- **20 billion compounds**
- **< 100 Euro per compound**
- **3 – 5 weeks delivery time**

https://nbis.se/support/structural-chemical.html

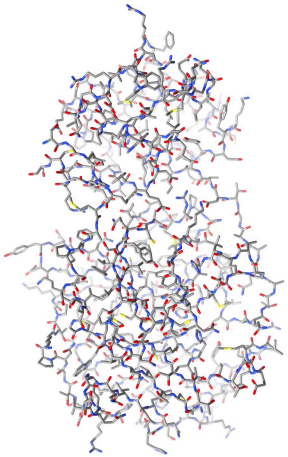




MAX IV

FragMAX beyond fragments

"automation and standardization of experiments"



fragments for exploring conformational landscapes

Today: "MX as an assay"

- FragMAX is a generic facility for large-scale crystal preparation
- Versatile platform for bespoke experiments…
- Link between MAX IV and LP3 (see Wolfgang Knecht's talk)

Tomorrow(ish): "Screening by RT & SSX experiments"

- Scientific advantages (unbiased protein conformations)
- Procedural advantages by avoiding crystal mounting step
- Complementary to MicroMAX and BioMAX developments

How?

- Work with MicroMAX, BioMAX team & MX user community
- We need your experience with cutting-edge experiments and science
- **Get in touch if you are interested! How can we help?**