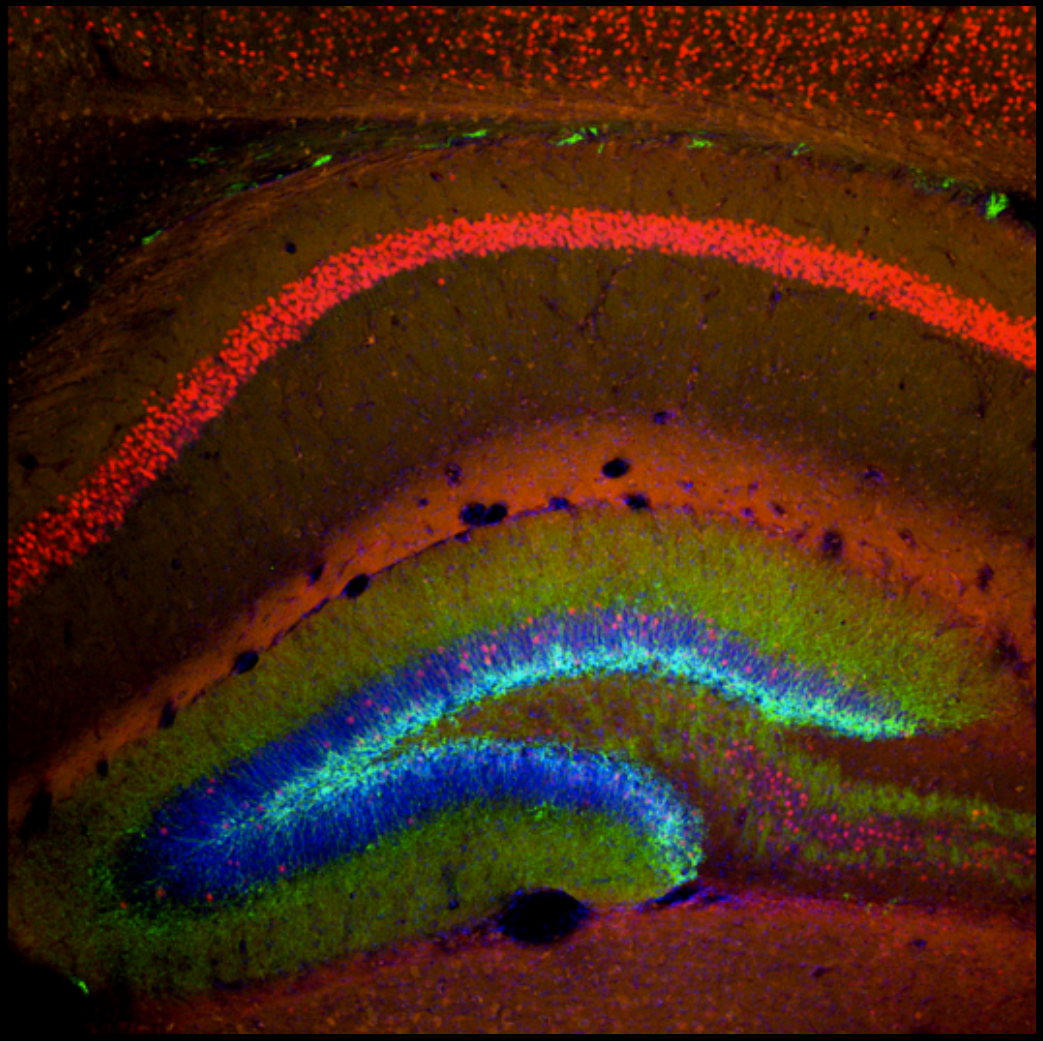
What do you notice?



Adult Neurogenesis

the birth of new neurons in the adult brain

By Lara Rangel

COGS 1: April 18, 2019

The number of neurons in the brain is *constantly changing*

New estimates of the number of neurons in the human brain range from roughly **80 billion** to **120 billion**.
Herculano-Houzel 2009

We can **lose** neurons for many reasons such as disease, injury, stress, and normal aging.

We can also **increase** this number through a process called *adult neurogenesis*.

On the replacement of lost cells

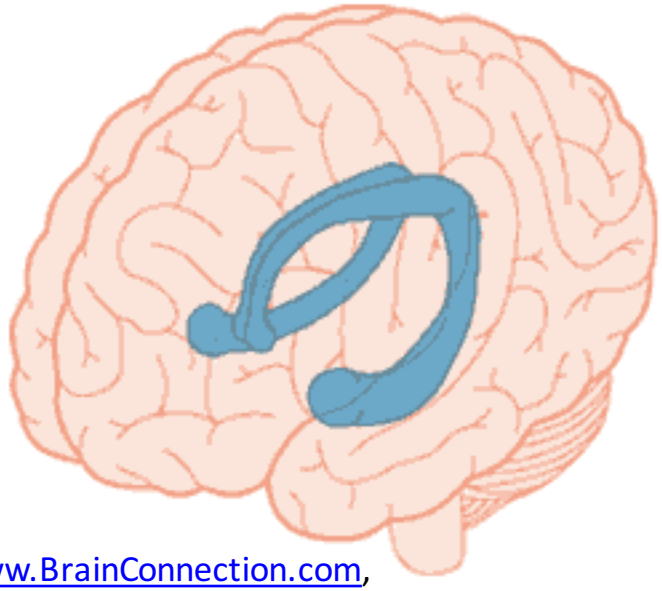
Question:

If we could **gain** a neuron for every neuron that we **lose**, could the new neurons take over the job of the lost neurons?

Or are lost neurons irreplaceable?

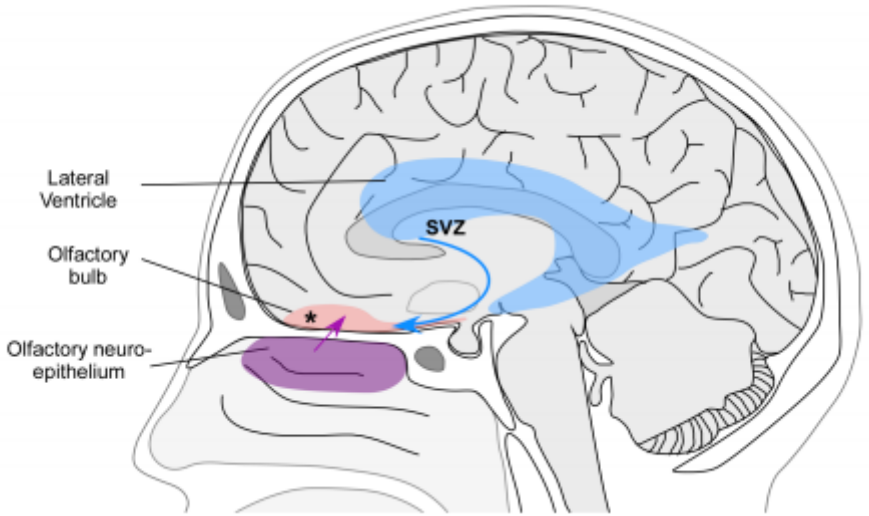
There are two main neurogenic regions

The **subgranular zone** of the dentate gyrus:

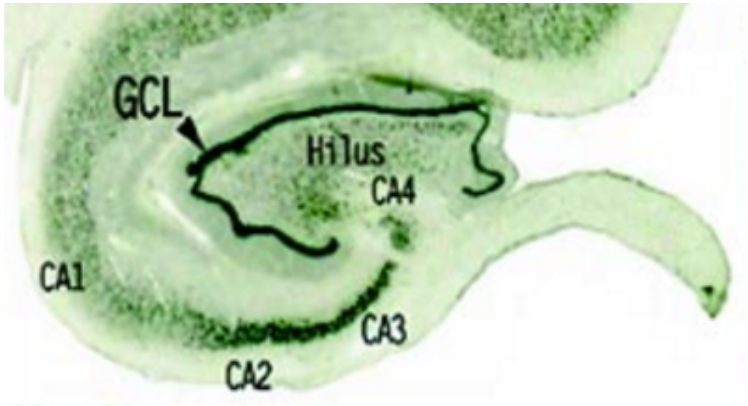


www.BrainConnection.com, Scientific Learning Corp., 1999

The **subventricular zone** of the lateral ventricle:



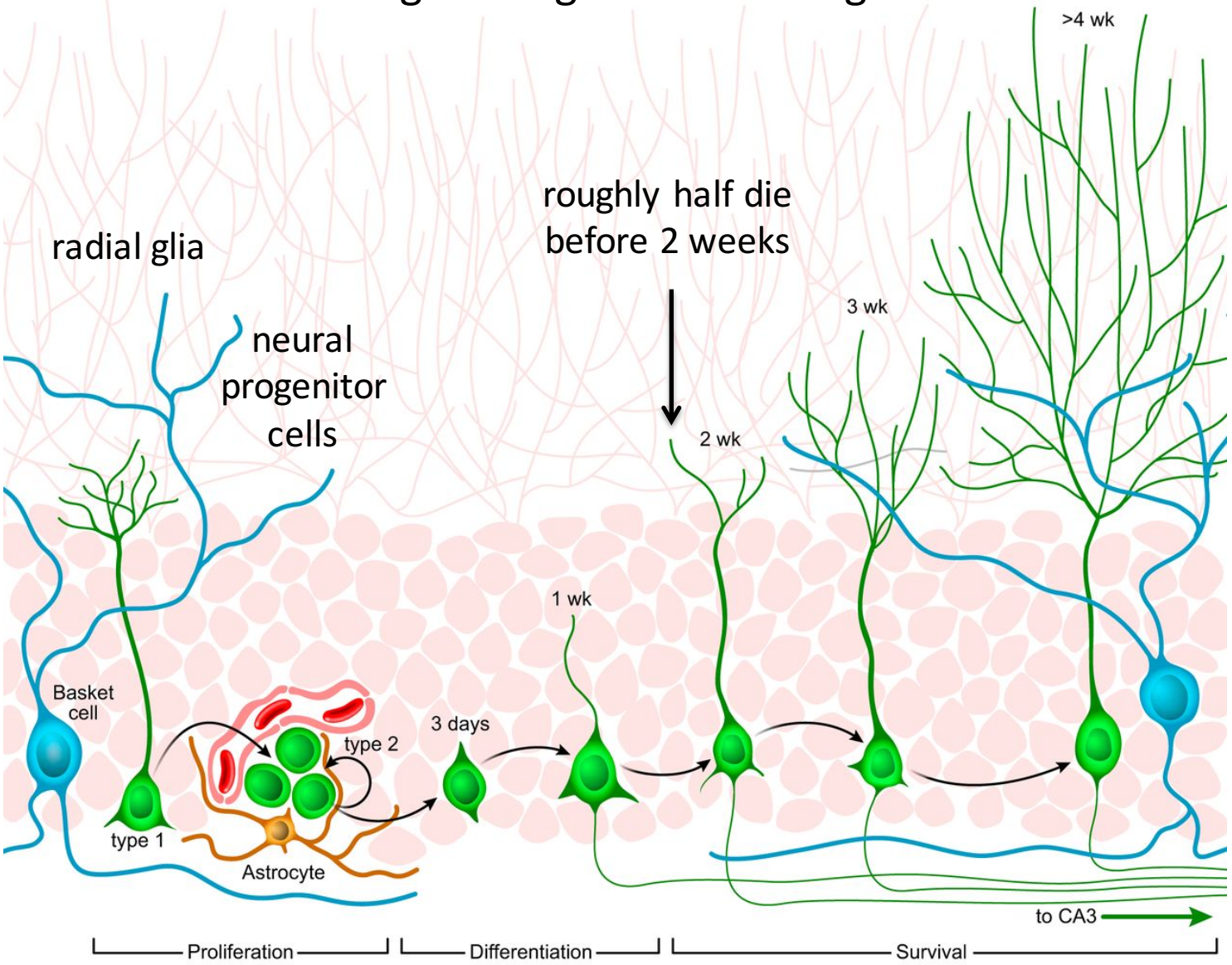
Huart, Rombaux, and Hummel, 2013



Eriksson et al., 1998

New neuron development:

from dividing radial glia to mature granule cell

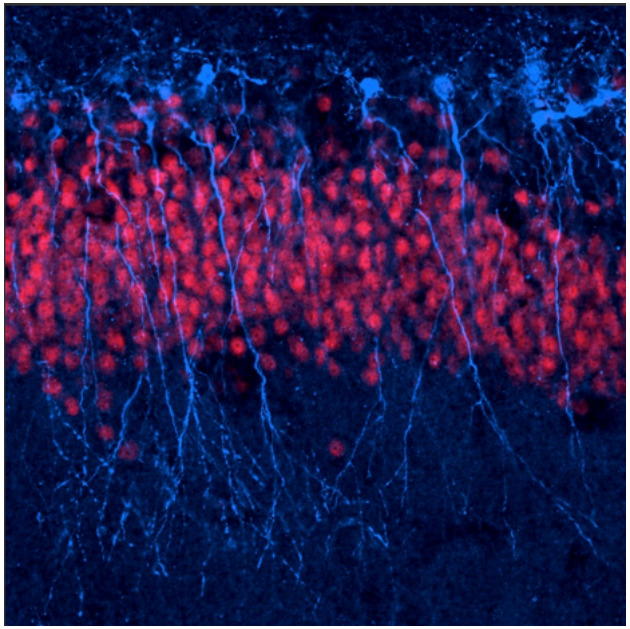


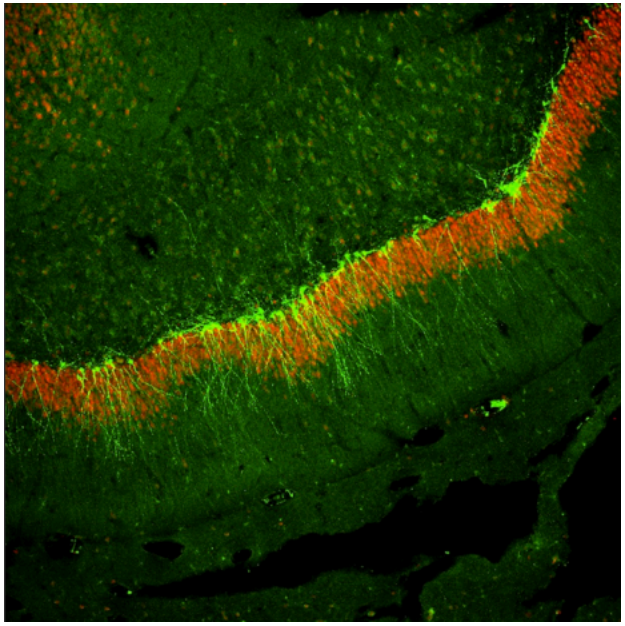
This process is **highly regulated**

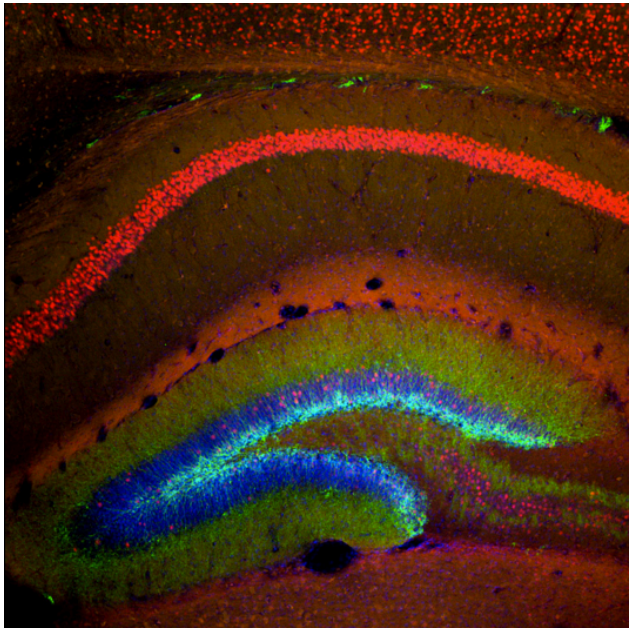
Aimone et al., 2014

Quantifying neuron **proliferation** (rate of division) and **survival**

Doublecortin: a mictrotubule-associated protein expressed in the first 2-3 weeks



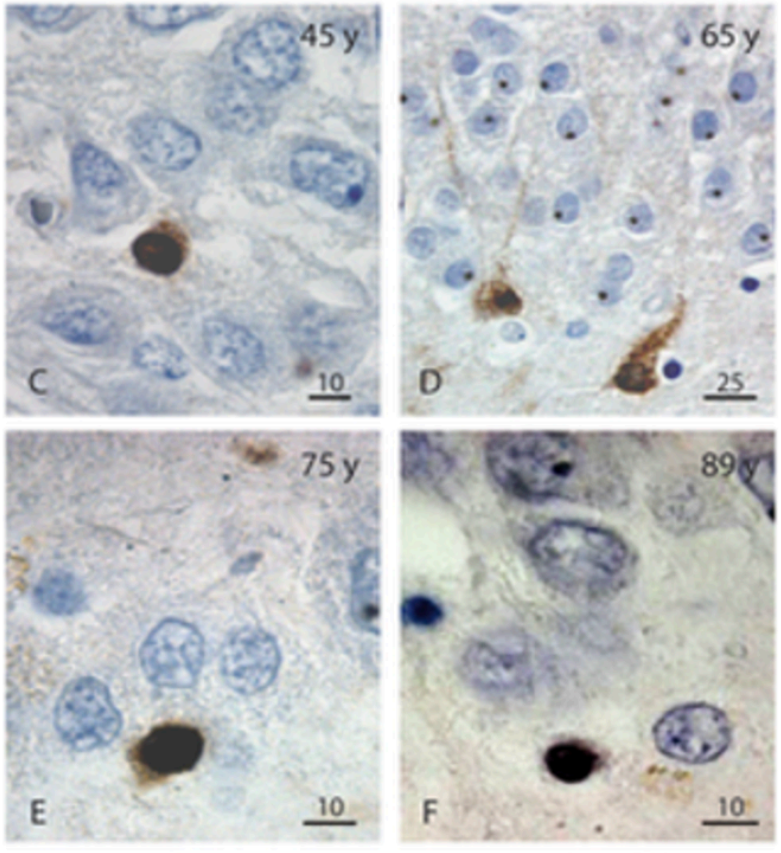




functionalneurogenesis.com
thebeautifulbrain.com

Quantifying neuron **proliferation** (rate of division) and **survival**

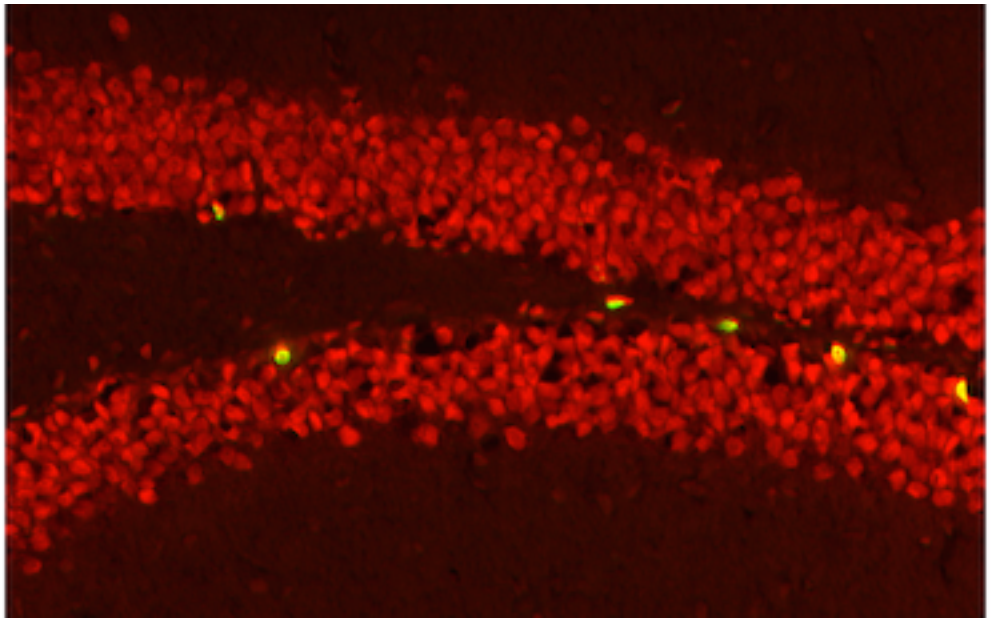
Doublecortin: a mictrotubule-associated protein expressed in the first 2-3 weeks



Knoth et al., *PLOS One*, 2010

Quantifying neuron **proliferation** (rate of division) and **survival**

5-bromo-2'-deoxyuridine (BrdU): a thymidine analog that is incorporated into the DNA of dividing cells during their S-phase

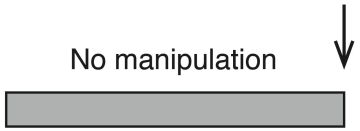


Mak et al., 2013

Quantifying neuron **proliferation** (rate of division) and **survival**

Measuring Proliferation

Control: **BrdU, DCX, Ki67**



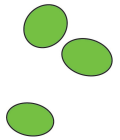
How many cells are dividing
or are immature at this time?

Many things can influence adult neurogenesis

proliferation is highly regulated

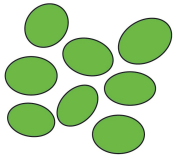
<u>Proliferation (rate of division)</u>:

- Stress
  Schoenfeld and Gould, 2012



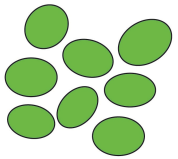
decreases

- Physical Exercise
  van Praag et al., 1999



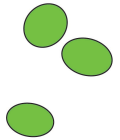
increases

- Antidepressants
  Boldrini et al., 2009



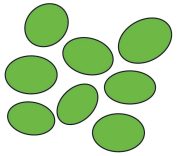
increases

- Aging
  Kuhn et al., 1996



decreases

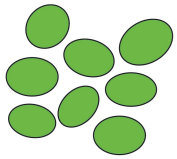
- Seizures
  Jessberger and Parent., 2015



increases

Many things can influence adult neurogenesis

survival is highly regulated



Survival:

- Learning

  Dupret et al., 2007

- Alcohol

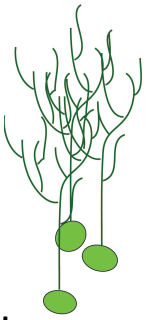
  Crews and Nixon, 2004

- Dietary Restriction

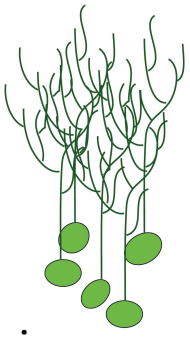
  Kitamura et al., 2006

- Enriching Environments

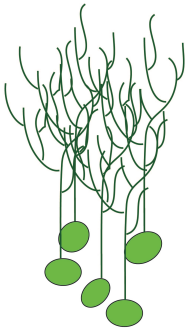
  Tashiro et al., 2007



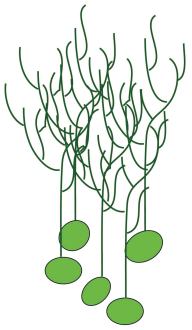
decreases



increases



increases



increases

On the regulation of adult neurogenesis

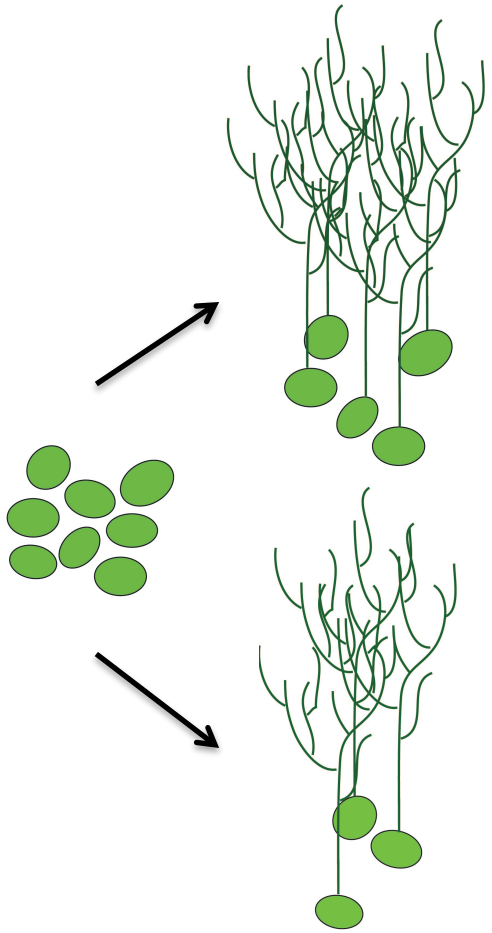
Question:

Is more neurogenesis a good thing?

Many things can influence adult neurogenesis

survival is highly regulated

- Adult neurogenesis can be regulated at different stages of neuron development.
- Increased proliferation does not necessarily mean that there are more that survive.
- The fact that this process is highly regulated suggests that these cells may serve a special function.
- Is more neurogenesis a good thing?

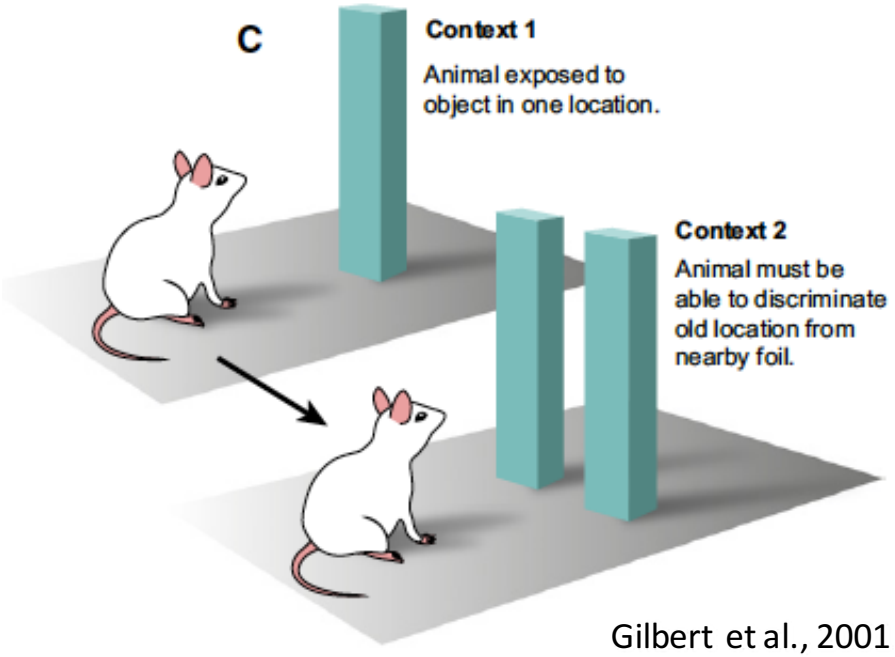


Adult neurogenesis occurs in the hippocampus

a brain structure important for **learning** and **memory**

The dentate gyrus (in the hippocampus) is important for being able to discriminate between similar experiences.

Rats require a dentate gyrus in order to discriminate between a new and old spatial location.



Gilbert et al., 2001

Aimone et al., 2011

Adult neurogenesis occurs in the hippocampus

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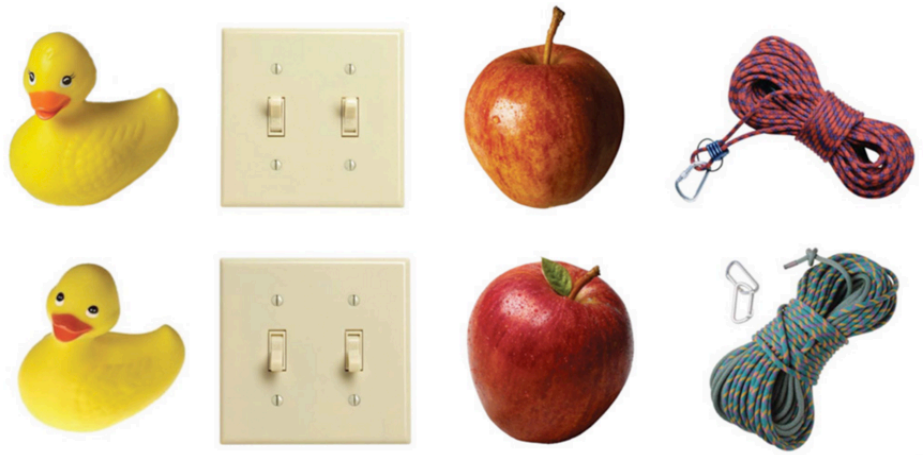
The dentate gyrus (in the hippocampus is important for being able to discriminate between similar experiences.

Humans show stronger activation of dentate gyrus when presented with an object subtly different from another object seen previously.



Bakker et al., 2008

Adult neurogenesis occurs in the hippocampus

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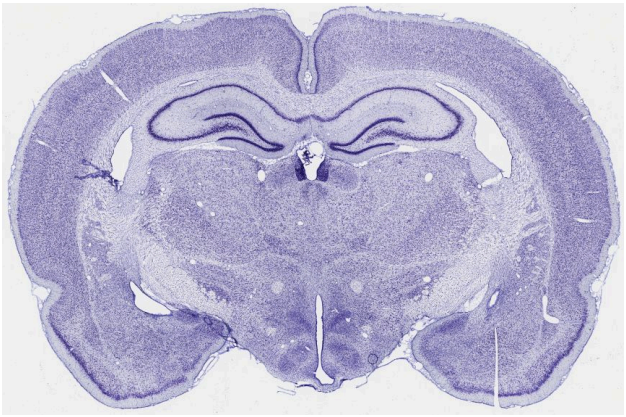
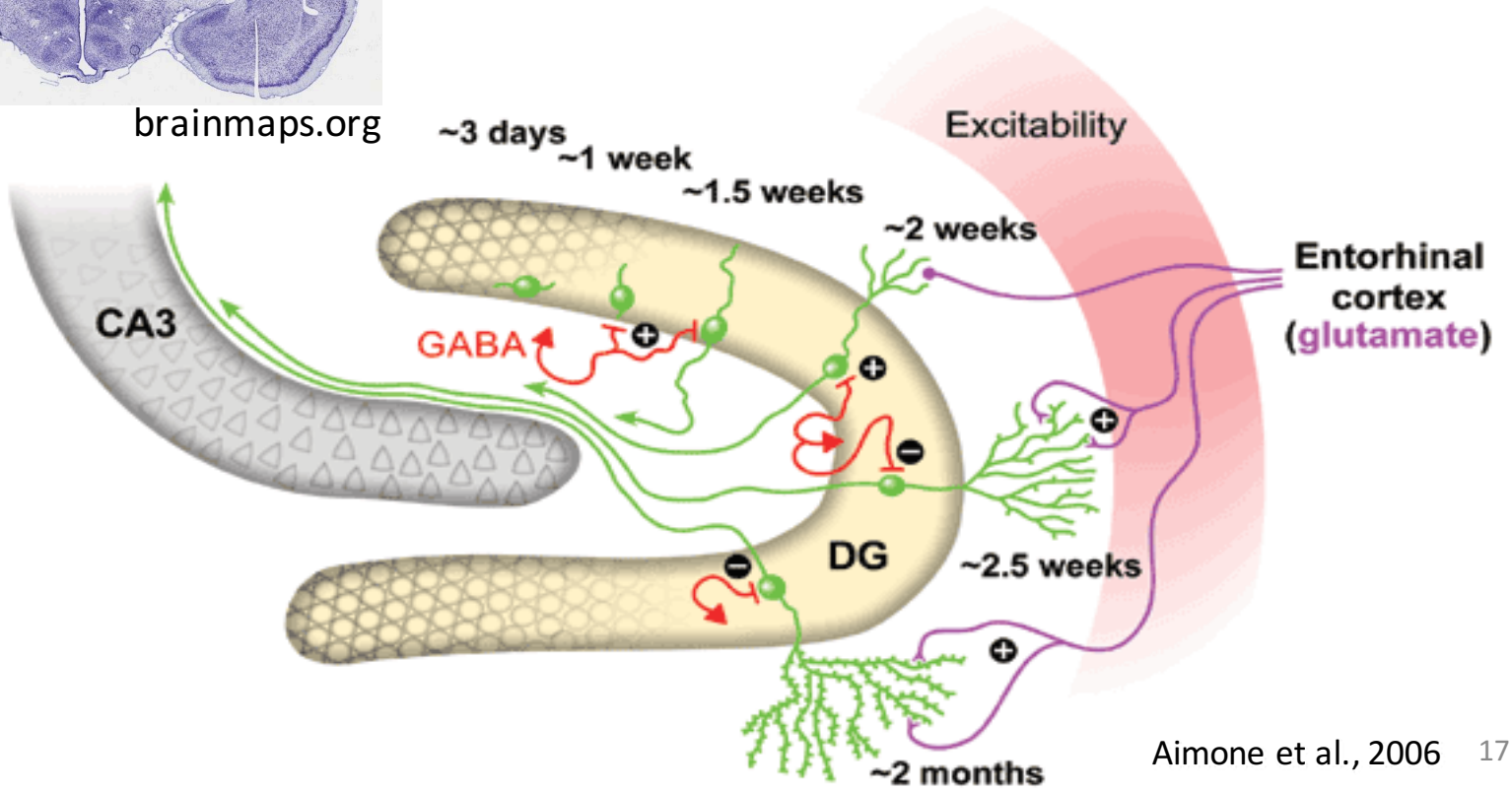
The **rat** hippocampus:



brainmaps.org

The time course of new neuron development may help us understand their role.

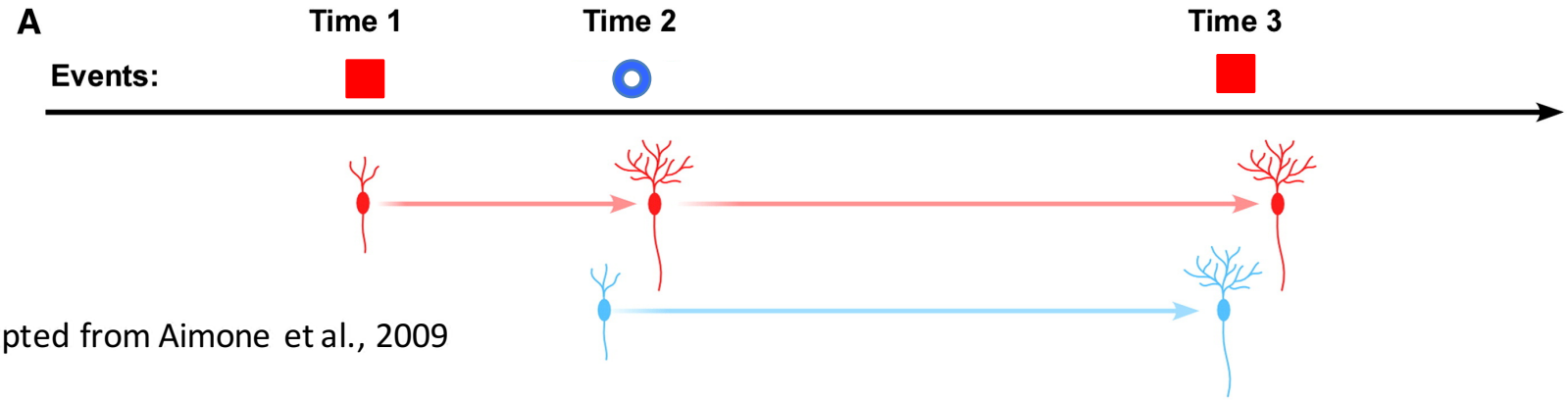


Aimone et al., 2006

Adult neurogenesis occurs in the hippocampus

a brain structure important for **learning** and **memory**

Hypothesis: Young cells may exhibit activity that is **selective** for experiences that occurred at a particular time point.

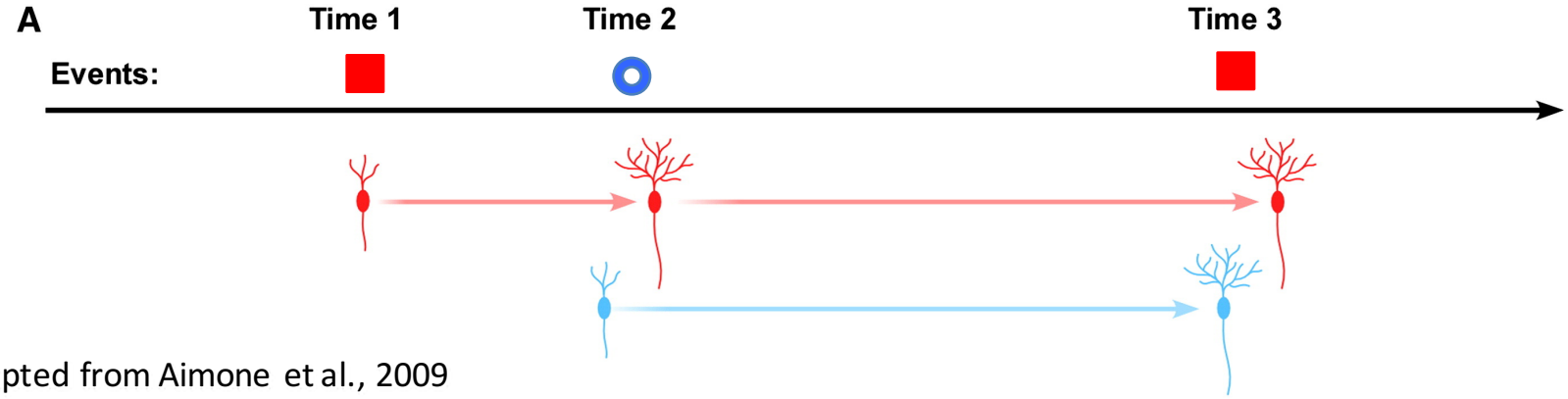


Adapted from Aimone et al., 2009

Events that occur **far apart in time** should engage **different** populations of adult-born neurons.

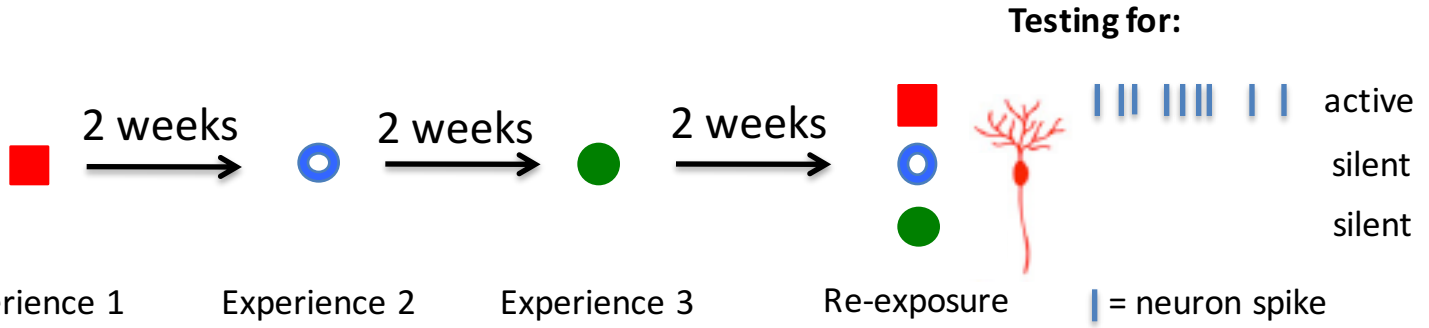
Adult neurogenesis occurs in the hippocampus

a brain structure important for **learning** and **memory**



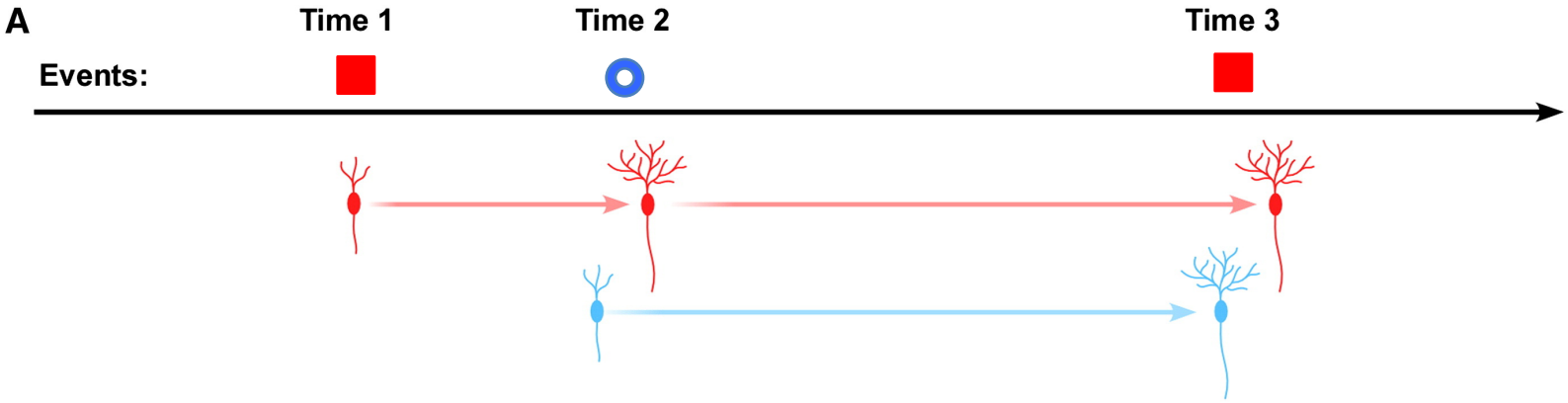
Adapted from Aimone et al., 2009

For experiences occurring weeks apart, granule cells exhibit activity selective to one experience.

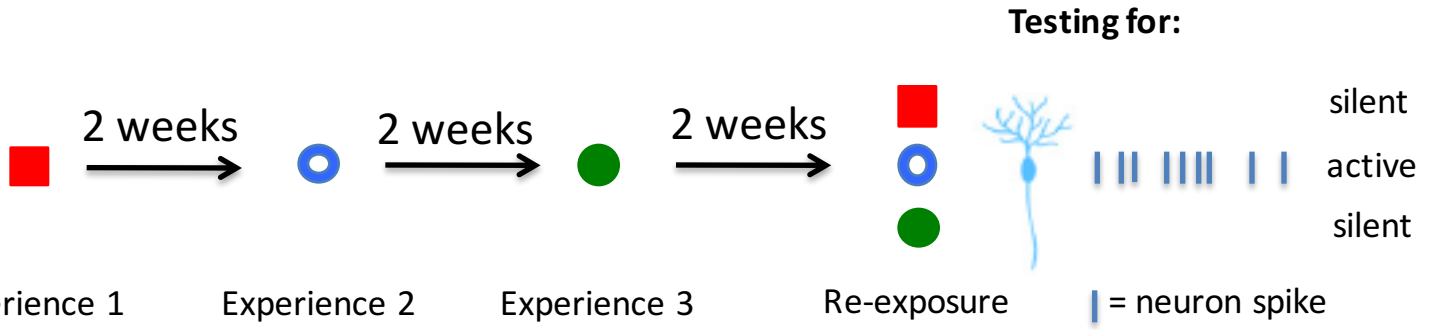


Adult neurogenesis occurs in the hippocampus

a brain structure important for **learning** and **memory**



For experiences occurring weeks apart, granule cells exhibit activity selective to one experience.



Adult neurogenesis occurs in the hippocampus

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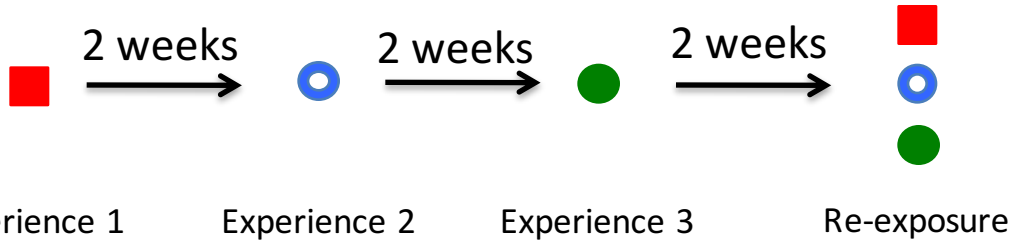
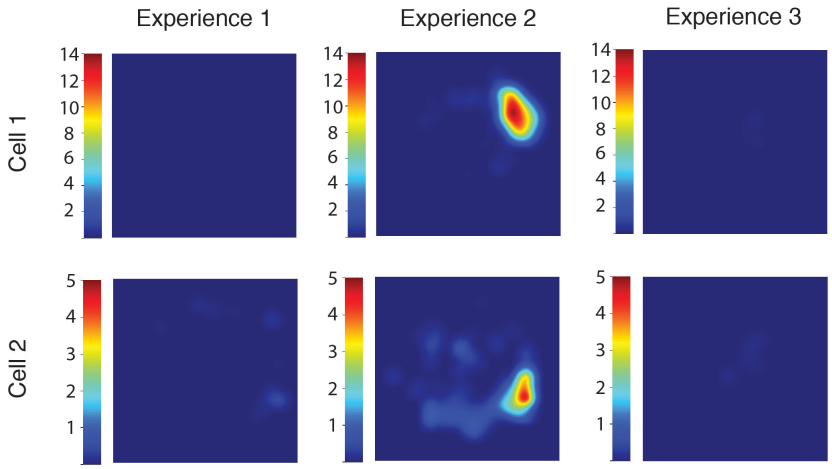
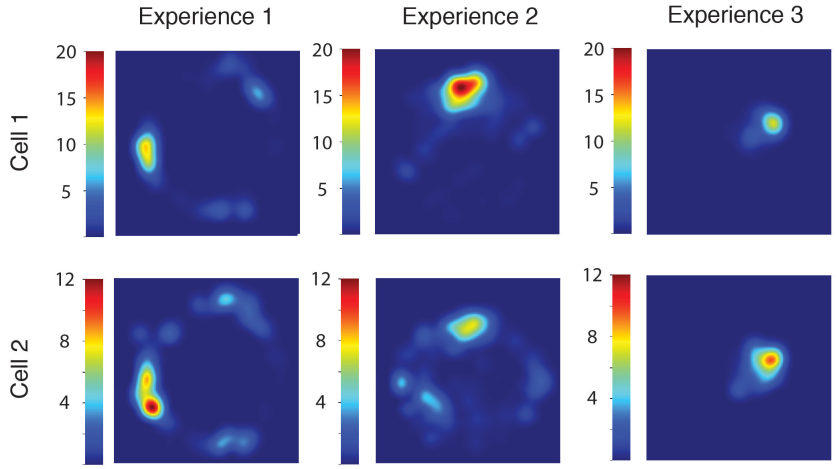


For experiences occurring weeks apart, granule cells exhibit activity selective to one experience.

with neurogenesis



neurogenesis **knockdown**



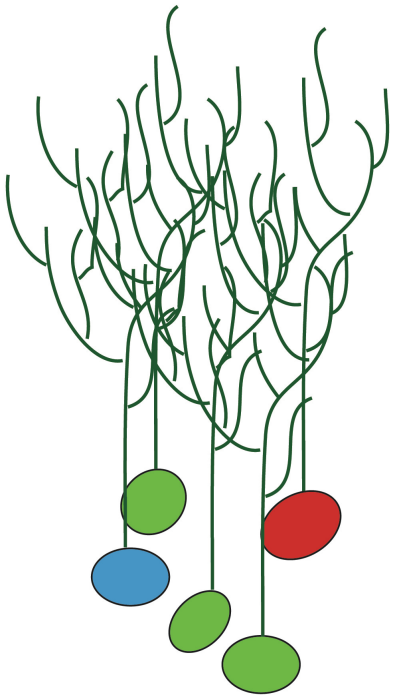
Rangel et al., 2014

Adult-born neurons may enable discrimination between temporally separated events through activity that is selective for experiences occurring at a particular time during their development.

Adult neurogenesis occurs in the hippocampus

a brain structure important for **learning** and **memory**

- The dentate gyrus is important for helping us discriminate between similar experiences.
- Neurons in the dentate can detect differences between experiences by demonstrating highly selective and specialized activity.
- Adult-born neurons may facilitate the allocation of selective and dedicated activity for new experiences in the dentate gyrus.



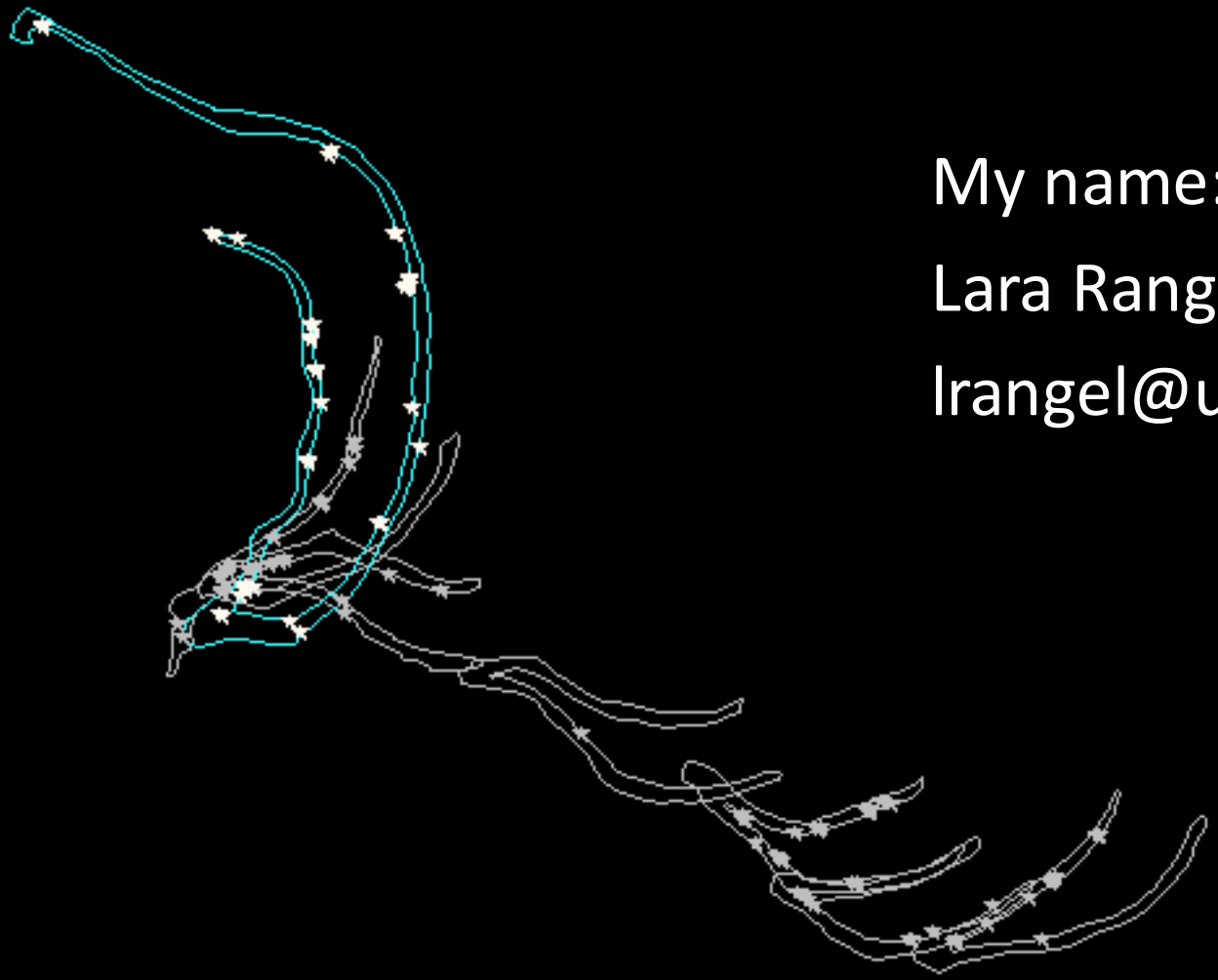
On the replacement of lost cells...

Question:

If we could **gain** a neuron for every neuron that we **lose**, could the new neurons take over the job of the lost neurons?

Or are lost neurons irreplaceable?

Thank You



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