

The Czodrowski Lab @ TU Dortmund

AIDD Kick-Off, January 26th 2021



www.czodrowskilab.org



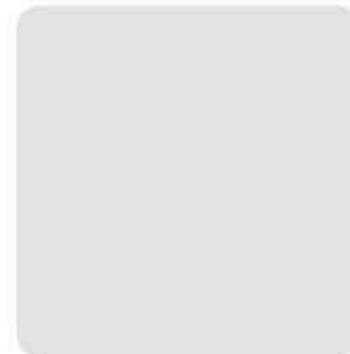
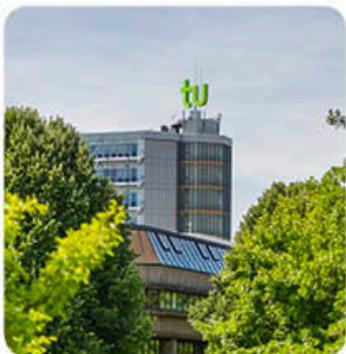
twitter.com/czodrowskipaul



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github.com/czodrowskilab



- University Professor in Dortmund since 2018
- Key research areas:



UC San Diego



Boehringer Ingelheim

MERCK

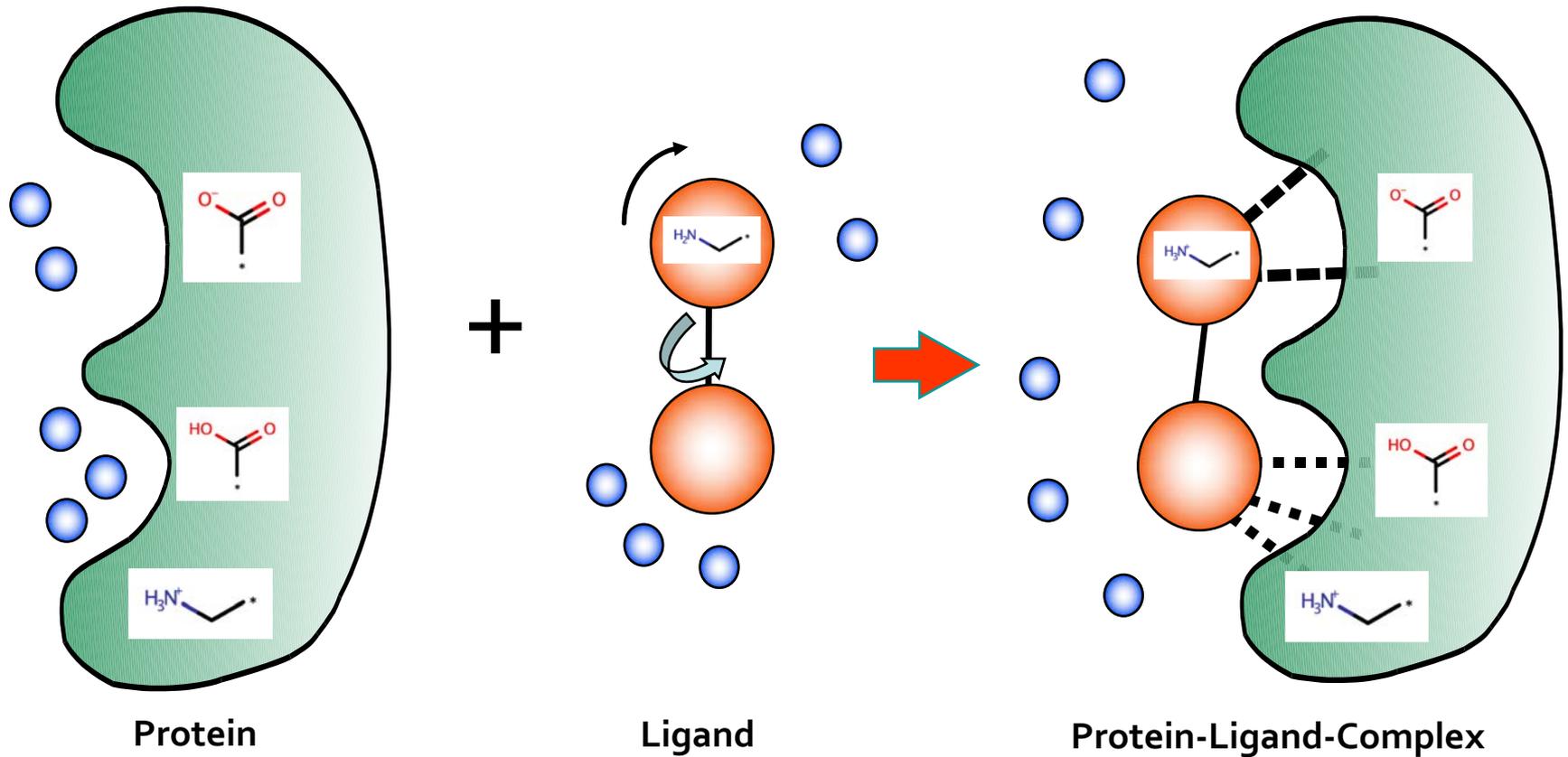


pKa measurements	Cheminformatics
ITC	Structure-based design
x-ray crystallography	Machine Learning



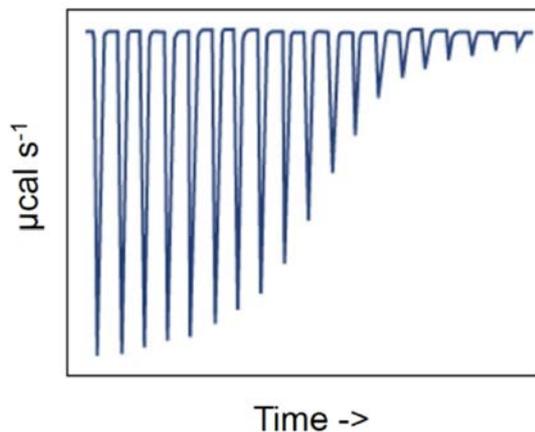
- Teaching:
 - Medicinal Chemistry, Computational Chemical Biology, Statistics
- Technologies in practice:
 - OCEAN, hERG me out, PDB2PQR 
- Community:
 - Euro-SAMPL (Statistical Assessment of Modeling of Proteins and Ligands)

Protonation effects in protein-ligand complexes

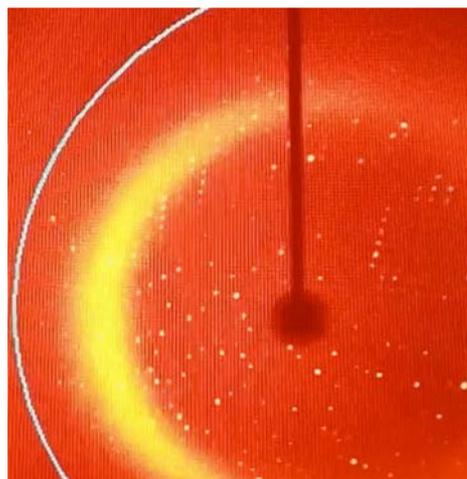


Protonation effects measured @CzodrowskiLab

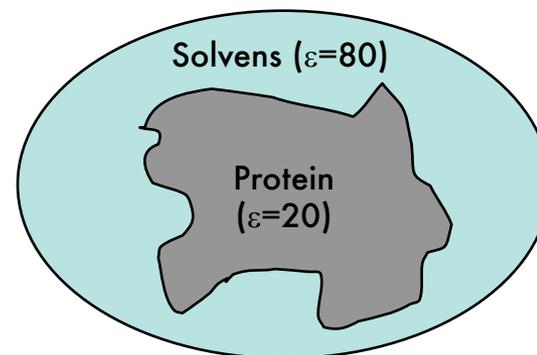
ITC



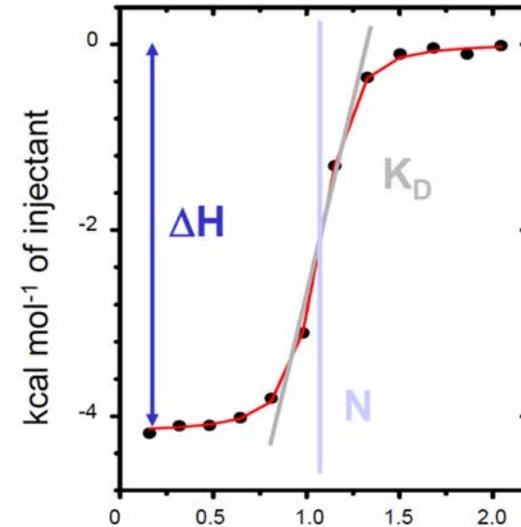
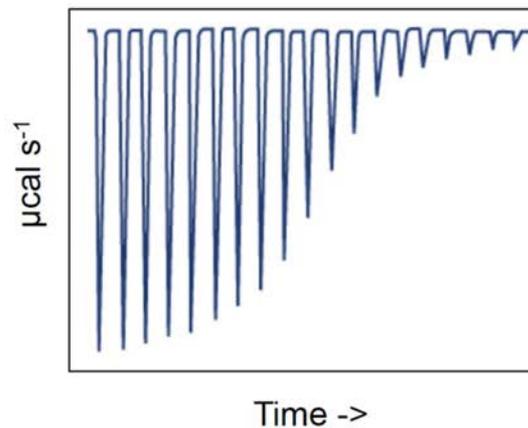
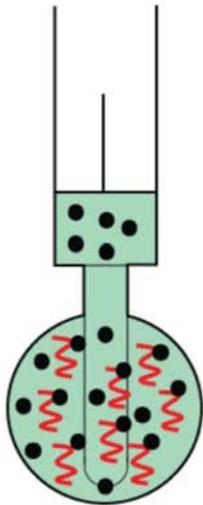
x-ray



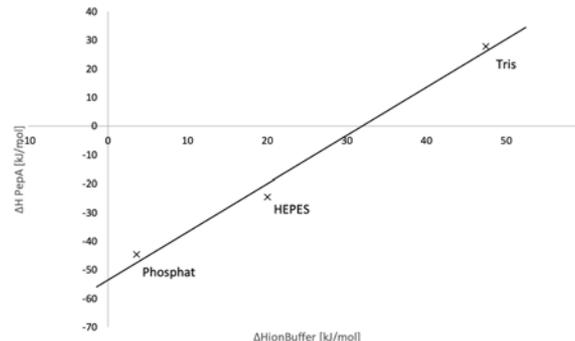
Poisson-Boltzmann



Protonation changes detected through ITC



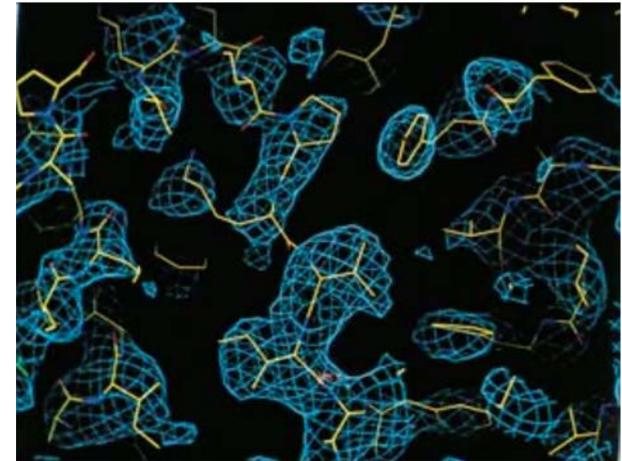
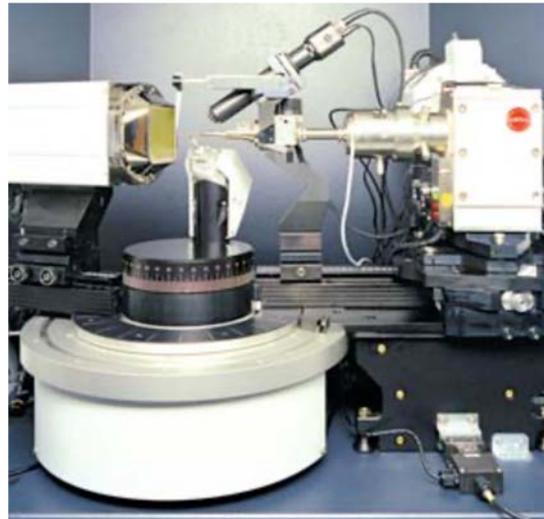
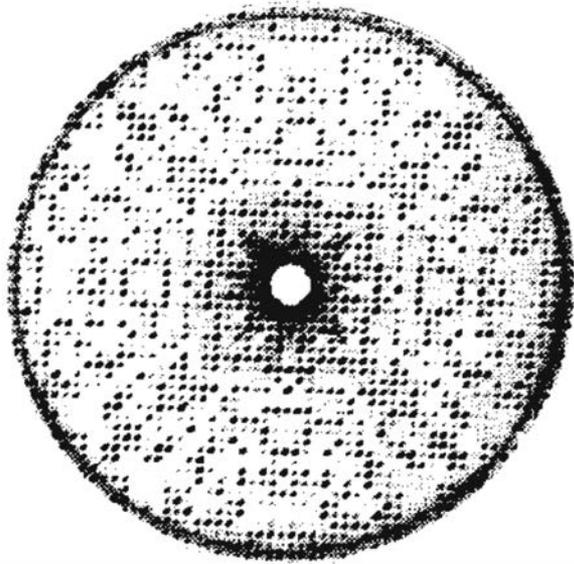
➔ Measurement in different buffers



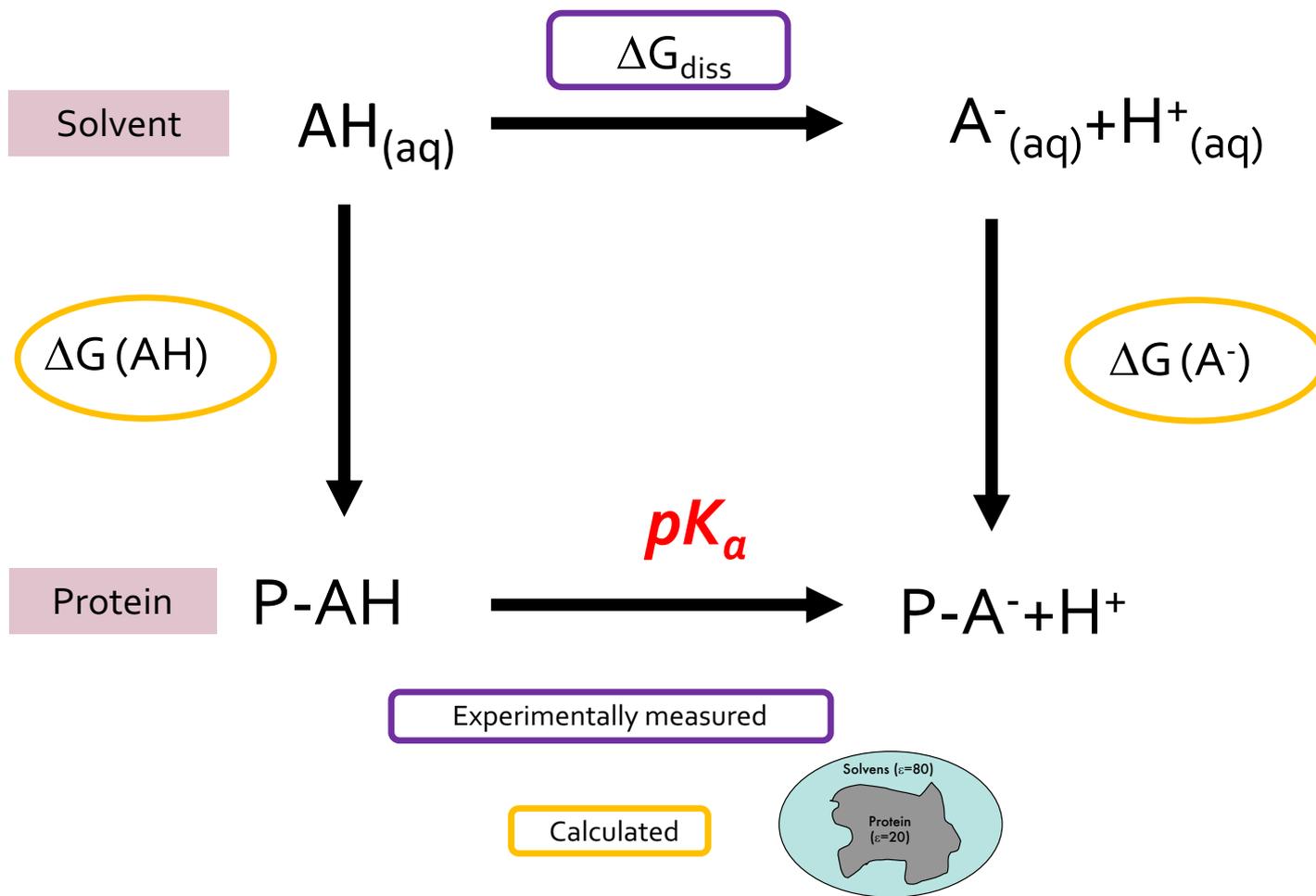
Slope of the straight line:
Macroscopic Protonation effect

$$\Delta H_{meas} = \Delta H_{bind} + n \Delta H_{ion}$$

Structure determination via x-ray



Poisson-Boltzmann calculations

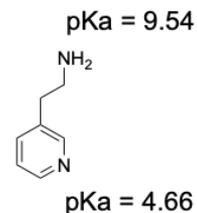
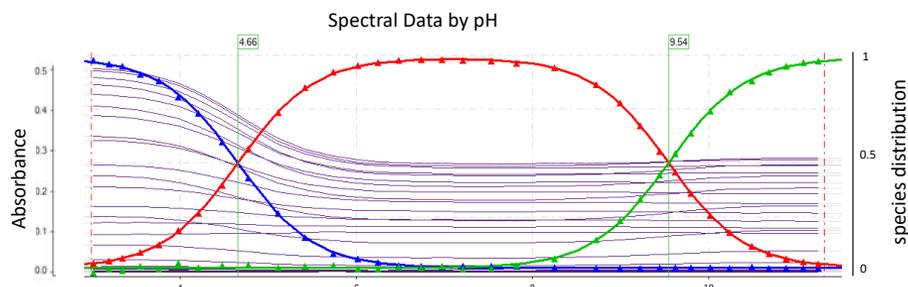
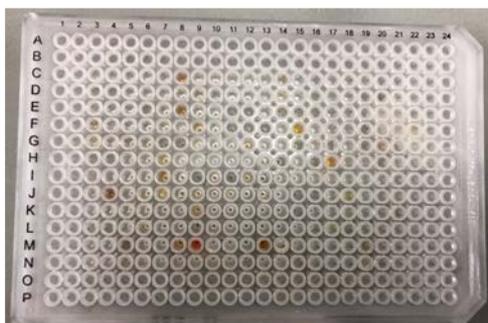




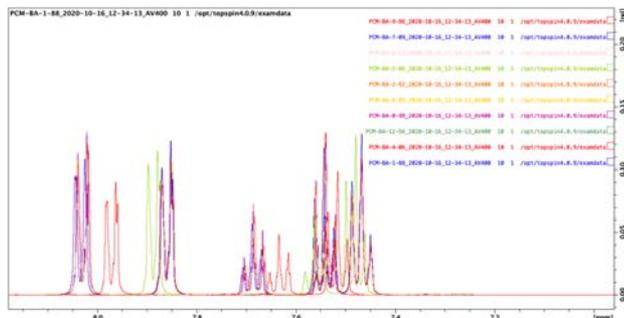
SMOL pKa measurements/predictions

600 Fragments

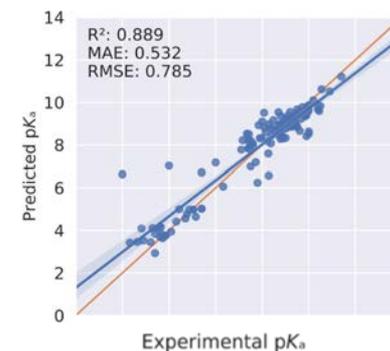
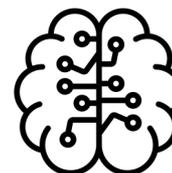
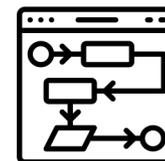
pKa-Measurement via UV/Vis



pKa-Measurement via NMR



Machine Learning



More research projects

Kudos to the team!



Presentations at the RDKit.UGM.2020 and GCC.2020

[Let it flow: VSFlow as versatile open-source tool for virtual screening](#)

[Same same but different: investigations of two almost identical kinase inhibitors](#)

[SAMPL + NFDI₄Chem = EuroSAMPL](#)

[Open source application for small molecule pKa predictions](#)

There is one more thing



A quick introduction to Cell Painting Assay

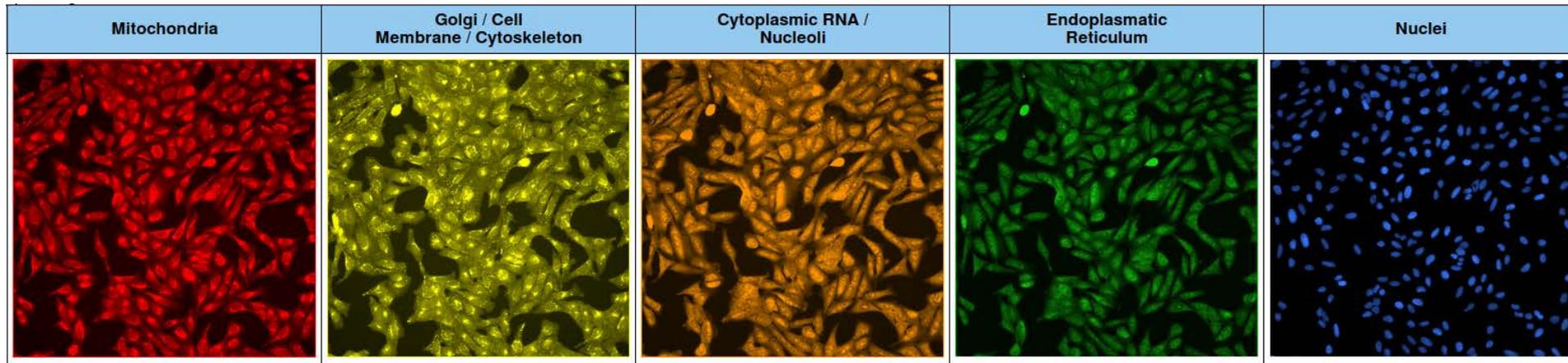
- Developed by the Carpenter group from Broad Institute (Bray et. al 2016)
- This assay involves staining of different cellular components by different dyes with distinct excitation-emission range
- Result: an unbiased, multiparametric, high-throughput and high-resolution image-based cell assay where changes in cells' morphology caused by different treatments are quantitatively recorded

Bray, M., Singh, S., Han, H. *et al.* Cell Painting, a high-content image-based assay for morphological profiling using multiplexed fluorescent dyes. *Nat Protoc* **11**, 1757–1774 (2016).

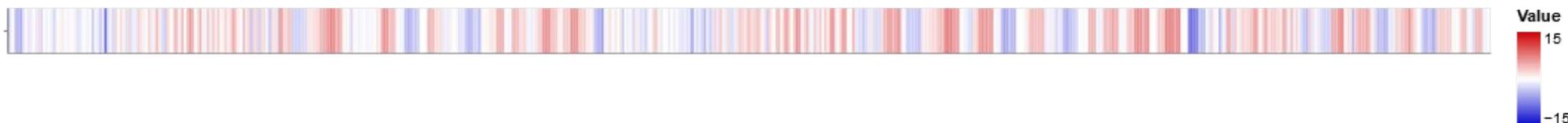


The MPI Cell Painting Dataset

25k measurements of 14k compounds (4k reference, 10k research compounds)

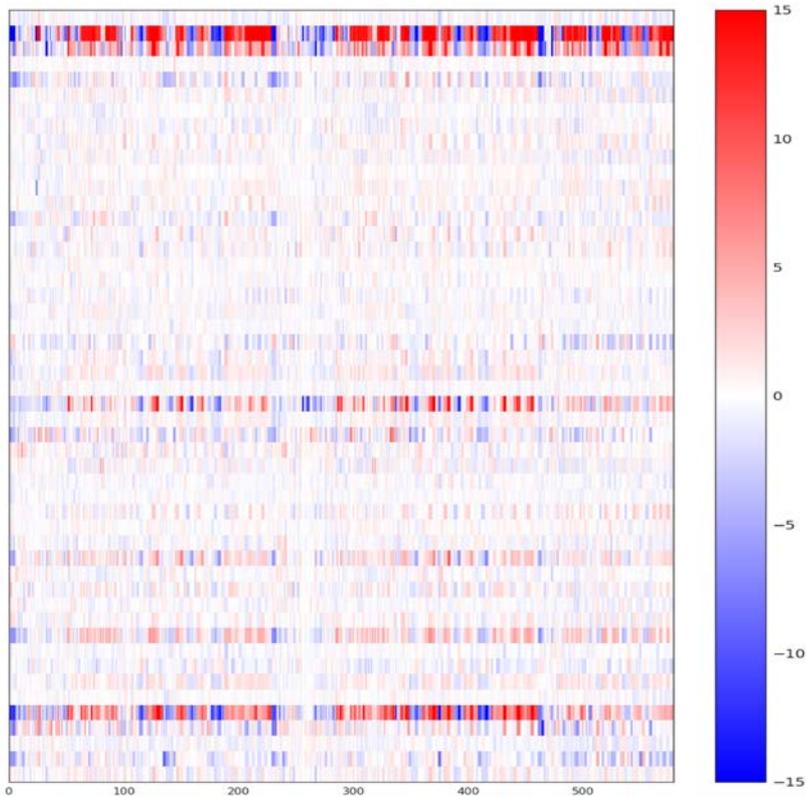


CellProfiler (open-source software developed by the Broad Institute) extracts numerical features from microscope images and then the MPI pipeline calculates morphological features per test compound.

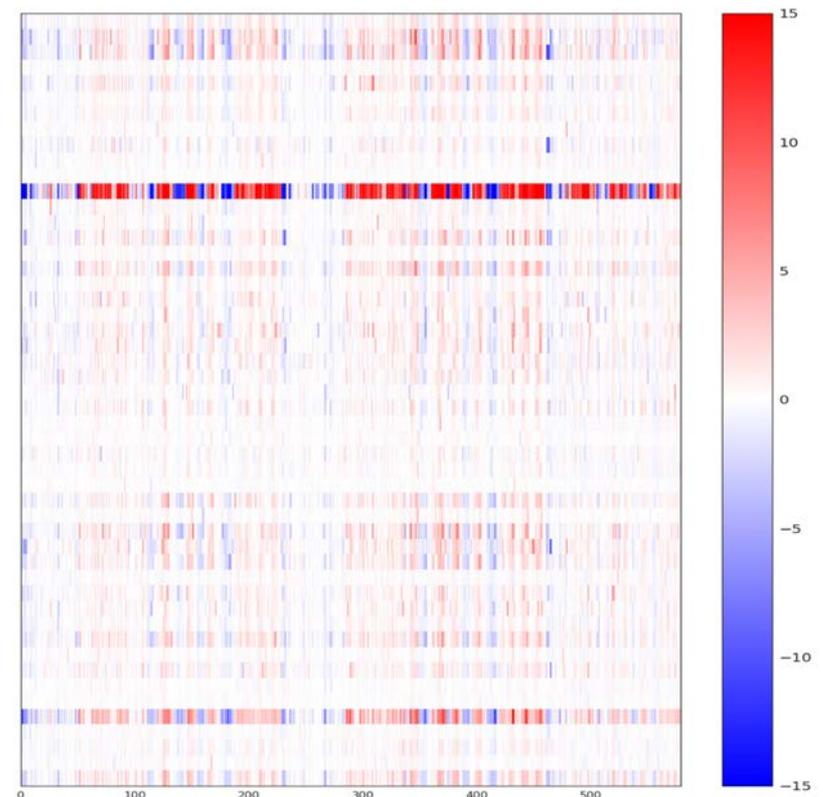




Ensemble Model Approach



Original CP Profile of 50 compounds



Predicted CP Profile of the same compounds

More to come soon...