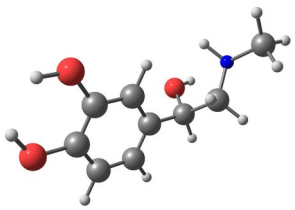
UNIVERSITY OF CAMBRIDGE

The modern day alchemist

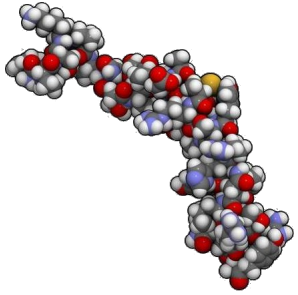
Gareth Conduit

Theory of Condensed Matter group

Action of a drug



Drug

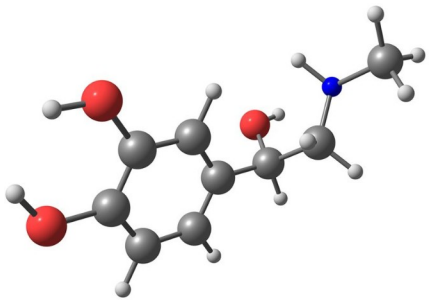


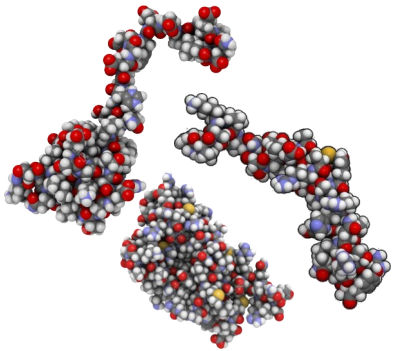
Protein

Effect

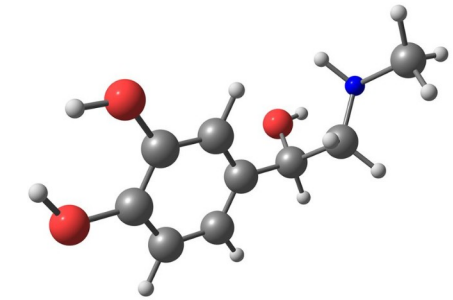
Black box prediction of drug behavior

Traditional approach is to study in a lab



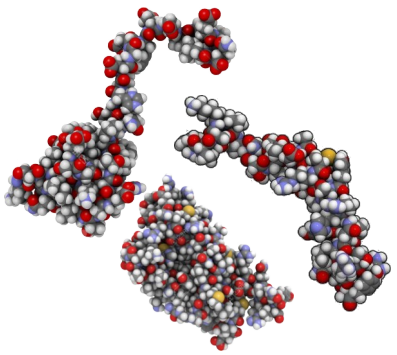


Machine learning black box

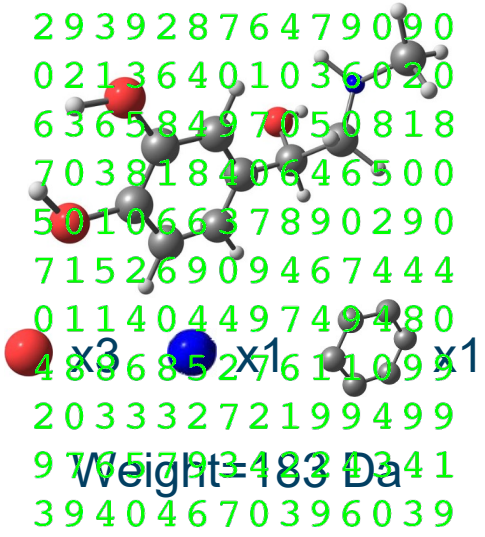


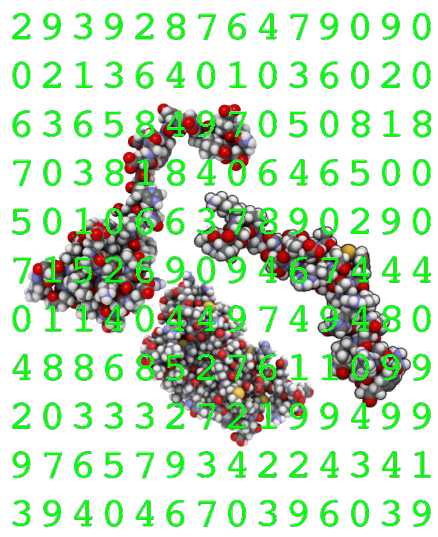
x3 x1 x1

Weight=183 Da

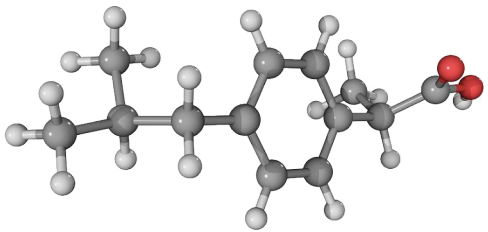


Train from existing data



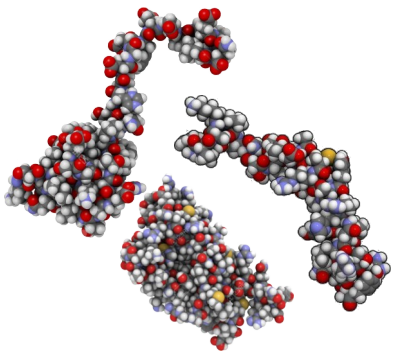


Predict properties of ibuprofen



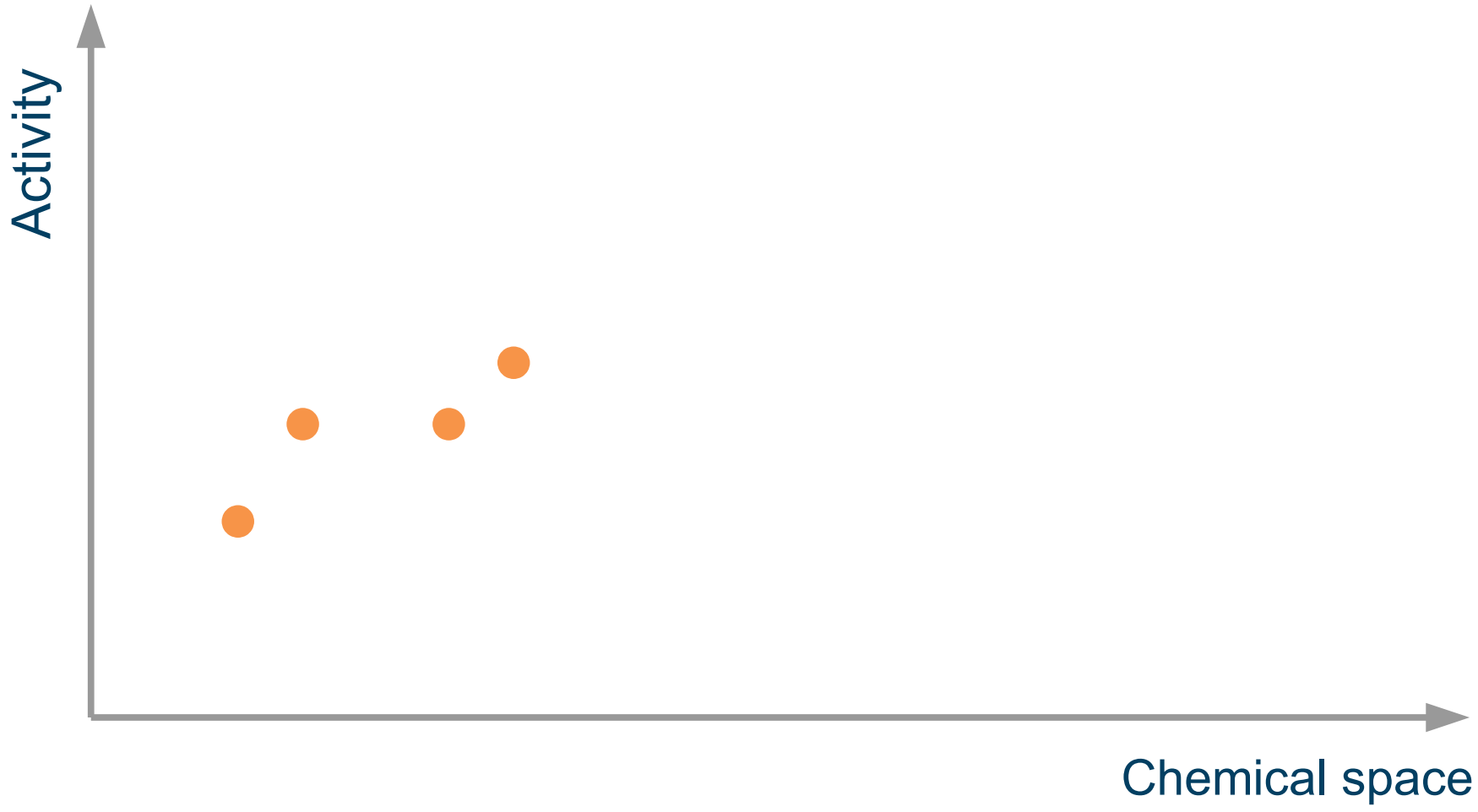
x2 x0 x1

Weight=205 Da

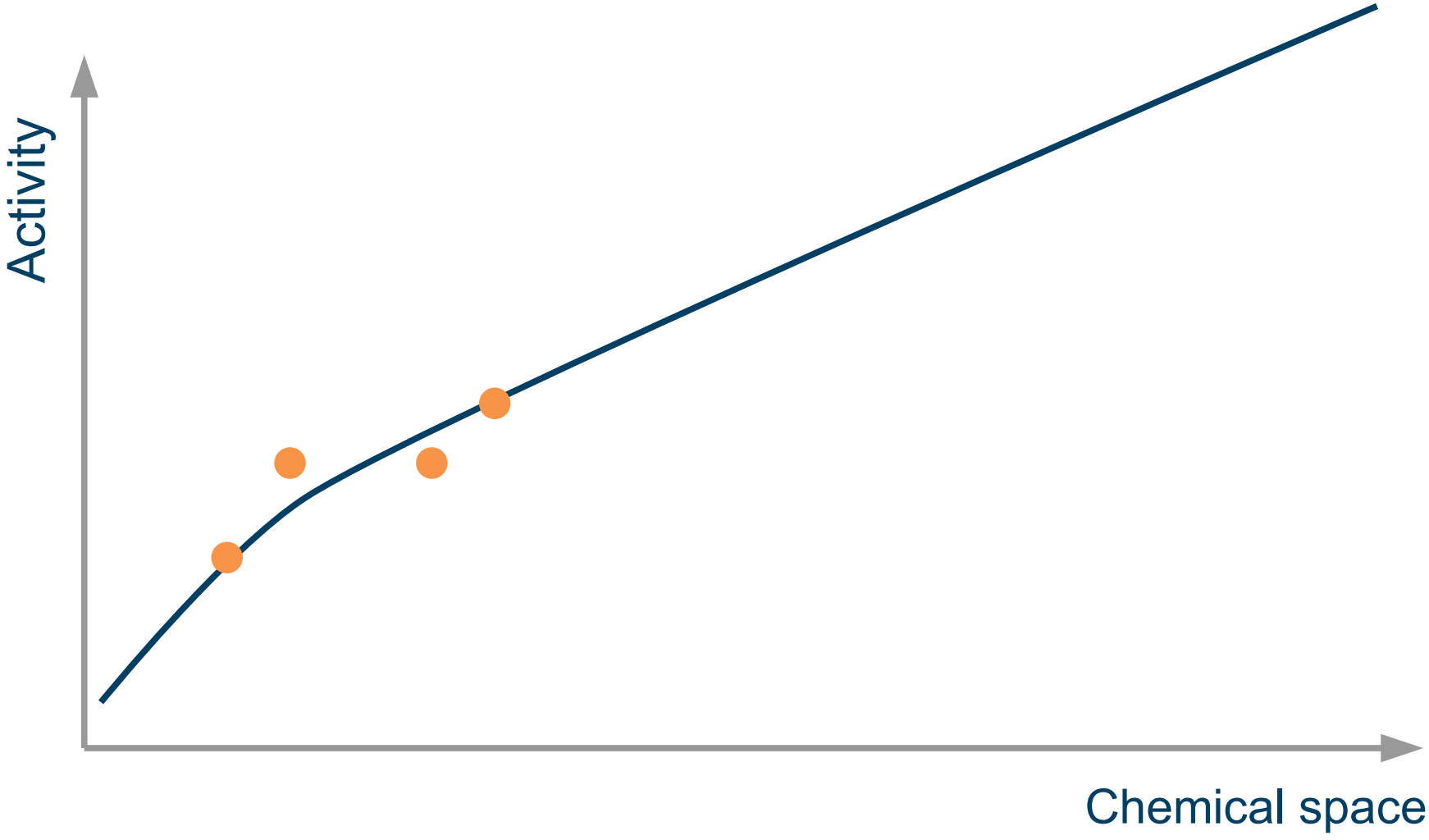


The elemental Gordian knot – MCR-SCR talk April 2015
Imputation of Assay Bioactivity Data using Deep Learning
Journal of Chemical Information and Modeling, 59, 1197 (2019)

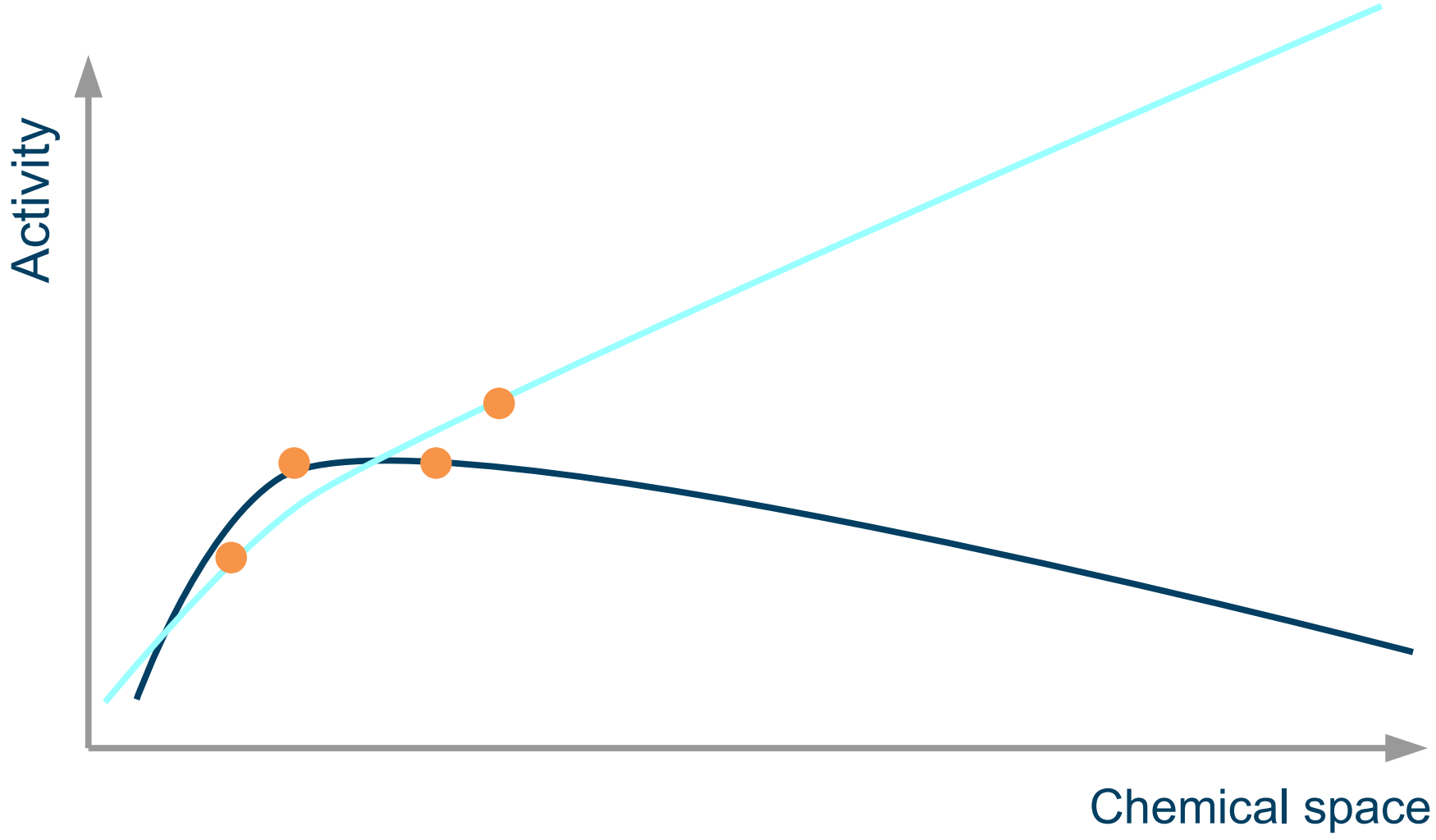
Training data for machine learning



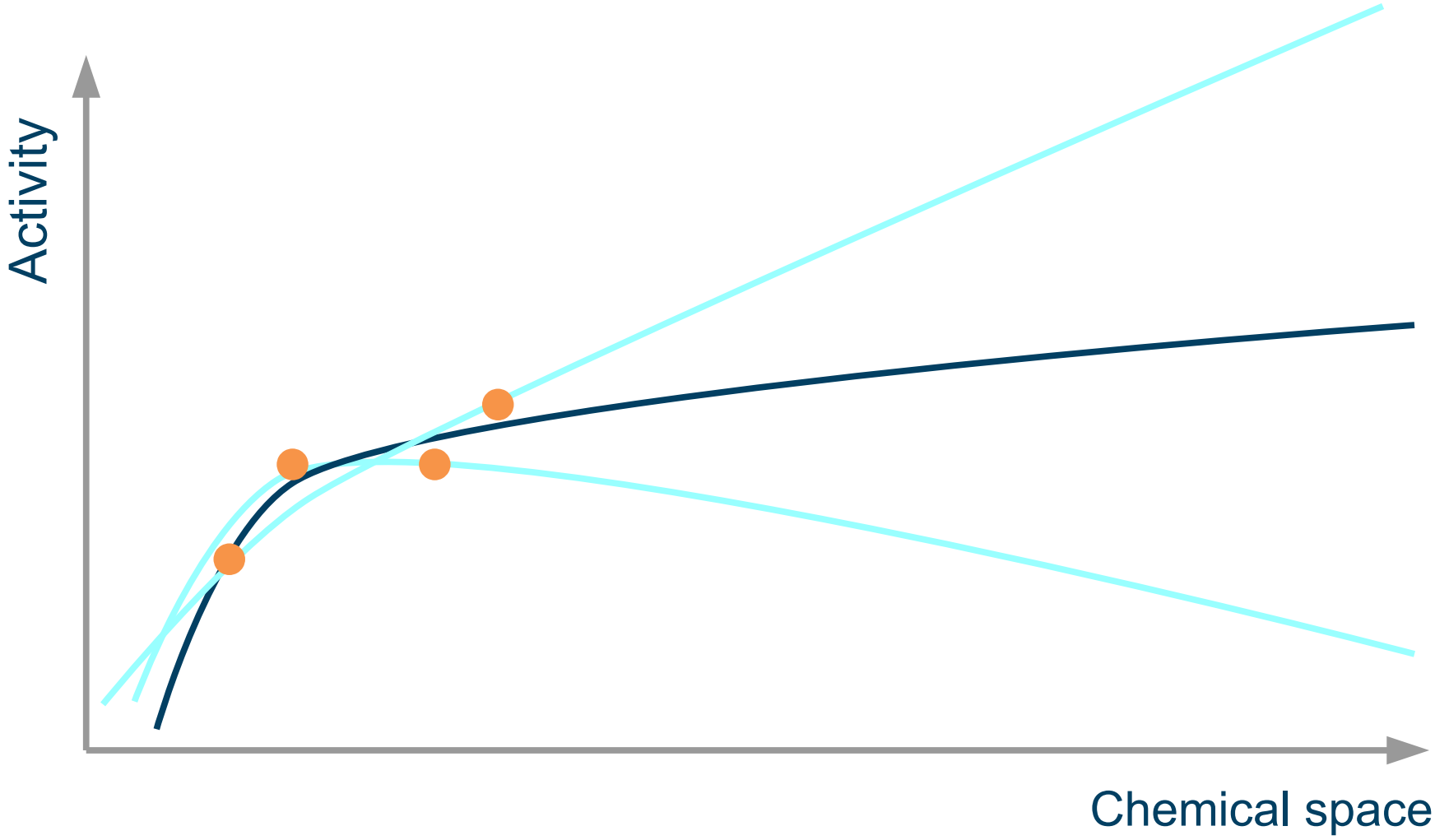
One curve that fits the data



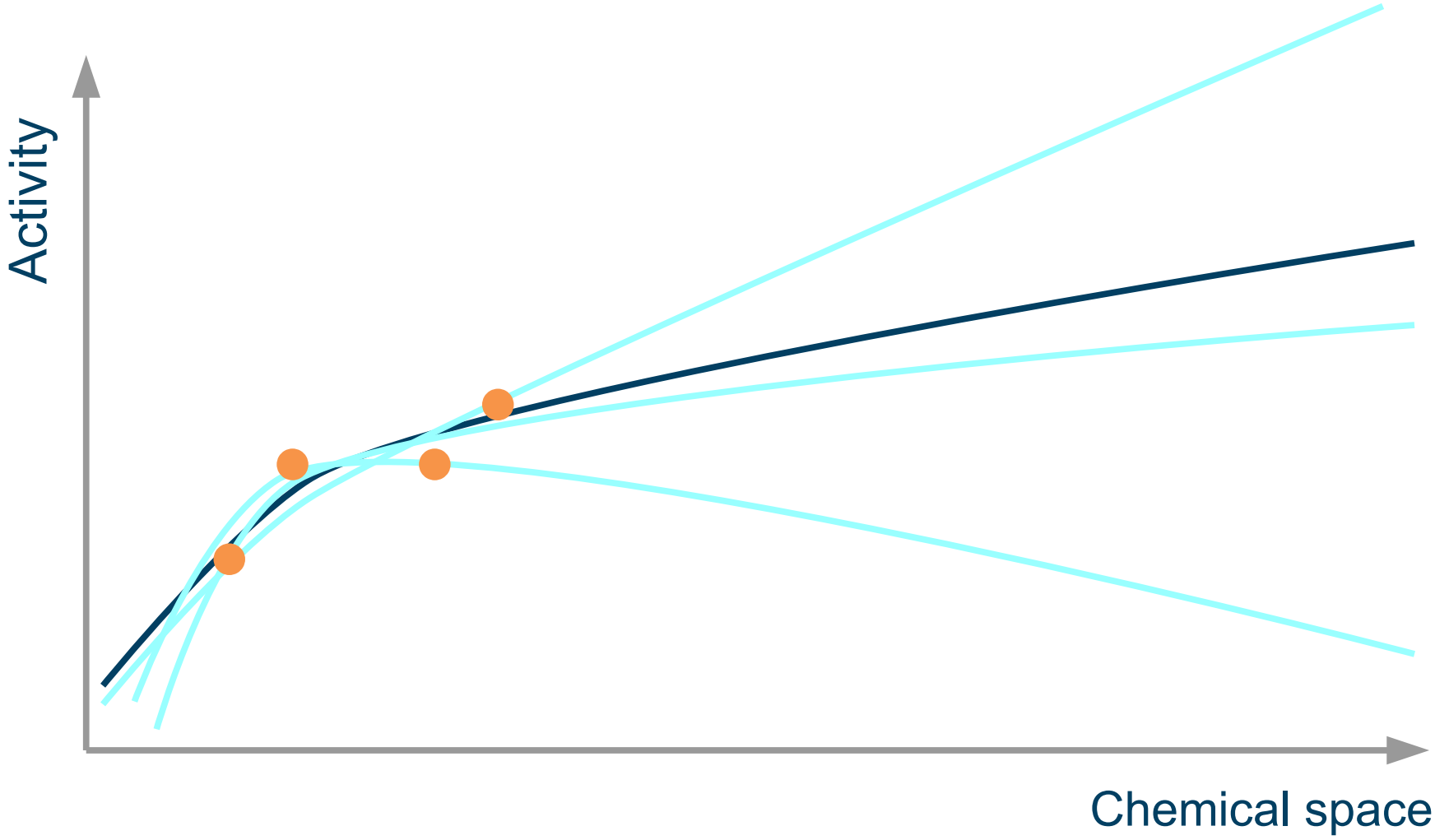
Another curve that fits the data



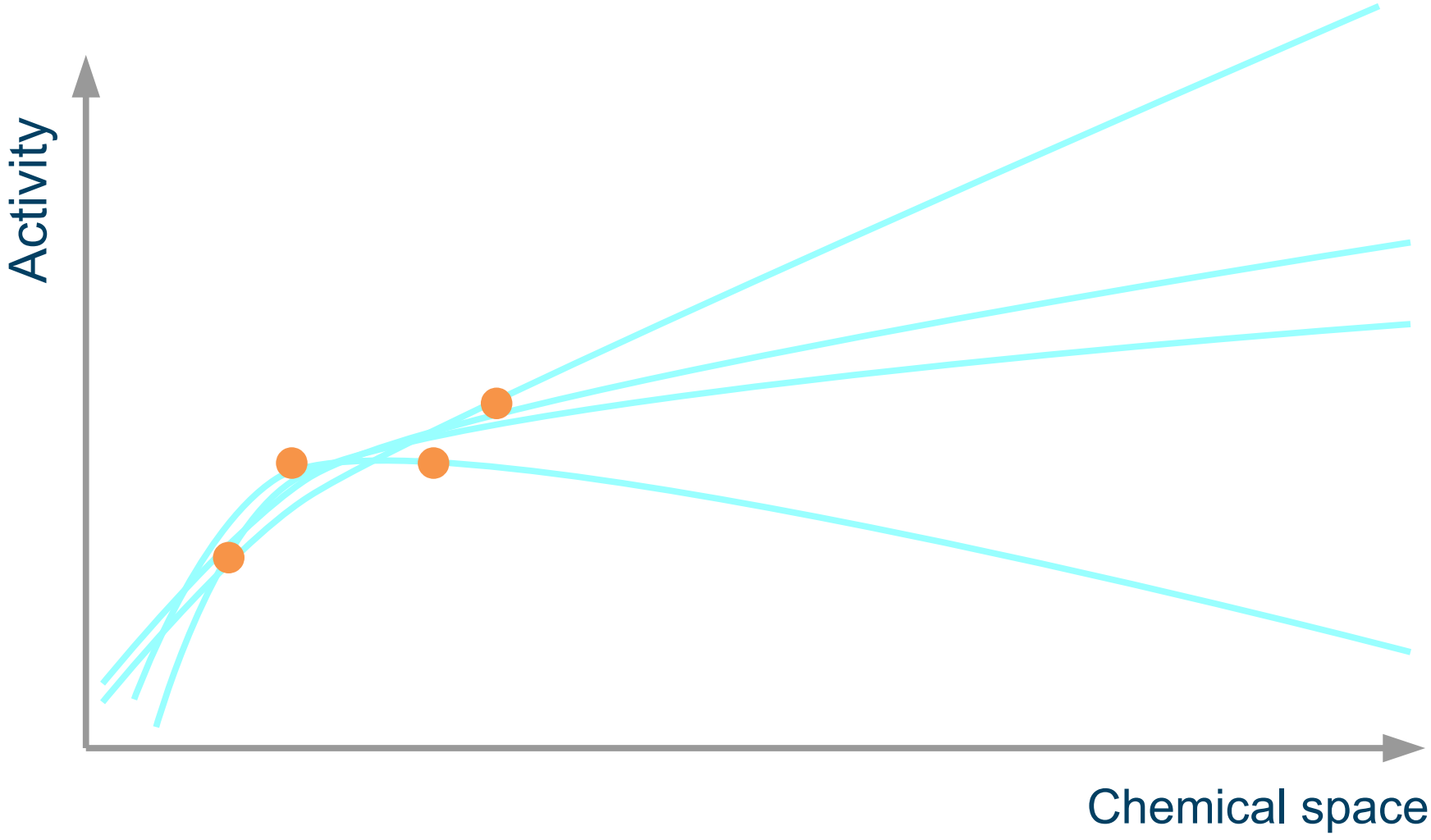
Third curve that fits the data



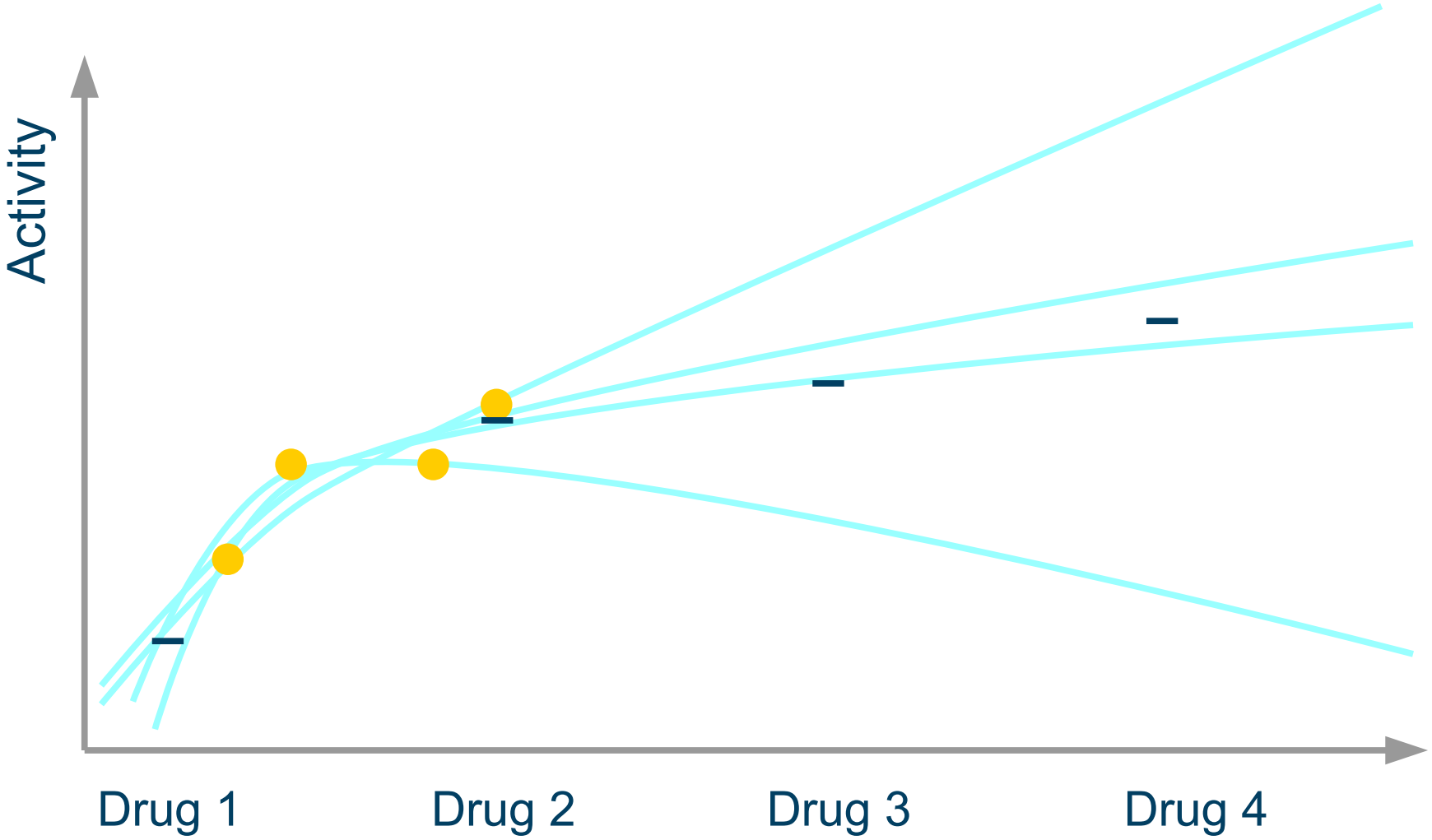
Fourth curve that fits the data



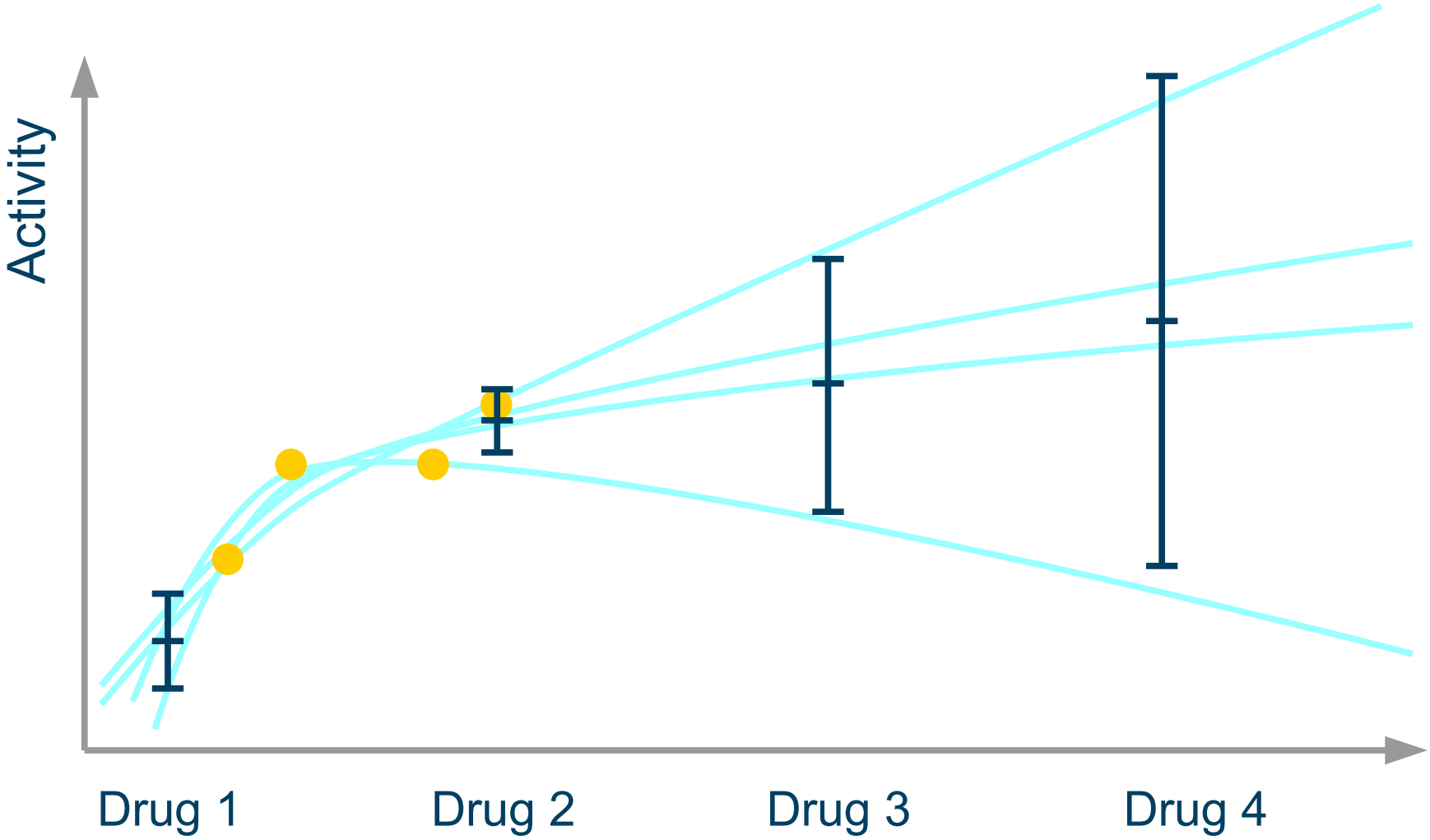
Many curves fit the data



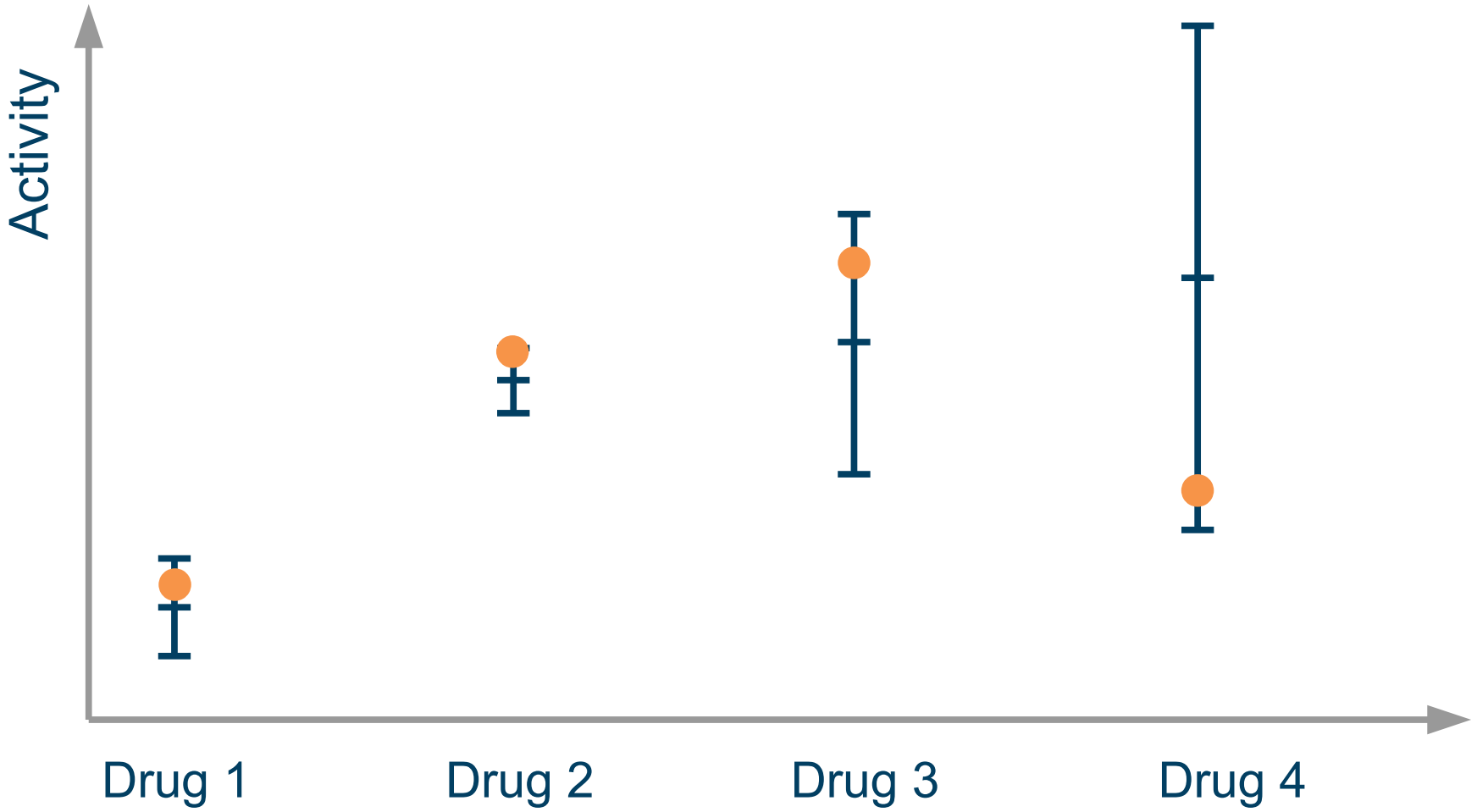
Summarize the model by the average for each drug



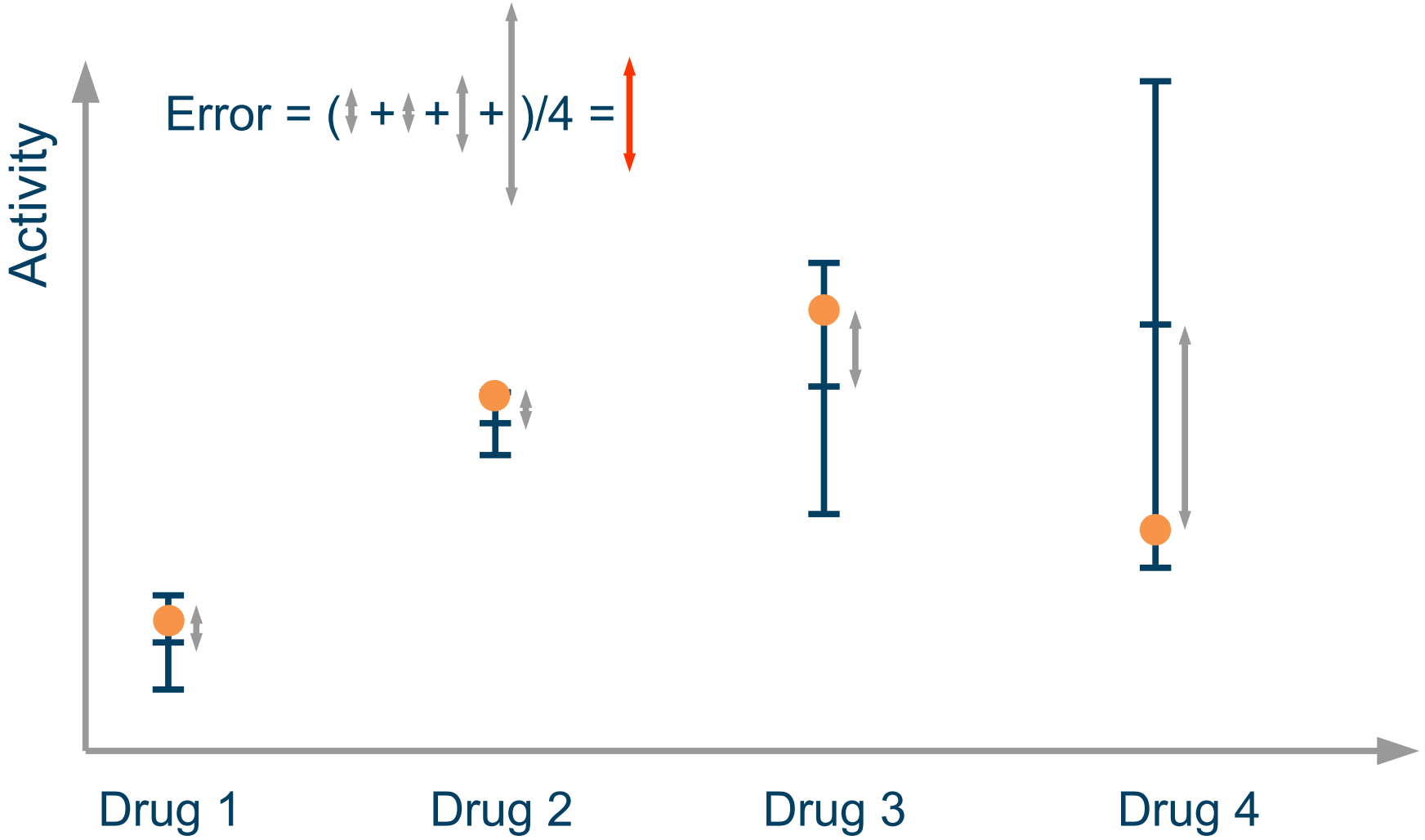
Capture the range of predictions



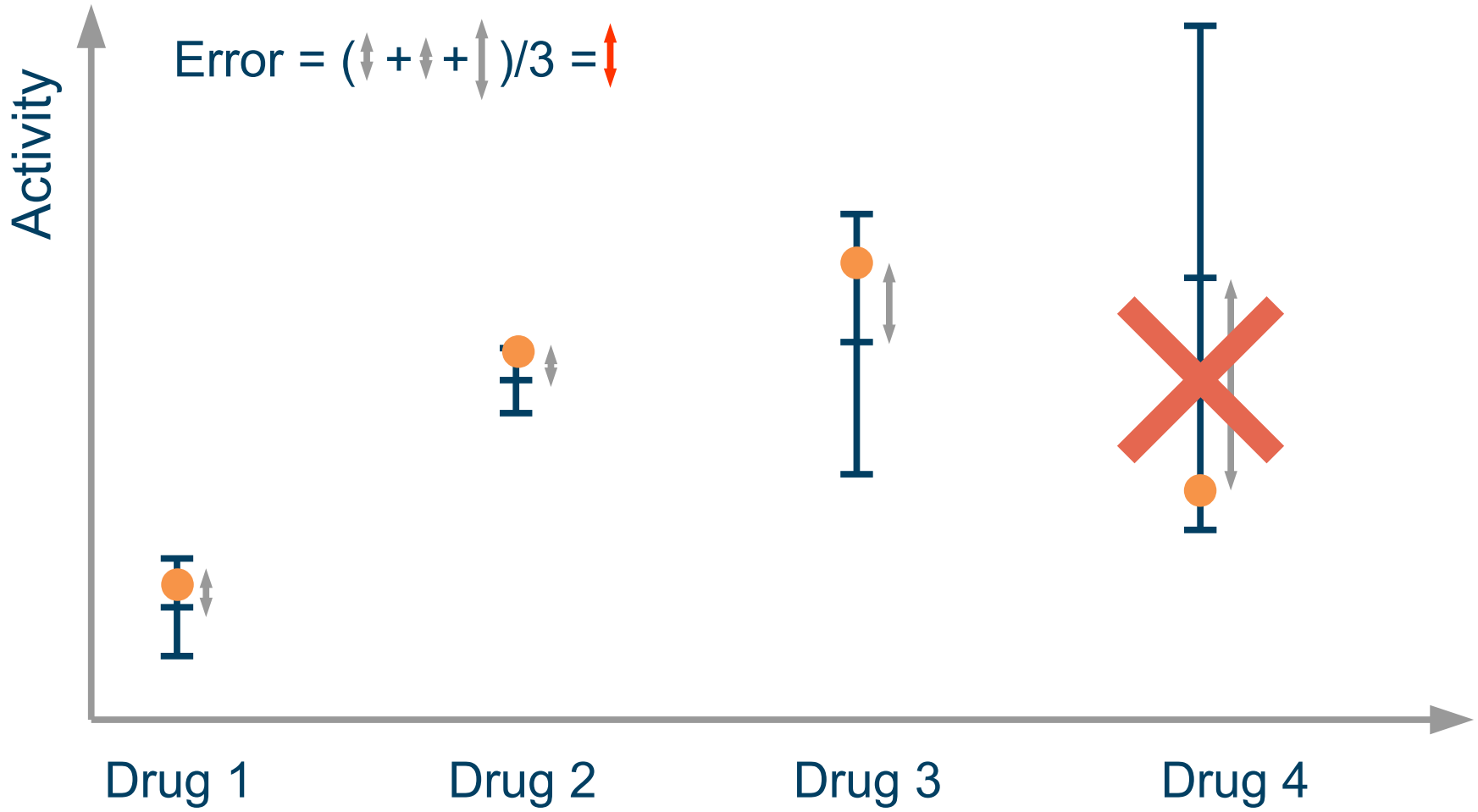
Validation data typically within one standard deviation



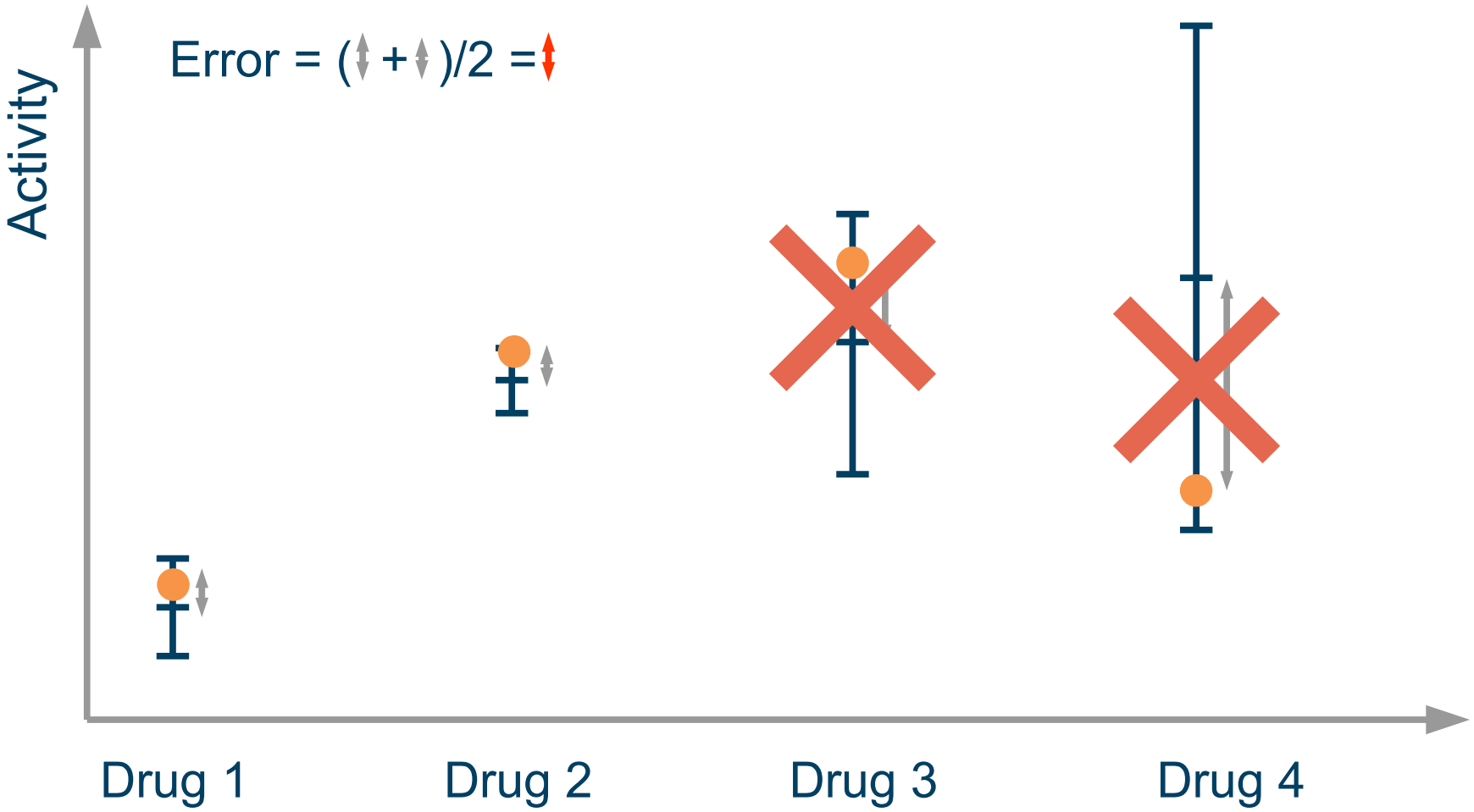
Average error is average of arrows (squared)



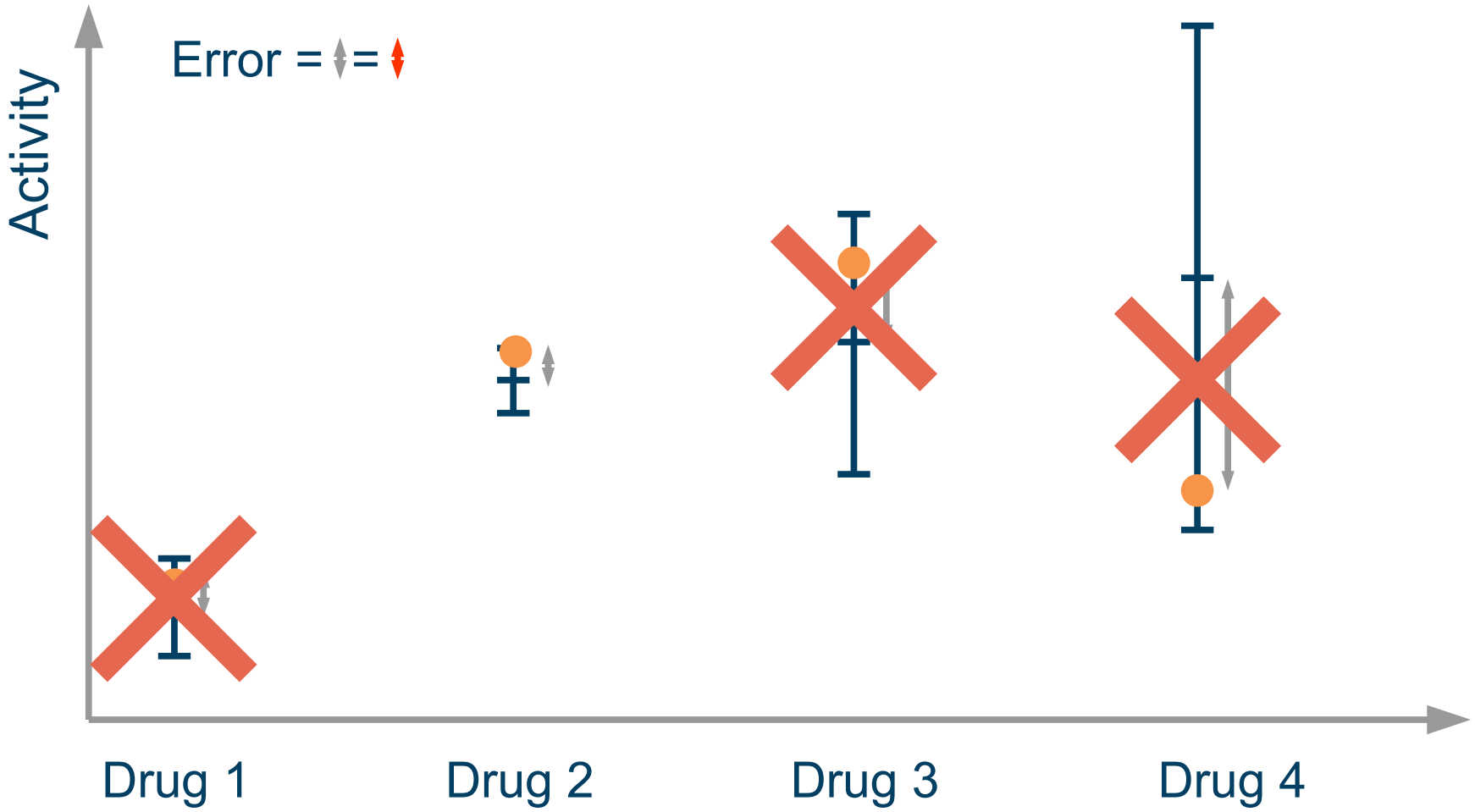
Impute 75% of data with smallest uncertainty



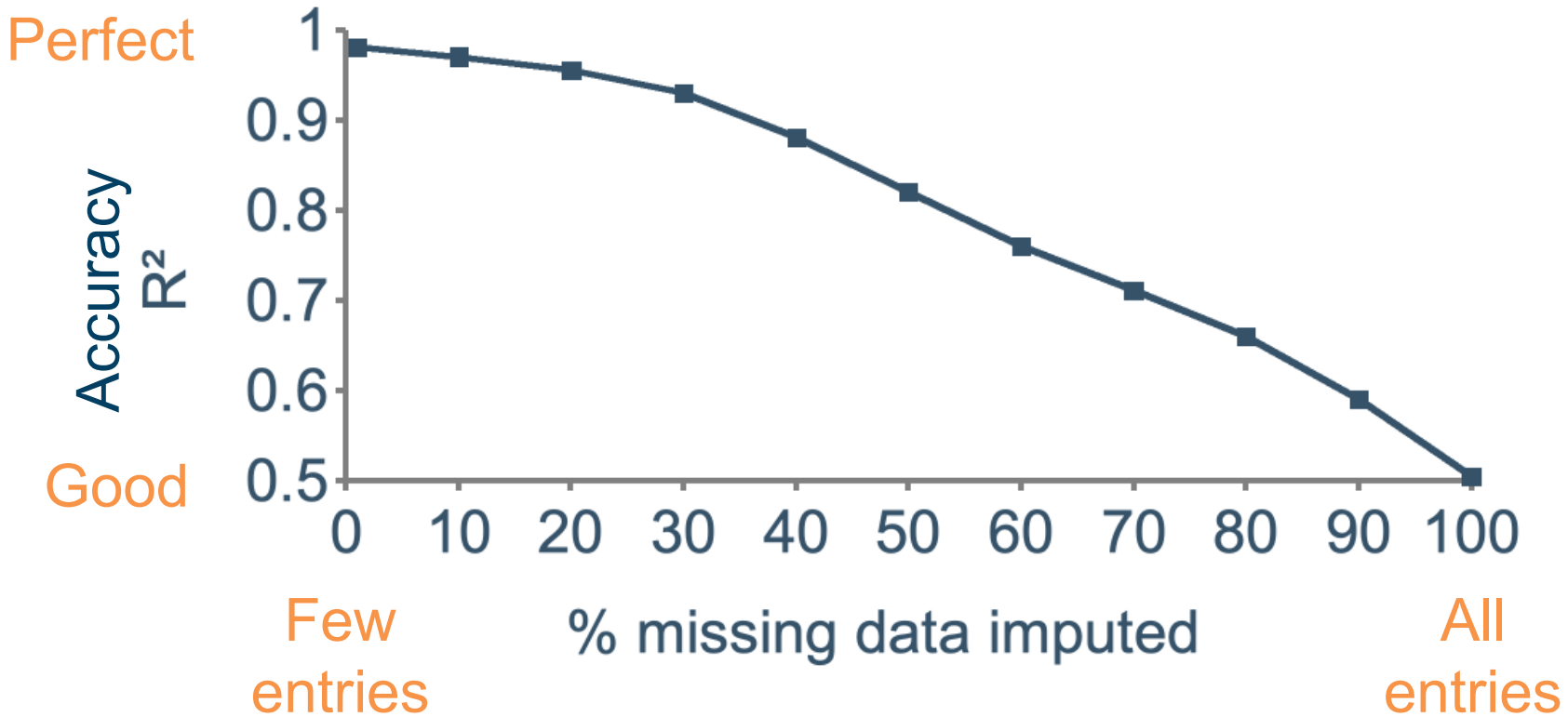
Impute 50% of data with smallest uncertainty



Impute 25% of data with smallest uncertainty

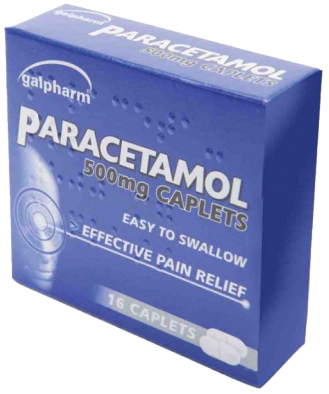


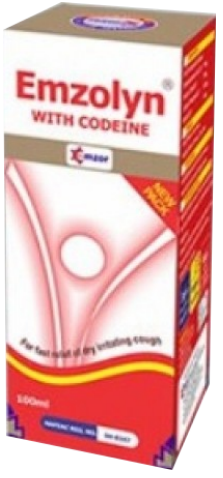
Improved performance by exploiting uncertainty



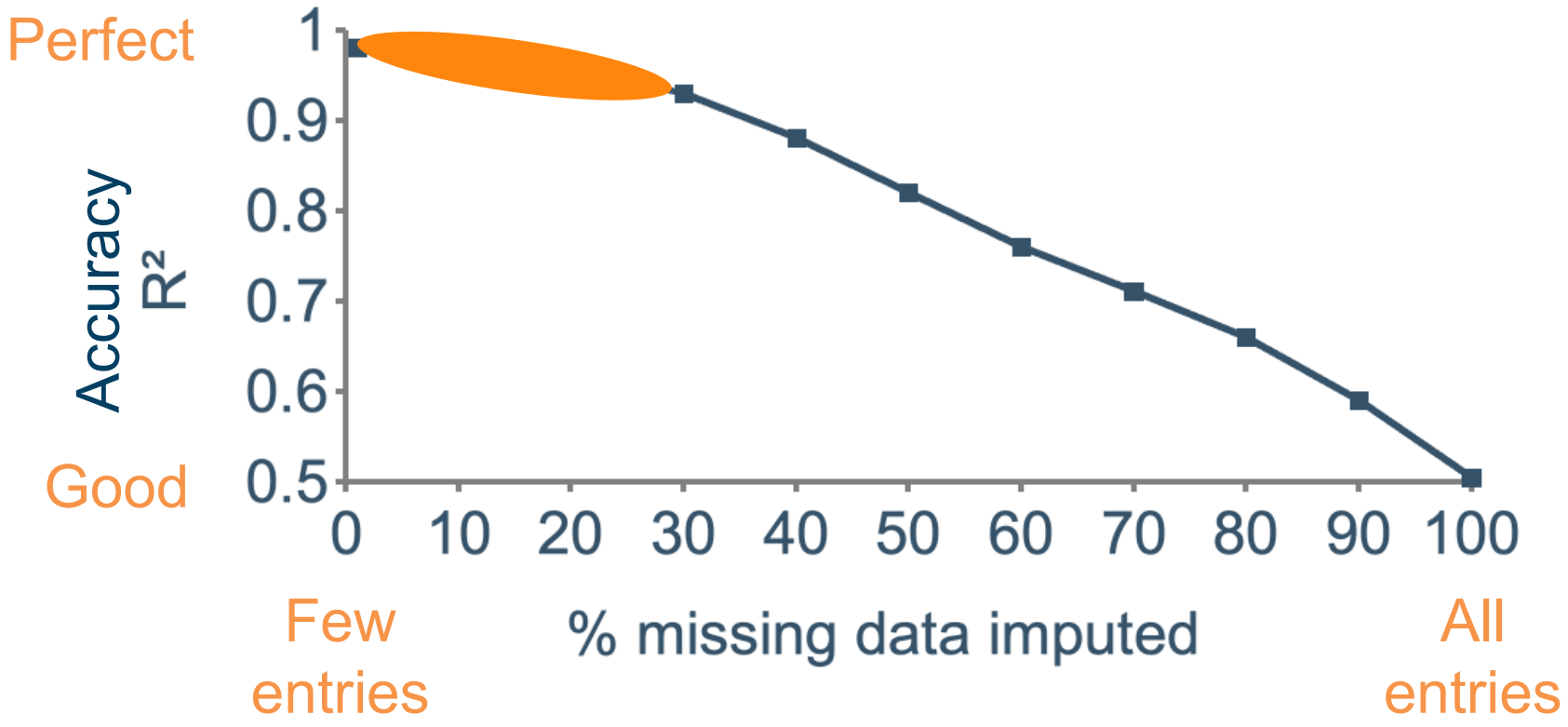
Kinase virtual screening accuracy comparable to four-concentration IC50s for realistically novel compounds
J. Chem. Inf. Model., 57, 2077 (2017)

Different drugs can treat the same ailment





Focus on just high quality predictions



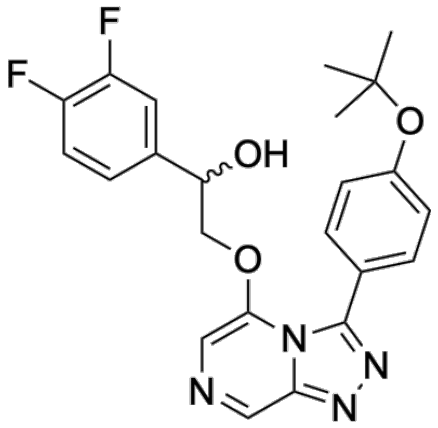
Open Source Malaria contest

OPEN SOURCE MALARIA

Looking for New Medicines

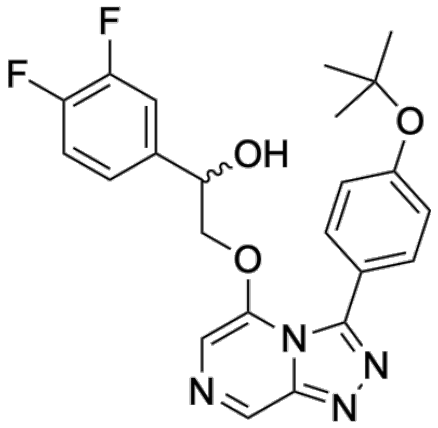
Focus on compound most likely to work

Proposed molecule



Irwin, Whitehead, Wade,
Segall, Conduit

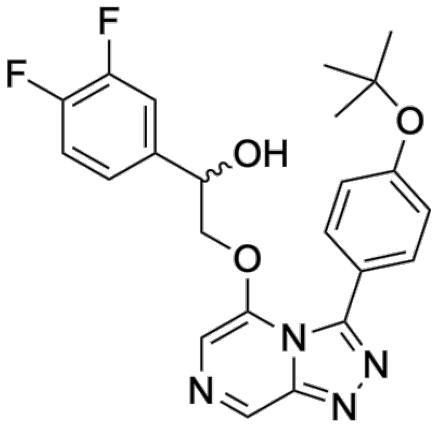
Experimental validation



Irwin, Whitehead, Wade,
Segall, Conduit

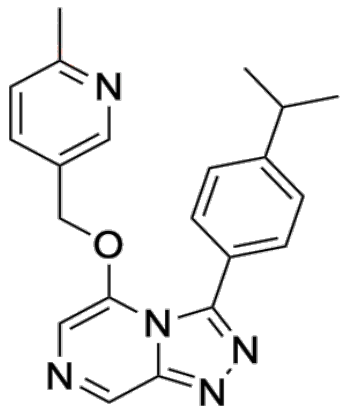
0.647 μM

Molecules proposed by other competitors



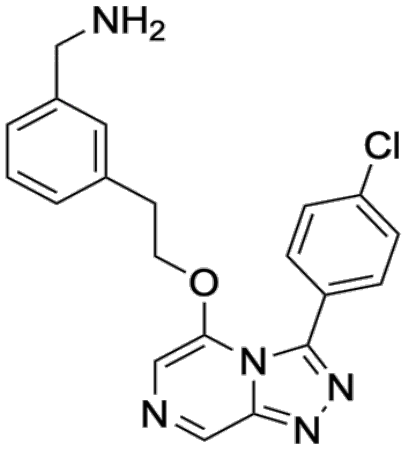
Irwin, Whitehead, Wade, Segall, Conduit

0.647 µM



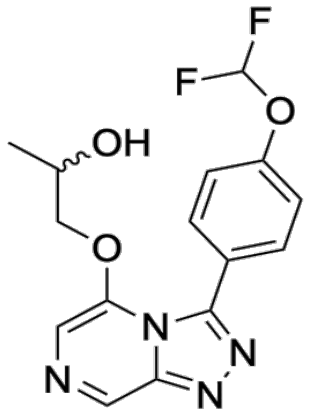
Davy Guan

>25 µM



Exscientia

10.9 µM



Molomics

>25 µM

Experimental Validation of Predictive Models in a Series of Novel Antimalarials
ChemRxiv.13194755

Summary

Exploit uncertainties to drill down on drugs most likely to work in practice

Designed experimentally verified drug in Open Source Malaria competition

Methodology also used in materials design

Taken to market through Optibrium and startup Intellegens