

# Neural Circuit Development Notes

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### 1 Thoughts

**Ortus basic premise:** entire system works similarly to the CO<sub>2</sub> and O<sub>2</sub> regulation mechanism. Aim is to keep a balance. E.g., if IFEAR goes up, this should inherently be bad. Could be that the reason for this is that it is tied to a very basic system, like breathing. So, if system is wired such

that as INO2 increases, IFEAR increases, and an increase in INO2 causes an intake of O2, which decreases INO2, the system *inherently* wants to minimize INO2 and IFEAR. Everything should build off of and/or expand this basic idea/structure.

Take *C. elegans*, for example. It only has 302 neurons, and is a relatively simple organism, with its connectome nearly entirely known. Despite its relative simplicity, it is capable of avoiding toxins (cite toxin avoidance), and withdrawing from a touch to the head. Both of these actions show a tendency to minimize certain conditions. In the context of an organism as simple as *C. elegans*, it becomes clear that this tendency arises from a circuit configuration that causes certain “pre-wired” responses to be preferred over others. **This another premise of Ortus:** The idea of “emotions”, as we know them, are simply the rise and fall in activation of different groups of neurons, tied to very fundamental behaviors. The concepts of “good” and “bad” sensations or emotions only carry meaning to us because of their associations to circuits that are either desirable or undesirable from a longevity perspective.

1. perhaps use a “chemical” to signal that a synapse may be created
2. may also need to factor location in... that would be a pain, because each synapse would need a 3D coordinate.
3. classical conditioning – two stimuli paired, instrumental conditioning – stimulus -> response -> reward
4. as things get repeated, the pathway between input and output shortens (creates a “reflexive reaction”, though not the same as a real reflex, like a knee jerk)
  - i) **Ortus premise:** Essentially, complex behaviors are more nuanced reflexes. A reflex goes from a sensory neuron to the spinal cord where interneurons redirect the signal to a motor neuron. Complex behaviors originate from some combination of existing neural activity and sensory input, which combine and, after being passed through a number of different interneurons, end up as signals to motor neurons, or loop back around to continue the “thought” process.
5. Should have a loop that re-energizes (in a decaying way) neural pathways/circuits that were recently used. In this way, perhaps we can implement instrumental learning, and time-based/sequence-based knowledge.
6. rodent and human brain have same basic structure, it seems. things tend to be organized fairly similarly, relative to each other. 32.2
7. 32.2 are discussing rodent experiments that cause lesions to regions of the brain, so ortus should be able to function by using single neurons to represent groups of neurons, while there isn't a requirement for greater behavioral nuance.

## 2 DNA, Genes, Proteins, and Cells

Genes...

### 2.1 How Genes work

<https://publications.nigms.nih.gov/thenewgenetics/chapter1.html> [https://online.science.psu.edu/biol011\\_sandbox\\_7239/node/7260](https://online.science.psu.edu/biol011_sandbox_7239/node/7260) <http://genetics.thetech.org/about-genetics/how-do-genes-work>

## 2.2 Cell Signaling

<http://www.nature.com/scitable/topicpage/cell-signaling-14047077>

## 2.3 From DNA to protein

Video: From DNA to protein - 3D <https://www.youtube.com/watch?v=gG7uCskU0rA>

My understanding is:

1. DNA is made up of nucleotides
2. Sections of DNA encode various genes
  - i) Intergenic DNA (DNA between genes) seems to play a part in determining which genes are turned on/off, among other things. (this is part of the 98% of DNA not coding for genes)
    - a) There is also DNA that sits in the middle of genes at times
      - A) Exons → coding sequences, introns → intervening sequences
3. Enzymes unzip the DNA, and one side is transcribed to generate RNA—a single strand of nucleotides
  - i) This happens for genes that are “turned on”
  - ii) Each cell only “turns on” the genes it needs to do its job; this is due to proteins on the RNA polymerase
4. Codons are groups of 3 nucleotides, from the RNA strand, that code for amino acids
  - i) There are “start” and “end” codons that mark the start and end of each gene
5. Amino acids are protein building blocks
6. The ribosomes then convert the codons from the RNA strand to proteins
  - i) Prior to this, parts of the RNA are cut out during RNA splicing
    - a) Exons are stitched together, using introns to dictate things like “alternative splicing”
  - ii) genes are instructions for making certain proteins
7. The proteins “made” by some genes can act as switches
  - i) If something goes wrong, a leg could grow instead of an antennae, for example.
    - a) **This suggests that as replication happens, slight changes in the expressed genes are (more or less) deterministically carried out to ensure that things like arms, legs, vertebrae, etc. grow exactly as they should**
8. Some of these proteins are receptors for neurons
  - i) Some of these receptors are ligand-gated ion channels, that open to allow ions into or out of the neuron/cell.
    - a) AKA ion-channel-linked receptors
    - b) ligands are the neurotransmitters

### 3 Parts of the Brain

1. cerebral cortex (cerebrum)
  - i) frontal lobe (top front) – reasoning, planning, parts of speech, movement, emotions, problem solving
  - ii) parietal lobe (top middle)– movement, orientation, recognition, perception of stimuli
  - iii) occipital lobe – visual processing
  - iv) temporal lobe – perception and recognition of auditory stimuli, memory, and speech
2. cerebellum (little brain)
  - i) associated with regulation and coordination of movement, posture, and balance
  - ii) evolutionarily really old; reptiles have this as more or less their full brain
3. limbic system (emotional brain) – buried within cerebrum, like cerebellum, fairly old
  - i) Thalamus - relays sensory impulses from receptors in various parts of the body to the cerebral cortex. Experts think of it as a gate. 98% of sensory input is relayed by it (not olfaction? – maybe olfaction is a more primitive sense that routes to cerebellum, and is similar to chemosensors in *c. elegans*?).
  - ii) Hypothalamus – controls release of 8 major hormones, involved in temperature regulation, control of food and water intake, sexual behavior, daily cycles in physiological state and behavior, and mediation of emotional responses.
  - iii) Amygdala – integrative center for emotions, emotional behavior, and motivation. where memory and emotions are “combined”. combines many different sensory inputs.
    - a) Amygdalofugal Pathway (link whereby motivation and drives can influence responses, and where responses are learned, rewards and punishments), stria terminalis (similar to fornix) – both important, come back to this.
  - iv) Hippocampus – associated primarily with memory. looks like a seahorse.
4. Brain Stem – underneath limbic system, responsible for basic vital life functions such as breathing, heartbeat, and blood pressure.
  - i) Midbrain – (tectum, the ‘roof’, and tegmentum, in front of the tectum). Tectum responsible for visual reflexes. Tegmentum coordinates sensorimotor information.
  - ii) Pons – connects the spinal cord to higher brain levels, and transfers info from cerebrum to cerebellum, some of which are part of the reticular formation, which regulates alertness, sleep, and wakefulness.
  - iii) Medulla – transmits signals between the spinal cord and higher parts of the brain, controls autonomic functions like heartbeat and respiration. Also holds part of reticular formation.
5. grey matter: pinkish-grey, contains cell bodies, dendrites, and axon terminals – so, this is where the synapses actually are. On outside of brain, but inside of spinal cord.
6. white matter: axons, which are connecting the different parts of grey matter to each other. On inside of brain, but outside of spinal cord.

So, basically, input goes into thalamus, and is then relayed, in this way, associations can be built. Thalamus has three groups of cells:

1. Sensory relay nuclei – These include the ventral posterior nucleus and lateral and medial geniculate body. Relay primary sensations by passing specific sensory information to the corresponding cortical area.
2. Association nuclei – receive input from specific areas of the cortex, which is projected back to the cortex to “somewhat” generalized association areas, where they regulate activity.
3. non-specific nuclei (intralaminar and midline thalamic), which receive input from cerebral cortex and project information diffusely through it. Most of these interconnect brain activity between different areas of the brain and play a role in general functions such as alerting.

**Note:** brain part info from

1. <http://www.news-medical.net/health/What-does-the-Thalamus-do.aspx>
2. <http://neuroscience.uth.tmc.edu/s4/chapter06.html> – talks about fear response and amygdala
3. Britannica, and other places too...

#### **4 Neural reuse: a fundamental organizational principle of the brain. [1]**

Test...

#### **5 Functional roles of short-term synaptic plasticity with an emphasis on inhibition [2]**

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#### **6 Emerging roles of astrocytes in neural circuit development. [3]**

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## **30 Neural plasticity and behavior ??? sixty years of conceptual advances [27]**

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## **31 Homeostatic Plasticity of Subcellular Neuronal Structures: From Inputs to Outputs [28]**

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## **32 Mechanisms of Neural Circuit Formation [29]**

(Note: this is a book comprised of research articles, title of relevant articles as subsections)

### **32.1 Introduction to mechanisms of neural circuit formation**

Topics in book:

1. cell adhesion molecules (and downstream roles in cell identity, recognition, and synaptic specificity)
2. axon guidance, formation of terminals, and dendritic arborization
3. formation of synaptic structures themselves (remains subject to remodeling and plasticity throughout development and even in adult animals)

### **32.2 Wired for Behaviors: from development to function of innate limbic system circuitry, 2012**

1. “Limbic system links external cues possessing emotional, social, or motivational relevance to a specified set of contextual and species-specific appropriate behavioral outputs”

2. Some enhanced through experiential learning and reinforcement, but others are innate
  - i) courtship, maternal care, defense, establishment of social hierarchy → all ensure survival of individual or offspring, and thus propagation of species
  - ii) regulated and influenced by sensory stimuli
3. “Emotional salience, produced in the amygdala, is generally thought of as a prime driving force behind innate human behaviors, typically social in nature”
4. This review focuses on the rodent, and because sensory inputs to rodents are primarily smell, audio, and touch, (with minimal visual inputs), the review focuses on chemosensation and how it relates to mating, maternal care, etc.
5. innate rodent behaviors, e.g.: female prefers male urine odors to female, or no odors (naive); mouse that has never encountered a predator will display signs of fear in response to predator odors.
  - i) These chemicals are detected in the nose, processed by the Main and Accessory Olfactory Bulbs (MOB, AOB), projections from the AOB and MOB (directly or indirectly) synapse onto a number of higher order structures (olfactory cortex, amygdala), and the amygdala sent projections to the hypothalamus for further integration and coordination with the brain stem to initiate “fight or flight” responses.
    - a) although they will focus their attention on this circuit, they state that: “we would like to emphasize that these brain hubs and their many feedback loops are not the sole components of a highly complex neural network important for the regulation of sociability an innate emotions”
      - A) This is probably dumb.
6. disabling different parts of the aforementioned circuit, when looking at mating behaviors, can all have different effects on mating behavior (e.g., males seeking males)
7. defensive behaviors trigger slightly different areas of the amygdala and hypothalamus, depending upon whether the stimulus is a predator or a conspecific animal.
  - i) NOTE: this seems to back up the idea of building on / expanding existing structures to grow the brain in Ortus
8. VNO organ (receptors) appear(s) to have evolved specifically to respond to cues that depend upon the animal’s survival in the wild (so, to react to specific species)
9. TEMP

### **32.3 Protocadherins, not prototypical: a complex tale of their interactions, expression, and functions**

## **33 Synaptogenesis: A synaptic bridge [30]**

Test...

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