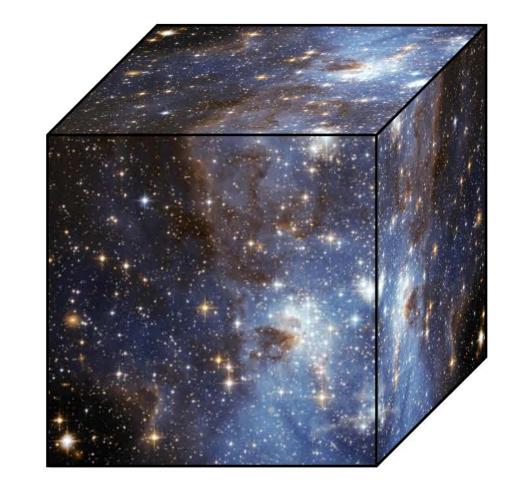# F2X-Universal and F2X-Entry:
structurally diverse compound libraries for crystallographic fragment screening

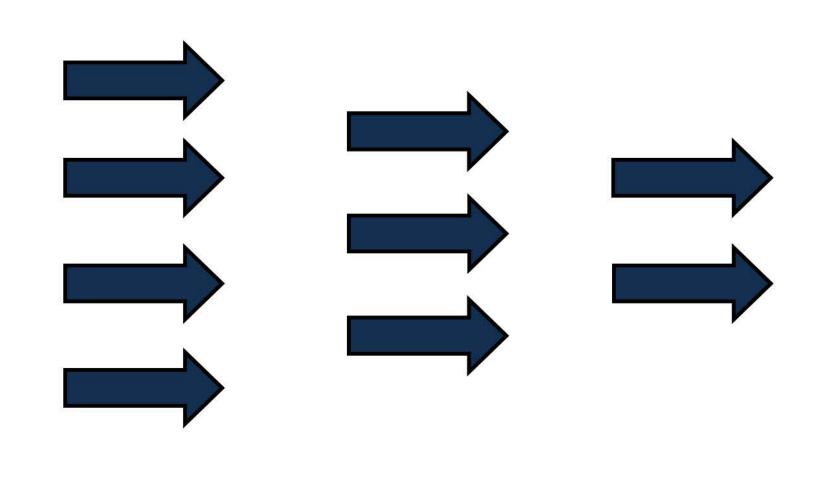Jan Wollenhaupt[1,2], Alexander Metz[1], Tatjana Barthel[2], Gustavo M. A. Lima[3], Andreas Heine[1], Uwe Müller[2,3],
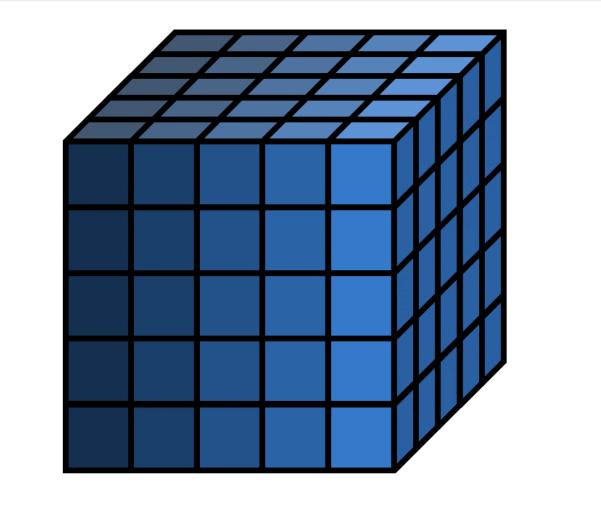
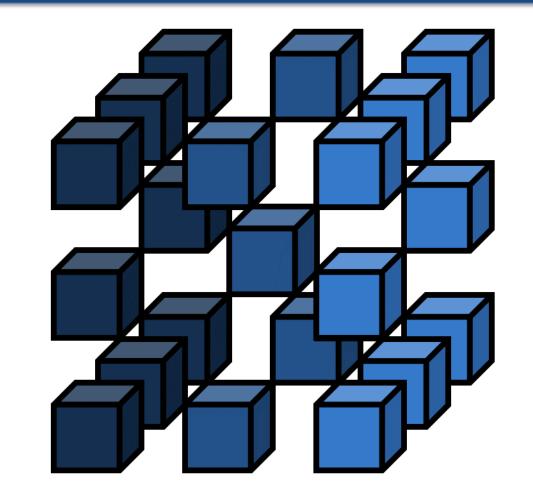Gerhard Klebe[1], Manfred S. Weiss[2]

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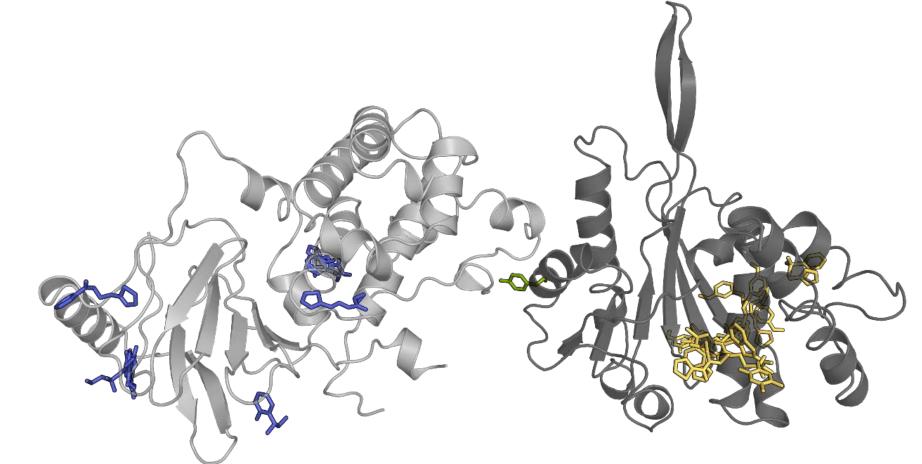manfred.weiss@helmholtz-berlin.de

Chemical space of commercially available fragments

medicinal chemistry filtering & clustering by pharmacophors + shape
Details on poster of Alexander Metz

1103 cluster representatives

F2X-Universal Library

96 representatives

F2X-Entry Screen

Validation campaigns for F2X-Entry Screen - high hit rates and diverse binding sites

Endothiapepsin

29 hits (30%)
37 binding events

Hits reproduced w/o DMSO
(non-binders not tested)

21 hits i.e. 72% of original hits
22 binding events with same poses
8 binding events with new poses

AR protein complex

20 hits (21%)
23 binding events

Hits reproduced w/o DMSO
(non-binders not tested)

15 hits i.e. 75% of original hits
16 binding events with same poses, 1 binding event with new pose

Largely automated analysis with FragMAXapp

Using pipelines for:
- auto-processing (i.a. XDSAPP)
- auto-refinement (i.a. fspipeline)
- Hit identification (PanDDA)

2mFoDFc mFoDFc   PanDDA   + fragment

A07

C04

E11

The efficient and versatile F2X-Entry Screen is now routinely applied for crystallographic fragment screening at HZB.

Further user examples:

Bacterial enzyme	Hit rate:	26%	(resolution ~1.3 Å)
Metabolic enzyme	Hit rate:	14%	(resolution ~2.2 Å)
(44/96 fragment screened, t.b.c.)			
Two cystein proteases	Hit rates:	4 and 7%	(resolution ~1.8 Å)
Secretory protease	Hit rate:	27%	(resolution: ~1.7 Å)

At present, the F2X-Universal Library and the F2X-Entry Screen are available for users of the macromolecular crystallography beamlines of the BESSY II synchrotron in Berlin free-of-charge on the basis of a collaboration contract. Moreover, the F2X-Entry Screen is available to everyone on the basis of a material transfer agreement for academic use.

References

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