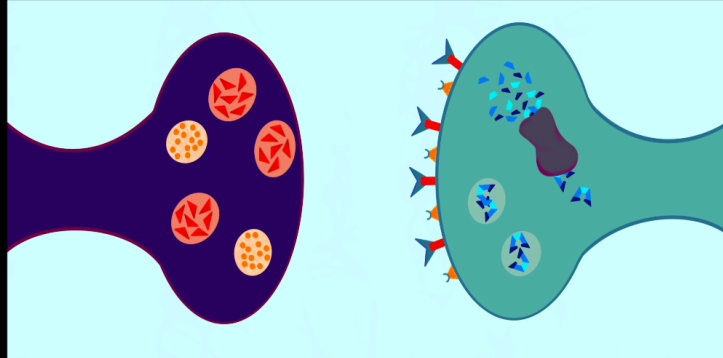


**Locally
Synthesized eCB
on Synaptic Shape
and Memory**

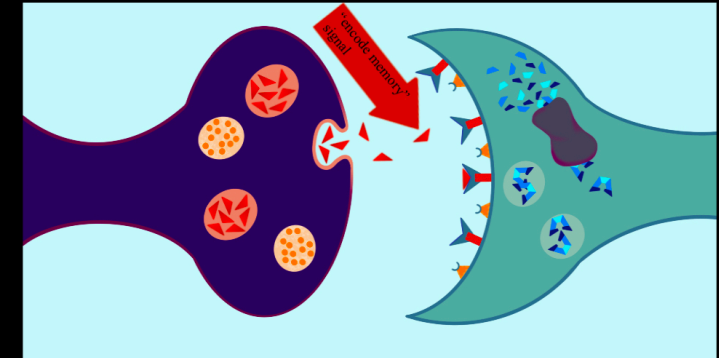
Question: On a biophysical level, what is a memory?

Hypothesis: Communication between neurons strengthens as the two neurons “talk” across the synapse between them (a.k.a. the neuron on one side of the synapse stimulates the neuron on the other side of the synapse). Biophysical changes in one cell of this neuron pair, across a neural pathway, encodes a memory.

Let’s break this down and focus in on a single synapse between two neurons. The neuron on the left is called the **presynaptic cell**, and we will name her **Margot**. Margot sends a signal across the synapse to **Lily**, who is our **post synaptic cell**. Lily’s job is to receive the signal from Margot and respond. Because no other neurons have given Margot information that needs to be passed on to Lily, the synapse between them is dormant.

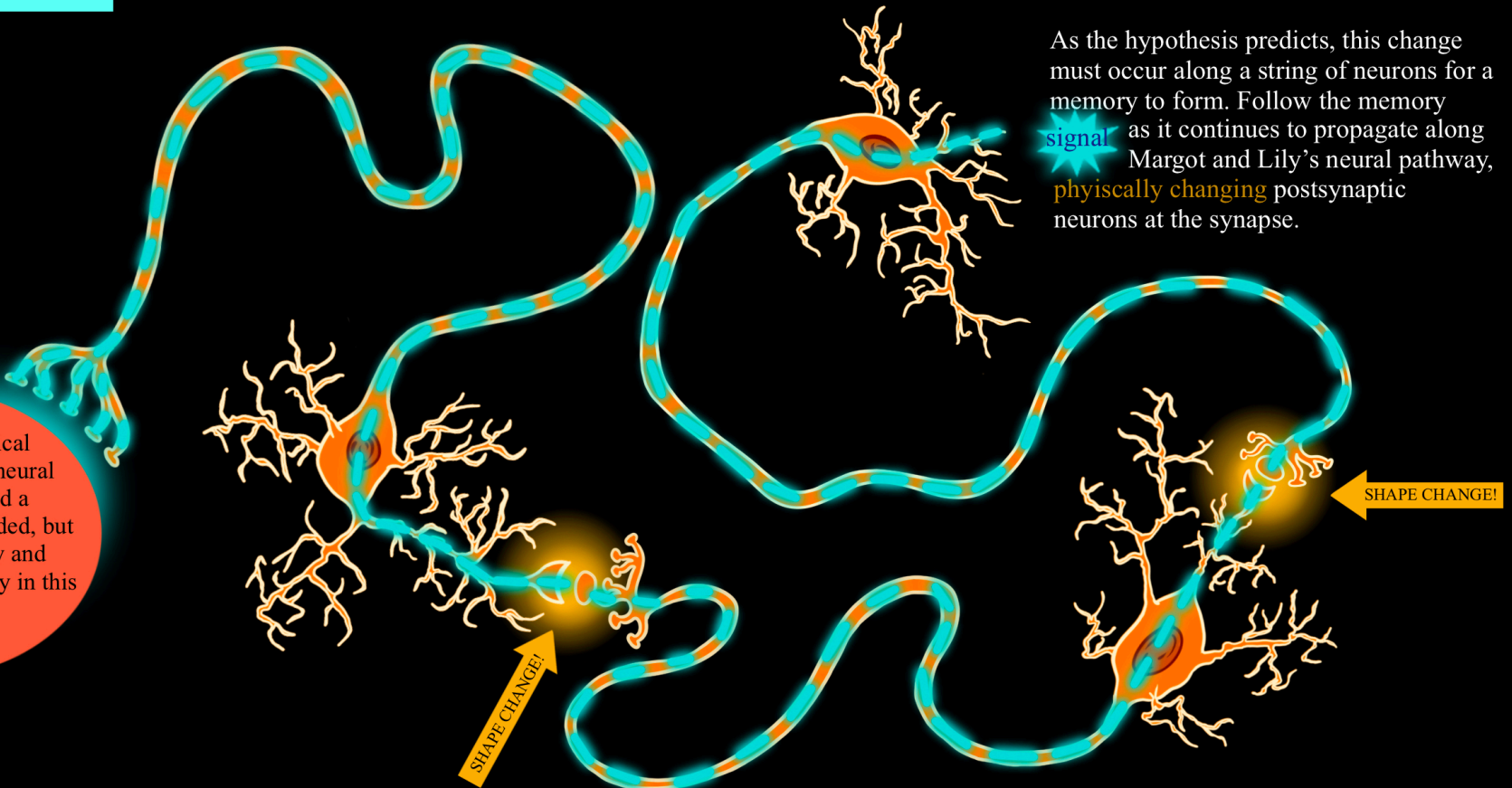


Margot has just received a signal from a neighboring neuron telling her that a new memory must be encoded using the neural pathway that Margot and Lily belong to. Margot passes this message on to Lily by sending a chemical “**encode memory**” signal across the synapse, and Lily responds by changing her shape to accommodate the new memory.



As the hypothesis predicts, this change must occur along a string of neurons for a memory to form. Follow the memory signal as it continues to propagate along Margot and Lily’s neural pathway, **physically changing** postsynaptic neurons at the synapse.

A series of biophysical changes along this neural pathway has allowed a memory to be encoded, but do neurons like Lily and Margot have any say in this process?

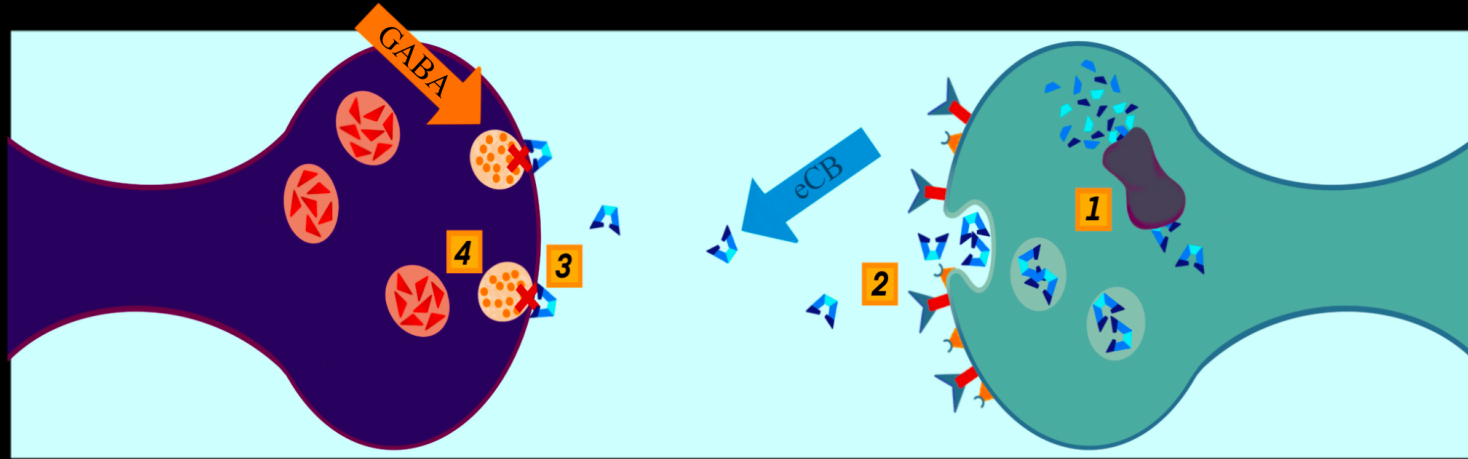


In fact, a postsynaptic cell like Lily can influence whether she “hears” Margot’s signal or not. Along with the “encode memory” signal that can be sent to Lily, Margot produces **GABA**, an inhibitory neurotransmitter which counteracts Margot’s other chemical signals.

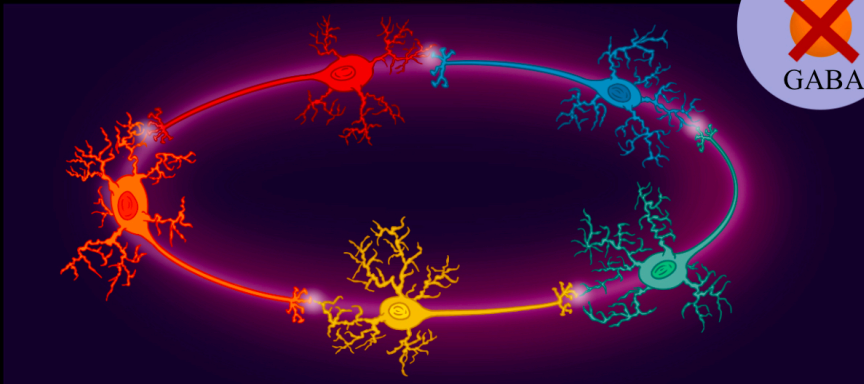
For Lily to pass on the “encode memory” signal to the next cell, she needs to “hear” this message enough times - say, 10 times. Every time she receives the “encode memory” signal from Margot, she counts +1 towards her threshold of 10. But every time she receives a GABA signal from Margot, she takes away -1. Thus, GABA can block Lily from passing on the “encode memory” signal, even while she is actively receiving this signal from Margot.

However, Lily can synthesize a molecule called **eCB** locally (meaning eCB is made in the dendrites - the part of Lily that interact with the synapse to Margot - instead of the cell body farther away). eCB can go back across the synapse to block Margot from releasing GABA, meaning that Margot’s “encode memory” signal cannot be blocked and will be clearly “heard” by Lily. Let’s take a look at this process:

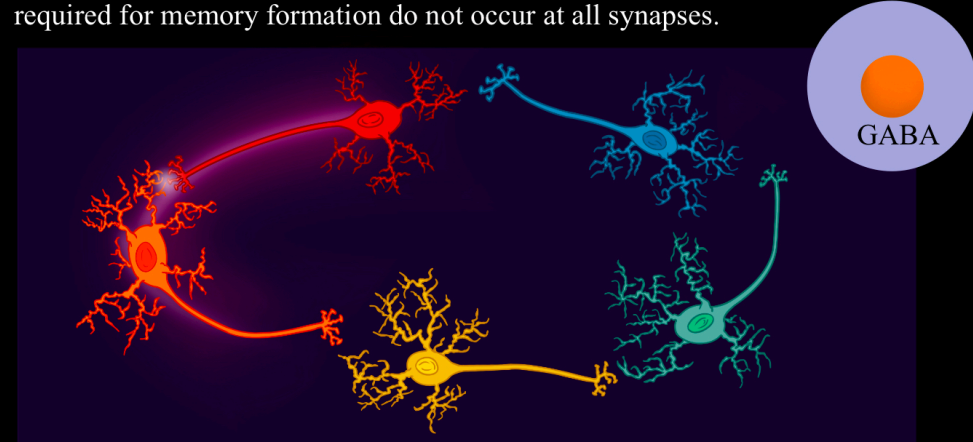
- 1** Inside Lily’s dendrites, eCB is synthesized.
- 2** eCB exits the postsynaptic cell and diffuses back across the synapse to Margot, our presynaptic cell.
- 3** At the presynaptic membrane, eCB blocks the release of neurotransmitter GABA.
- 4** GABA cannot leave Margot to counteract other chemical signals. Lily successfully “hears” Margot’s “encode memory” signal.



If Lily is producing eCB, GABA is blocked. Lily is able to propagate the “encode memory” signal to other neurons in the pathway, which induces the necessary biophysical changes for memory encoding to occur.



If Lily doesn’t produce eCB, GABA can silence the “encode memory” signal, meaning Lily can’t pass on the message. The biophysical changes required for memory formation do not occur at all synapses.



And so, we see how local synthesis of a specific molecule can regulate whether or not certain signals are received, and therefore what shape the synapses of neurons take on. Through regulating synaptic plasticity, locally synthesized eCB impacts the formation of memory.

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