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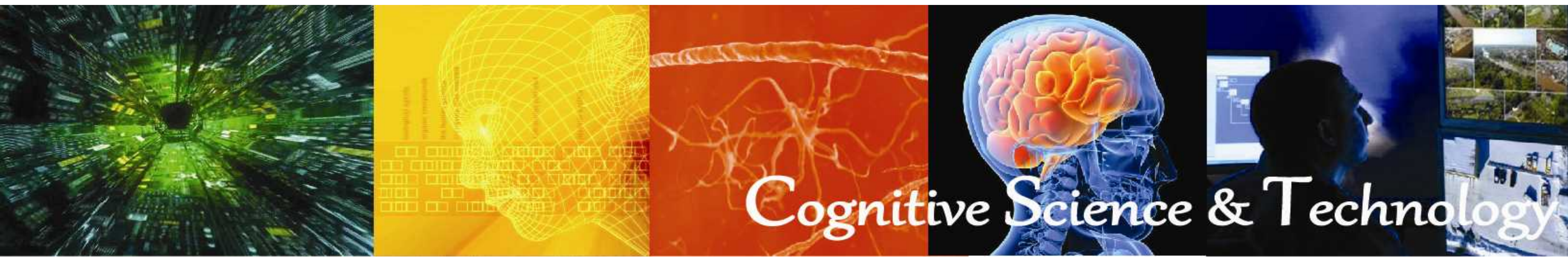

Adult neurogenesis and scale: how important are large scale neural simulations?

Brad Aimone

U.S. DEPARTMENT OF ENERGY · NNSA National Nuclear Security Administration · LDRD Laboratory Directed Research & Development

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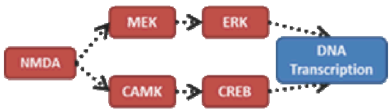
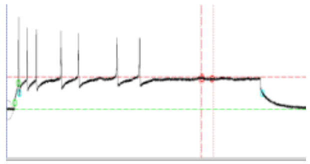
Neuroscience spans many scales

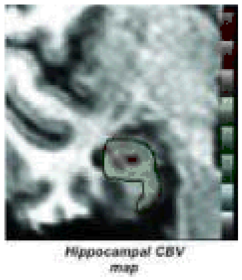
Molecular



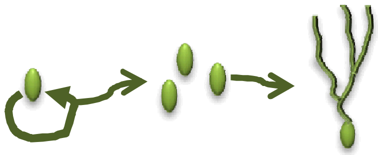
Electro-physiology



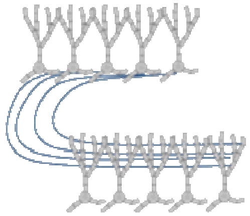
Cognitive



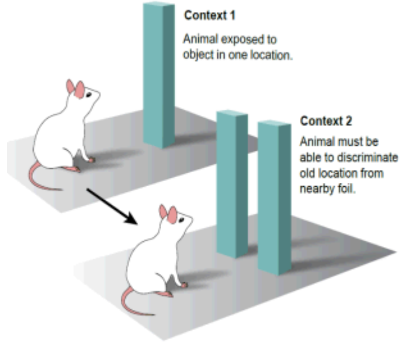
Developmental



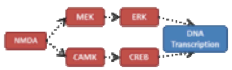
Systems



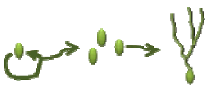
Behavioral



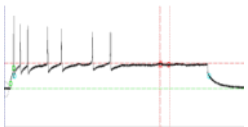
Computational neuroscience integrates across scales and drives applications



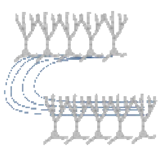
Molecular



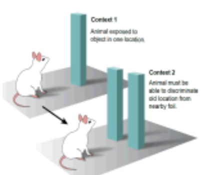
Developmental



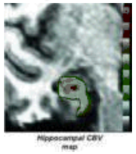
Electro-physiology



Systems



Behavioral



Cognitive

Computational Neuroscience

Applications

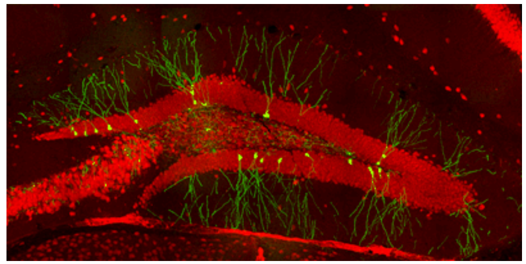
Computing

Health

More than just NIH health

Computational Neuroscience at Sandia

- Computational Neuroscience



Adult Neurogenesis LDRD

- Simulation Design Platform

Neurons to Algorithms LDRD

- Simulation Engine and Analysis

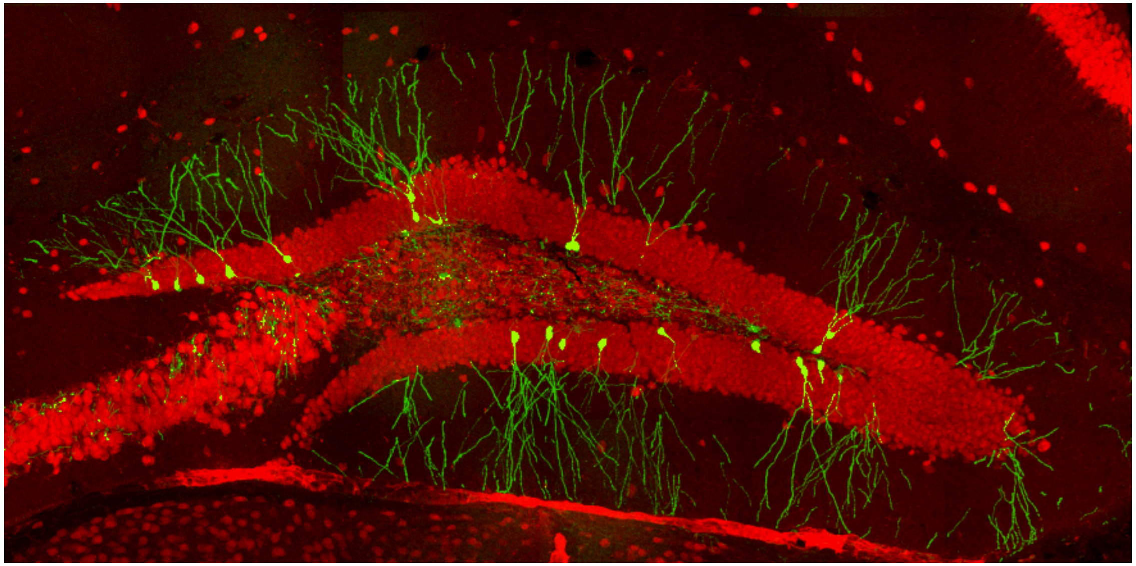
*Emerging Brain Maps LDRD**

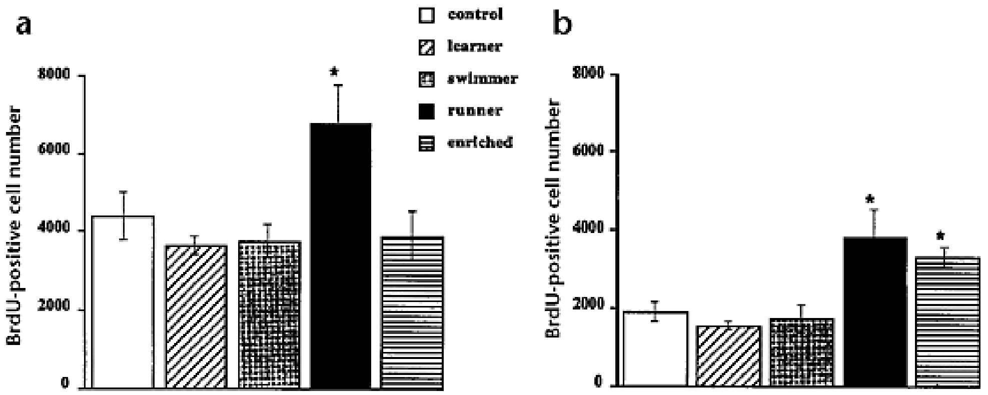
Stretching from data to a useful model

- Case study: adult neurogenesis
  - Biologically very well characterized at low levels
  - Big questions
    - Relevance in humans
    - What types of cognition would it affect?
  - Substantial application impact
    - Target for in psychiatric and neurological therapeutics
      - Beyond NIH: PTSD, depression, and traumatic brain injury?
    - Novel form of algorithm – plasticity at neural scales?
      - Pattern recognition in dynamic, big data?

What is adult neurogenesis?

- Robust process
  - Thousands of new neurons integrate into dentate gyrus monthly
- Highly regulated
  - Both proliferation and survival controlled
  - Activity, enrichment, stress, diet, aging, disease…



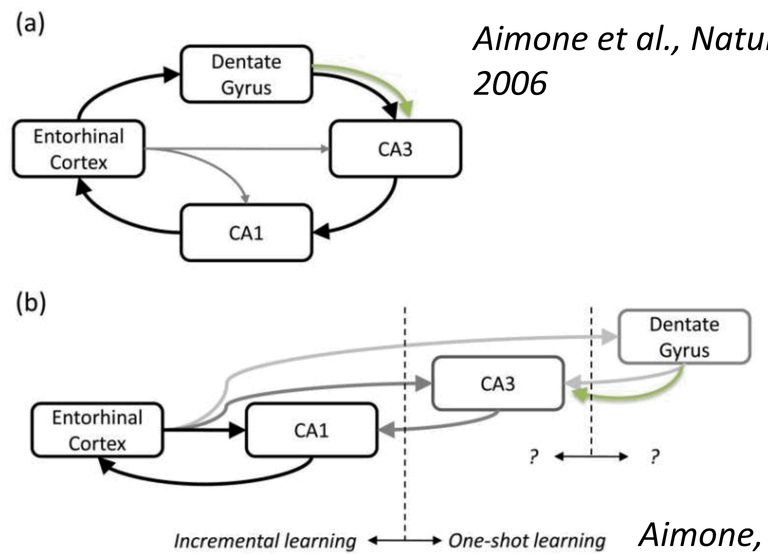


van Praag et al., 1999

What is adult neurogenesis?

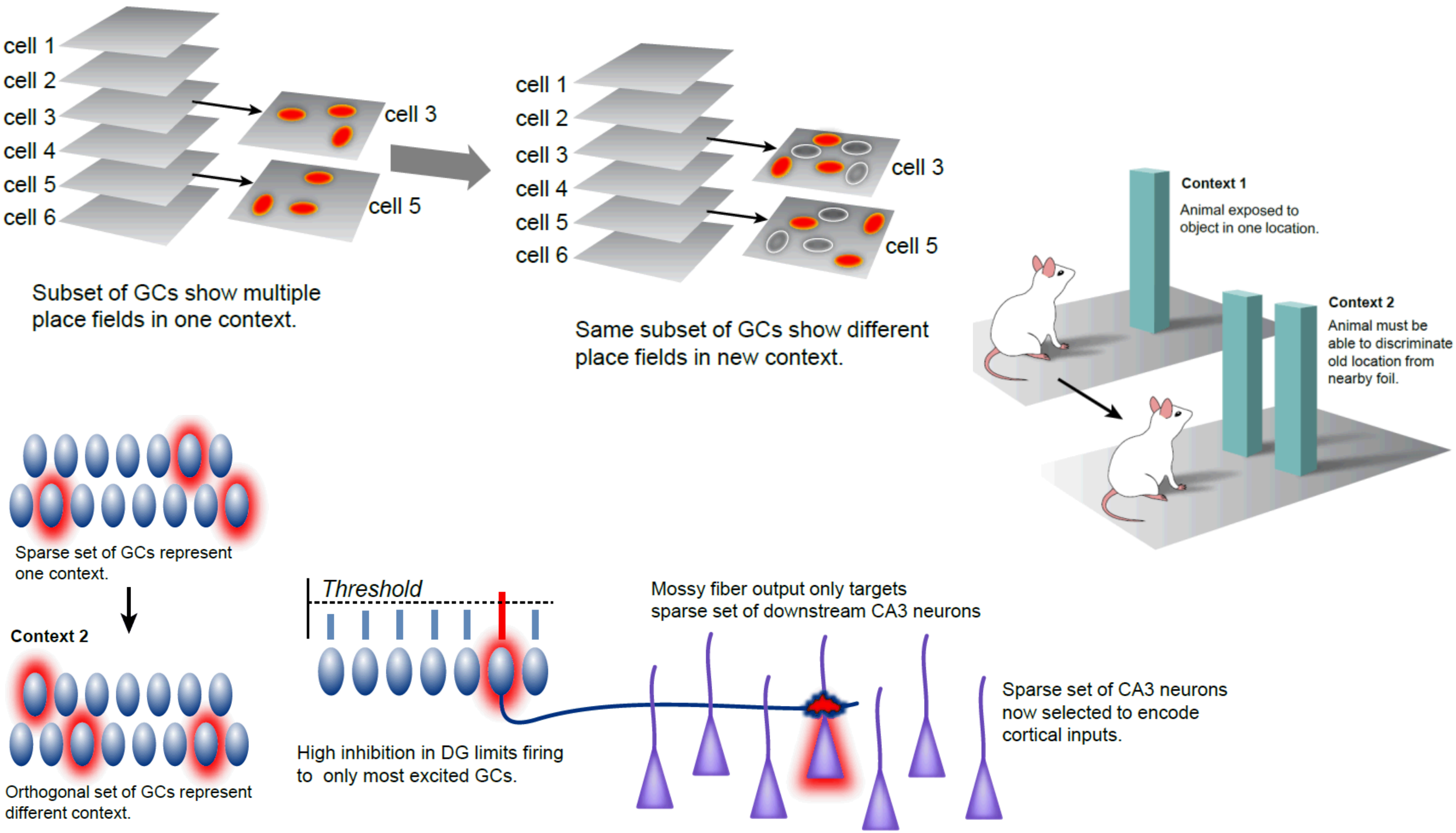
- Extended maturation
  - Several weeks to begin integrating into circuit
  - Still “immature” several months later
- Positioned to make an impact
  - Dentate gyrus is initial stage of hippocampus
  - Network amplifies effect of new neurons

Aimone et al., Nature Neuroscience 2006

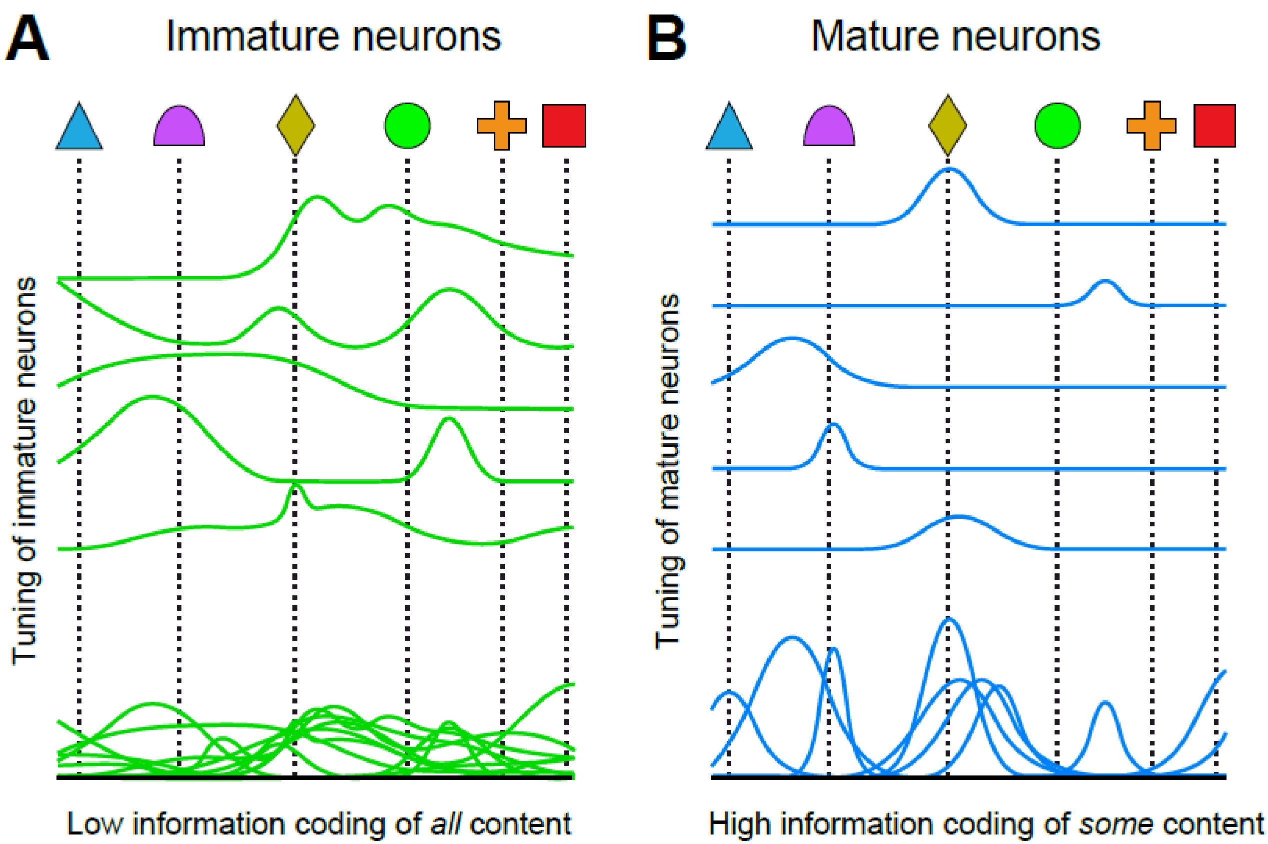


Aimone, Deng and Gage Trends in Cog. Sci., 2010

Mainstream theory: pattern separation

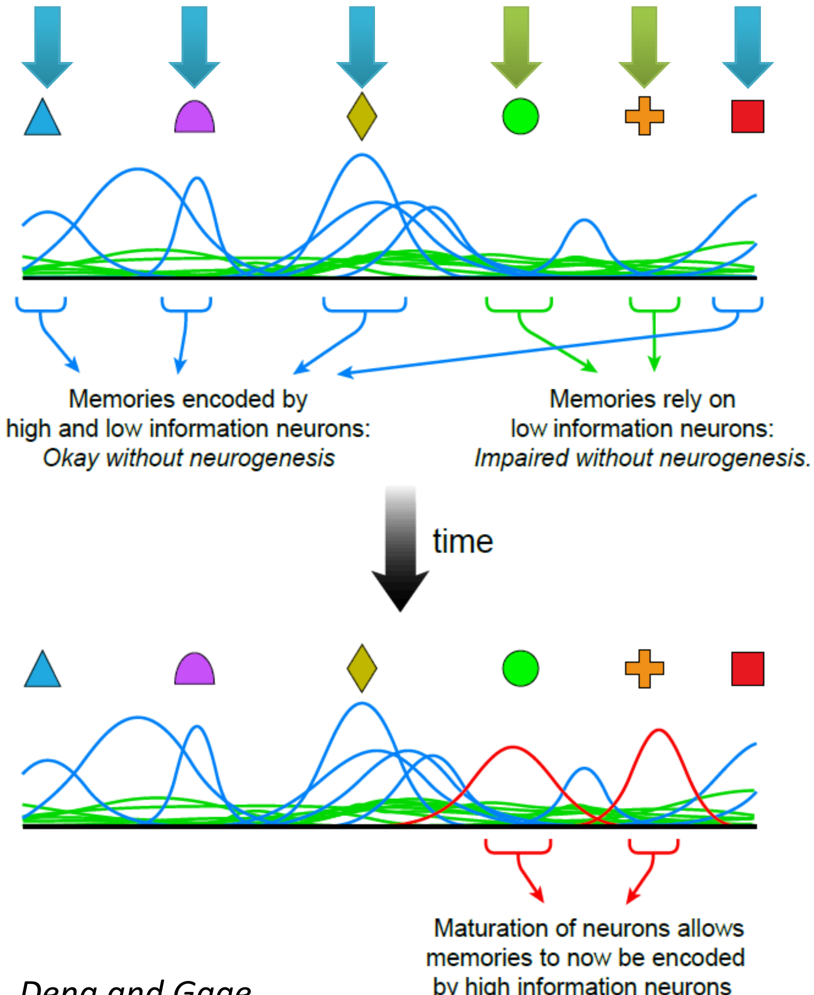


Alternative theory: young and old neurons encode information distinctly



Aimone, Deng and Gage
Neuron; 2011

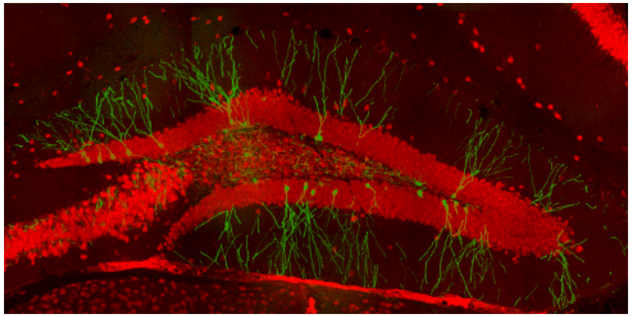
Alternative theory (continued): neurogenesis dynamically restructures coding scheme



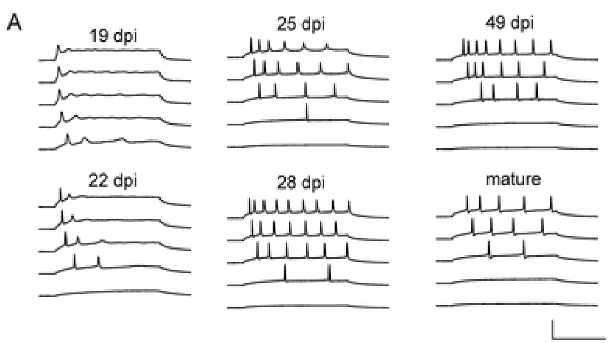
Aimone, Deng and Gage
Neuron; 2011

- Dentate Gyrus performs sparse coding for episodic memories
- Mature neurons are tightly tuned to specific features
  - *Not all events will activate mature neurons*
- Immature neurons are broadly tuned
  - *All events will activate some immature neurons*
- Neurons mature to be specialized to those events later
  - *Coding range of network gets more sophisticated over time*

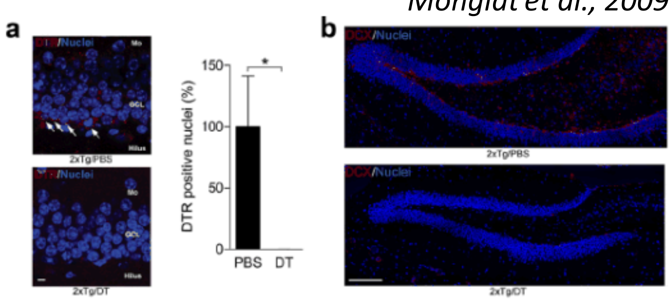
Realistic model of neurogenesis



courtesy Chunmei Zhao



Mongiat et al., 2009



Arruda-Carvalho et al., 2011

Neuroanatomy

- Circuit (principal neurons, interneurons, and how they are connected)
- Maturation of new neurons

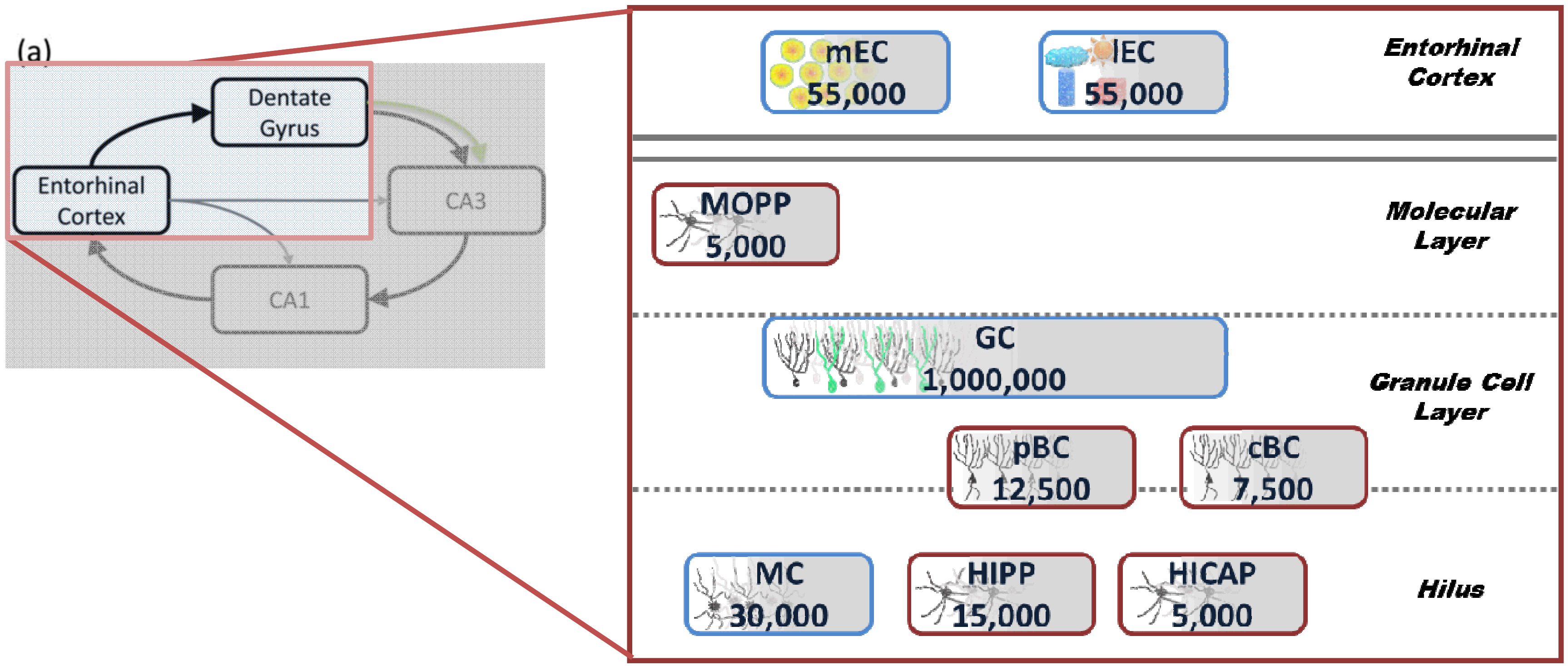
Dynamics

- Every neuron has unique dynamics
- Neurogenesis results in many different forms of GC dynamics

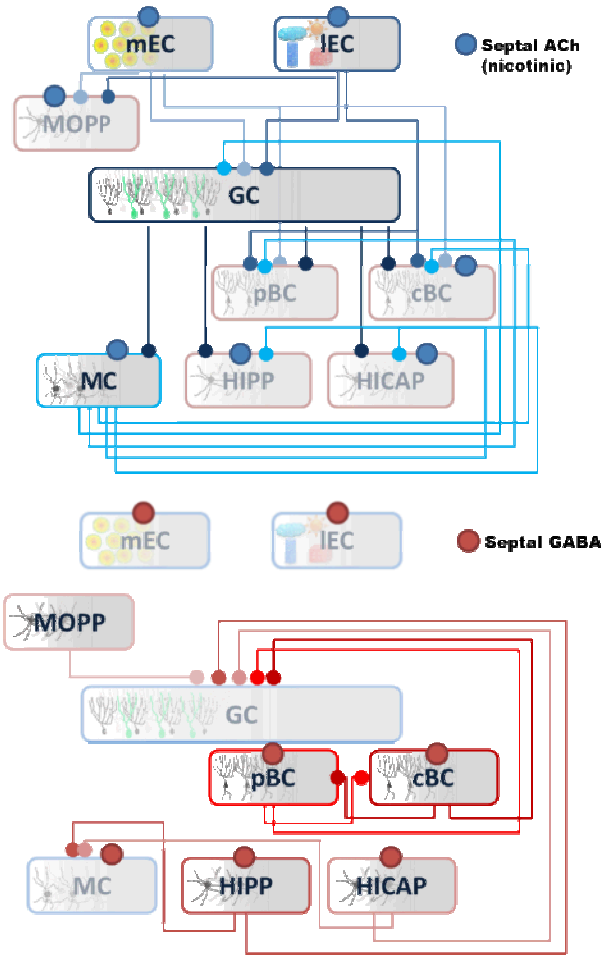
Behavior

- *In vivo* and immediate early gene studies of neuron behavior
- Behavior studies in lesion or knockdown animals

Goal: scale to realistic rat and human sizes

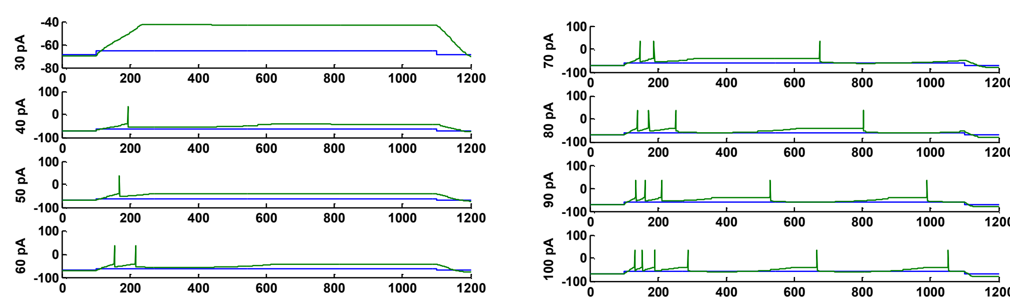


Goal: realistic connectivity and dynamics

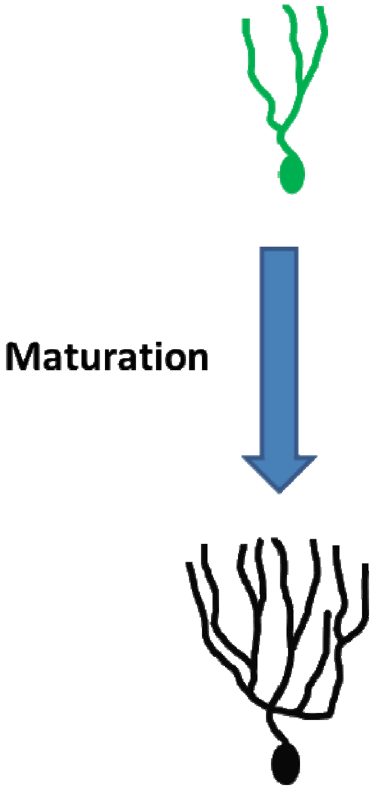


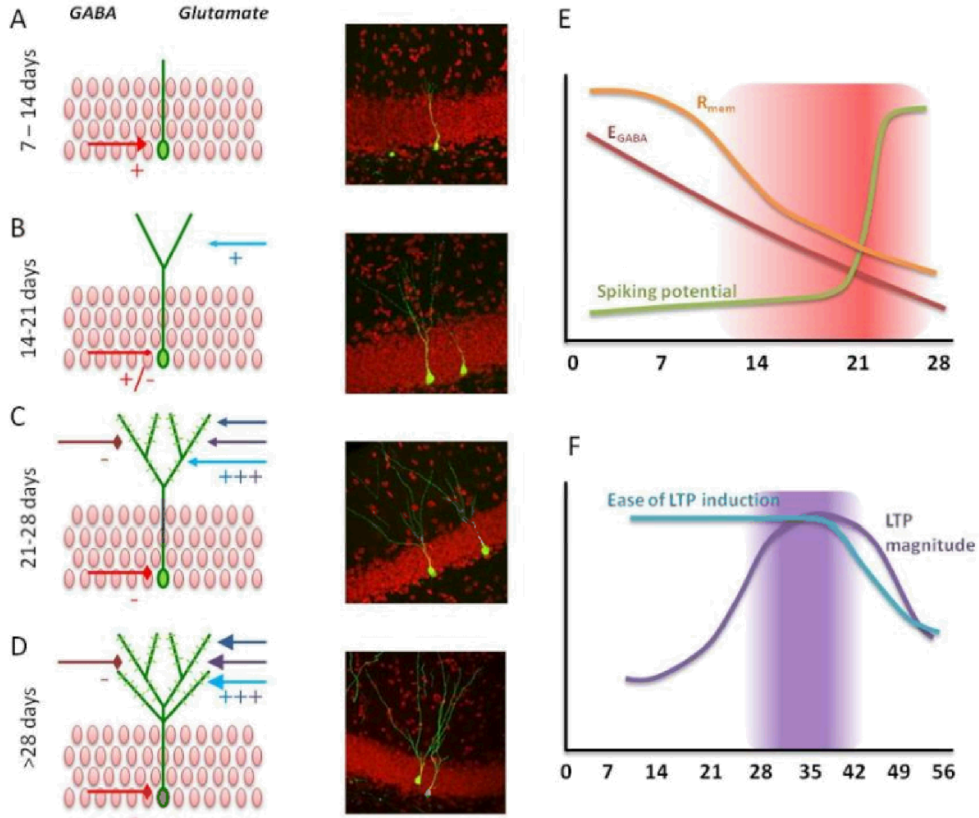
Physiology data

Modeled neuronal dynamics



Goal: represent neurogenesis with biological realism

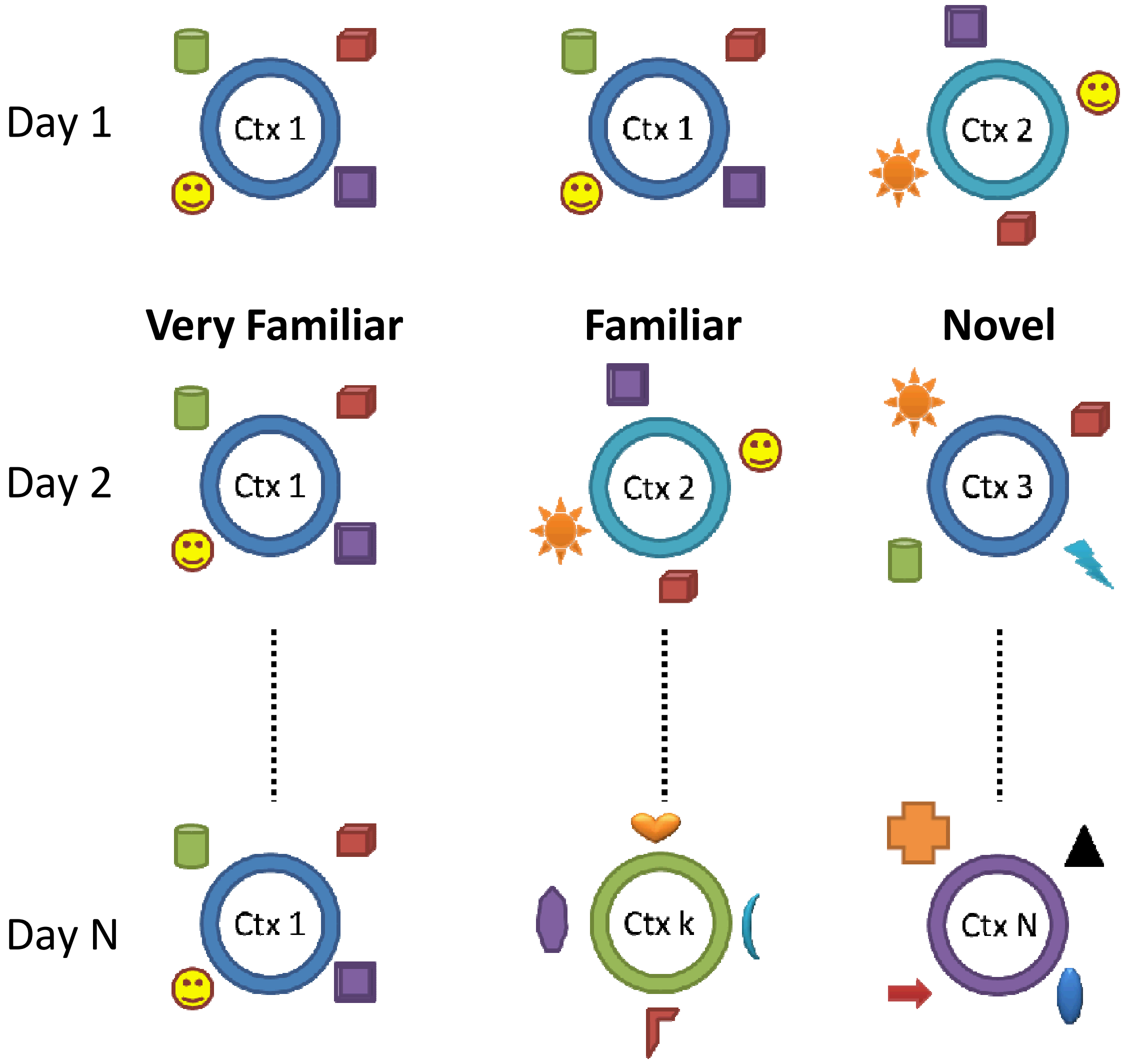




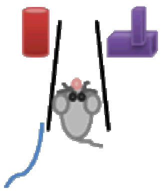
Aimone, Deng, and Gage
Trends in Cog. Sci. 2010

Goal: test model using realistic inputs

- Train network on series of different contexts
- Each day, network exposed to very familiar, familiar, and novel contexts and objects

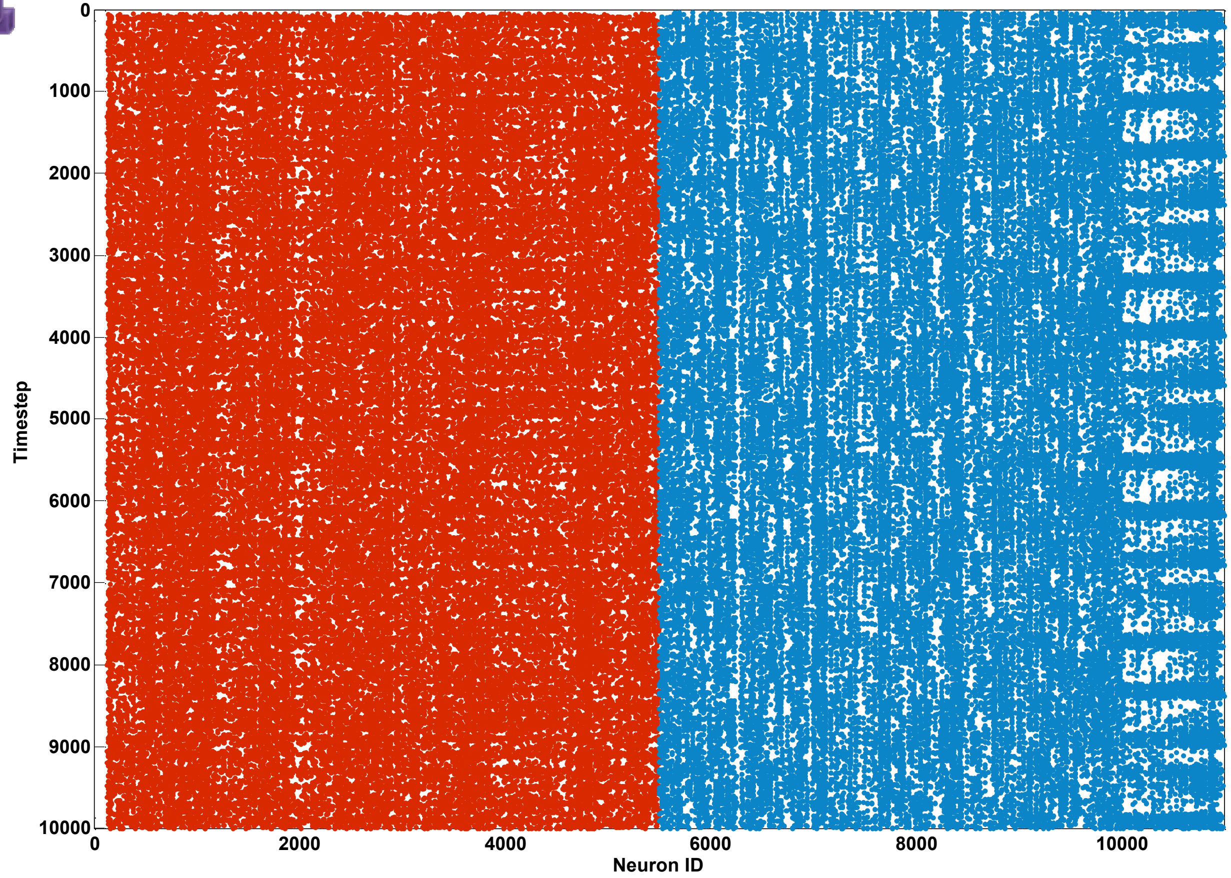


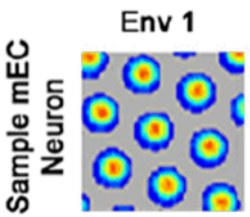
Activity of network – EC Inputs



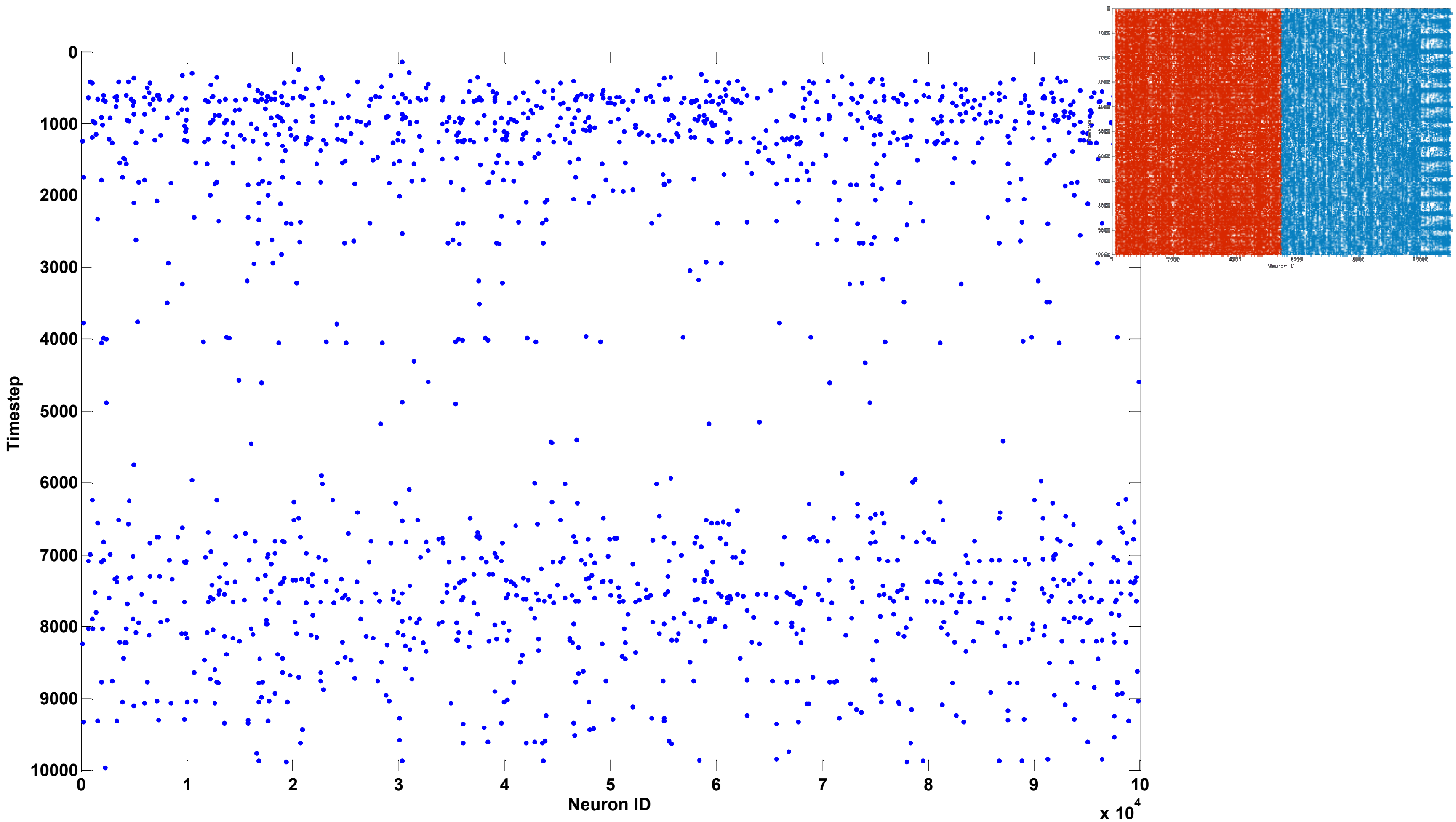
Lateral entorhinal (objects)

Medial entorhinal (space)

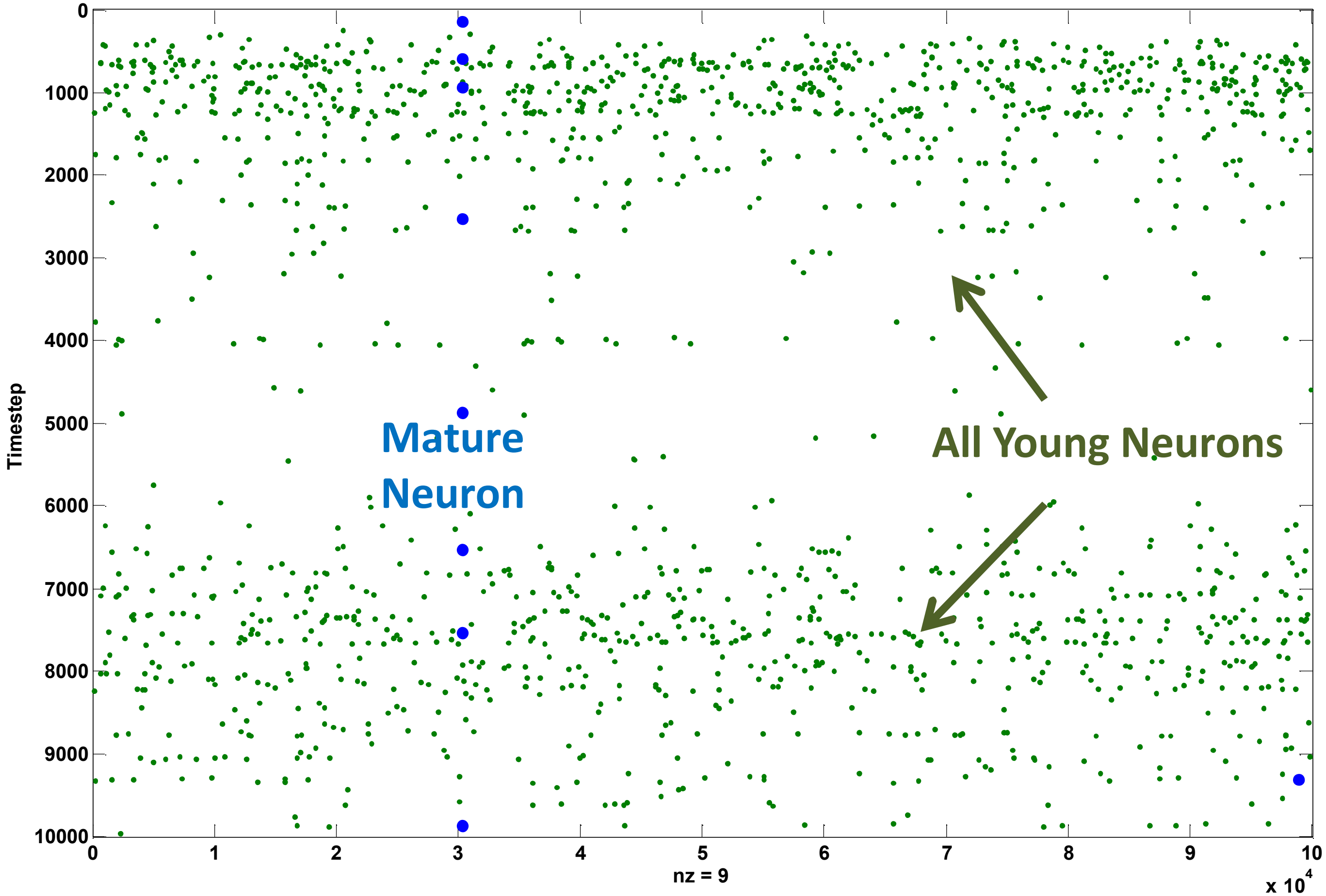




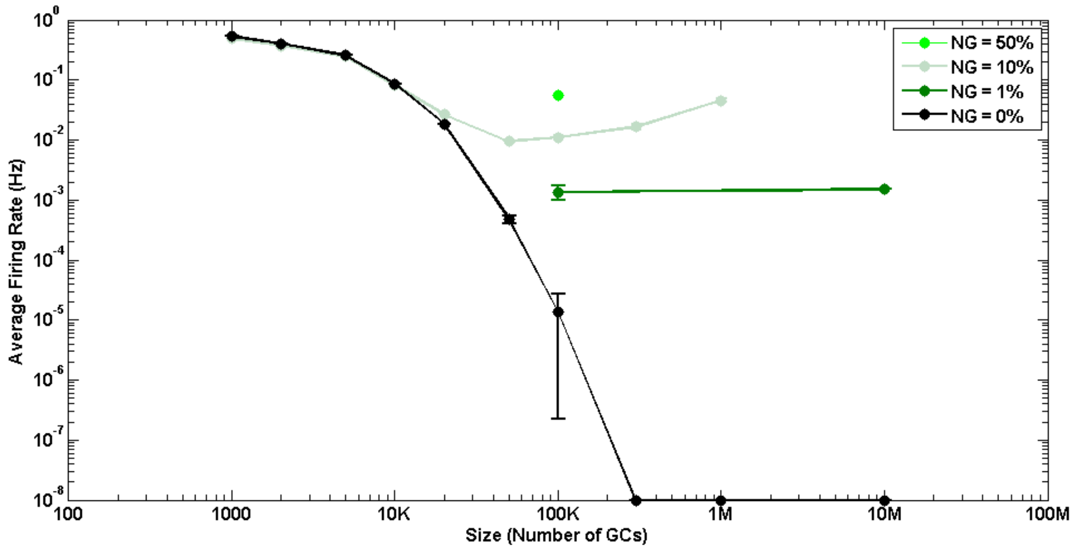
Activity of network – GC Outputs



Young GCs dominate activity in response to novel inputs

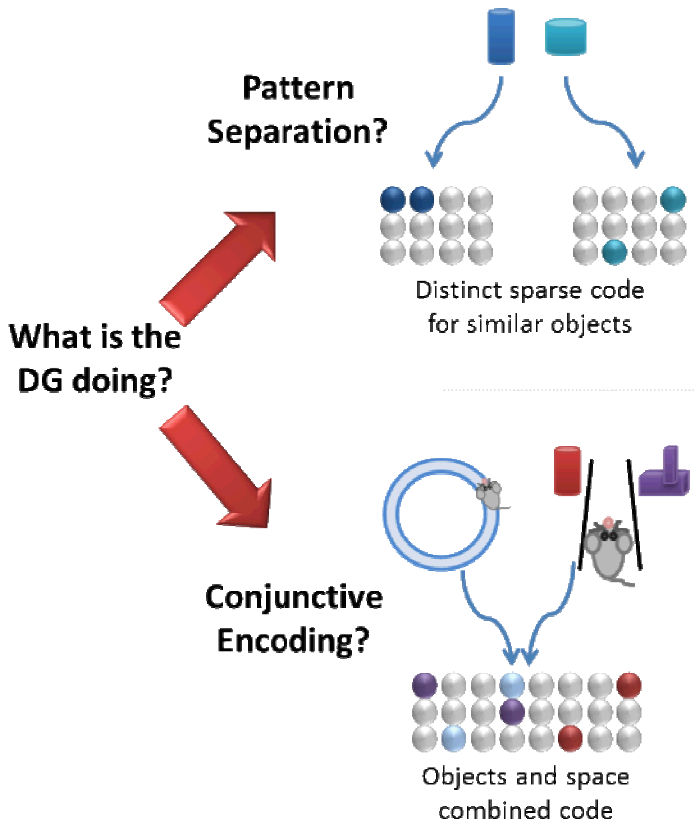


Lack of neurogenesis in large networks correlates with much lower activity



- Neurogenesis networks show activity to novel information at much higher scales
- As we approach human scales, mature neurons appear essentially silent in response to novel information
- Signal (immature) to noise (mature) is amplified in larger networks

How should large spiking networks be analyzed?



- Pairwise correlation / dot product

$$Sim_{t1,t2} = \frac{\left\| f_{GC,t1} \cdot f_{GC,t2} \right\|}{\left\| f_{GC,t1} \right\| \left\| f_{GC,t2} \right\|}$$

- Average covariance

$$\sigma_{t1,t2} = \sum_{GC} \left(f_{GC,t1} - \overline{f_{t1}} \right) \cdot \left(f_{GC,t2} - \overline{f_{t2}} \right)$$

How to combine over observations?

- **Linear compressability**

$$\kappa_{GC} = \sum\nolimits_{i=1..d} (\sigma_i - \lambda_i) \Big/ \sum\nolimits_{i=1..d} \sigma_i$$

- Average firing rate

$$f_{GC} = {}^{1}\!/_{N_{GC}} \sum_{GC} {}^{N_{spikes}}\!/_{T}$$

- Total variance

$$\sigma_{GC} = \sum_{T} \sigma_{GC,T}$$

- Information Content

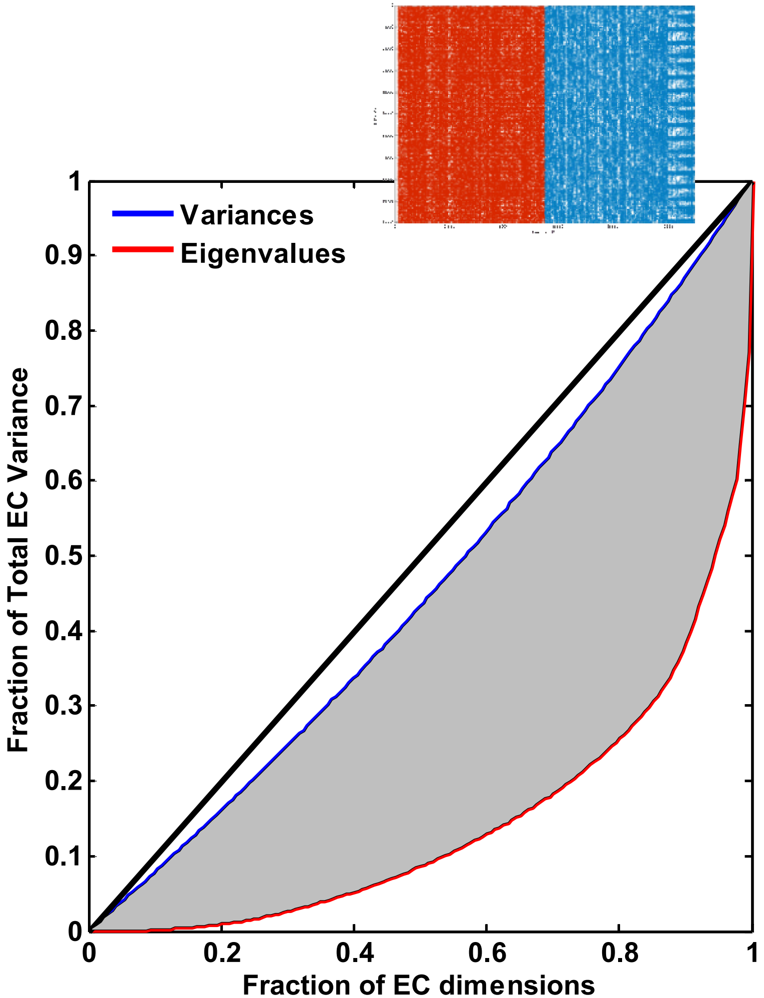
$$I = \sum_{ctx} p_{ctx} \, {}^{f}\!/_{\bar{f}} \log_2 {}^{f}\!/_{\bar{f}}$$

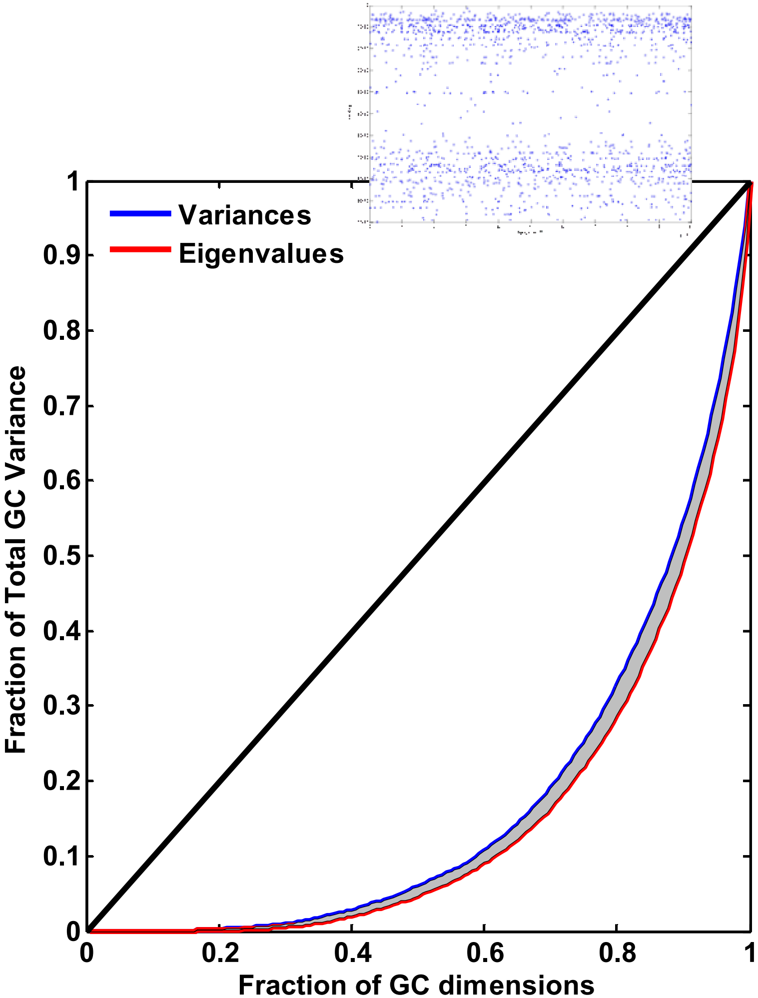
How to combine over neurons?

- **Independent variance**

$$\varphi_{GC} = \sigma_{GC} \times \kappa_{\lambda}$$

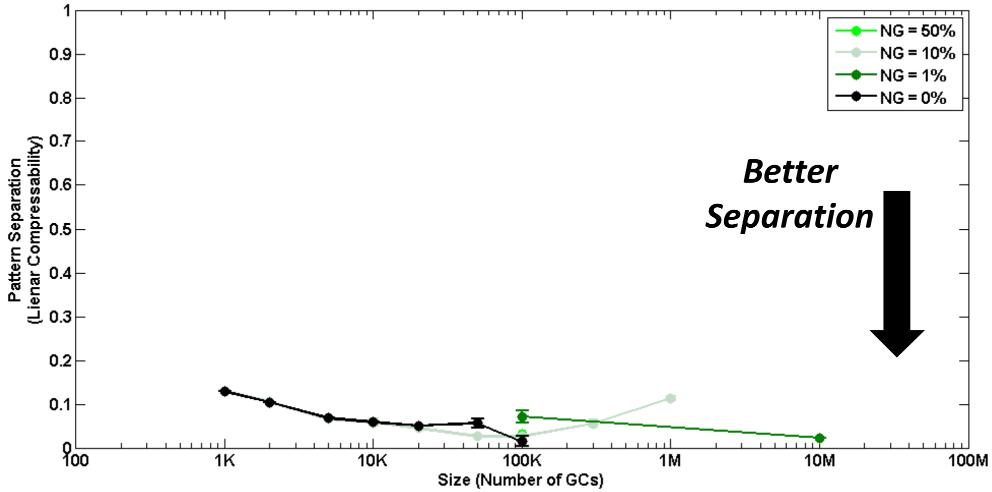
Proposal: Use compression techniques to quantify separation and independent coding



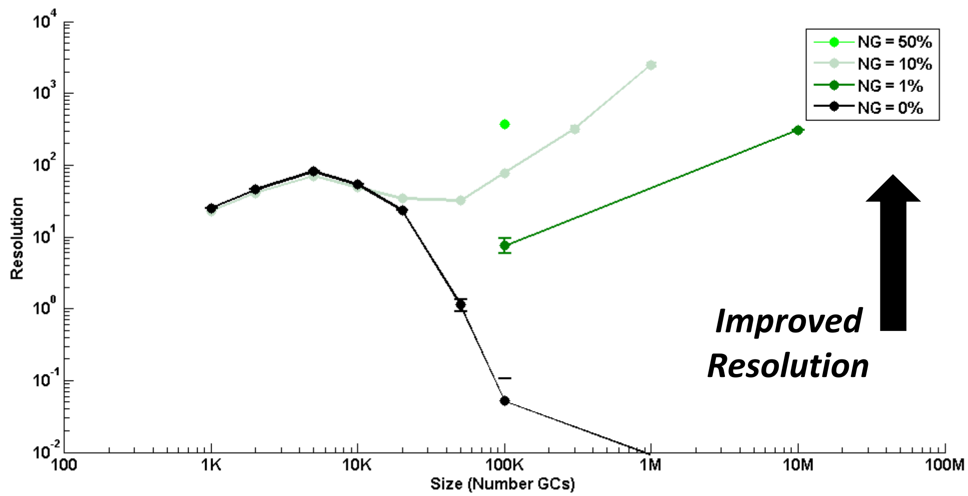


Neurogenesis maintains compressibility and increases total representation

Pattern Separation



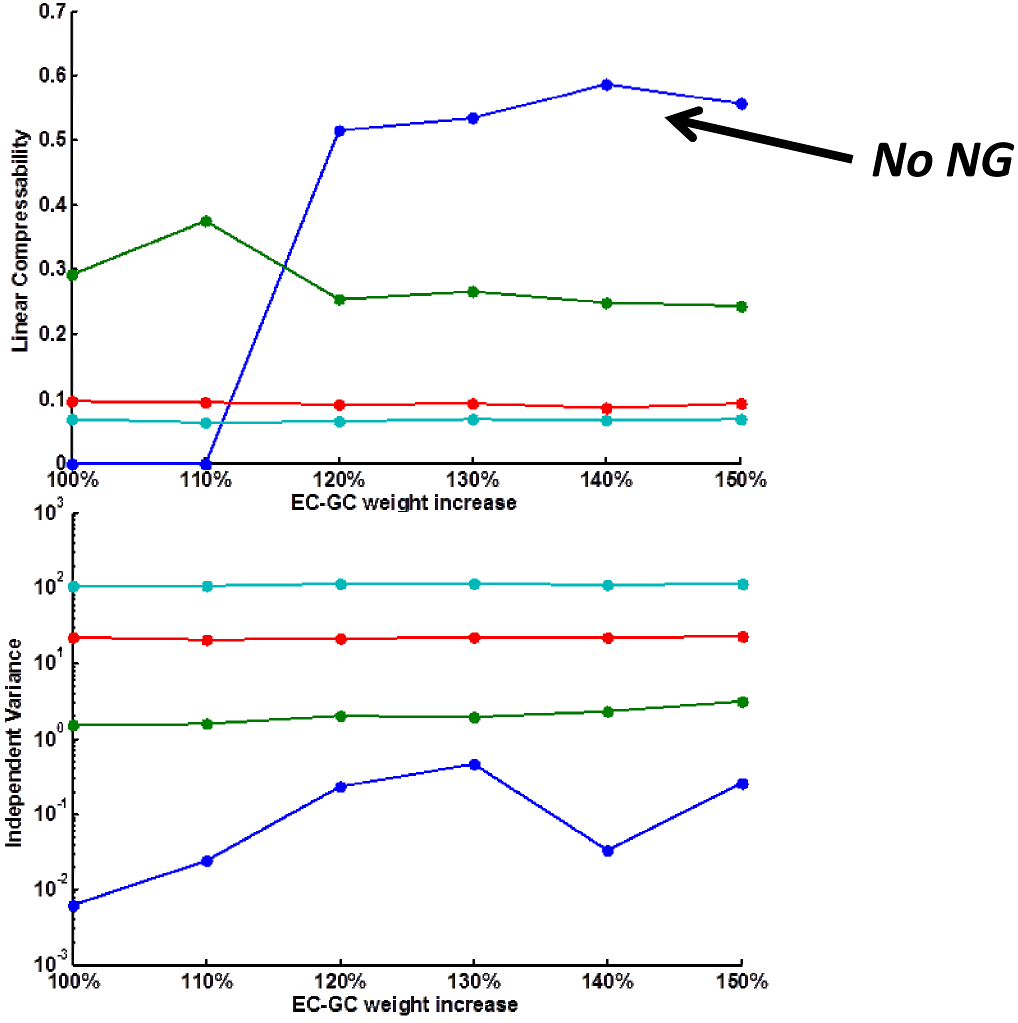
Memory Resolution



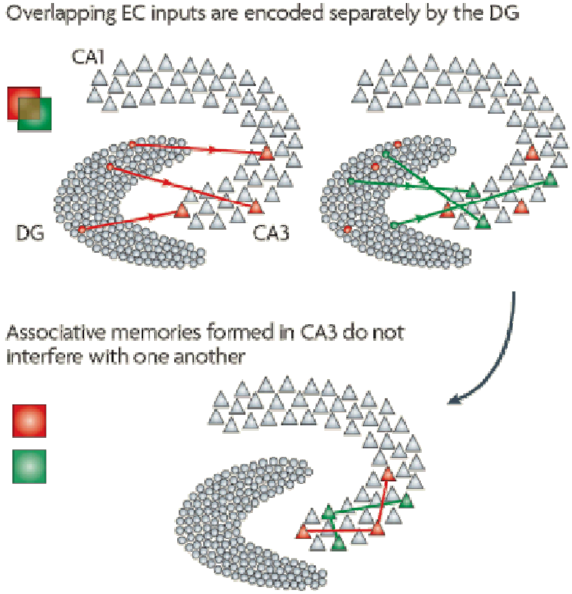
Increasing EC-GC weights impairs separation without improving coding

Pattern Separation

Memory Resolution

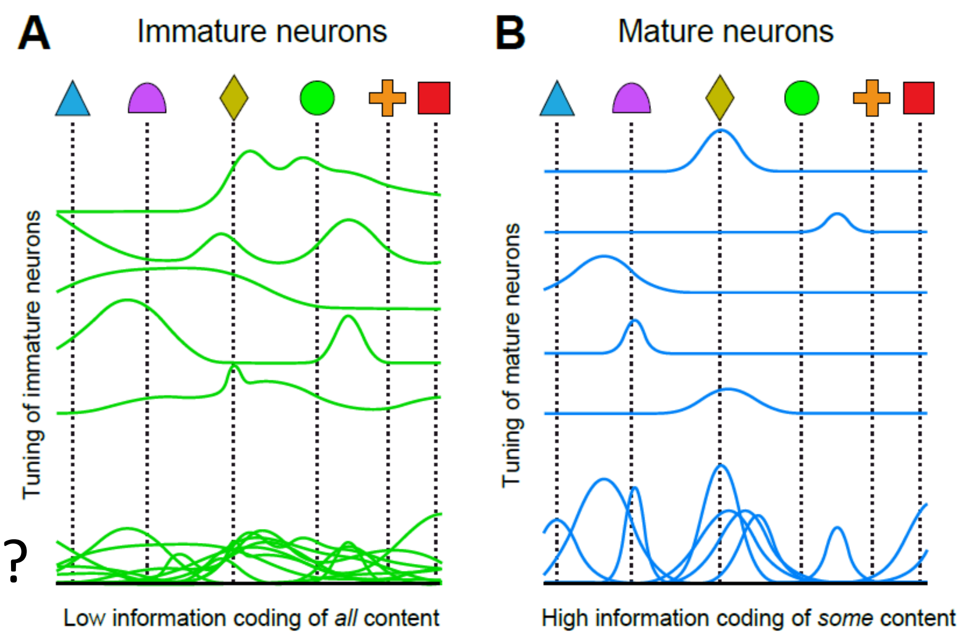


So which is right?

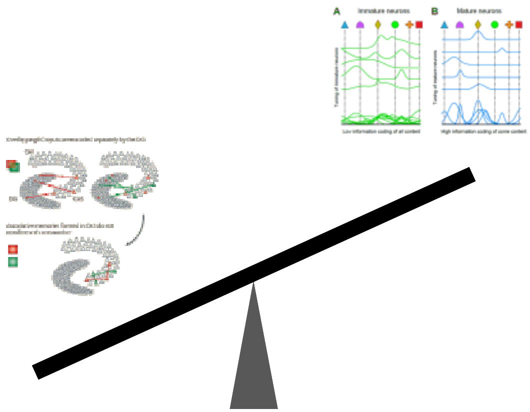


Pattern separation?

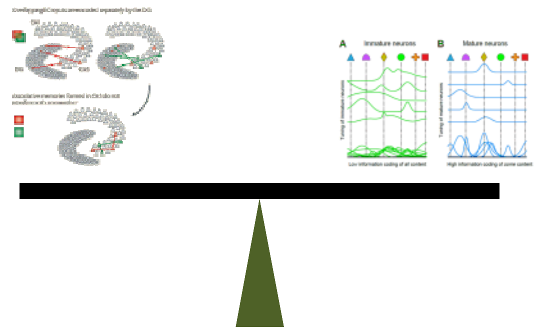
Or memory resolution?



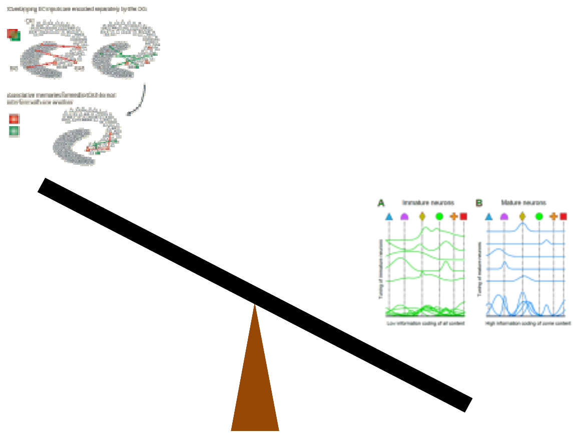
Neurogenesis strikes a balance



No neurogenesis yields very little activity
DG representations are separate but very sparse



Neurogenesis increases activity while preserving separation
DG representations increase their resolution but avoid interference



Increasing activity directly ruins pattern separation
DG representations are dense and informative but potentially interfere with each other

Next research steps

- UQ / SA on large scale simulations
  - ***Neuroscience does not do this***
- Apply principles to neural computing
  - How can we effectively emulate structural plasticity in silicon?
  - Explore algorithmic potential
- Impact on human decision making
  - Can insights into neurogenesis affect our interpretation / prediction of behaviors of individuals?

Accomplishments and Impacts

- **Among first** human scale simulations in computational neuroscience
- New methods for quantifying information in distributed and sparse neural networks
- Compromise between pattern separation and memory resolution debates in neurogenesis field

- Substantial health implication on aging, chemotherapy, and disease populations
- Interpretation and design of neural computing technologies

- **Grand Challenge Proposal**
- **Publications**
  - Rangel … & Aimone – "A Hypothesis for Temporal Coding by Young and Mature Granule Cells" *Frontiers in Neurogenesis* 2013
  - Vineyard … & Aimone – "   " Proceedings of HCI International 2013
- **Invited Talks & Meetings**
  - BU Biomedical Eng; UIUC Neuroscience; Virginia Tech Carillion
  - SfN Annual Meeting, Cosyne, HCI International, BICA

Translating Applications from Computational Neuroscience

- Health
- National Security
  - Brain Inspired Computing
    - Hardware solutions – new devices and capabilities beyond conventional computing
    - Software/algorithmic solutions – new algorithms to enable analysts
  - Understanding behavior of adversaries
    - e.g., DoD focus on understanding "Neurobiology of Aggression"

Differentiating Features of the Brain

- High connectivity
- Plasticity / Self-reconfigurable
  - Synaptic plasticity (weights between neurons change over time)
  - Intrinsic plasticity (neurons electrical properties change, for instance homeostatically)
  - Structural plasticity (architecture rewires itself)
    - Synapses come and go…
    - Neurons come and go…

Health and behavioral implications

Real world example

UAV Drone operators

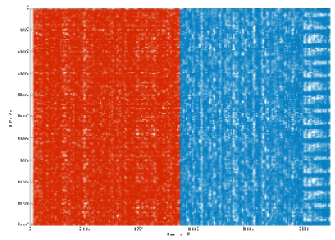
- Sleep deprived
- Low enrichment (isolated in trailer in desert)
- High stress environment

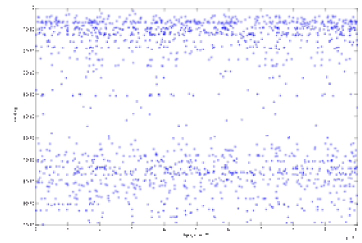
- Implications of NG on performance
  - Ability to react appropriately to novel, unpredicted events

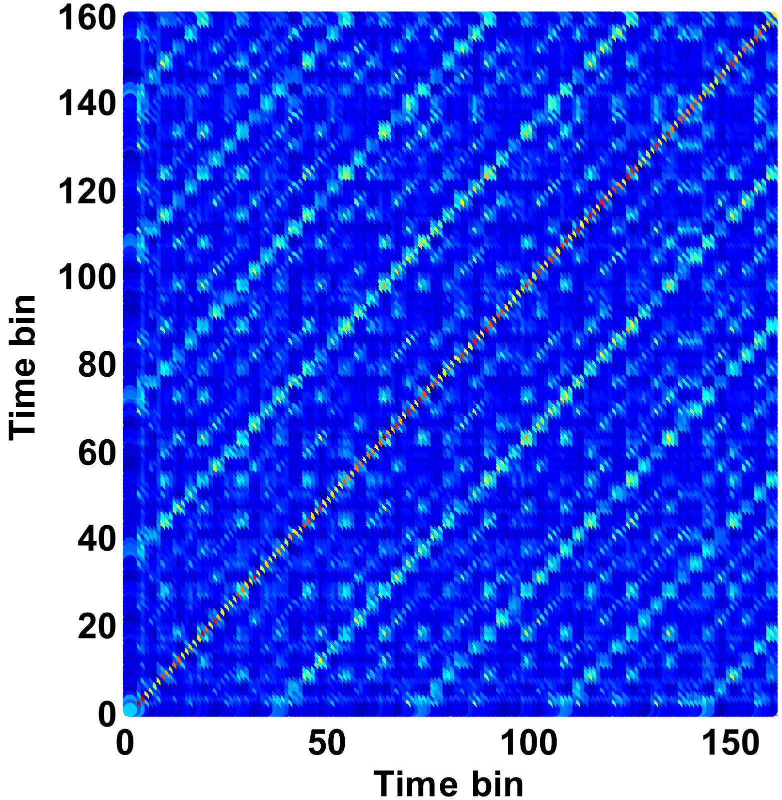
- Implications of uncertain outcomes
  - Post traumatic stress disorder
  - Depression

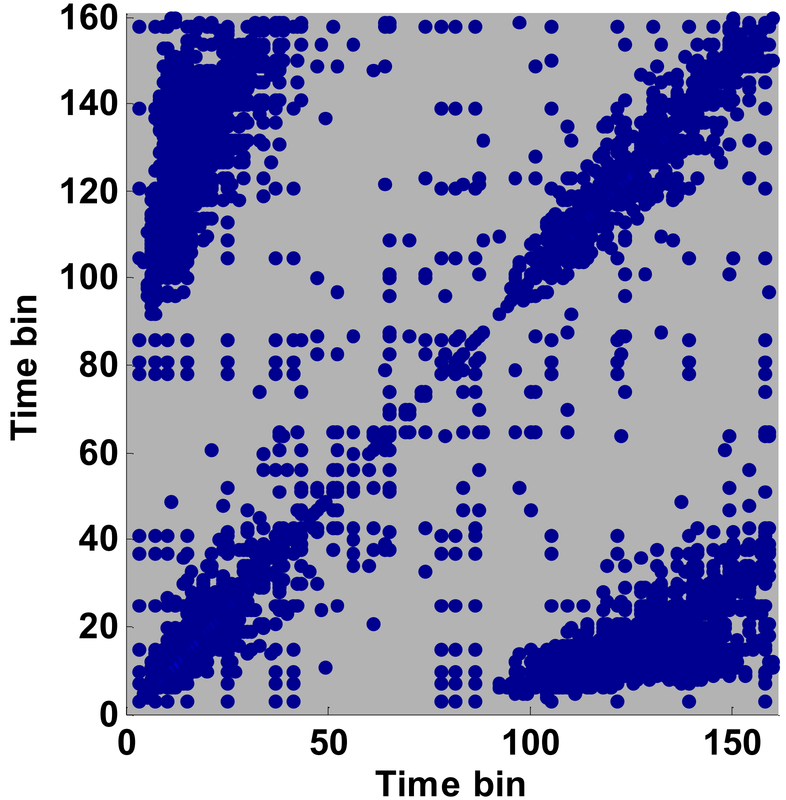
http://web.mit.edu/newsoffice/2012/boredom-and-unmanned-aerial-vehicles-1114.html

Information processing in large networks



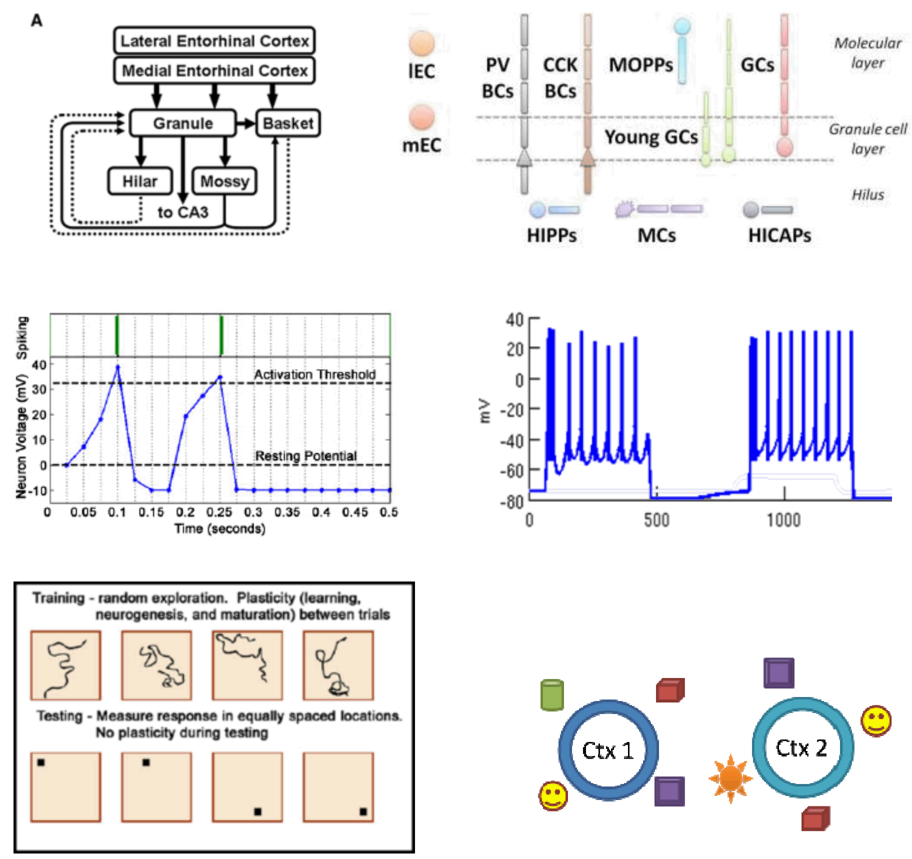






Limitations of past modeling work

- Between abstract and high fidelity
  - Time not particularly well represented
  - Details of DG architecture lost (e.g., feed-forward inhibition, modulatory inputs)
  - Experiment doesn't map to behavior



Aimone et al., Neuron 2009