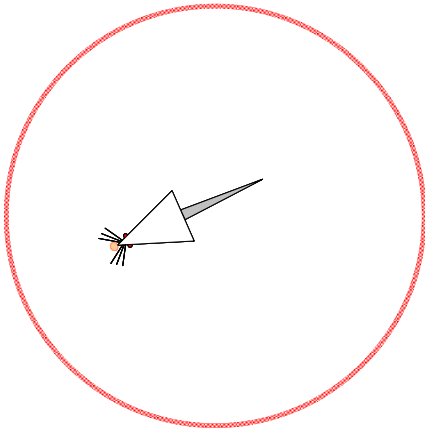
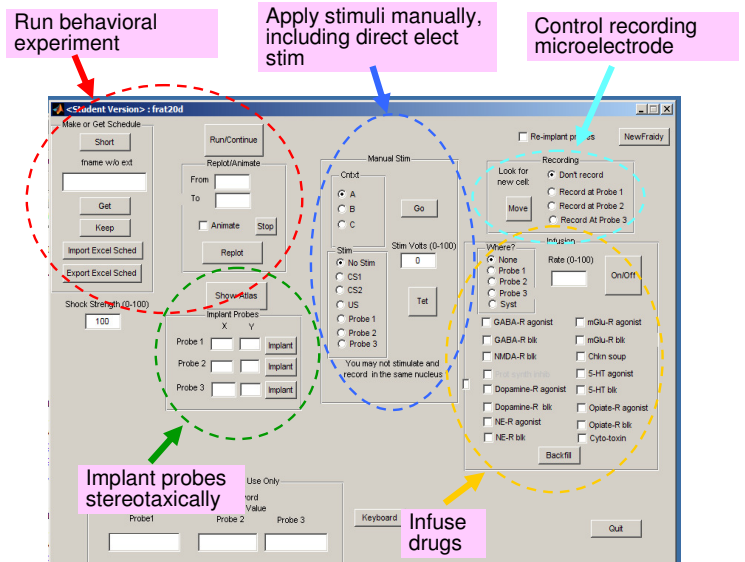


# FRAIDY RAT



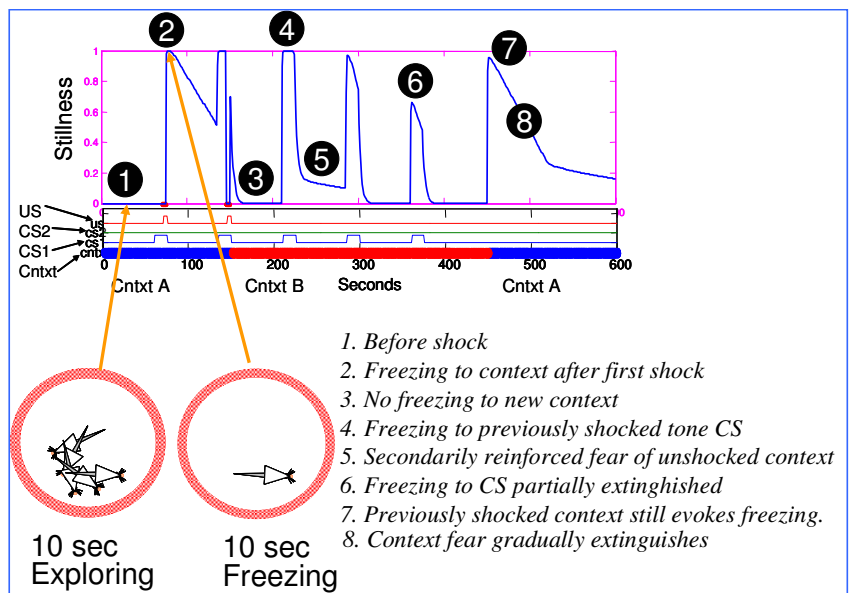
**Introduction.** Fraidy Rat is a computer simulated (i.e. "virtual") rat that can be used by students to do behavioral and neurophysiological experiments on Pavlovian fear-conditioning. The program utilizes mechanisms that have been hypothesized to operate in real animals. It was written for, and has been used extensively as, a module on mechanisms of learning in laboratory courses given at UCLA for students in the Psychobiology and Neuroscience Majors. The program is available on-line as a free download. A short book, entitled, **The FraidyRat Companion--FraidyRat: A Fictitious Rat for Real Research on the Neuroscience of Fear Conditioning**, which is based on the UCLA teaching materials, is in preparation and when finished will be made available at low cost. The brief introduction below is intended to give a feeling for the program in action.

**Control panel.** Fraidy Rat is controlled by a Graphical User Interface shown at the right.



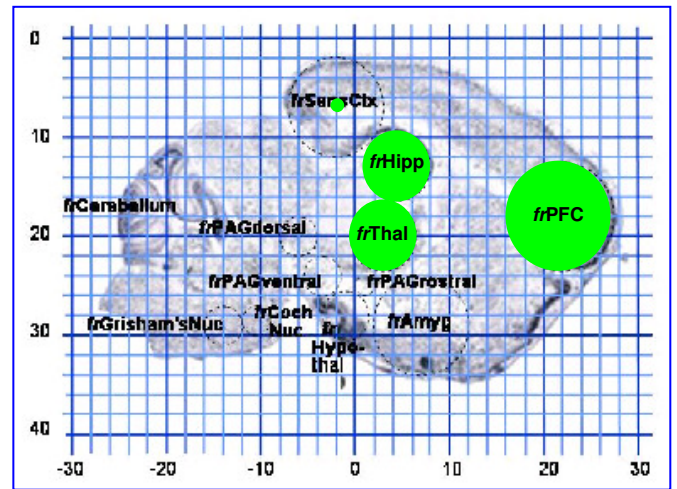
**An illustrative behavioral conditioning experiment.** In the experiment graphed at the right, Fraidy Rat was first given two pairings of a tone CS and shock in context A. Then it was given a brief extinction test to the tone in context B followed by additional extinction without the tone back in the conditioning context A. The X axis is time in seconds and the Y axis is degree of freezing [max stillness=1; maximal exploration of the environment (or jumping about trying to escape shock)=0].

**Fraidy Rat's nervous system controls an animation.** Students can run a cartoon animation of the animals movements (controlled by Fraidy's virtual nervous system; the animation does what the relevant parts of the nervous system tell it to do). Some superimposed frames of the animation from two points in the experiment are shown.

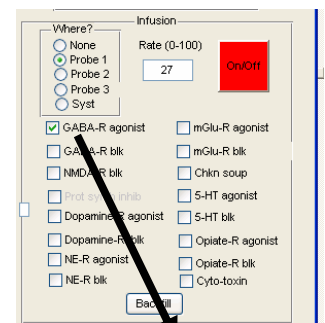


**Stereotaxic Atlas of Brain.** Fraidy Rat has a two dimensional brain with a stereotaxic atlas that is used to guide the implantation of probes for electrical stimulation, single unit extracellular recording, or infusion of a variety of drugs. Fraidy Rat's brain anatomy and physiology are somewhat parallel to, but not the same as that of a real animal, and students are told that Fraidy should be thought of as an "alien" or "mutant" rat that will have both similarities to and differences from real rats. So knowing about real rats and about real fear learning mechanisms can help guide them, but they will have figure out by experiments what the real story is for Fraidy Rat himself.

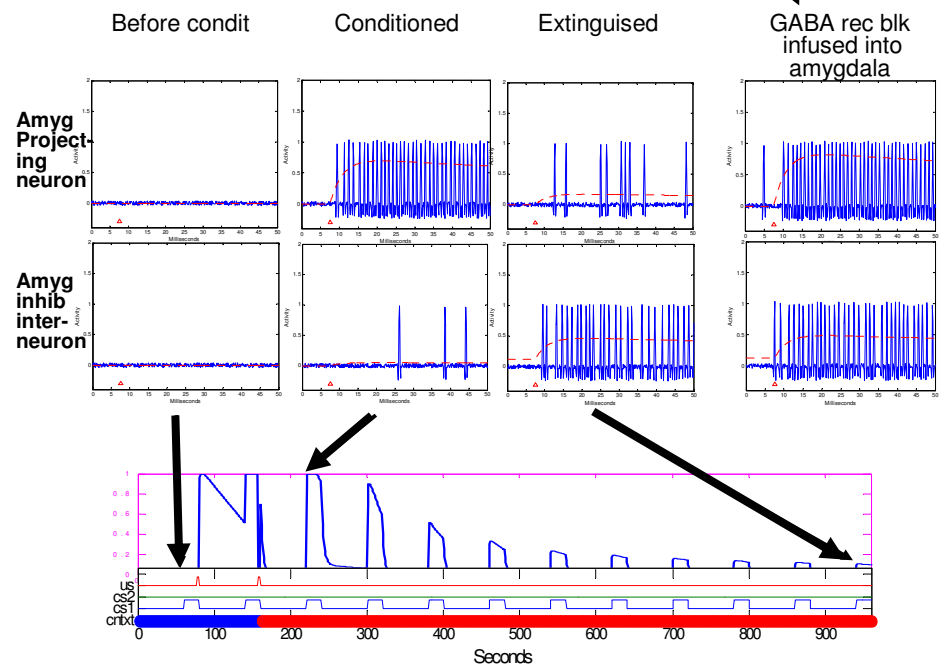
*Retrograde dyes* can be injected into brain regions to discover what nuclei project to a given spot, and students can use this to work out the gross connectivity of the brain. In the picture at the upper right, dye was injected into "sensory cortex" (a Fraidy Rat amalgam of visual, auditory, etc cortex) at the green dot which caused those regions having neurons that project to sensory cortex to turn green.



**Single unit recording.** Single units can be recorded by implanting a probe stereotaxically and then advancing a microelectrode from the probe shaft. Below are shown recordings from two different amygdala units of different types at several points in an experiment. In each case the CS occurred at the little triangle on the baseline of the recorded trace. One recorded cell was a neuron that projected downstream to PAGd that promotes freezing, and the other is a local inhibitory interneuron involved in extinction. Students can determine which of the two types of amygdala units a microelectrode has encountered by electrically stimulating the PAGd electrically and looking for an antidromic (backward-propagating) spike in the recorded amygdala neuron.

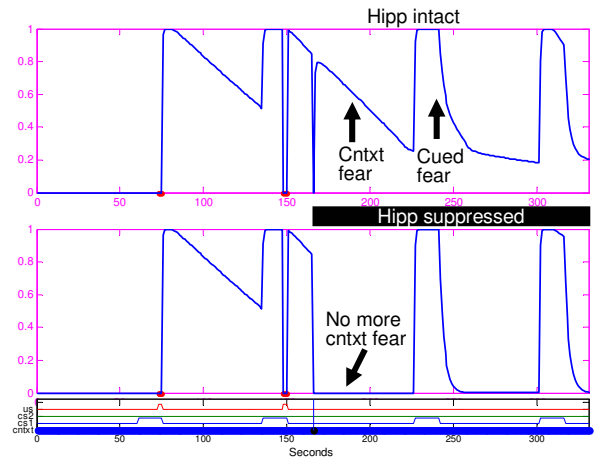


**An illustrative drug infusion effect.** A GABA receptor inhibitor was infused into the amygdala at the end of extinction in this experiment. Students must make infusion flow rate commensurate with the size of the amygdala so as to fully affect amygdala but not affect adjacent structures. During infusion of the GABA receptor blocker, amygdala inhibitory interneurons, whose activity was responsible for extinction, continue to fire, but because GABA receptors are blocked, the amygdala principal cells, whose activity was causing fear prior to extinction, resume firing to the CS since in Fraidy Rat extinction is due to inhibition rather than erasure. Further tests would show that freezing to the CS did in fact resume.



**Hippocampus, contextual fear, and consolidation.** As in real rats, suppression or lesion of the hippocampus soon after conditioning causes retrograde amnesia for context fear. At right, above, are contextual and cued fear during two conditioning trials and a the start of immediately following extinction. In the frame below the same experiment was done but hippocampus was suppressed with a GABA agonist during extinction. Context fear is lost, but cued fear remains.

However, systems type consolidation occurs if about 30 days of rest are allowed after training (which are easily programmed via the control panel), and in that case inactivation of the hippocampus causes no loss of contextual fear (not shown).



**And more.** Many other aspects of fear conditioning can be studied in Fraily Rat. Almost any experiment typically done in real animals can be executed in the Fraily Rat program. Reinforcement mechanisms, effects of expectation errors, neuromodulatory control of synaptic plasticity, LTP, cellular consolidation, renewal of extinction, and more aspects of fear conditioning can be investigated by the student.