***BYOB* detailed notes**

This document describes in detail the inner working of the website "*Build Your Own Brain*" (*BYOB*), in case anyone cares. It also describes some of its limitations. It does not deal with the GUI at all, since that is explained in the instructions for the website. This document is about the calculations behind the scenes. *BYOB* is written in Javascript and depends on *JQuery*, *FileSaver.js*, and the *Font Awesome* icon library. It should run on most newer browsers [Note: *BYOB* will not run on many versions of *Safari* or *IE*].

BYOB implements a very simplified, discrete-time, leaky integrate-and-fire model. The dynamics of neuronal communication are almost completely ignored. Potentials are not modeled and stimulations last only for the epoch in which they are generated; neurons integrate their momentary inputs only. It is therefore a Markov model. It allows for simulating some drug effects, in a way that shares some features with the Nossenson & Messer (2010) model (but much simpler).

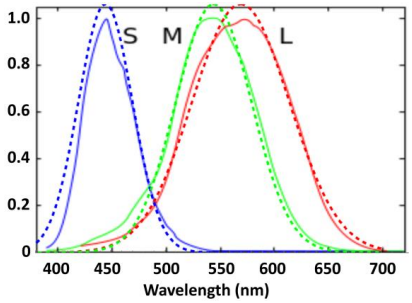
BYOB networks consist of 6 types of elements. Each element has a unique ID and 2D coordinates. The elements are:

1. **Neurons** have inputs and outputs. They have 4 additional user-set properties:
    a. *Neurotransmitter*: the name of the neurotransmitter (*NT*) this neuron emits. Each neuron can only emit one *NT* at all its axons. *NT*s are selected from predefined lists.
    b. *Spontaneous firing rate*: a number in the range [0, 1] that specifies the probability that a neuron self-generates depolarization in any epoch. In epochs where it does, it will internally generate stimulation equal to its activation threshold. This will sum with any external (excitatory or inhibitory) stimulation.
    c. *Excitatory/Inhibitory*: neurons can be either excitatory or inhibitory. The stimulation they provide to downstream elements is multiplied by 1 or -1 to reflect this. This also determines the list of possible *NT*s the user can choose from.
    d. *Threshold*: a value in the range [0, ∞) that determines the minimum amount of stimulation a neuron must receive in one epoch (summed over all inputs) to fire.

    At each epoch, a neuron can fire or not fire. Firing is deterministic: neurons always fire when stimulated at or above their threshold, never otherwise (note, however, that stimulation can be probabilistic, as in the case of spontaneous firing). Firing takes one epoch. In the following epoch, all the axons belonging to a neuron that fired will be activated.

2. **Sensors** are specialized neurons that react to external stimulation rather than synaptic inputs. They have outputs, like neurons, but no inputs. Their user-set properties vary by their type:
    a. *Type:* sensors can be of 6 different types: *Rod*, *Cone*, (cochlear) *Hair*, *Olfactory*, *Taste*, and *Touch*. The type of a sensor is set when it is created and cannot be changed.
    b. *Neurotransmitter:* as for neurons.
    c. *Excitatory/Inhibitory*: as for neurons.
    d. *Subtype* (cones only): the frequency response range of the cone cell. Can be *Red (Long)*, *Green (Medium)*, or *Blue (Short)*. Each subtype reacts differently to light stimulation at different wavelengths (see **Stimuli**, below). The response functions for all three

subtypes are normal distributions centered at wavelengths, *w*, of 570 nm (L), 545 nm (M), and 445 nm (S). The functions are shown in the figure at right. Solid lines are response norms for human cone cell subtypes; dashed lines are the *BYOB* functions. The response equations are:



i. Red: $f(w) = 1/e^{(w-570)^2/4050}$
ii. Green: $f(w) = 1/e^{(w-545)^2/2450}$
iii. Blue: $f(w) = 1/e^{(w-445)^2/1250}$

e. *Frequency* (Hair cells only): frequency response range of the hair cell. Hair cells respond to any stimulation that is within 10 Hz of their set frequency. Responding is all-or-none.

Unlike neurons, sensors do not fire spontaneously nor do they have activation thresholds. Since such cells do not usually fire action potentials, sensors in *BYOB* can change the strengths of their axons (see below) as a function of the stimulation they receive. Activated sensors will "fire" but will first change the strength of their axon, A_S, as follows:

- *Olfactory*: no change in axon strength. Sensor either fires or not.
- *Cone*: $A_S = I * f(w)$, where *f(w)* is the response function given above.
- *Others*: $A_S = I$, where *I* is the intensity of stimulation delivered (see **Stimuli**, below).

3. **Muscles** are the outputs of the system. They have inputs but no outputs. Muscles have:
   a. *Threshold*: as for neurons.

   In each epoch, muscles can fire (flex) or not, depending on the total stimulation they receive. Firing takes one epoch.

4. **Axons** serve as connections between the other elements. Each axon belongs to one element (neuron or sensor) and attaches to one element (neuron or muscle). Only one axon is permitted between any two elements. Though all incoming axons to an element appear (on screen) to converge at the same point, each axon is considered to have its own synapse and synapses operate independently of each other. Axons have:
   a. *Strength:* a number in the range [0, ∞) that determines the amount of stimulation this axon, when active, delivers to its target element.
   b. *Receptor:* the type of postsynaptic receptor present at the synapse (receptors are made properties of the [presynaptic] axon since that is the only place where *BYOB* distinguishes between synapses on the same postsynaptic element). Receptors are selected from predefined lists, which depend on the *NT* being emitted by the axon's owner. In other words, *BYOB* does not allow synapses where the receptors do not match the *NT*. Only one receptor type is allowed per synapse.

In each epoch, an axon can be active or not. Axons always deliver the same amount of stimulation when active (equal to their current strength) and no stimulation when inactive. The stimulation is multiplied by -1 if the axon belongs to an inhibitory neuron or sensor. Activation

takes one epoch to move down an axon; the length of the axon is ignored. Stimulation is delivered to the target element in the following epoch.

5. **Stimuli** are external events that can influence sensors. Stimuli are not connected to the network but can affect sensors that are nearby. Stimuli have:
    a. *Type*: there are 5 types of stimuli: *Light*, *Sound*, *Touch*, *Odor*, and *Taste*. Each stimulus will only activate sensors of the appropriate type. There is no limit to the number of sensors one stimulus can activate.
    b. *Radius*: A number in the range [0, ∞) that determines how far away the effects of the stimulus are felt. Active stimuli activate all appropriate sensors within range. On screen, the distance is measured from the center of the stimulus icon to the top-right corner of the sensor icon.
    c. *Intensity*: A number in the range [0, ∞) that determines the strength of stimulation provided. Note that intensity does not decrease with distance: any sensor within range receives the full intensity; anything outside the range receives no stimulation.
    d. *Frequency*: sound and light stimuli deliver stimulation at a specific frequency or wavelength, respectively. Sensors will only be affected if their sensitivity matches the stimulus frequency (see above).
    e. *Schedule*: each stimulus can be on or off in each epoch. The stimulus' schedule is a comma-separated list of numbers in the range [0, 1] that determine its probability of being active in each epoch. The list can be of any length and the simulation will cycle through the list for as long as it is running. If the stimulus is active, it always delivers its full intensity (i.e., activation is all-or-none).

6. **Drugs** are a type of stimulus that acts at the synapse instead of on sensors. They are also external to the network. Drugs have:
    a. *Class*: drugs have many different mechanisms of action, selectable from a predefined list. Currently, there are two classes: *(Ant)agonists* (*AG*) and *Reuptake inhibitors* (*RI*).
    b. *Target*: the receptor (*AG*) or *NT* (*RI*) that the drug is specific to. Drugs can only affect one target type. Targets are selected from a predefined list for each class.
    c. *Radius*: as for sensors. Active drugs will affect any appropriate synapse (i.e., that has the corresponding target) that is within range. Distance is measured from the center of the drug icon to the blue dot (dendrite) on the postsynaptic neuron.
    d. *Affinity*: how strongly the drug binds to its target receptor (*AG*) or transporter (*RI*).
    e. *Efficacy* (*AG* only): how strongly the drug activates its target receptor.
    f. *Schedule*: as for sensors.

    Though all incoming axons to a target neuron may fall within range of a specific drug, drugs operate at the level of the synapse. Co-located synapses with non-matching receptors or *NT*s will not be affected. Drugs compete for binding sites with each other and, for *AG*, with any endogenous *NT*s. The two classes of drugs affect synapses differently:

i. *(Ant)agonists*: bind to receptors, proportionately to their affinity, and stimulate them, proportionately to their efficacy. All within the same epoch.
ii. *Reuptake inhibitors*: cause any endogenous stimulation (coming from an axon) from the immediately preceding epoch to remain, proportionate to the drug's affinity.

Drugs compete with each other, within their class. Each drug's (of either class) *affinity*, *A*, is first normalized by $A_i' = (A_i Max(A))/\Sigma A$, where *Max(A)* is the maximal affinity of all drugs of the same class active at that synapse in that epoch. The final stimulation at a given synapse for the current epoch *t*, F_t, is then given by:

$$F_t = IS_t\big(1 - Max(A_{AG})\big) + \sum_{AG} A_i' E_i + \sum_{RI} A_i' S_{t-1}$$

where *I* is the excitatory/inhibitory coefficient for the presynaptic neuron (1 or -1), S_t is the level of endogenous stimulation (i.e., from incoming axons + spontaneous firing) at that synapse at time *t*, $Max(A_{AG})$ is the maximal affinity of all *AG*, and E_i is the efficacy of AG_i. In other words, final stimulation is the sum of endogenous, *AG*, and *RI* effects.

Plasticity

BYOB allows changes in the strengths of axons, to simulate LTP and LTD. Only synapses where the receptor is set to "*NMDA/AMPA*" are plastic, and only where the synapse is onto a neuron (i.e., not at neuromuscular junctions). The rules are as follows:

- *LTP*: the strength of a plastic synapse that receives endogenous stimulation (the incoming axon is active) in an epoch when the postsynaptic neuron is already firing will increase by 0.1. This is independent of the strength of the stimulation (i.e., even if it is sub-threshold) and of the source of the stimulation that caused the postsynaptic neuron to fire (e.g., it could have come from a different synapse). There is no limit to the maximal strength a synapse can attain.
- *LTD*: the strength of a plastic synapse receiving sub-threshold endogenous stimulation in an epoch where the postsynaptic neuron is not firing will decrease by 0.1. LTD will only happen if the incoming axon is active. In other words, the axon must be delivering stimulation greater than 0, but less than the threshold of the postsynaptic neuron. The minimal allowed synapse strength is 0.1.

LTP and LTD are implemented presynaptically, by changing the strength of the incoming stimulation, not by altering the postsynaptic threshold (since that is set at the level of the neuron, not by synapse). The current strength of an axon is represented on-screen by its thickness.

Every model is wrong…

BYOB obviously contains many oversimplifications, some of which have been noted above. Below, I highlight a few other places where it does not accurately reflect what we know about the brain.

- The network is static: no neurogenesis, no new axons or axon branches, no new dendrites, no apoptosis, no change (or differences) in receptor sensitivity or trafficking.

- There are no dynamics of neuronal communication. No EPSPs (activation either reaches threshold and causes an AP, or dies immediately). The shape of the AP is not simulated. In this sense, *BYOB* is not really a classical integrate-and-fire model.
- There are no glia.
- There are no hormones.
- APs move down all axons at the same speed. Axon length is not considered – it always takes one epoch to go from the axon hillock to the synapse.
- Sensors, such as retinal cells, have axons just like generic neurons. They fire APs, though the strength of those does vary based on the stimulation they receive.
- LTP and LTD happen only presynaptically. All plasticity is NMDA-dependent. Changes in axon strength, barring further plasticity, are permanent. There is no required frequency of stimulation for LTP – it all happens in one epoch.

Pedagogy

BYOB is intended as a pedagogical tool for an undergraduate neuroscience course. Students can be given challenges (e.g., "make me an associative learning circuit") and can send instructors their resulting networks, which can be loaded and viewed on the website. I also have some Python scripts that will run multiple files at once and check if they conform to some criterion, which may help in grading files from large classes. There are some anti-cheating measures incorporated into *BYOB*, which should allow instructors to tell if a network has been copied or is original. For details of those, contact me. *BYOB* is free to use and I am happy to share my code. I welcome bug reports, suggestions for improvement, and unsolicited compliments. Contact me at: *nmiller@wlu.ca*