Dopamine (DA) contributes to critical functions in the central nervous system. By introducing electrical stimulation *in vivo* at the rat's medial forebrain bundle, evoked DA signals can be measured at a carbon fiber electrode with fast scan cyclic voltammetry (FSCV). Previously, our lab discovered that DA kinetics are highly heterogeneous. Hypothetically, the slow responses result from autoinhibition, which exists prior to the stimulus, presumably due to the occupation of pre-synaptic D2 autoreceptors by basal DA in the extracellular space. Fast responses have minimal autoinhibitory effect because the DA can be observed within 200 ms while it can require more than 2 s for the slow sites.

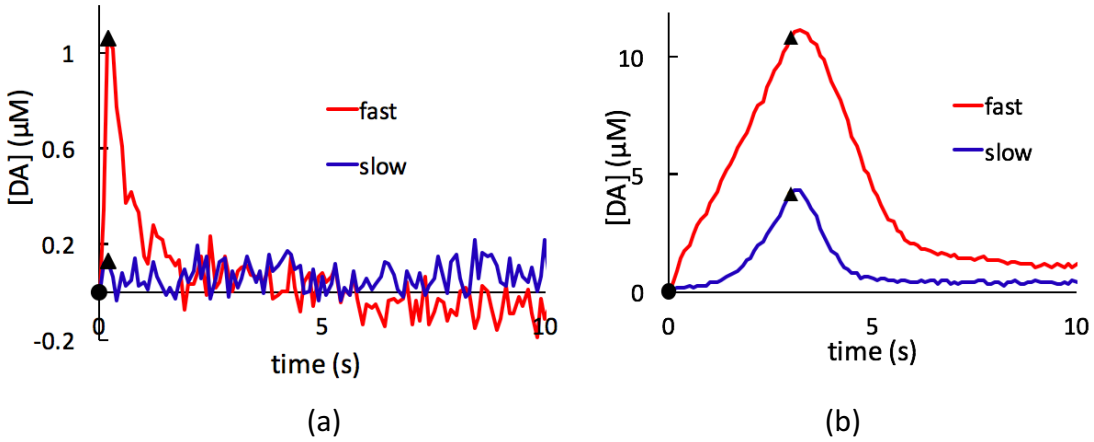
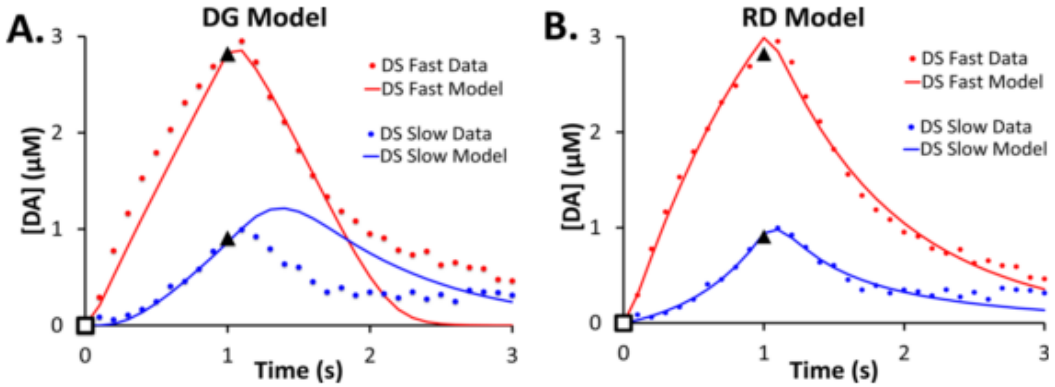



**Figure 1. (a)** After giving a 0.2 s stimulation at 60 Hz, there is an evoked response in fast site but not in slow site. **(b)** There is an initial "lab" in slow sites but no delay in fast sites at 60 Hz 3s simulation.

The Diffusion Gap (DG) model was the reigning explanation of this heterogeneous kinetics. This model proposes that there is a physical gap between the DA terminal and the recording site. However, if there is a delay at the onset of the stimulus, the fall of the response should have the same delay when the stimulus ends, which is not always observed. In addition, raclopride, a D2 antagonist, can eliminate this delay in a slow site.



Therefore, a new model was introduced based on restricted diffusion (RD). It suggests that DA is released to an inner compartment (IC) then transported to an outer compartment (OC). DA is detected in the OC and then cleared by re-uptake. A study was designed to explore different super-physiological stimuli pulses and examine how these responses are seen in the dorsal striatum after raclopride was given. Modeling responses obtained with high-pulse stimuli, the RD model reveals new information about the kinetics of the slow kinetic domains.

As autoreceptors function in both domains, it seems that the domains are different in autoinhibitory tone which derives from different basal DA concentration required to activate the D2 receptors. Due to this effect, future experiments will be focused on investigating the fast sites kinetics and whether the refined RD model can portray the responses. By studying the physiological sources of DA kinetics, we can investigate the responses similar of human neurons.