Dr Christian Lemmen, BioSolveIT, gave this presentation at the "Streamlining Drug Discovery" symposiums held in San Diego, CA, USA on 21 April 2017 and Cambridge UK on 18 May 2017.

**Abstract**

20 years ago - 1996 - is when the first FlexX docking publication appeared, which is still cited on a broad average more than once every week. So is docking an old hat, or are there new developments still that should be rewarded with our hats off? We will demonstrate that the latter is the case. These 20 years have been 20 years of active research improving the basic strategy piece by piece, improving results and enlarging the applicability domain quite a bit.

In this presentation we focus mainly on one aspect of docking, namely the fact that in vast majority of cases the active site is actually not empty but provided as a protein ligand complex. Most docking applications throw out a most valuable piece of information, namely the bound ligand, before the docking is performed. This is meant not to introduce any bias and of course necessary if you do virtual screening of compound data bases - as we all did 20 years ago. However, here we want to focus on other applications: the optimization of a compound, the evolution of a fragment binder, or the SAR analysis of a comparatively narrow compound series.

In all these cases it would be stupid to throw away the information of the bound ligand instead of giving the search algorithm a hint as where to start the search. We developed a novel template based docking strategy that does exactly that, it calculates common substructures between the bound ligand and the newly designed compound and uses the fragments' binding modes as seed points for the compound placement. Not only does this lead to highly accurate placements, but it is also much faster compared to a generic docking. We describe the algorithm as well as several application cases.

REFERENCES

[1] FlexX, JMB, 261, 470–489, 1996.
[2] SeeSAR v6, BioSolveIT GmbH, www.biosolveit.de/SeeSAR

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