Alcohol use disorder is a global health issue with dire social and economic costs, understanding the neuronal pathways and its effect on neurotransmitter-signaling systems, and how they are altered, will help to design new gene targeting drugs to suppress alcohol addiction and alleviate withdrawal symptoms.

Biological question: Acute alcohol administration increases the firing of VTA dopamine neurons. My aim is to investigate the role of D1 dopamine receptors during alcohol relapse and to identify significant dopamine signatures during relapse[[1]](#footnote-1).

Research model

* To study the activity across the dopamine system, we will visualize dopamine release using the GPCR indicator dLight during alcohol-seeking period.
* Laboratories animals will be Th-Cre rats and will receive the genetically encoded CAG promoter pAAV-CAG-dLight1.1[[2]](#footnote-2) . LEDS will generate two excitation wavelengths at 405 nm (isosbestic control signal) and 465 nm (Ca2+ dependent signal).
* Optical measurements will be measured by femtowatt photoreceivers at various locations of the nucleus accumbens (core, above medial accumbens sheel, lateral accumbens shell).
* Signals will be downsampled and processed:
  + ratio will be calculated where:

, F: Ca2+ dependent signal, : isosbestic signal

* will be low-pass filtered
* within a time-window around events was compiled will be averaged
* remove noise: 95% CI will be calculated for each event and non-significant events will be filtered out
* The rats will be placed in a chamber with a pump located on the wall of the chambers. Activating the dispenser extinguishes a blue light, and triggers a syringe which delivers alcohol. The rats will be trained and tested following a context induced reinstatement procedure: to use context as a factor, two contexts with different olfactory and tactile and visual properties will be created.
* Rats will be initially trained in the context where an activated pump by the rat, stops the light and dispenses alcohol. Then the rats are trained in an alcohol-missing context where the same pump when activated stops the light but doesn’t deliver alcohol. The training phase is followed by a testing phase, the rats are self-controlling the nose: they are first in the alcohol-missing context then they are in the alcohol-context. Signals will be recorded at each stage of this procedure.

We will use (RSA), for data analysis to compare similarities between brain activity and the measurements. A first order representational dissimilarity matrix (RDMs) will be constructed. From the pairwise correlation distances, indicating the degree to which each pair of waveforms are similar or dissimilar. A second-order Brain RDN will also be generated to factor out the stages of the experiments and keep correlations between each pair of brain regions.

1. Relapse being defined as humans going back to drinking after stopping, and similar behavior has been observed in rodents, humans re-exposed to alcohol return to pre-abstinence levels of drinking [↑](#footnote-ref-1)
2. From addgene [↑](#footnote-ref-2)