# 3D Model of Dopamine Receptor Ligand Interactions

A. Traeger, K. Ward, J. Haslam, J. Harvey & R.Penton
University of North Carolina at Chapel Hill

## Purpose:

Bridge the gap in science education between viewing receptor binding as a "lock-and-key" to more biologically accurate mechanism of dopamine receptors.

## Background:

-D1-like receptors (D1 & D5) are GPCRs
-They are 80% homologous in transmembrane domains but differ slightly in residues in the third cytoplasmic loop & C terminus [1,2]
-Binding pockets are identical except for additional residue, Ile169, on D5 [3]
-

## Methods:

- Conducted research on current models of D1 and D5 receptors
- Created initial prototypes using MakerSpace design kits (fig. 1)
- Completed 3D printing training
- Drew sketches of receptors (fig. 2)
- Designed 3D model using TinkerCAD and SWISS software[4]
- Printed 3D model at BeAM Makerspace using altermaker with CPE filament assembled using deryun magnets and rubber bands

## Design Process:

We planned to create 3D printed models of D1&D5 (fig. 1), but after difficulty replicating that degree of detail, we decided to focus on a general binding mechanism of dopamine GPCRs for our 3D printed model. We also changed the original design from a sphere to a cylinder to better reflect the structure of the receptor (fig. 3).

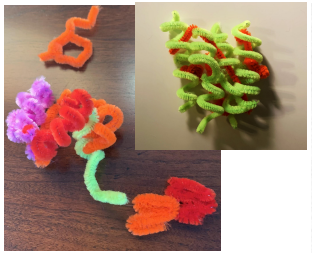

*Fig. 1 Early prototype*

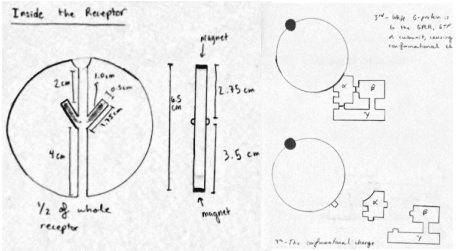


*Fig. 2 Binding mechanism sketches*

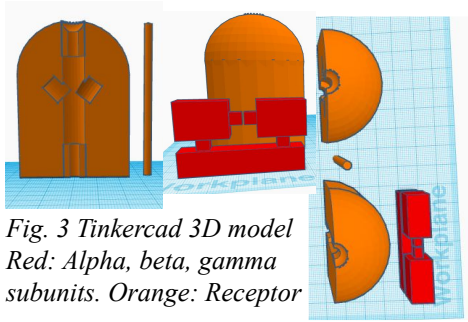


*Fig. 3 Tinkercad 3D model Red: Alpha, beta, gamma subunits. Orange: Receptor*

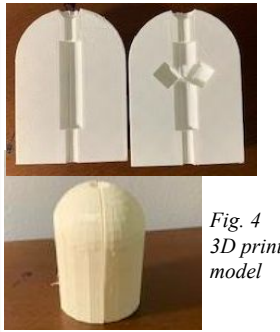

*Fig. 4 3D printed model*

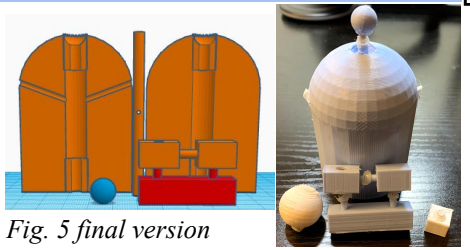

*Fig. 5 final version*

## Discussion and Implications:

Our model demonstrated the complexity of dopamine receptor binding. Dopamine "binds" above the shaft pushing on a spring which exposes a magnet that the G-protein binds to. As a result, the G-protein will dissociate into its signaling subunits. (fig 3)
Through iterations of design, we discovered the limits of modeling receptor function with 3D printing. While other models may focus on alpha helice representations, our model highlights the internal mechanism of conformational changes in a receptor when ligand binds.
Our next steps would be to incorporate protein structures to make the model more realistic.

## Contributions:

A. Traeger: Research & poster content J. Harvey: Design and poster content, K.Ward: Research & spark video design, J. Haslam: 3D model creation

1. Bhatia A, Lenchner JR, Saadabadi A. Biochemistry, Dopamine Receptors. . In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK538242/ 2. Pivonello, R. *et. al.* Novel insights in Dopamine receptor physiology. *European Journal of Endocrinology* 156 S13–S21 (2007). 3. Chapter IV, A Comparison of the Dopamine Binding Sites of the Human Dopamine Receptors. CalTech. https://thesis.library.caltech.edu/1599/4/Chapter4NEW.pdf 4. P21728: SWISS-MODEL Repository. SWISS Available at: https://swissmodel.expasy.org/repository/uniprot/P21728?csm=64E062D765D0DBA7.