SAND2013-4286P

Quantifying the effects of neurogenesis

From information theory to CA3 modeling

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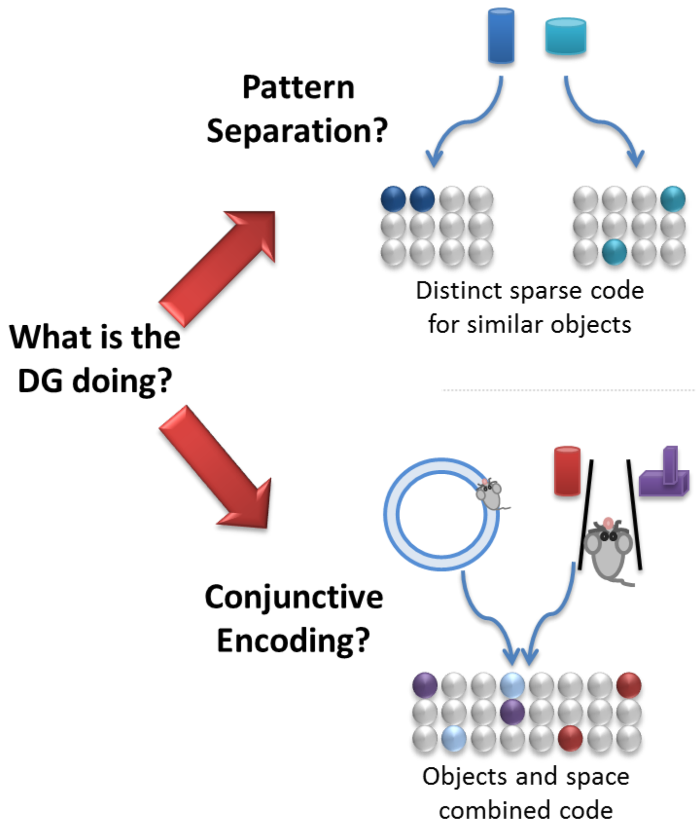
Metrics for understanding NG model



- Pairwise correlation / dot product

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

- Average covariance

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

How to combine over observations?

- **Linear compressability**

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

- Average firing rate

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

- Total variance

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

- Information Content

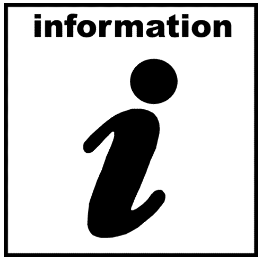
$$I = \sum_{ctx} p_{ctx} \, f/\bar{f} \, \log_2 f/\bar{f}$$

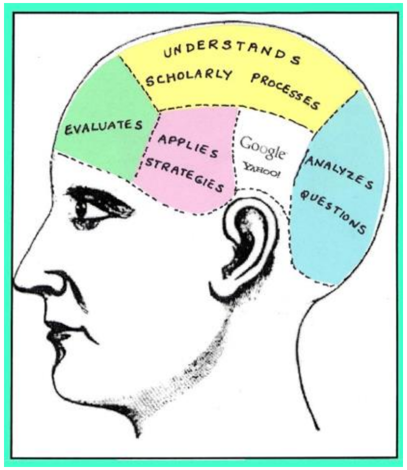
How to combine over neurons?

- **Independent variance**

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

What is Information?





What is Information?

Apparently these people have it —

What is Information?

It looks like it was around back in the old days too

What is Information?

- Claude Shannon (1948) suggested that we measure the information in a message as roughly the inverse of probability — more precisely, as the base 2 logarithm ($\log_2$) of the inverse of the probability.
- The intuitive idea behind Shannon's measure is that the more surprising a message is, the more information it conveys.
    - Ex: If I tell you that none of you will win the lottery tomorrow, this is not very surprising. But if I say that one of you will, this is very surprising indeed, and in some intuitive sense more informative.

What is Information?

- Shannon’s 1948 paper, “A Mathematical Theory of Communication”, marks the birth of modern information theory.
- Precise notions about information, not to mention tools that could be used to study it, did not exist prior to this time.
- Prior to Shannon, those that considered information primarily did so from a qualitative perspective.
- Shannon’s measure of information, because it was quantitative, with intuitively appealing operational interpretations, immediately caught the interest of engineers, scientists, and mathematicians.

What is Information?

- Information theory provides entropy of a discrete random variable as a quantitative measure of information

$$H(X) = \sum_{x \in X} p(x) \log(\frac{1}{p(x)})$$

- So what?

So what?

- Can be applied to neuroscience to quantitatively measure the information content of firing neurons.
  - And it has been with various methods such as:
    - Plug-in Entropy
    - Jackknife debiased
    - Asymptotically debiased
    - Ma bound
    - Bayesian/Dirichlet prior
    - Coverage-adjusted
    - Best upper bound

Neural Information Theory

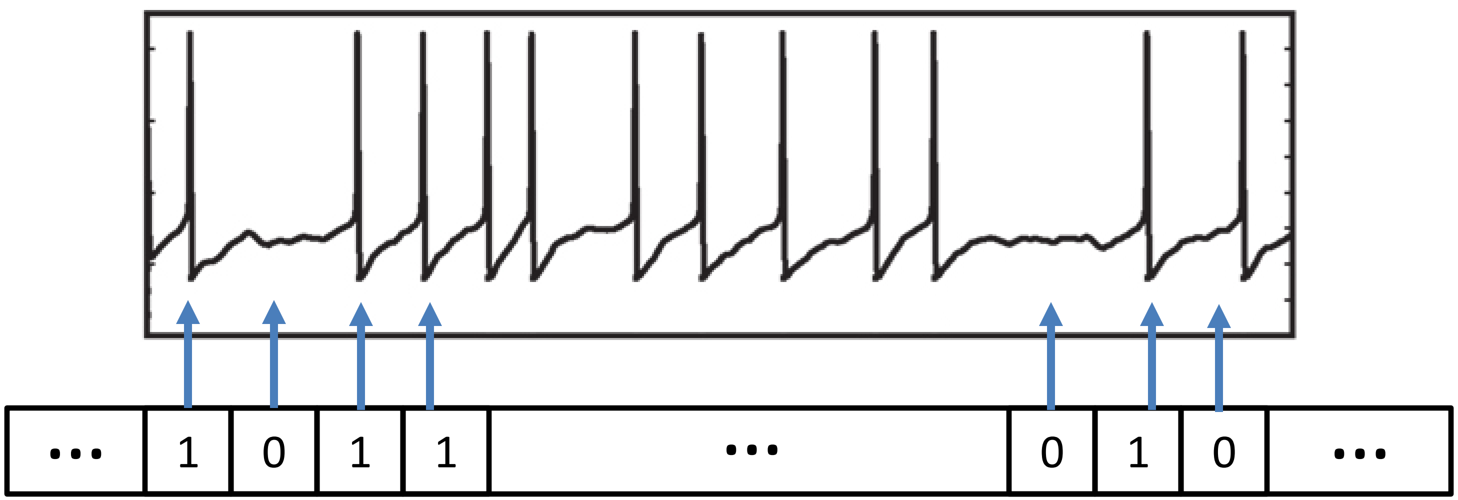
- But there are issues…
  - Entropy (and many other concepts from information theory) calculations require knowledge of the firing behavior probability distributions for the neurons - however
    - Limitations to in vivo recording capabilities
    - Neurons are somewhat deterministic
    - Neural plasticity effectively creates non-static distributions
    - Applicable to single neurons but not ensembles

Compression

- Instead - we have used complexity as a measure of compressibility in order to estimate entropy to quantitatively assess the information content of a signal.
- Szczepanski et al. applied the general Lempel-Ziv complexity (LZ-Complexity) measure to estimate entropy of real and simulated neurons.
- LZ Compression is a dictionary technique that does not require a probabilistic model.
  - Rather dictionary compression techniques exploit redundancies in the data.
  - LZ compression has been used in applications such as UNIX compress command and GIF compression.

Compression

- LZ-Complexity is based upon measuring the rate of generation of new patterns along a sequence of characters in a string being compressed.
- Applied to neuron spike trains, this technique looks for repeated spiking behavior over time.



Compression

- Once the spike signal is converted into a binary signal, where an action potential is encoded as a one and the absence of activity by a zero, the normalized complexity may then be computed as follows:

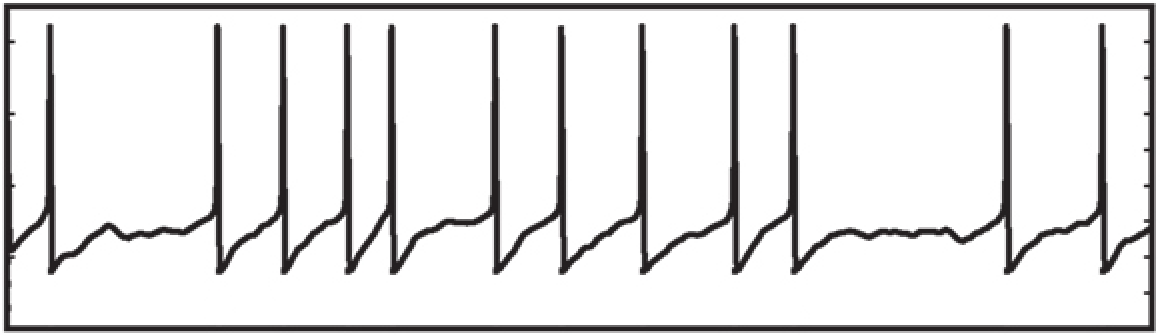
$$c_\alpha(x^n) = \frac{C_\alpha(x^n)}{n} * log_\alpha n$$

- Normalized complexity measures the generation rate of new patterns along a word of length n with letters from an alphabet of size α (in this case two).

Compression

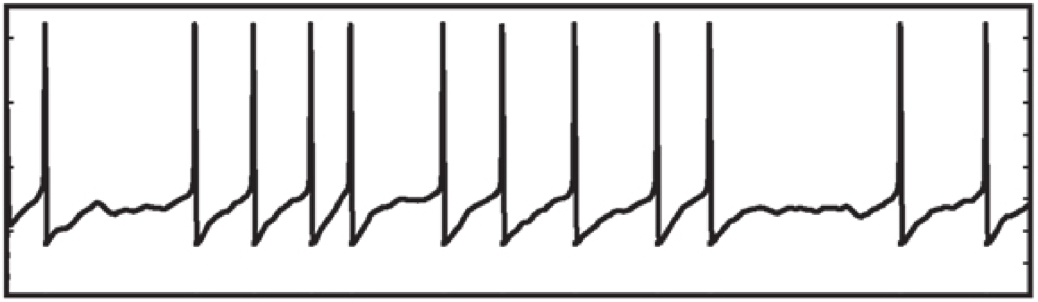
- But unlike the work of Szczepanski et al., rather than applying LZ-Complexity analysis to individual neuron spike trains, we have applied the approach to a neural population as a whole.
- Instead, by applying it across an entire neural ensemble, we assessed repeated patterns of neural co-activity.

Compression



10011110111101100011

Compression



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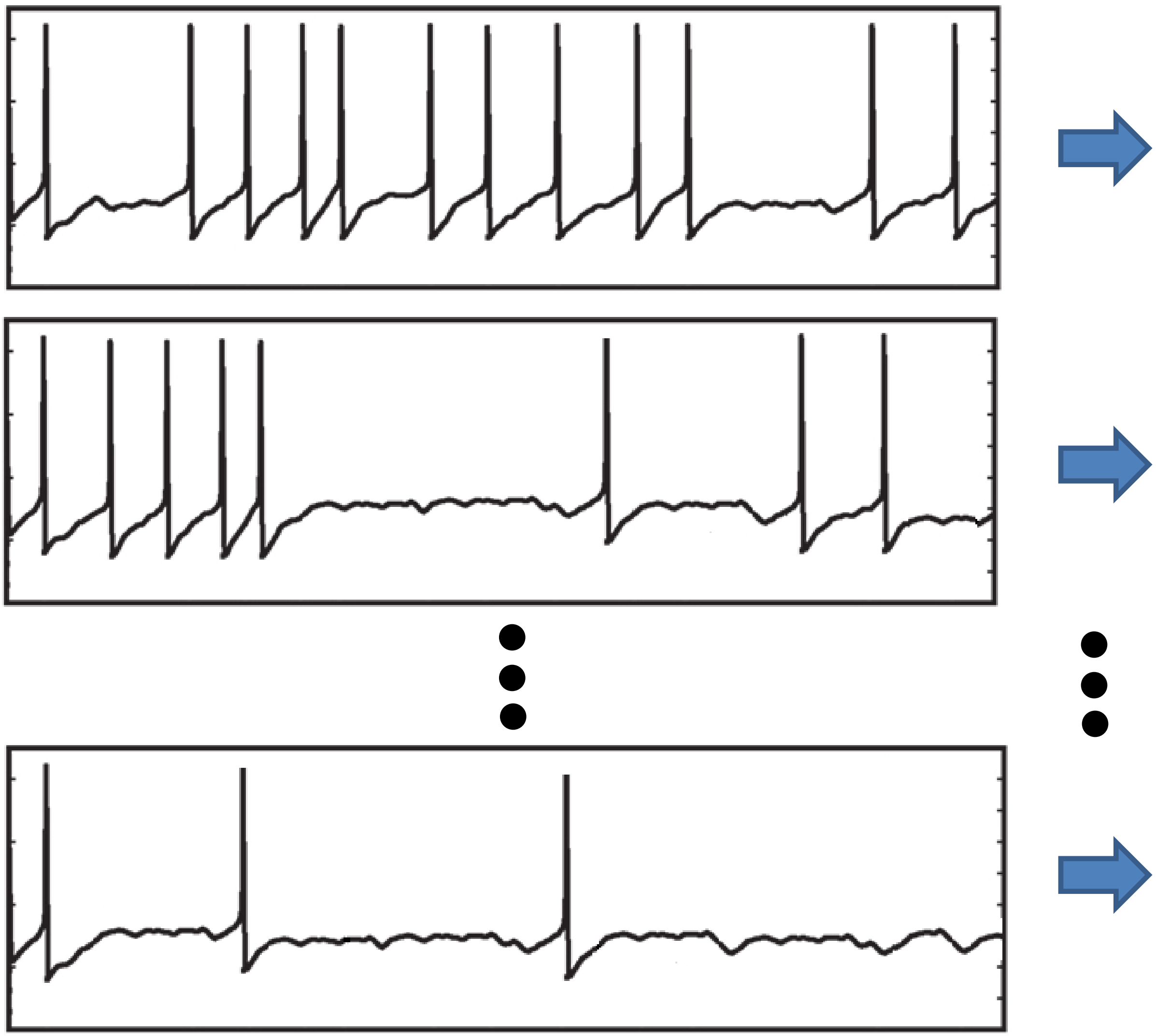
Compression



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Compression

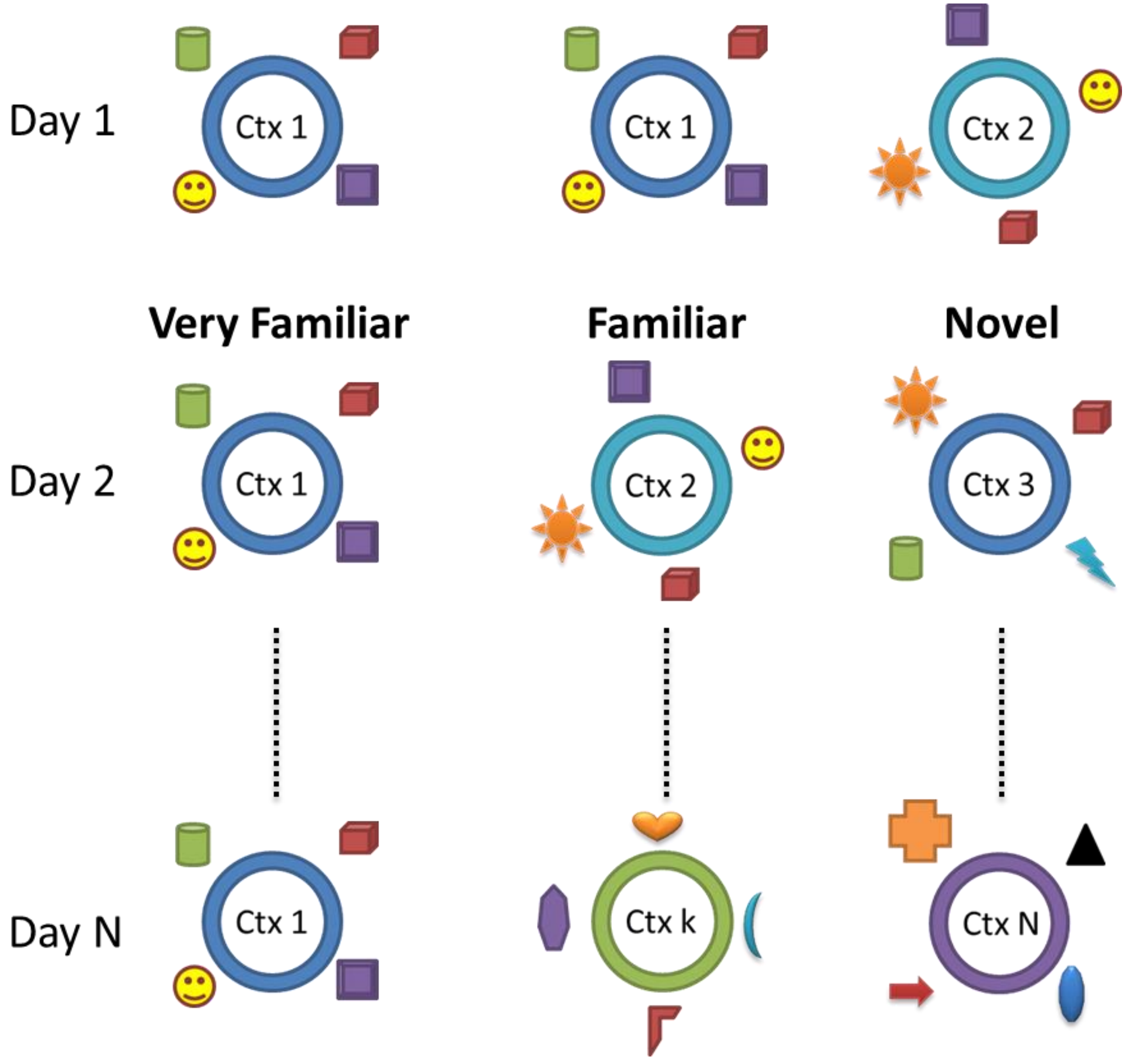
- Synaptic modifications alter the firing behavior of the neural network through learning.
- In order to account for this plasticity of the network, rather than computing the ensemble complexity at each timestep, we concatenated all of the firing outputs of the entire neural ensemble (while presented a single input context) into a long spike signal.

Compression

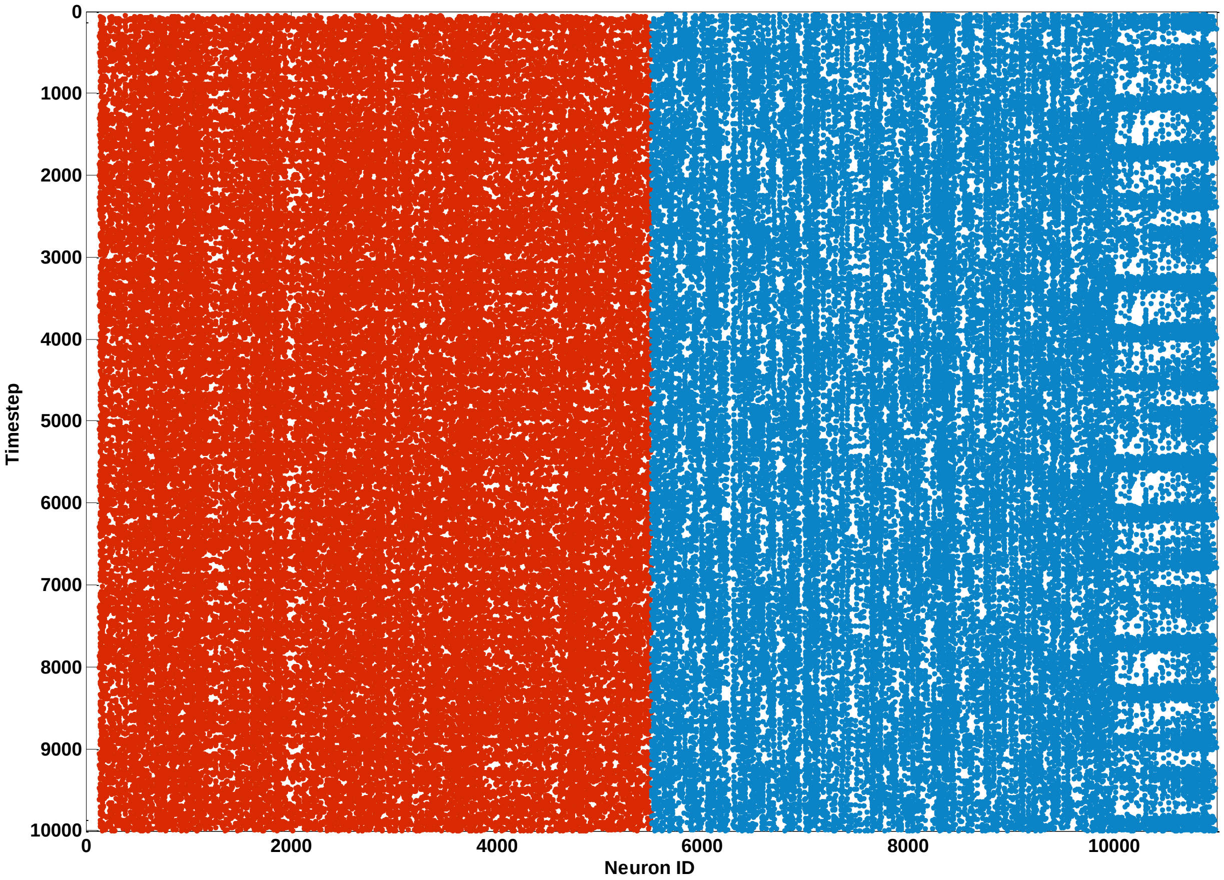
- It can be proven that as the string length (our series of neural firings in this case) goes to infinity, the supremum of the normalized complexity approaches the entropy of the signal S:

$$\lim_{n \to \infty} \sup c_{\propto}(x^n) \leq H_{\alpha}(S)$$

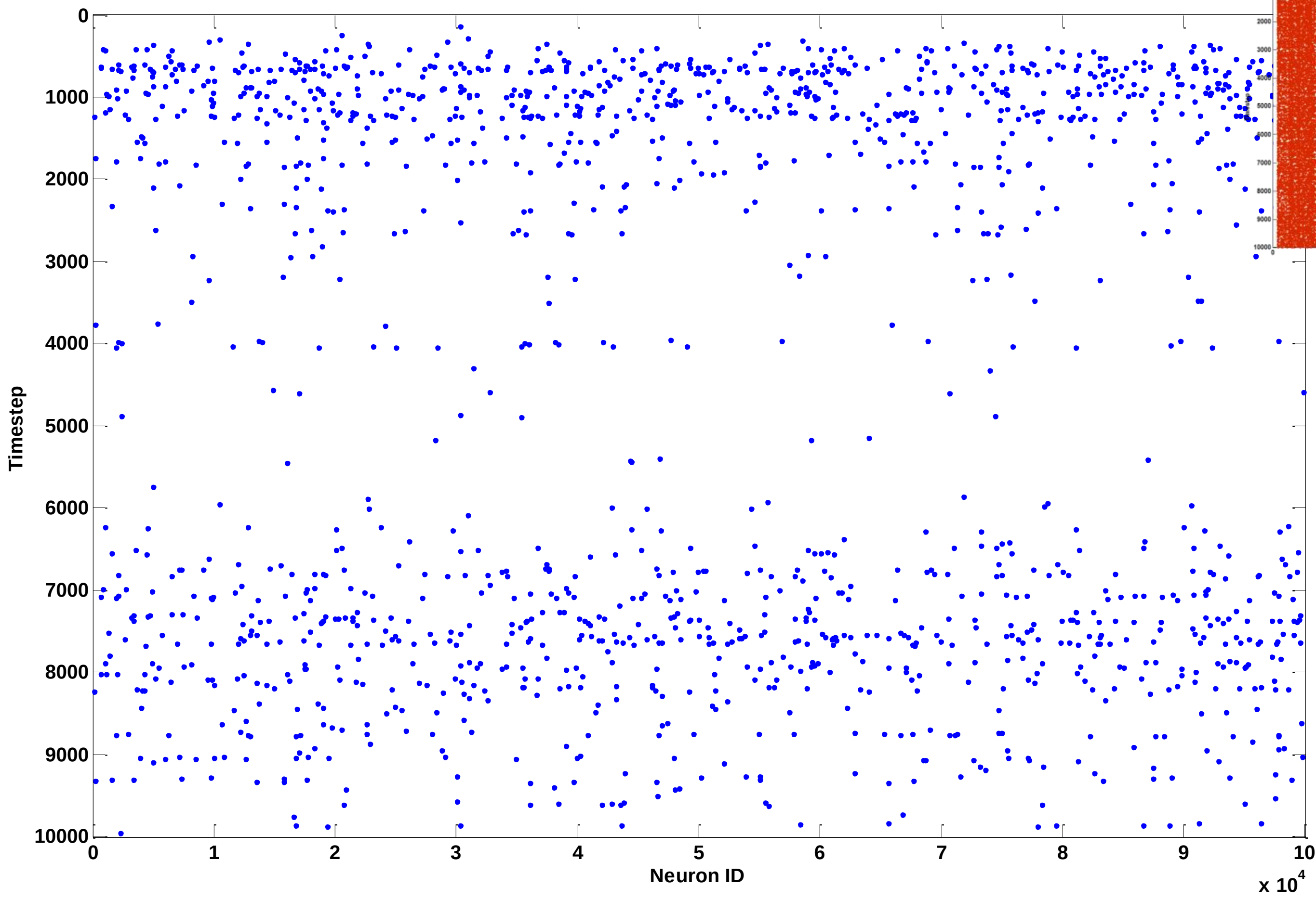
Experimental Paradigm

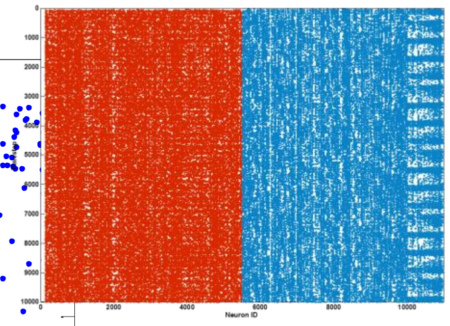


Activity of network – EC Inputs

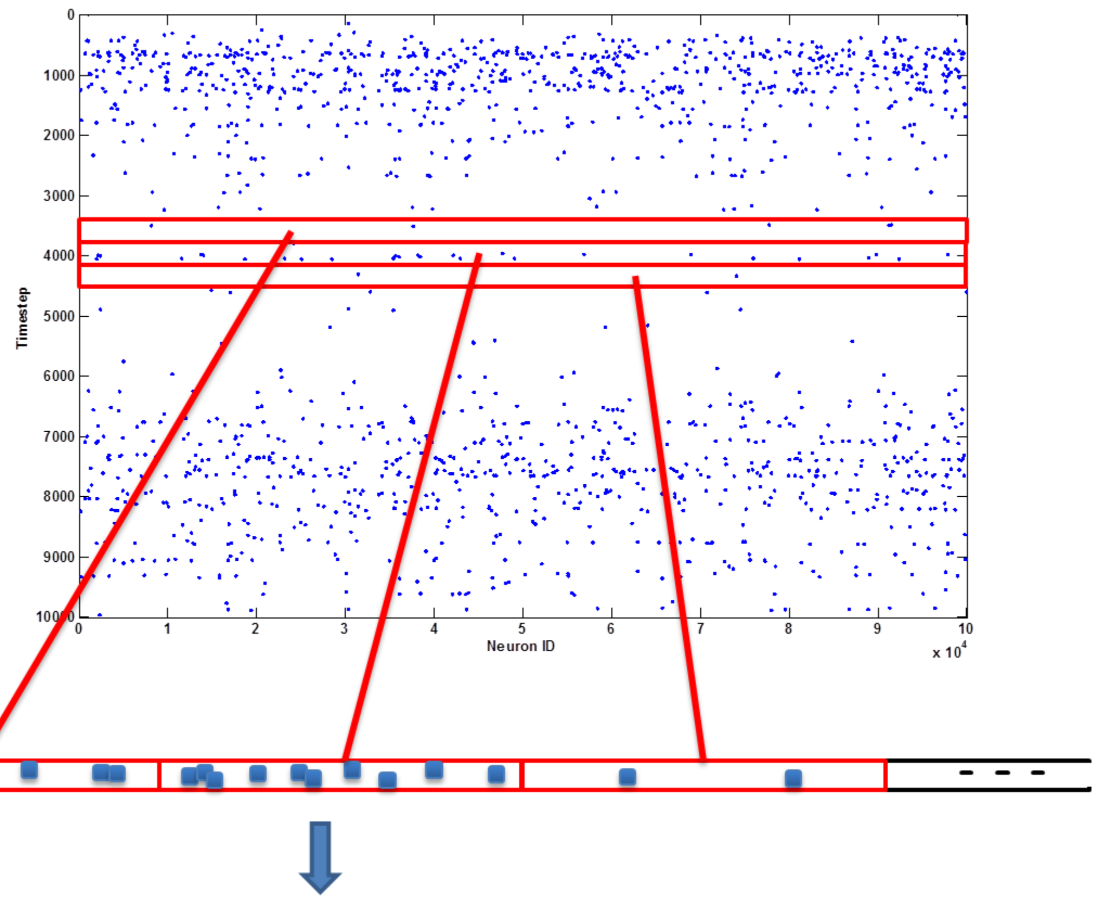


Activity of network – GC Outputs





Ensemble Spike Signal



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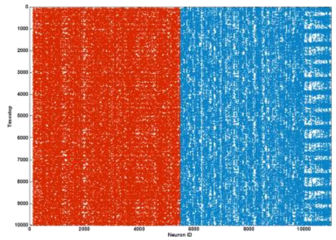
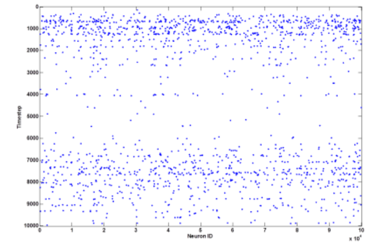
Normalized Complexities

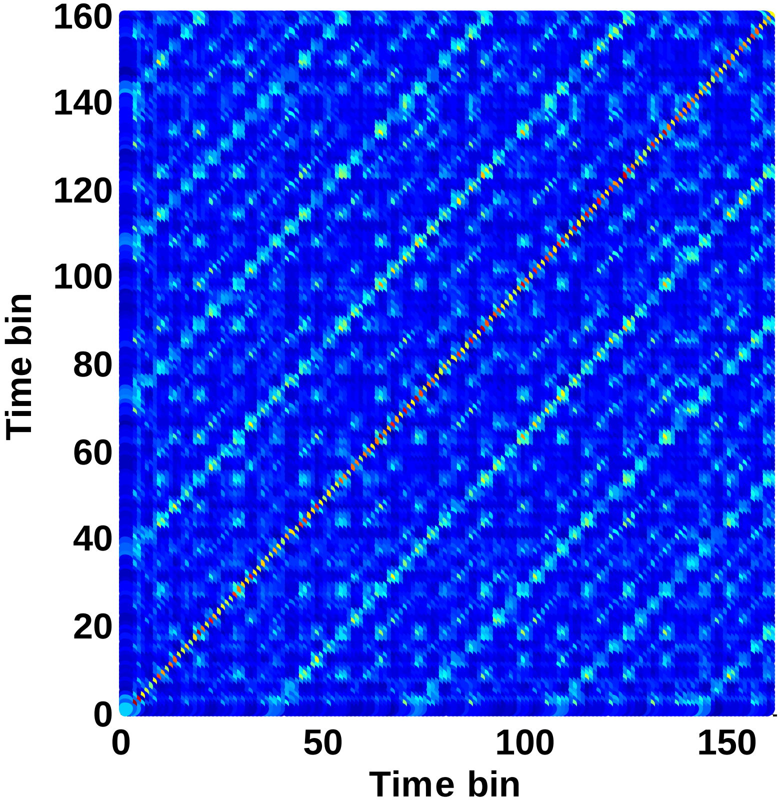
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
No NG	0.000003 0.000003 0.000003	0.000002 0.000002 0.000003	0.000002 0.000002 0.000002	0.000002 0.000002 0.000003	0.000002 0.000002 0.000002	0.000002 0.000003 0.000002	0.000002 0.000002 0.000002
10% NG	0.000032 0.000031 0.000031	0.000033 0.000035 0.000033	0.000861 0.000618 0.000747	0.000898 0.000846 0.000748	0.000789 0.000872 0.000824	0.001201 0.000458 0.000676	0.001298 0.001250 0.001050

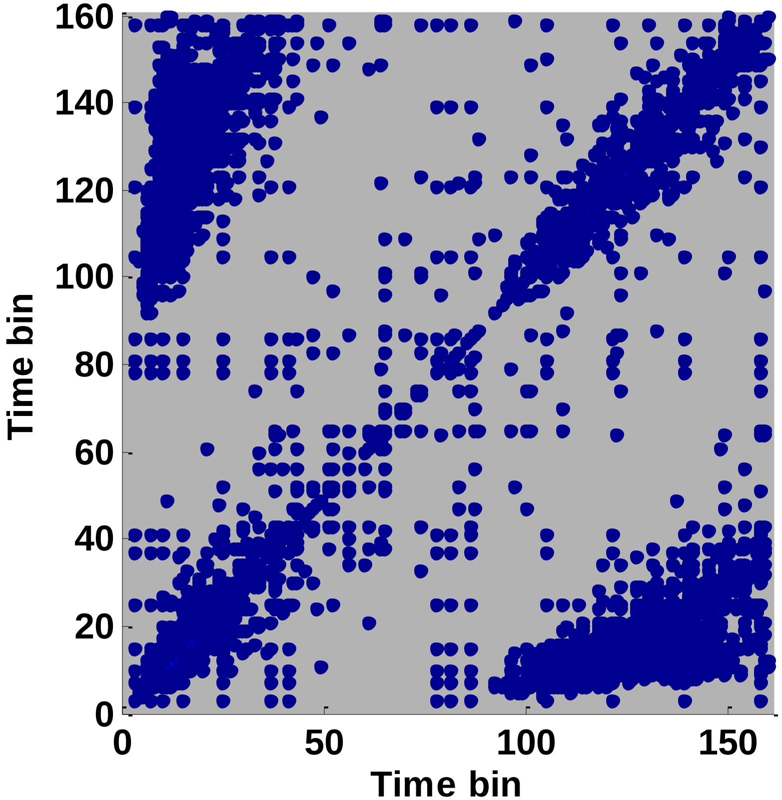
Entropy (Information) Estimates

Information processing in large networks

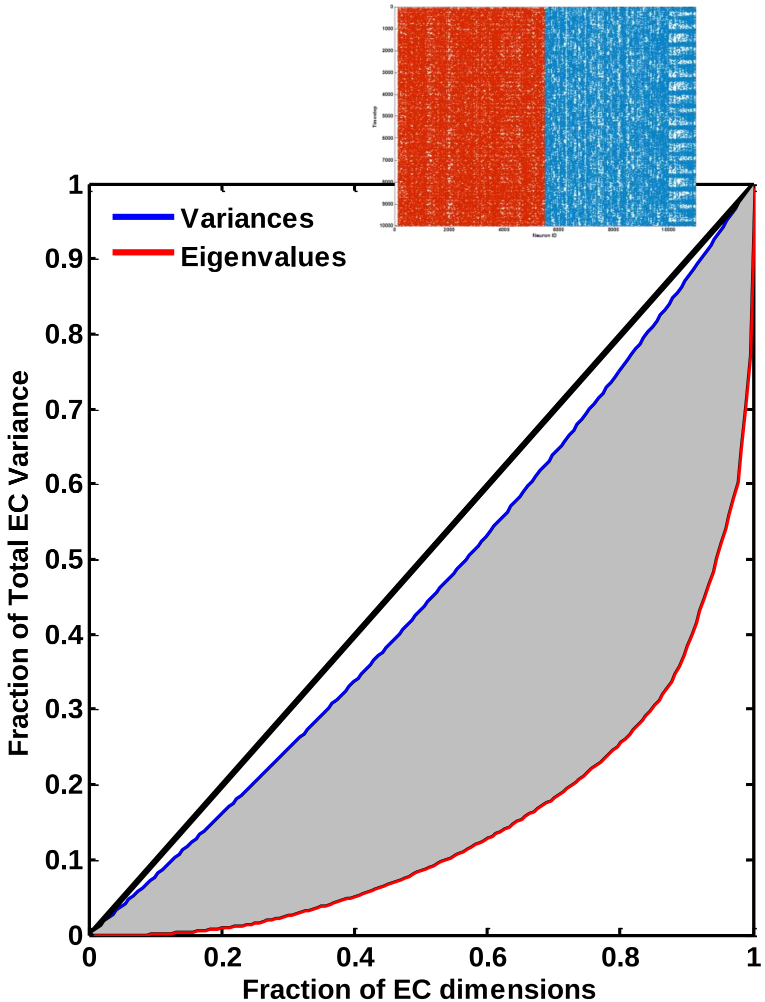


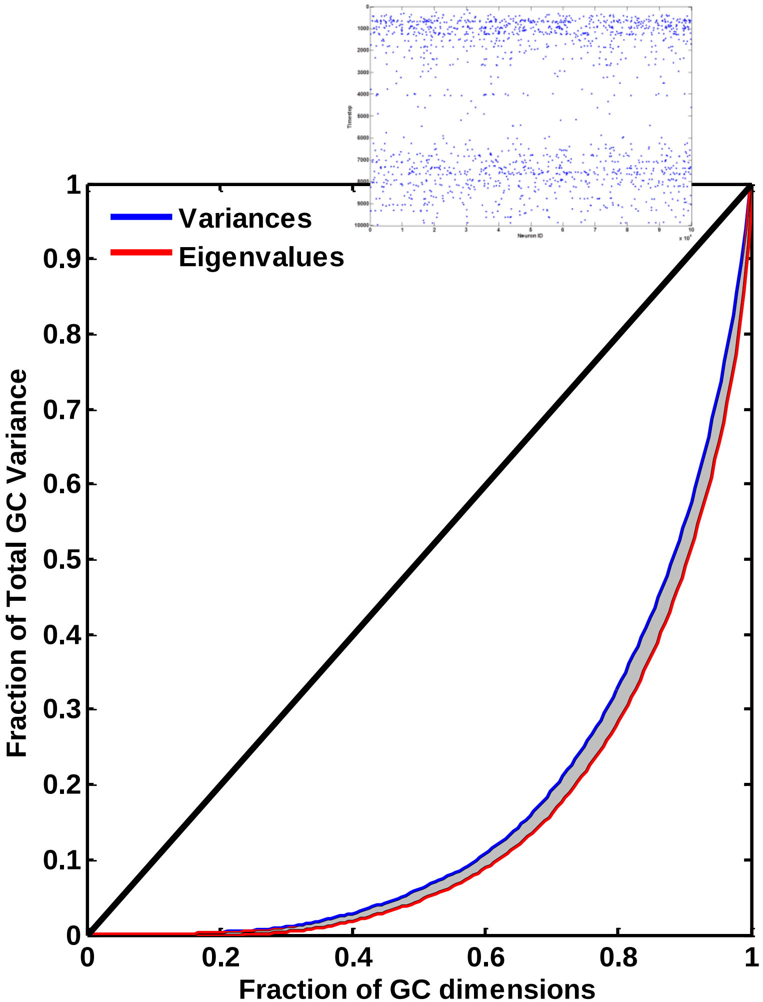




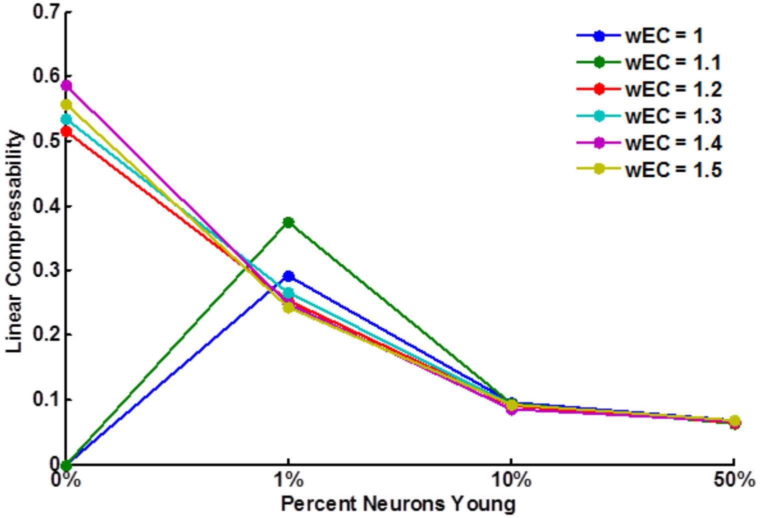


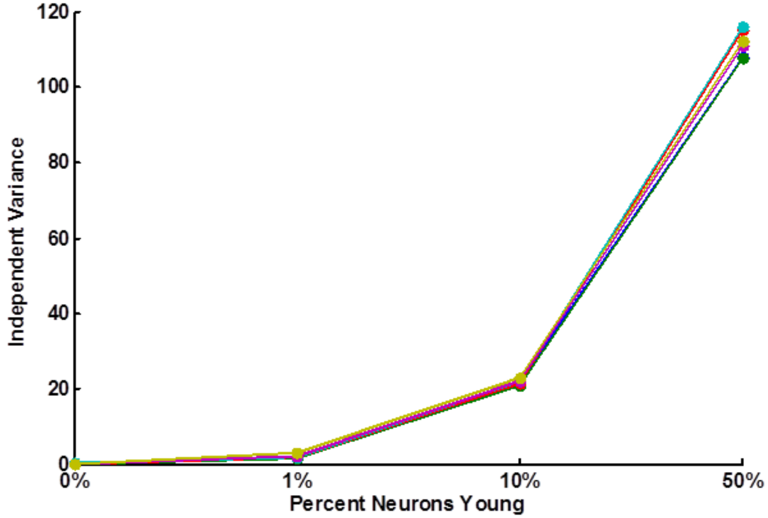
Information processing in large networks



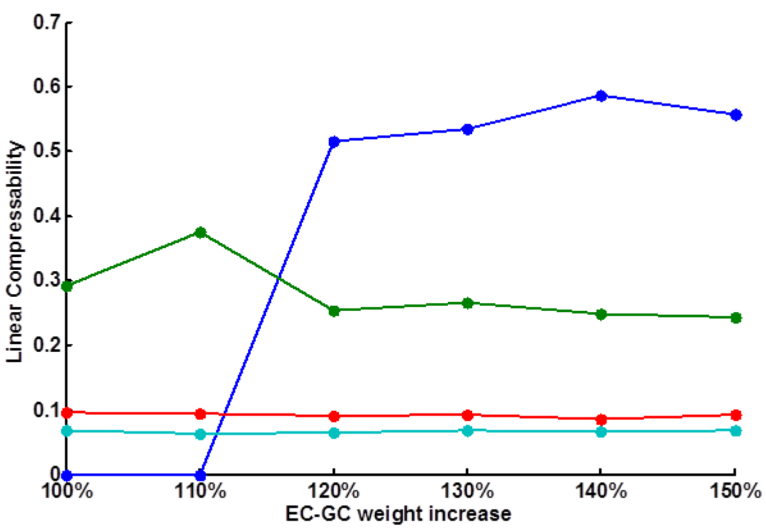


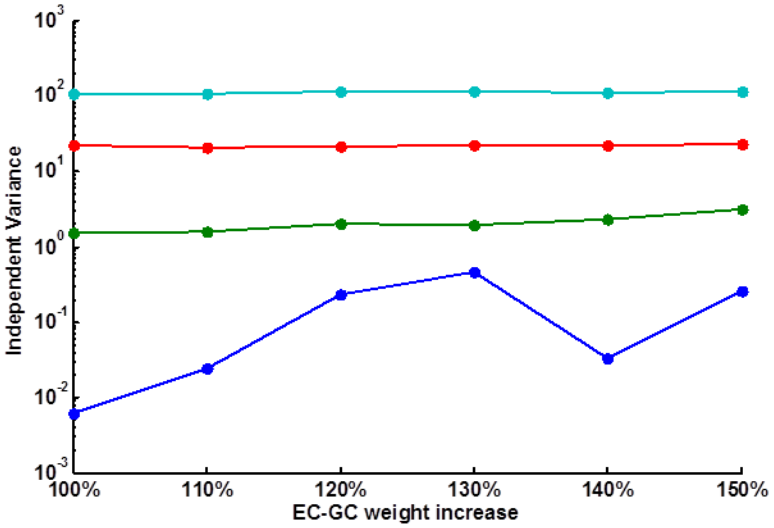
Neurogenesis decreases compressibility and increases total representation



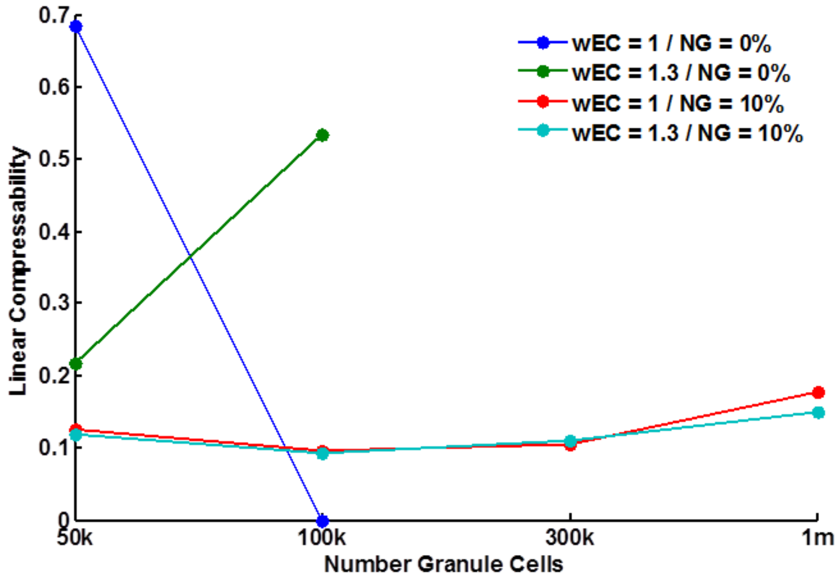


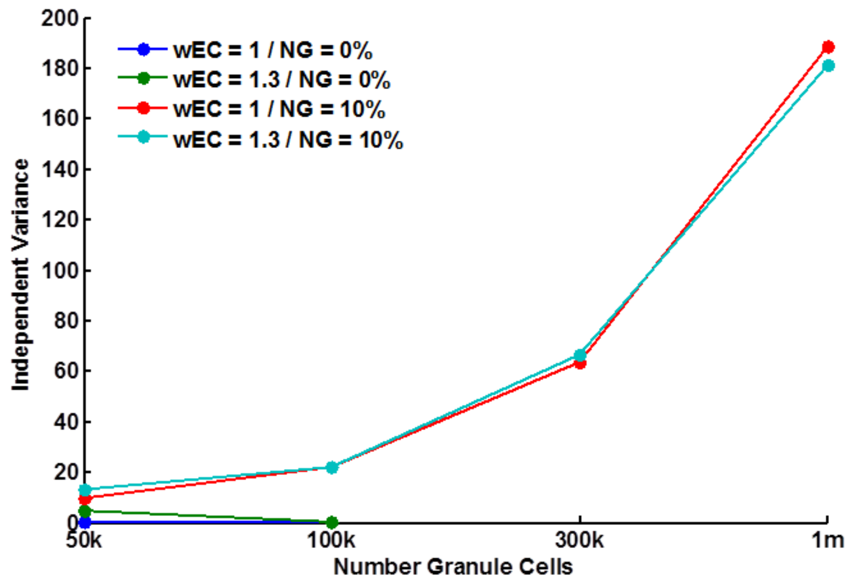
Increasing EC-GC weights impairs separation without improving coding





Increased size networks need neurogenesis for balancing separability and representations





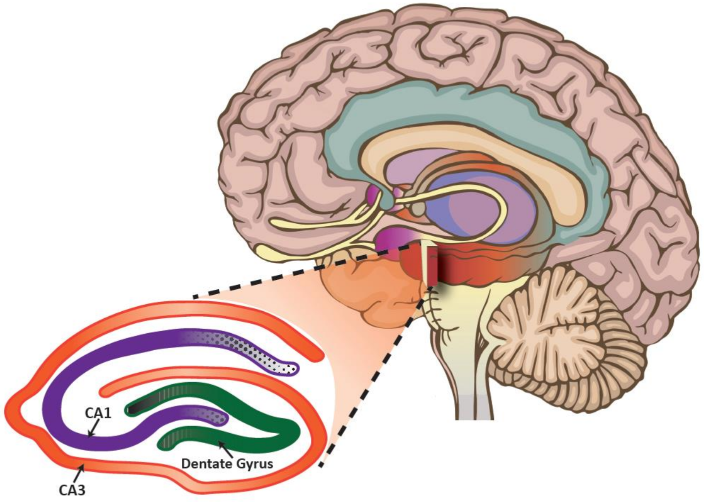
Next Steps

Next Steps

- We propose to further the understanding of adult neurogenesis in humans through computational modeling with two aims:
  - Develop a biologically realistic scaled spiking model of the CA3
  - Quantitatively analyze this model to examine the effects of neurogenesis on attractor dynamics and learning

Aim 1

- Expand Neurogenic DG model to incorporate downstream CA3 network
  - Neurogenesis itself of course takes place in the DG, however the functional significance of neurogenesis may require additional neural circuitry to become apparent



Aim 1

- Mathematics of chaos theory studies the behavior of dynamic systems in which small variance in initial conditions leads to vastly divergent outcomes
  - In the context of neurogenesis - possibility that by varying the memory resolution of the DG encoding, this slight modification of inputs to CA3 could result in significantly different associative memory encodings
- Potential ramifications:
  - Greater separation between attractor basins
  - Increased resolution of attractors
  - Different understanding of the mapping of the CA3 attractor landscape

Aim 1

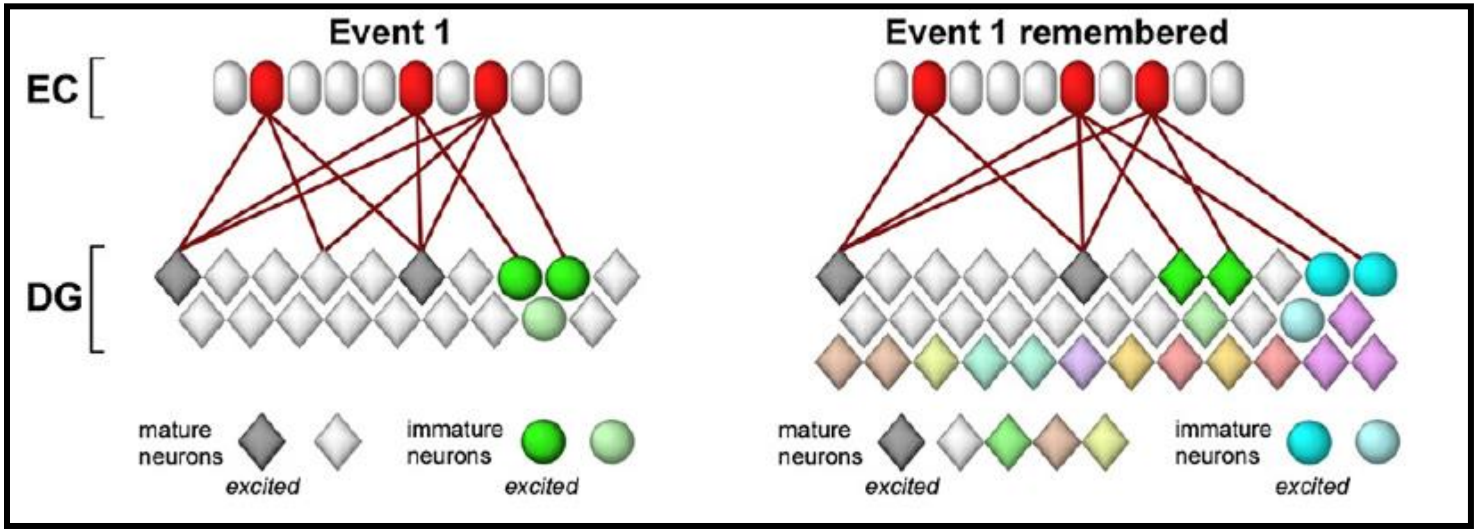
- To do so:
  - Develop a high fidelity biologically realistic spiking model implementing Izhikevich neurons with recurrent feedback
  - First develop a reduced scale model which operates upon the output of the Aimone developed DG model
  - As the model progresses
    - Increase biological fidelity by incorporating turning parameters guided by imaging/physiology work
    - Increase scale towards ~ 3 million neurons

Aim 2

- Develop quantitative metrics for memory dynamics in spiking neurogenesis DG-CA3 model
- Potential analysis techniques include:
  - Information theoretic analysis of neural encodings, information content, and channel capacity
  - Assessment of attractor formation and stability
  - Analysis of learnability.

Backup

Environmental commitment of adult-born neurons



Aimone et al., Neuron 2009

Hypothesis: The specialization of young neurons to the environments present during maturation allows improved encoding of new memories that relate to previously experienced contexts.

Why Computational Modeling

- The ability to create an accurate computational model depicts the state of understanding of the underlying neural processes
- Provides a platform amenable to test hypothesis not possible in humans or rodents
- In an iterated cycle, computational modeling and traditional laboratory work (such as experimental studies, imaging, and physiology analysis) are mutually beneficial.
  - Computational modeling may be able to provide predictions and insights which can be used to guide experimental studies, whose increased understanding subsequently leads to higher precision models.