

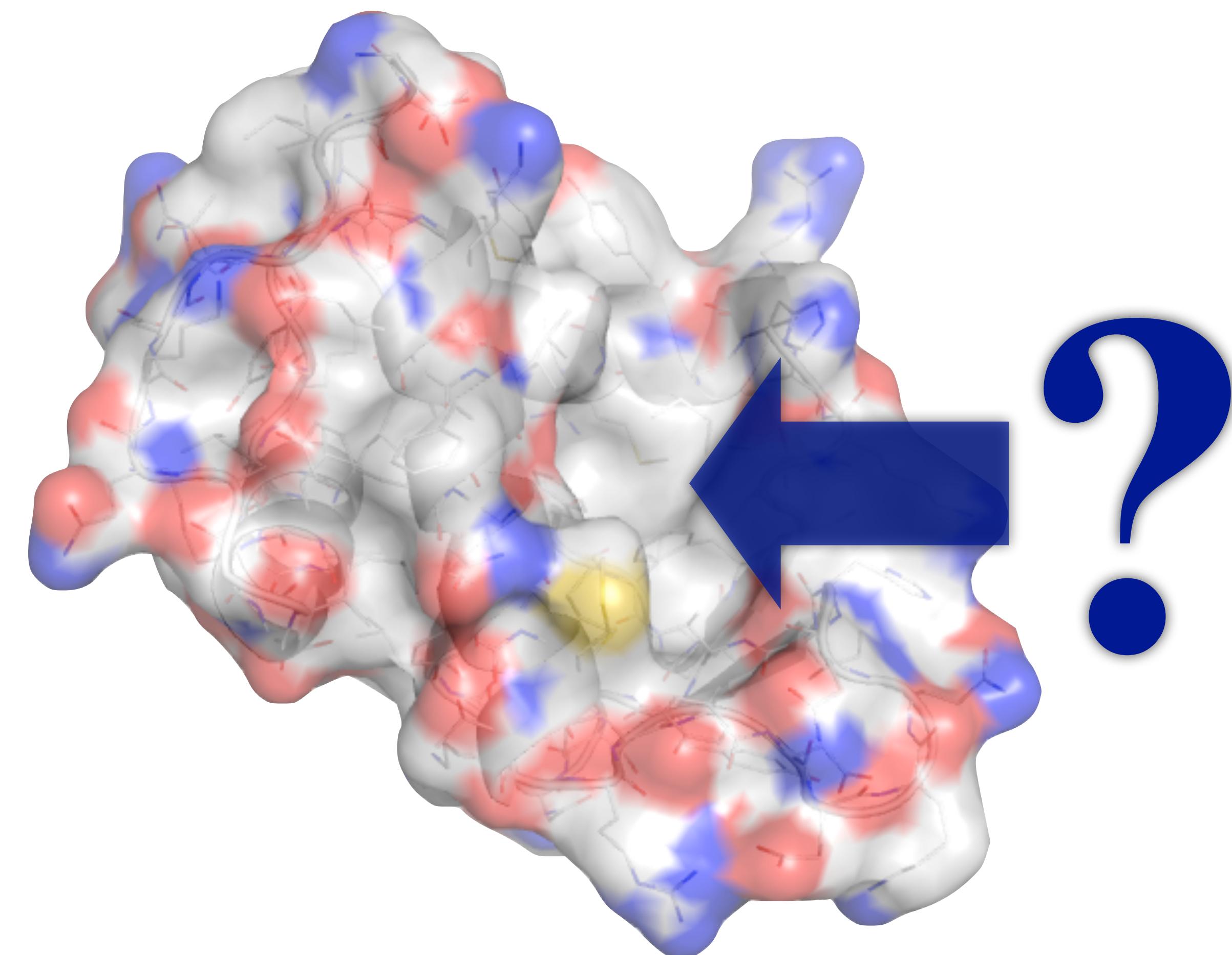
Koes Group Research Overview

*Removing barriers to
computational drug
discovery one bit at a time*

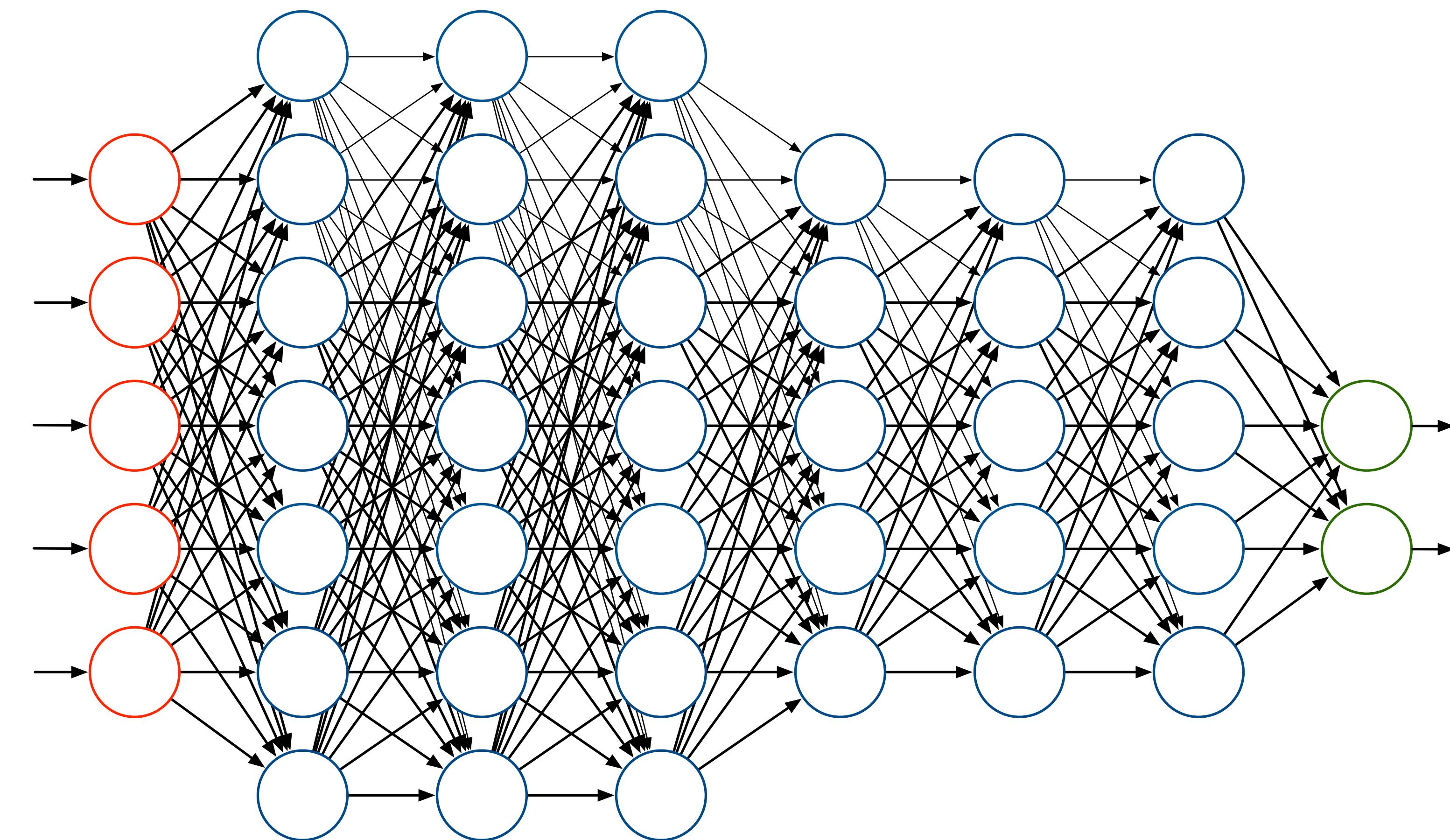
8/30/2019



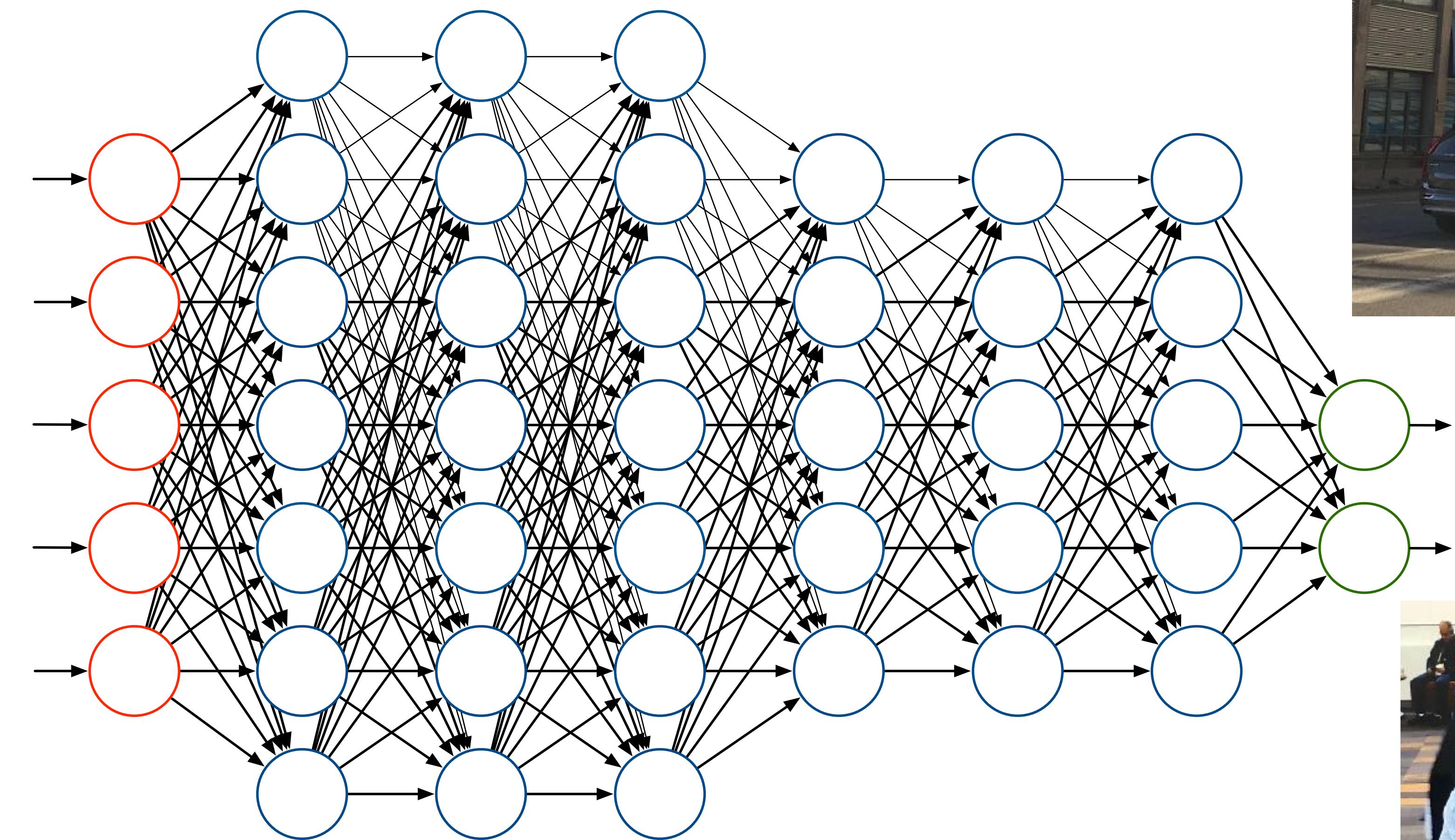
Structure Based Drug Design



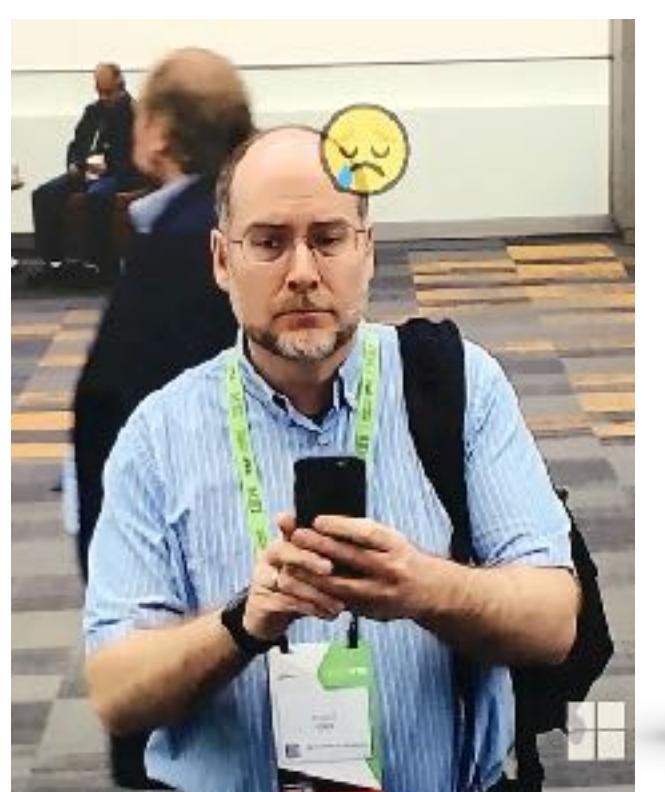
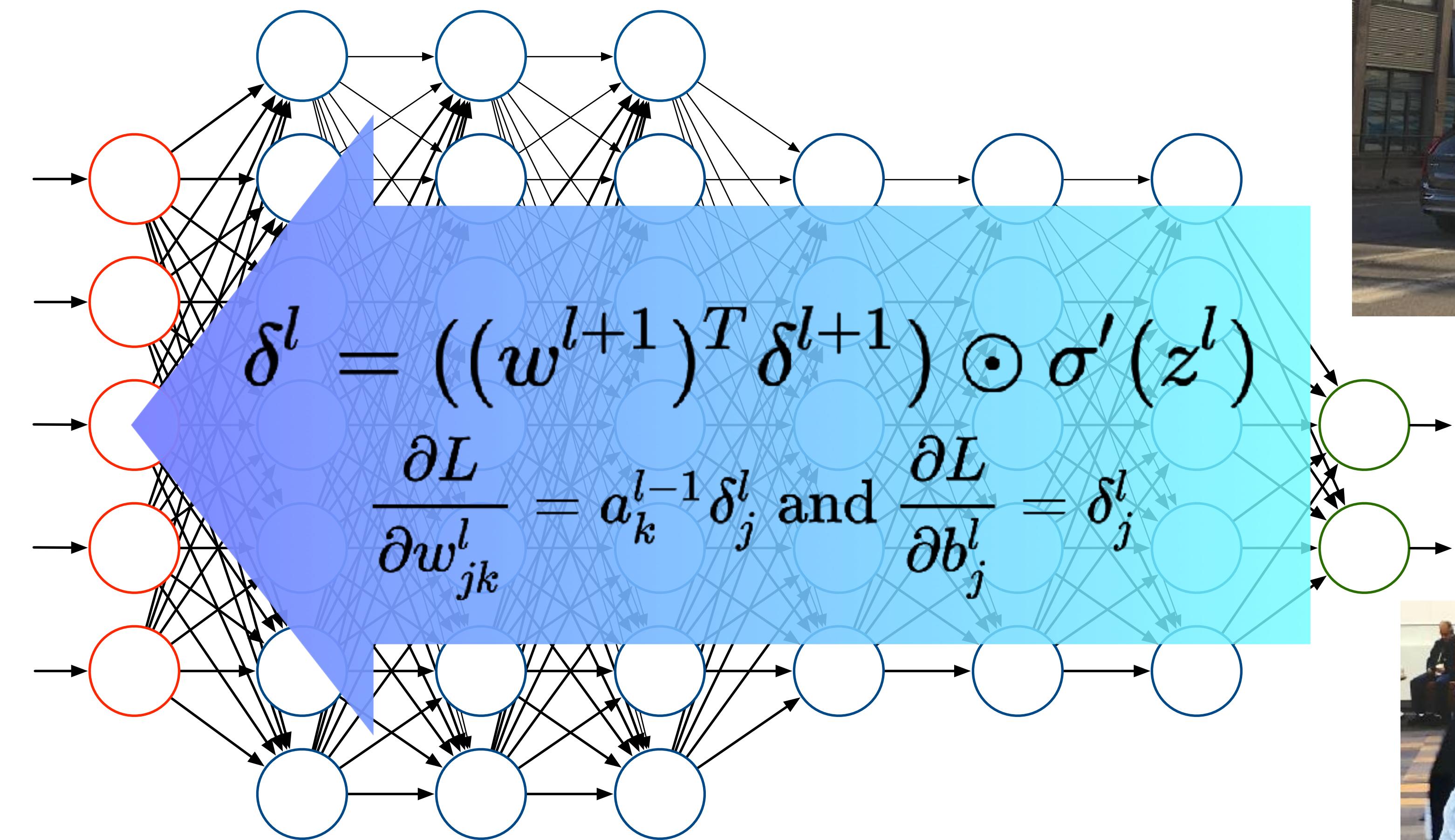
Deep Learning



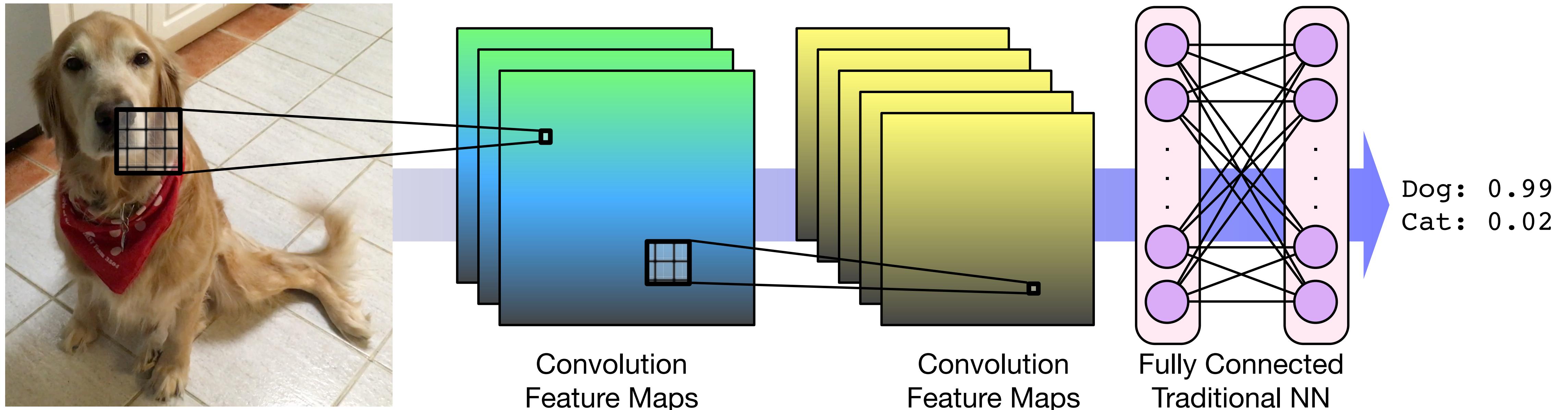
Deep Learning



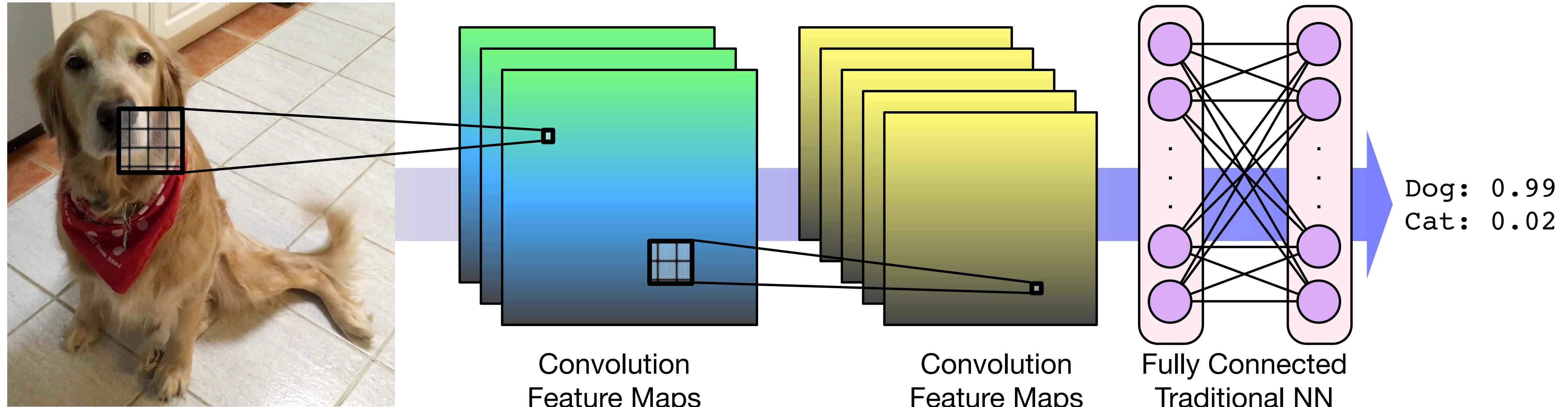
Deep Learning



Convolutional Neural Networks



Convolutional Neural Networks



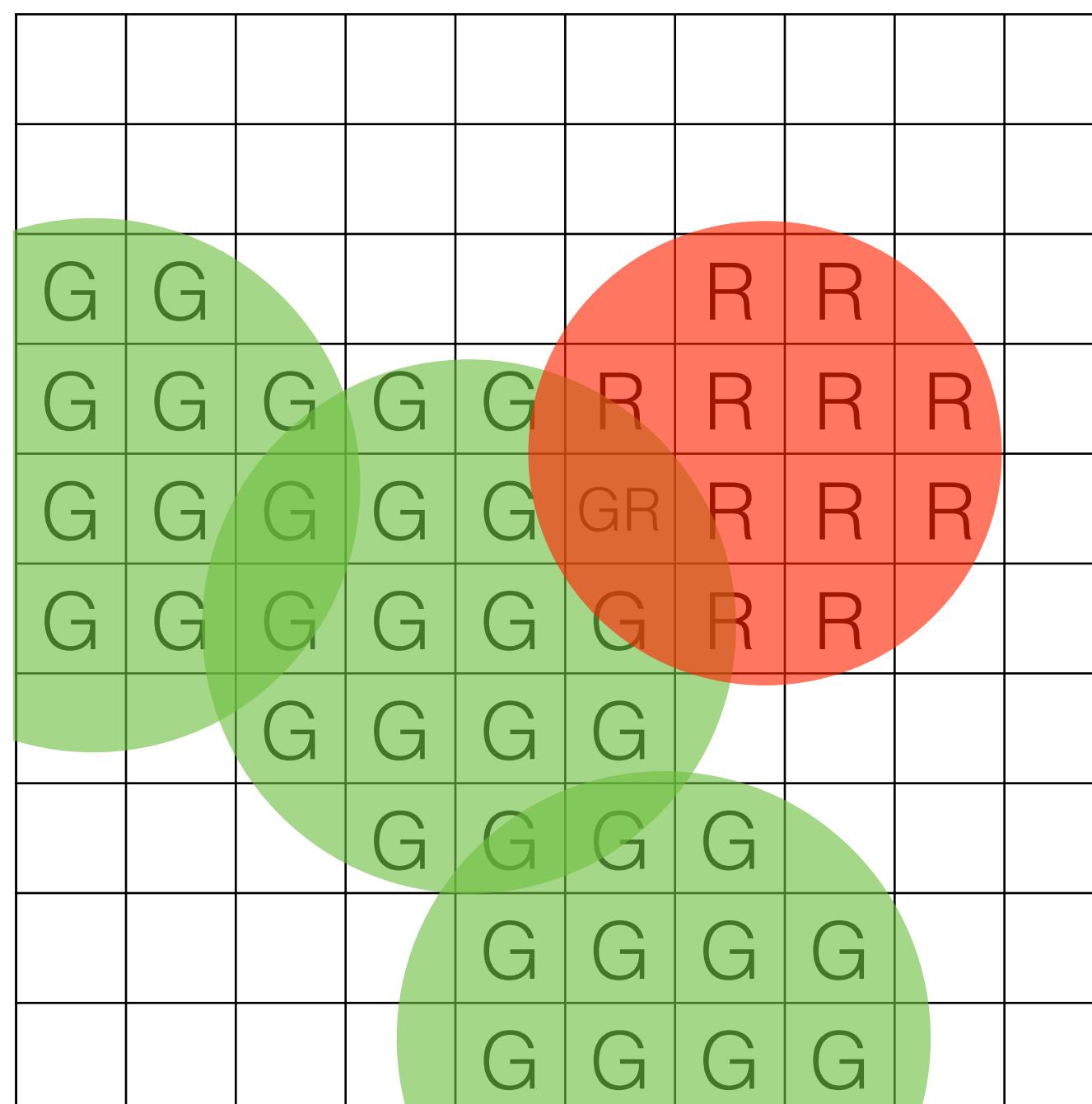
Sunseri J, King JE, Francoeur PG, Koes DR. Convolutional neural network scoring and minimization in the D3R 2017 community challenge. Journal of computer-aided molecular design. 2019 Jan 15;33(1):19-34.

Hochuli J, Helbling A, Skaist T, Ragoza M, Koes DR. Visualizing convolutional neural network protein-ligand scoring. Journal of Molecular Graphics and Modelling. 2018 Sep 1;84:96-108.

Ragoza M, Hochuli J, Idrobo E, Sunseri J, Koes DR. Protein-ligand scoring with convolutional neural networks. Journal of chemical information and modeling. 2017 Apr 11;57(4):942-57.

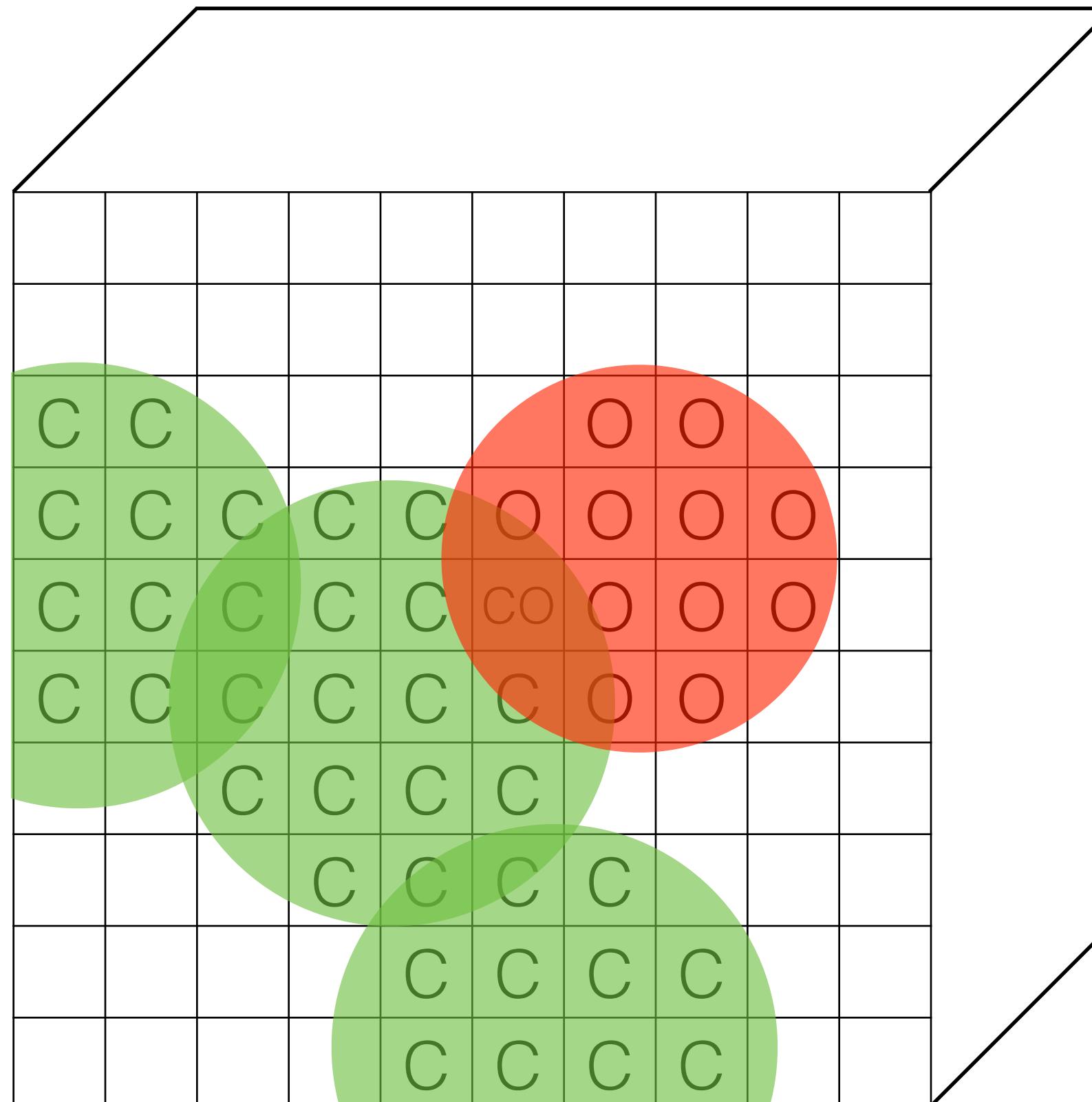
Sunseri J, Ragoza M, Collins J, Koes DR. [A D3R prospective evaluation of machine learning for protein-ligand scoring](#). J Comput Aided Mol Des. 2016 Sep;30(9):761-771.

Protein-Ligand Representation



(R,G,B) pixel

Protein-Ligand Representation

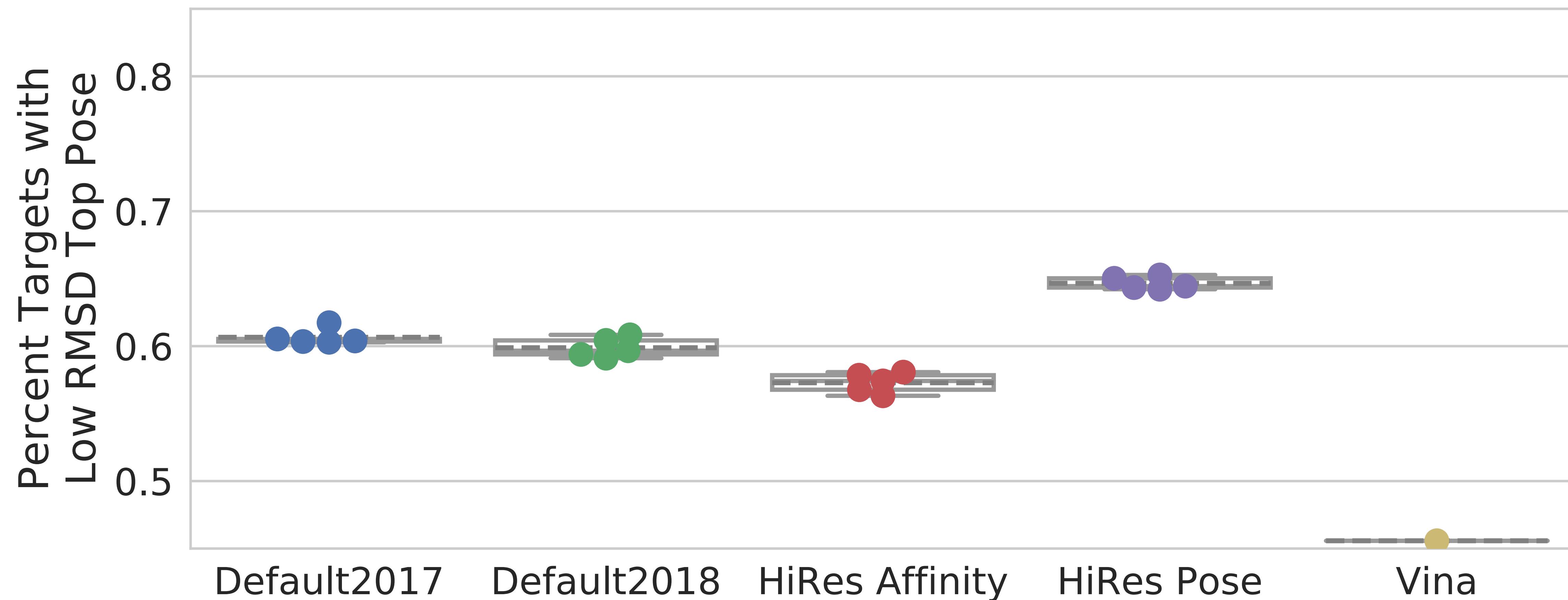


(R,G,B) pixel →
(Carbon, Nitrogen, Oxygen,...) **voxel**

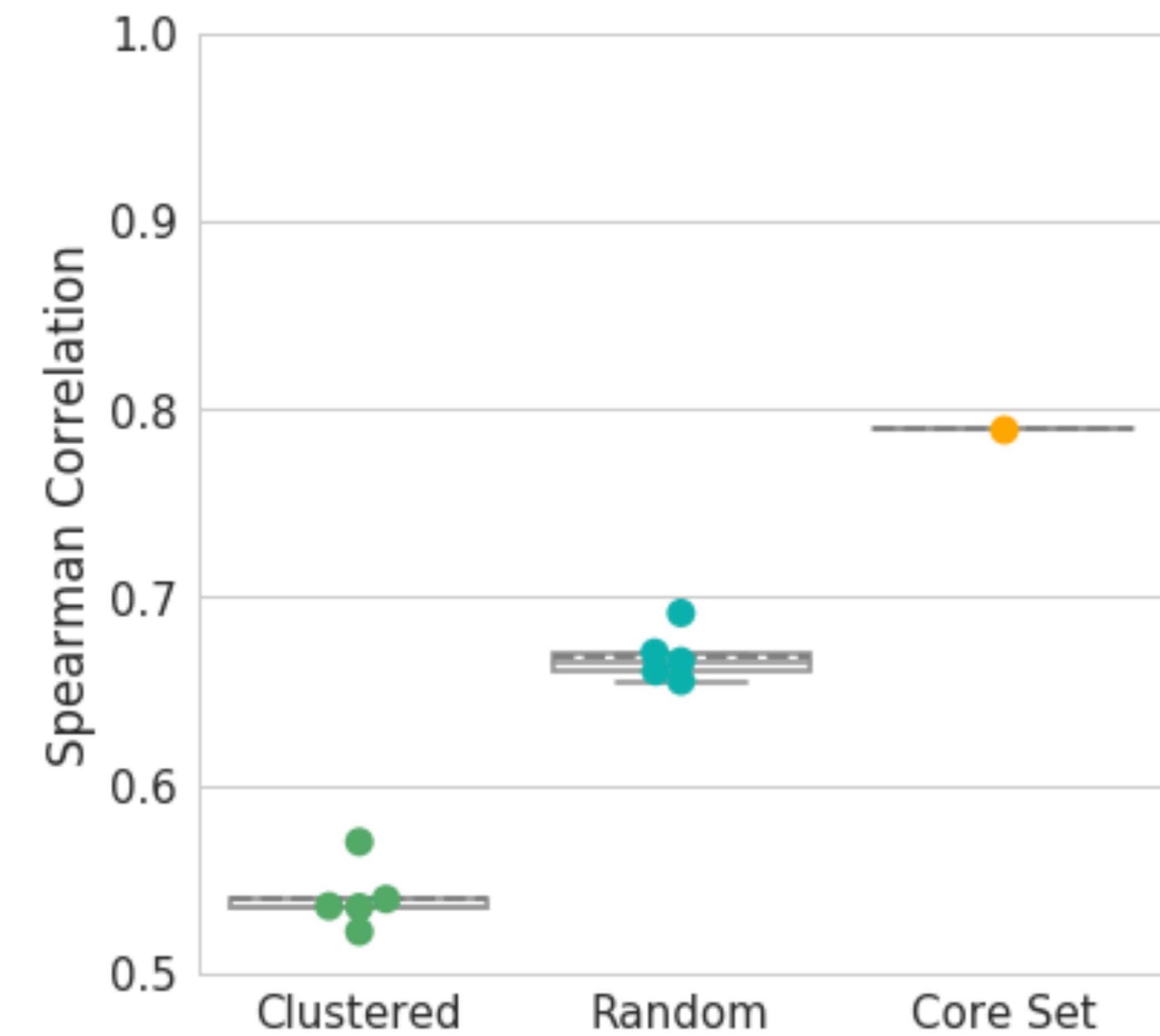
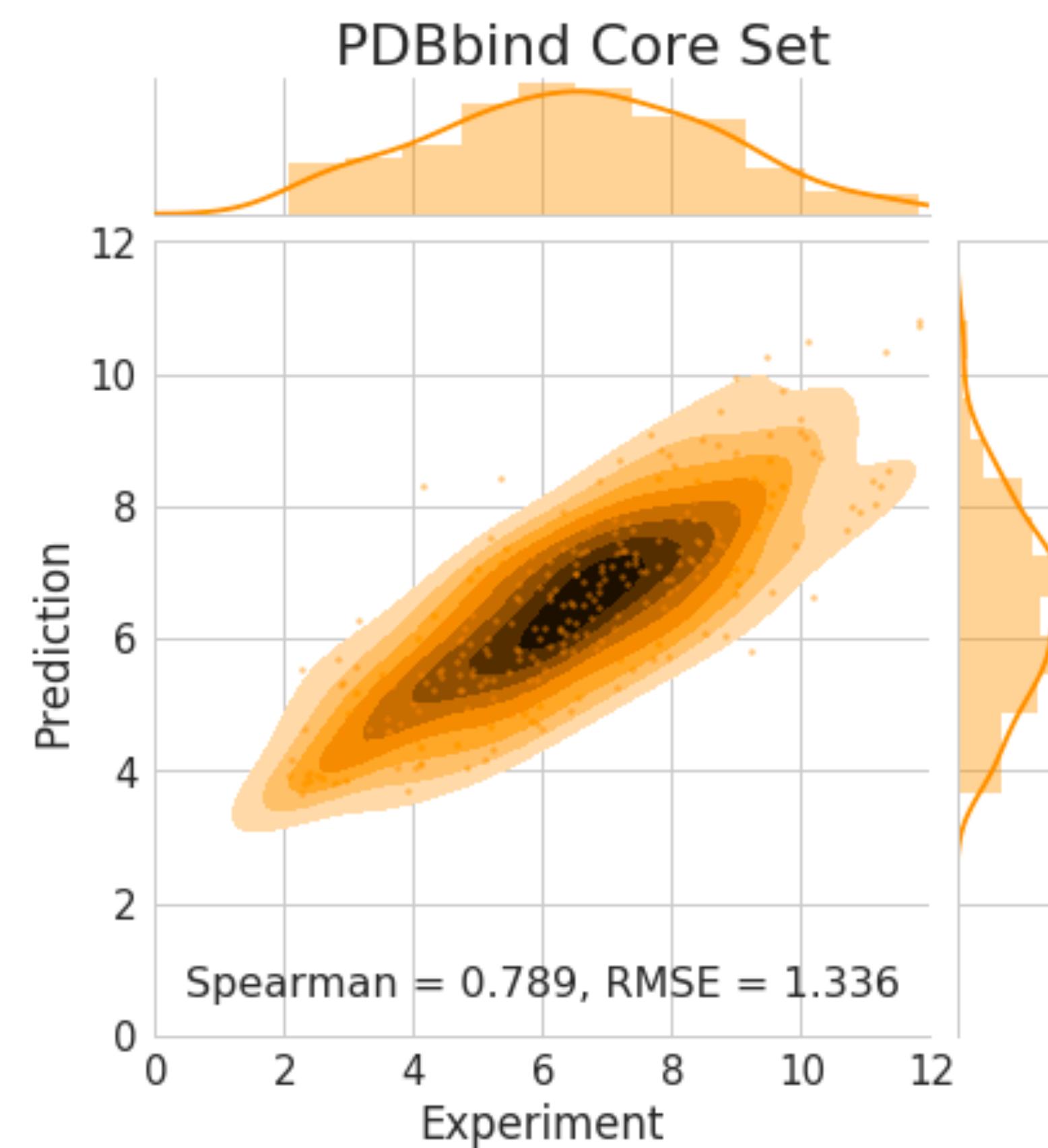
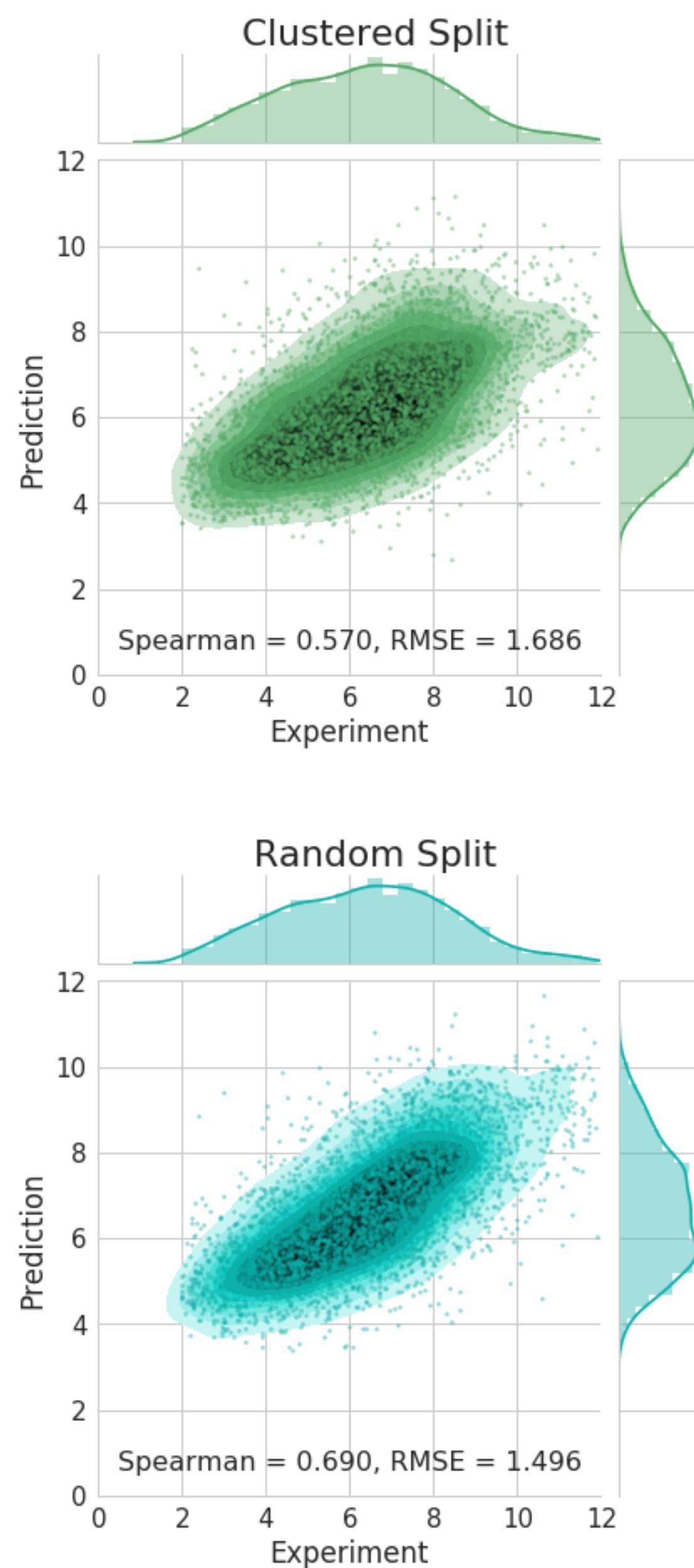
The only parameters for this representation are the choice of **grid resolution**, **atom density**, and **atom types**.

Pose Results

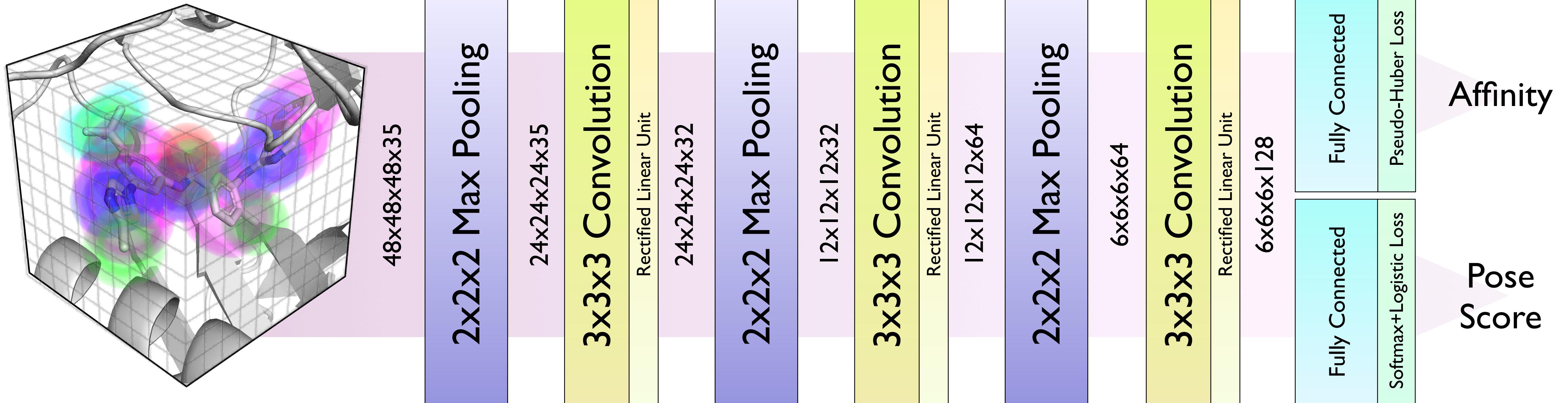
Crossdocked Pose



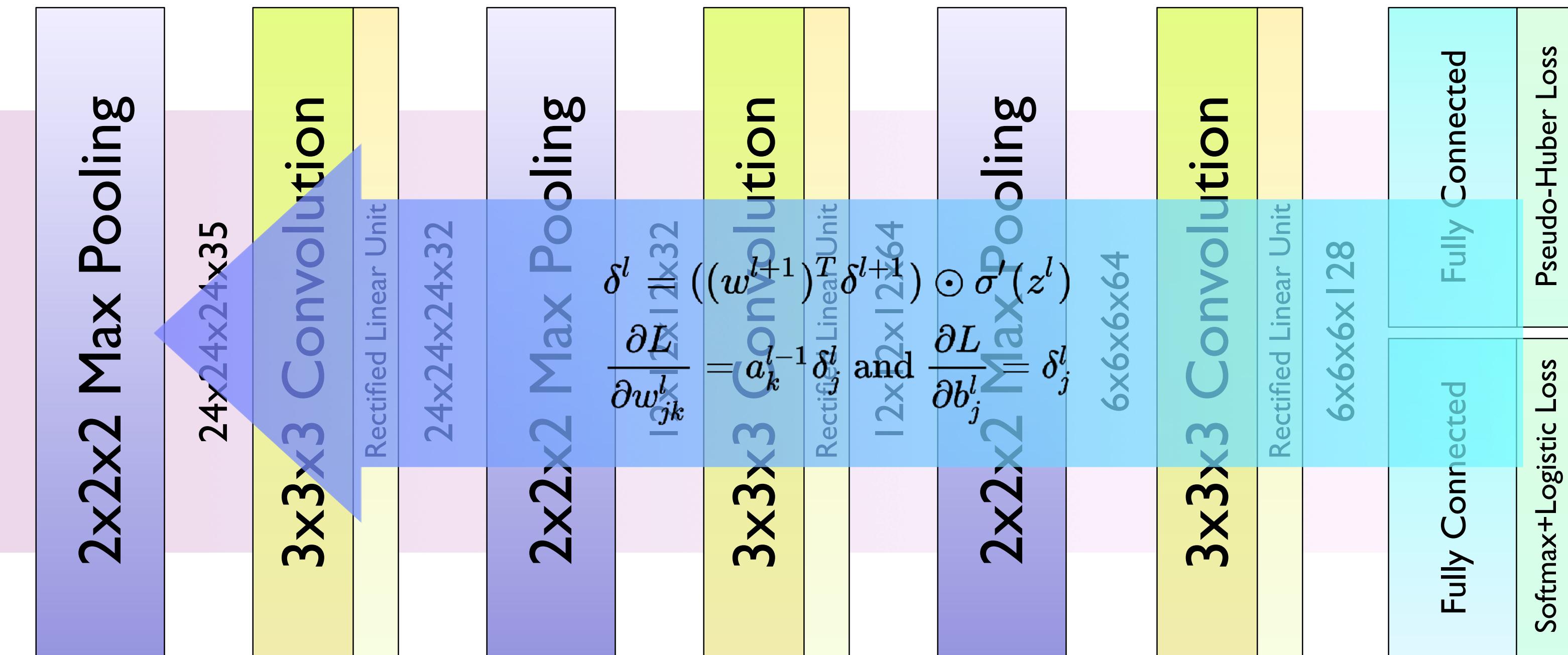
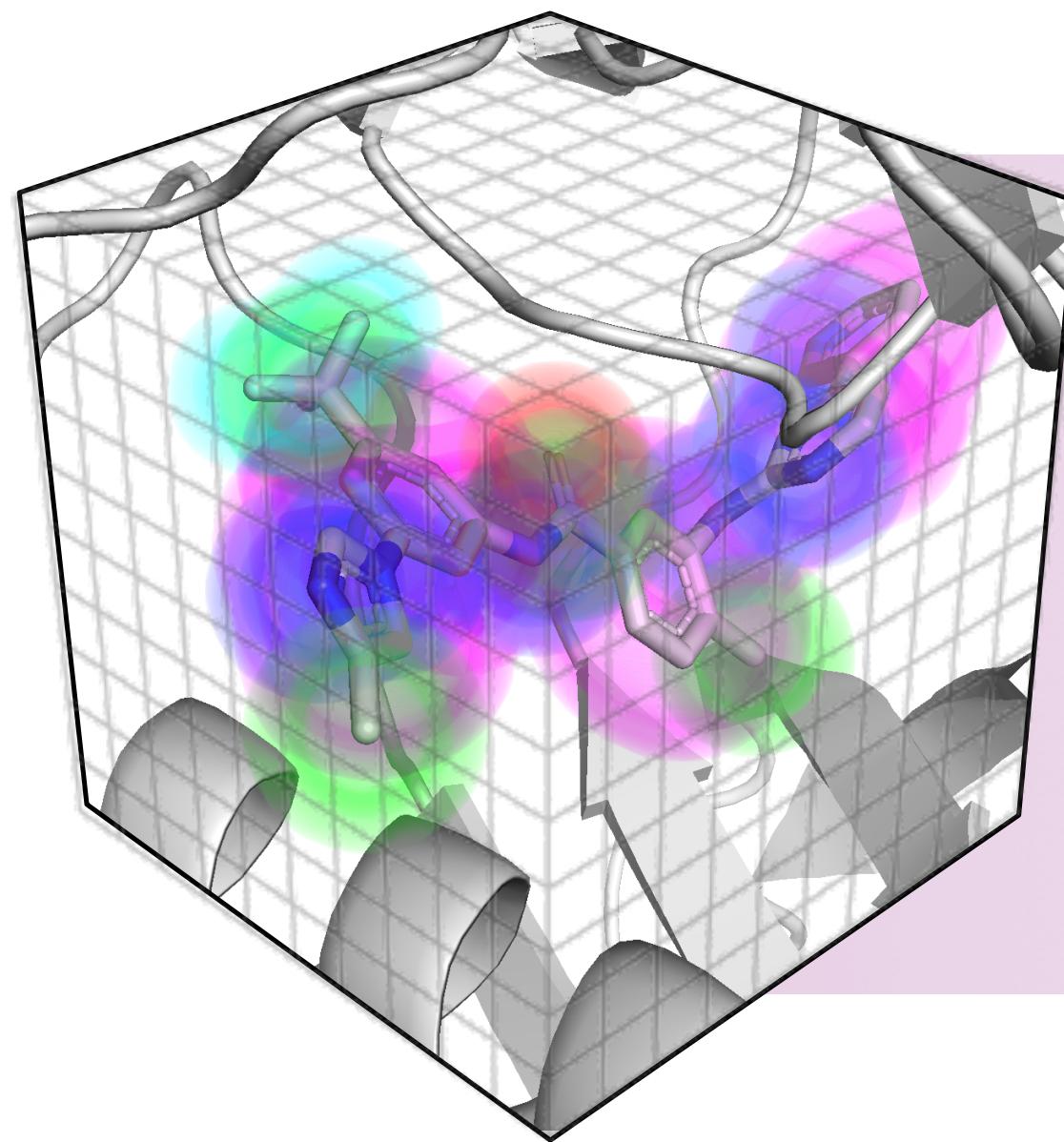
Affinity Results



Beyond Scoring



Beyond Scoring

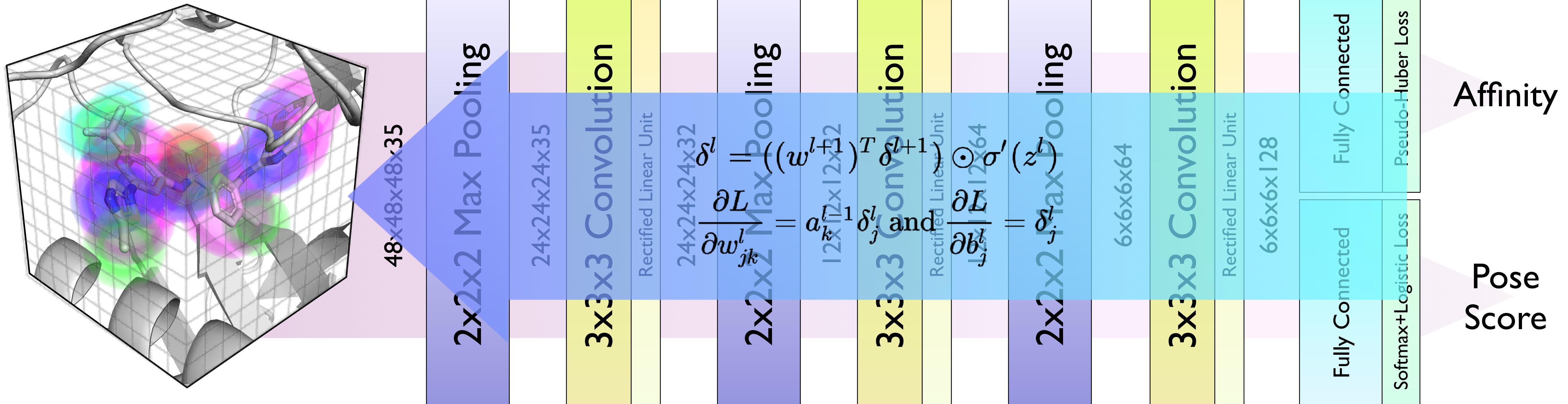


$$\delta^l = \frac{\partial L}{\partial z^l} \mid_{z^l = ((w^{l+1})^T a_k^{l-1}) + b_j^l}$$

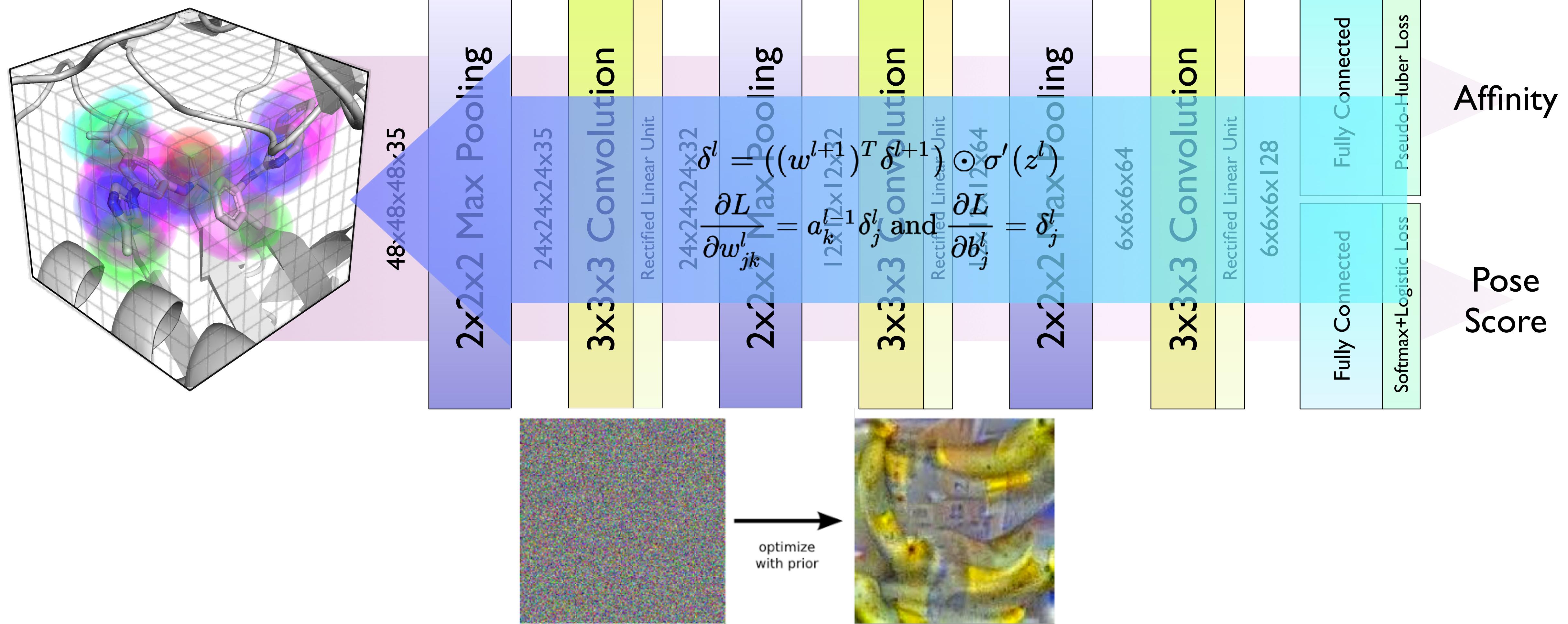
and

$$\frac{\partial L}{\partial b_j^l} \odot \sigma'(z^l)$$

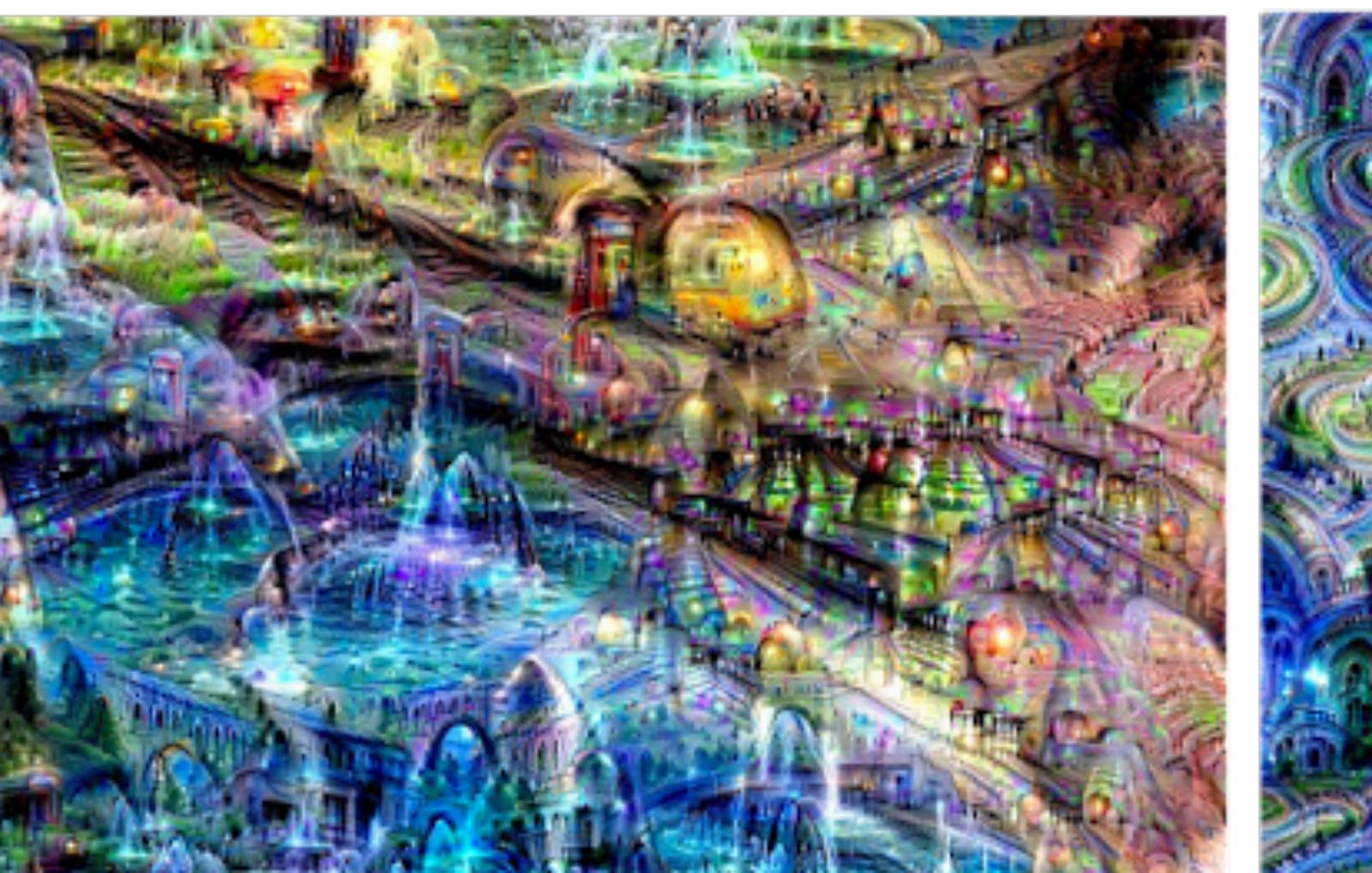
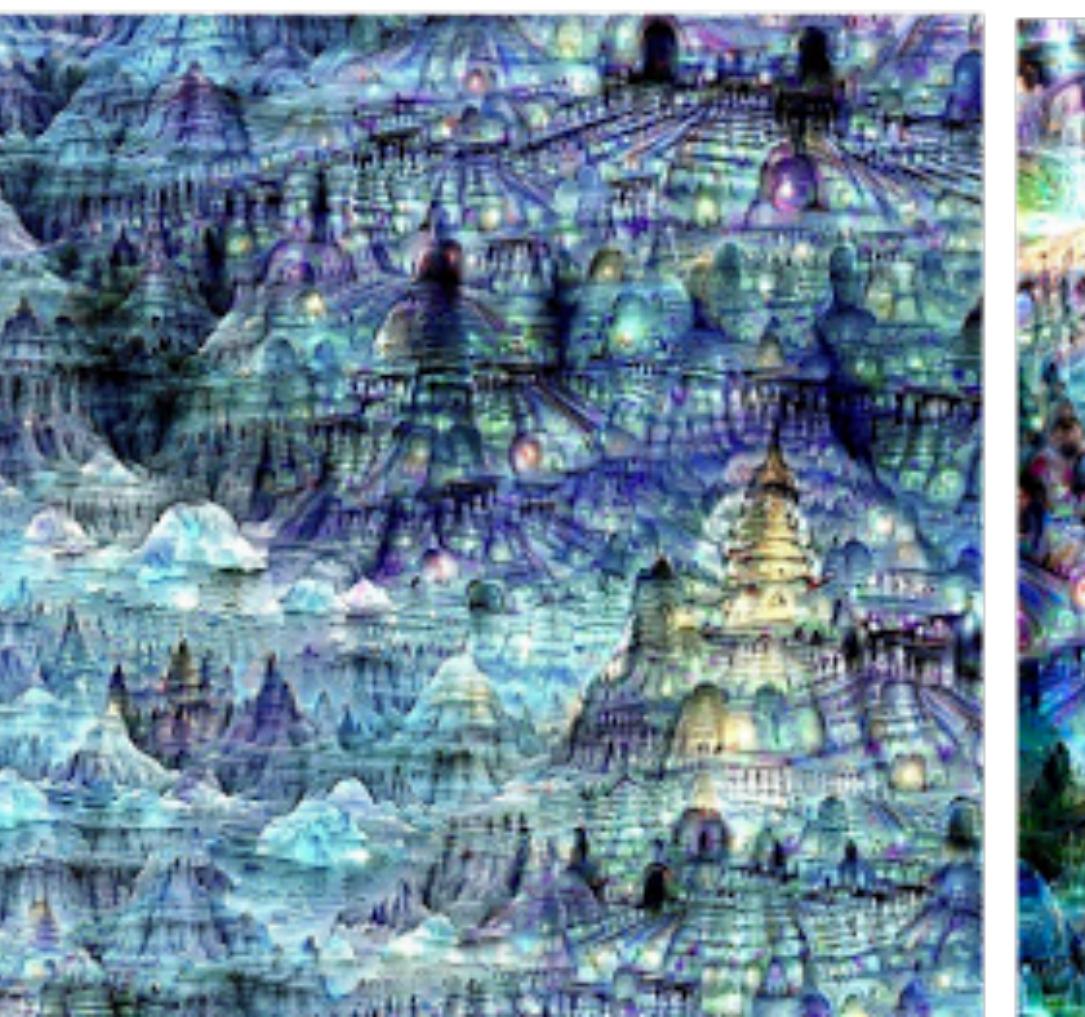
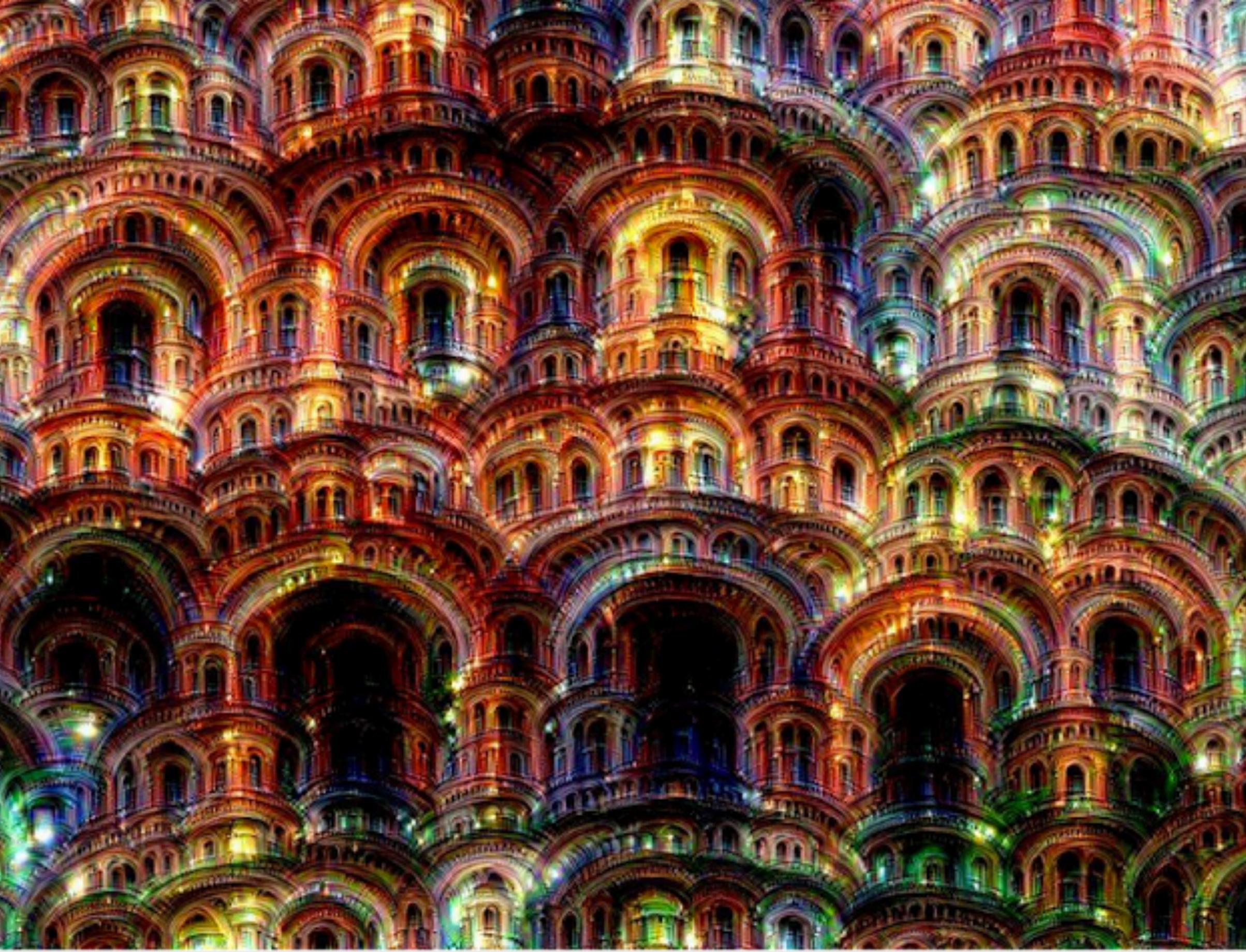
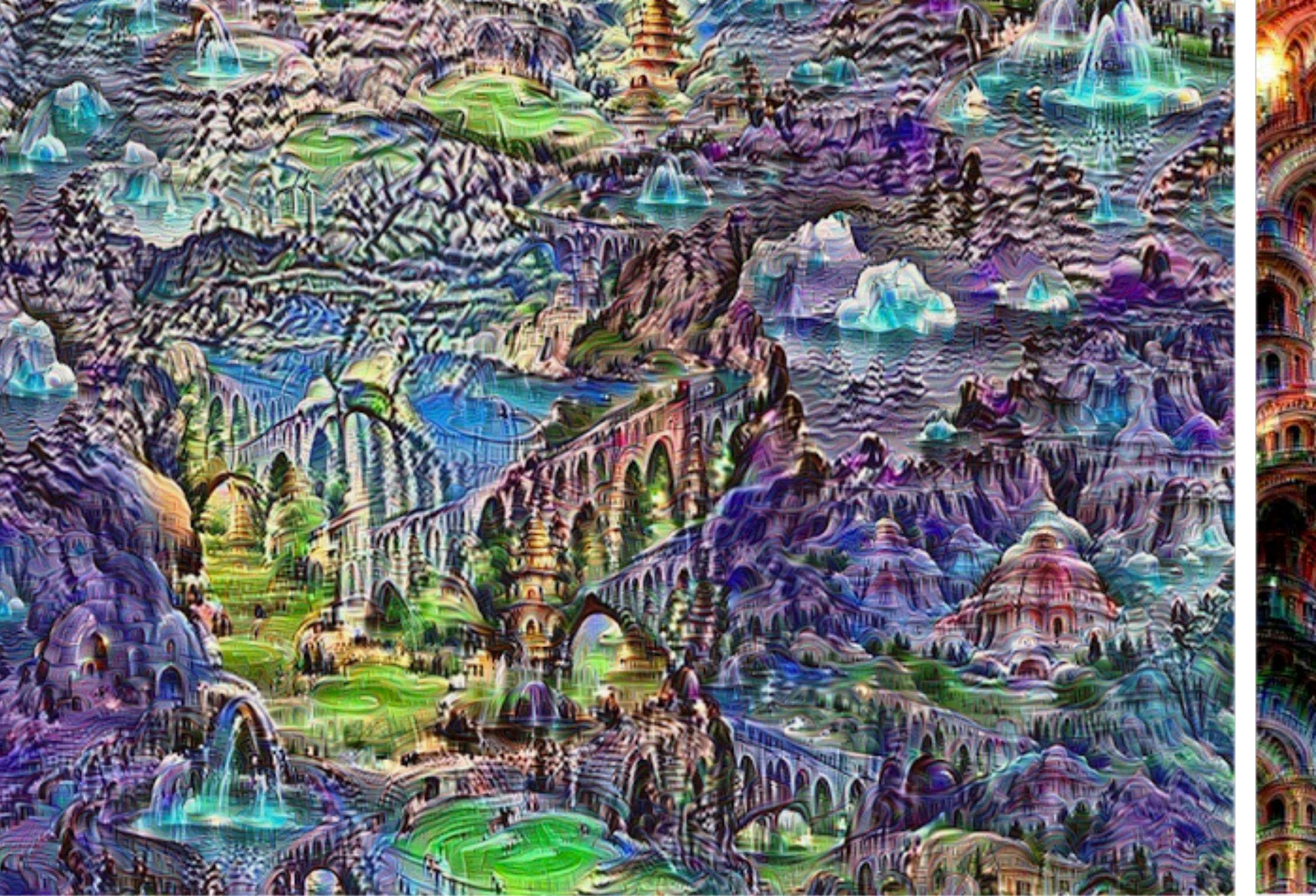
Beyond Scoring



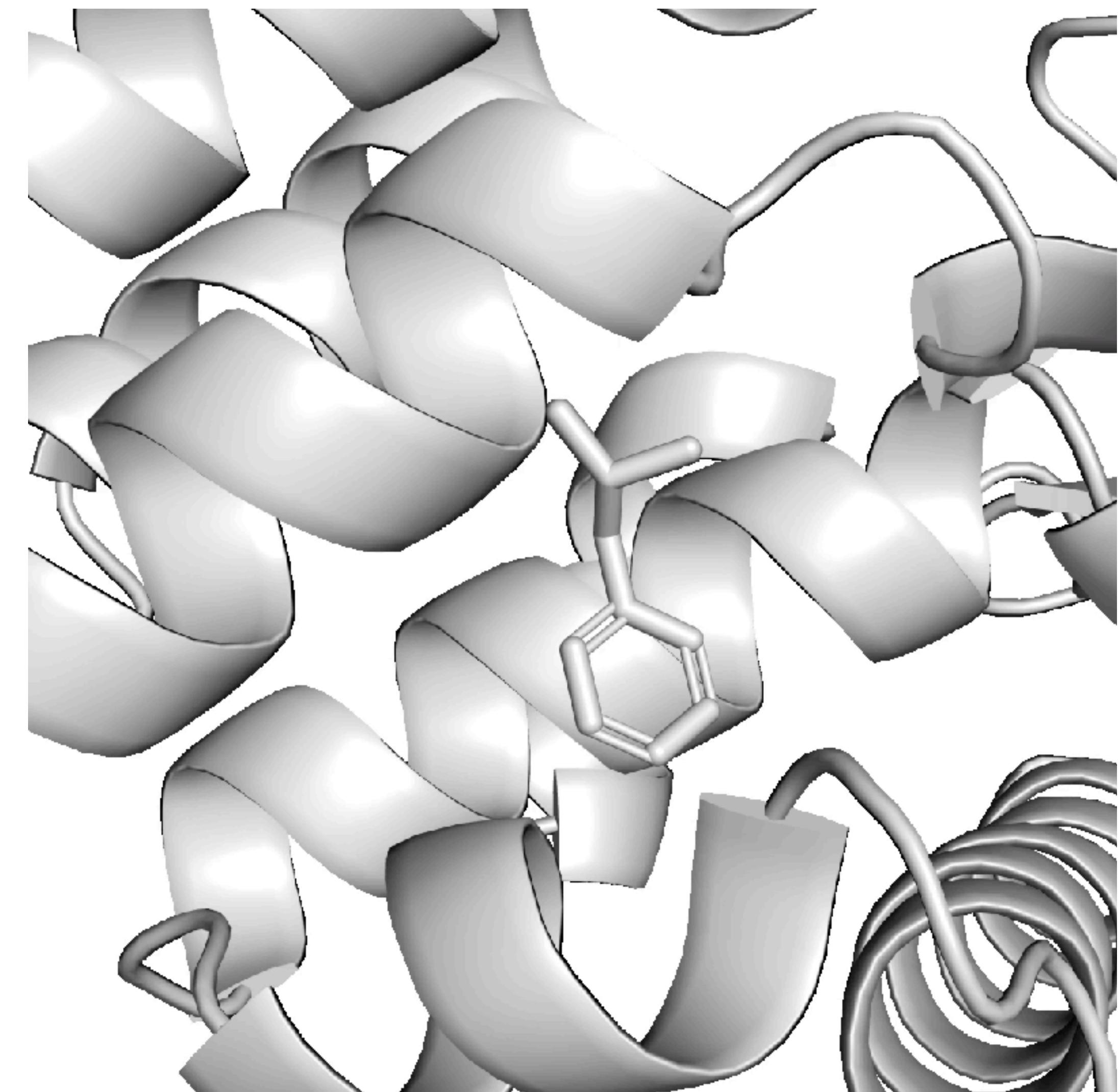
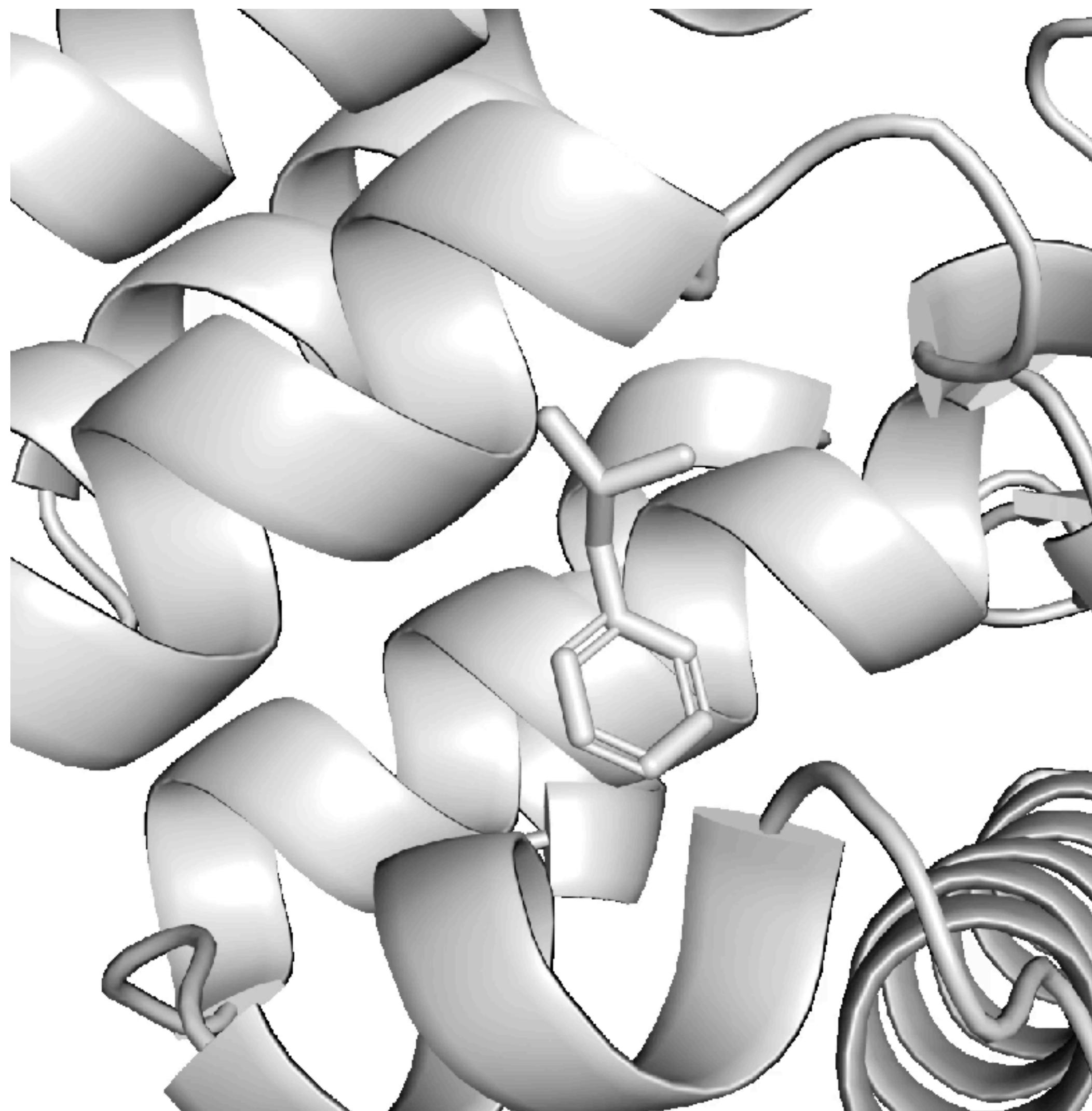
Beyond Scoring



<https://research.googleblog.com/2015/06/inceptionism-going-deeper-into-neural.html>

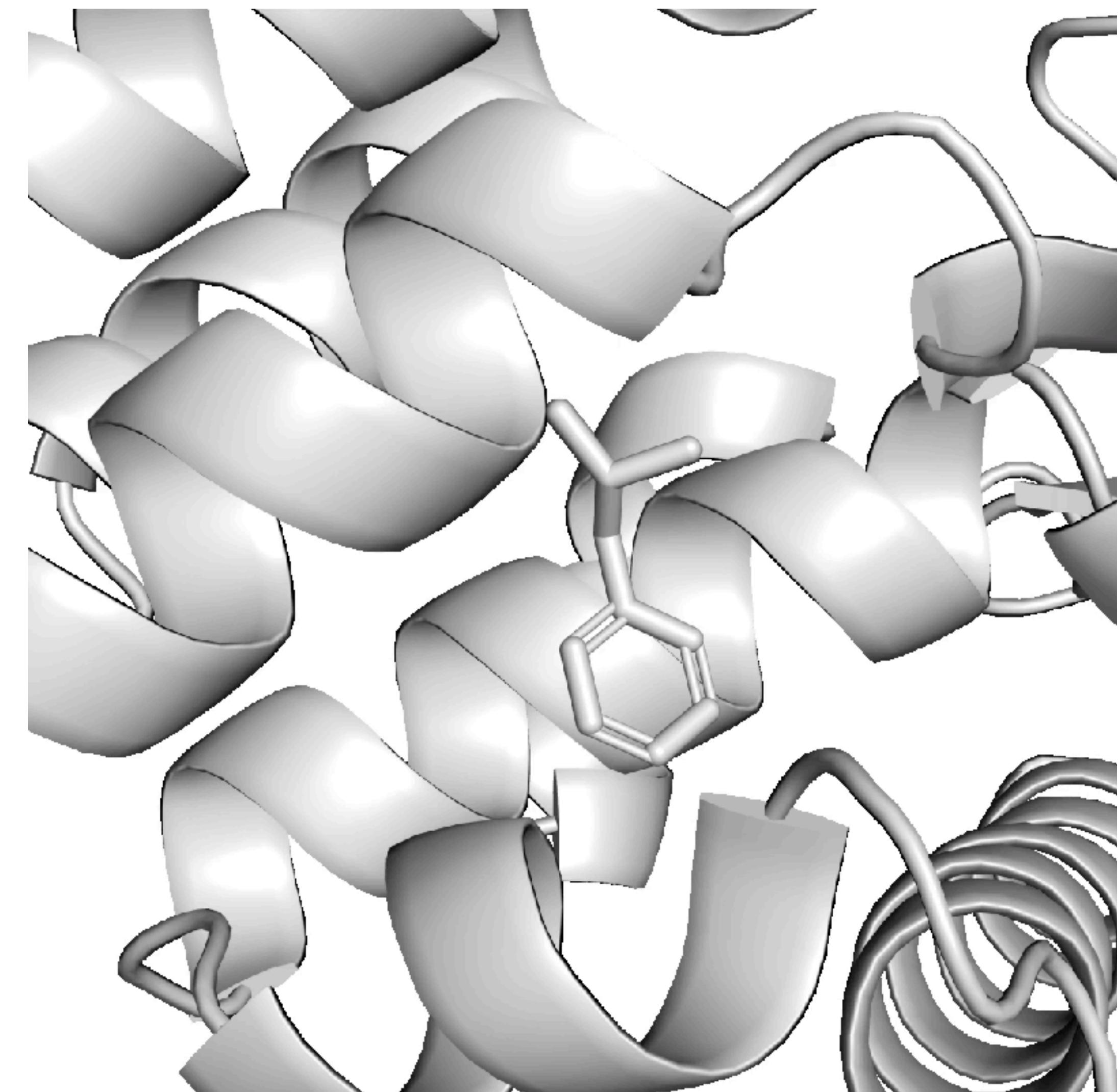
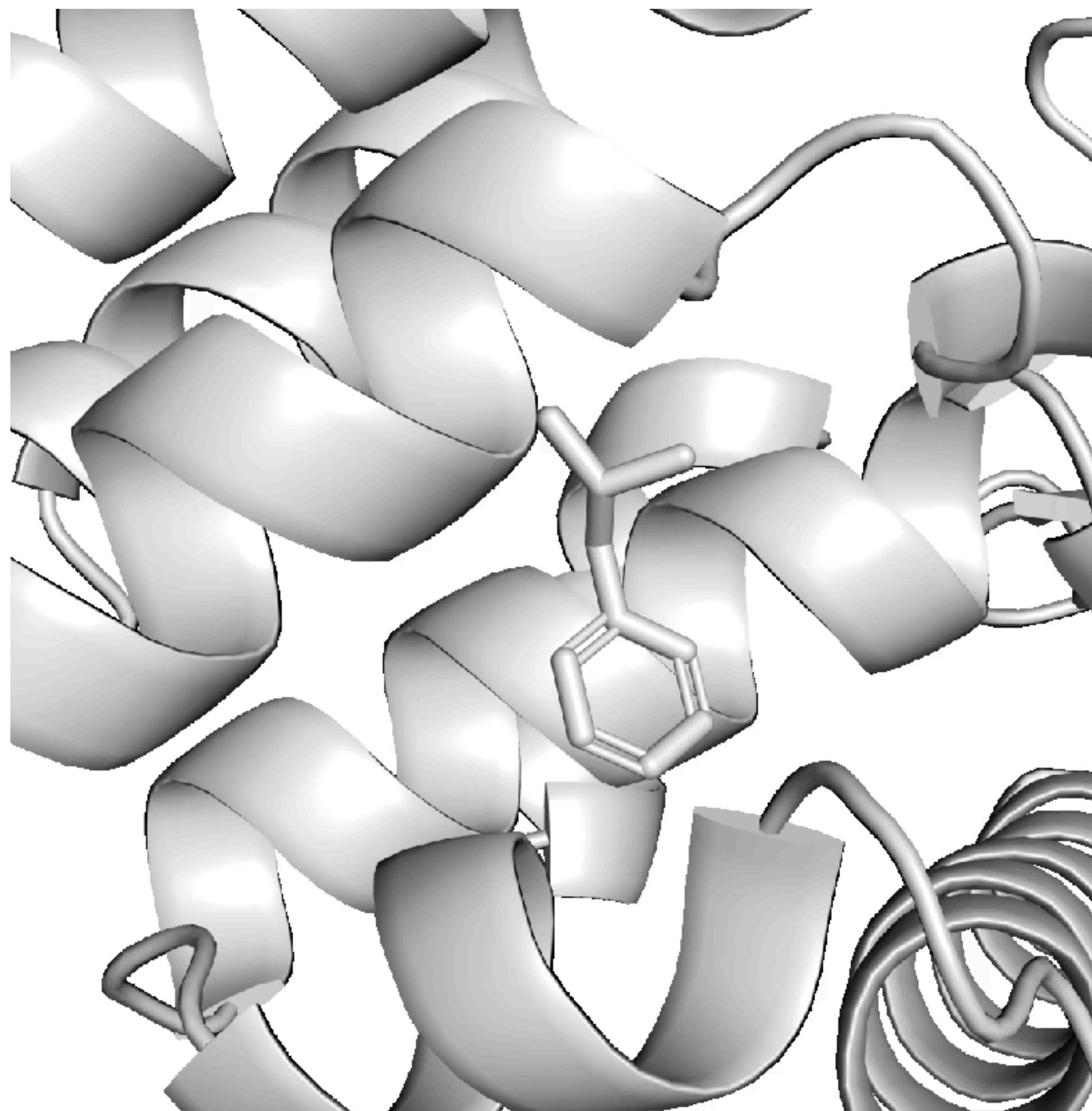


Deep Dreams of Molecules



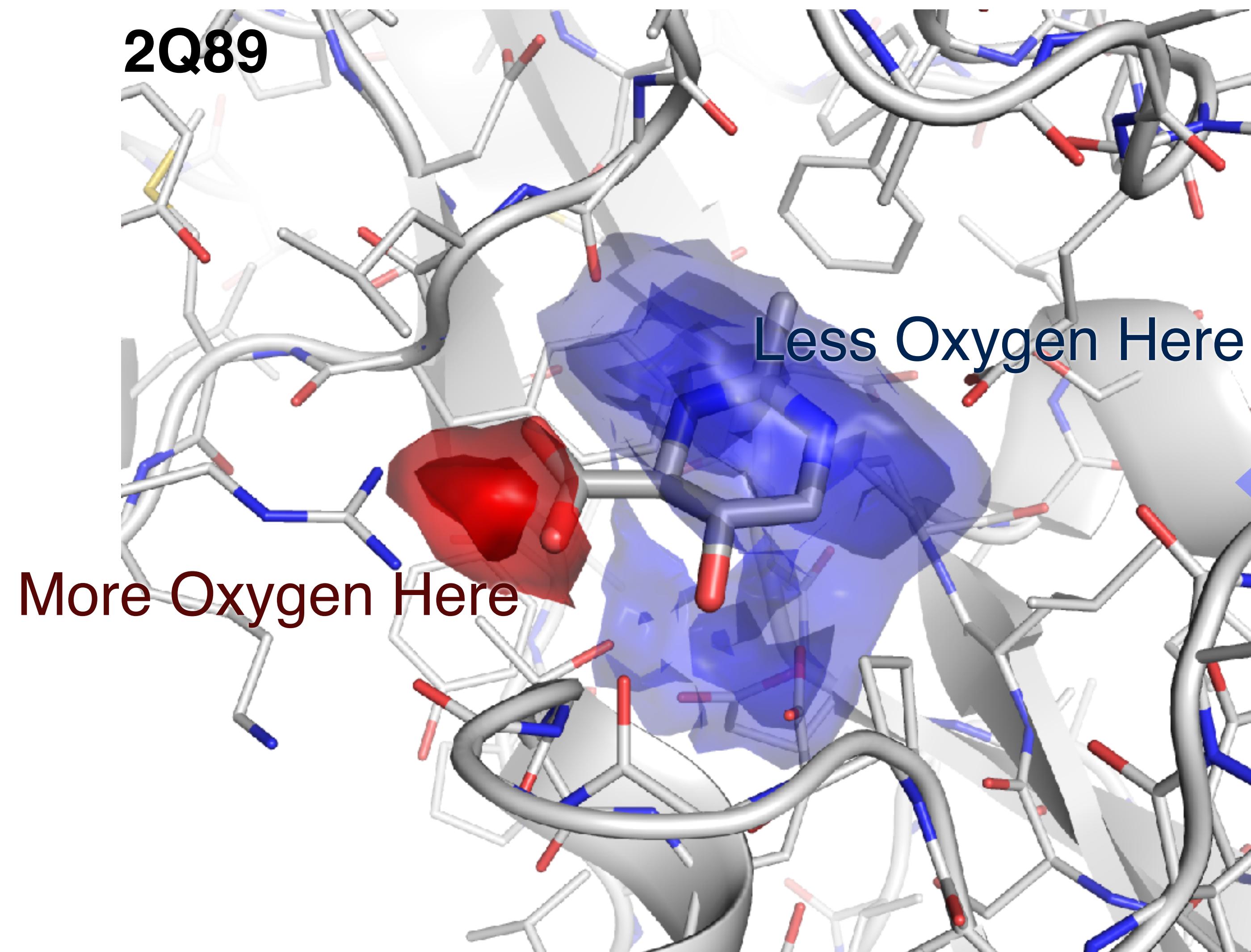
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Deep Dreams of Molecules



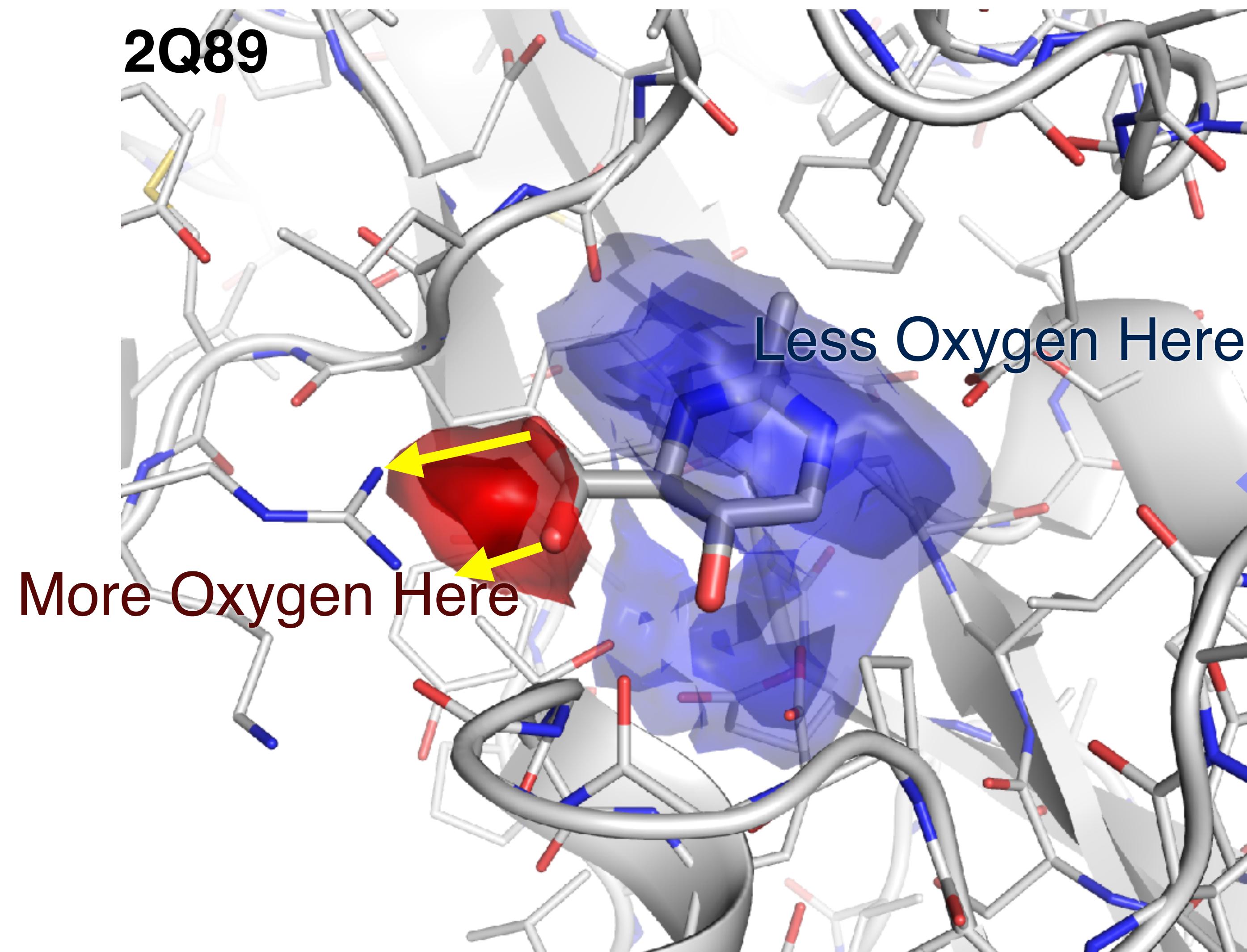
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Beyond Scoring



$$\frac{\partial L}{\partial A} = \sum_{i \in G_A} \frac{\partial L}{\partial G_i} \frac{\partial G_i}{\partial D} \frac{\partial D}{\partial A}$$

Beyond Scoring



$$\frac{\partial L}{\partial A} = \sum_{i \in G_A} \frac{\partial L}{\partial G_i} \frac{\partial G_i}{\partial D} \frac{\partial D}{\partial A}$$

