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Computational modeling of human adult neurogenesis - information theoretic analysis of biologically realistic dentate gyrus networks

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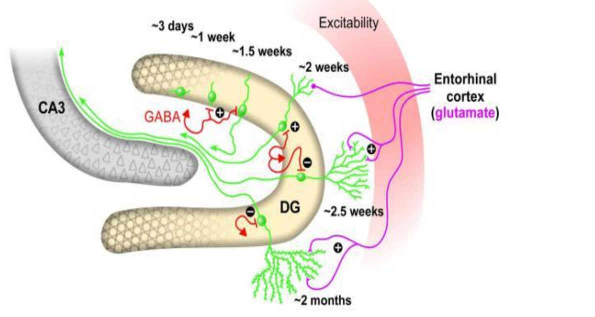
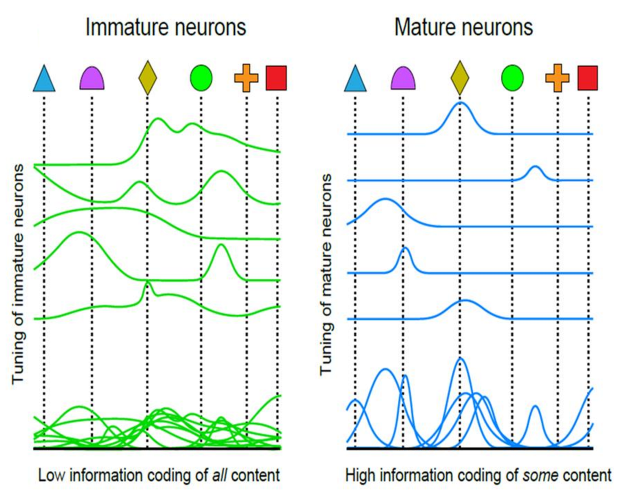
Overview of Adult Neurogenesis

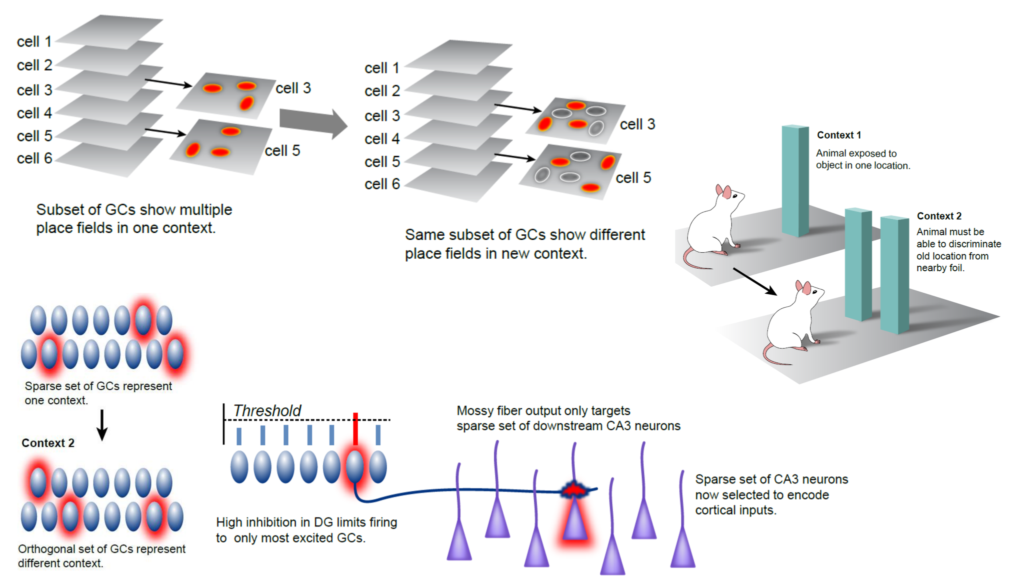
- 1000s of new granule cells integrate into DG monthly
- Only excitatory neurons are born; no new inhibitory neurons in DG
- Process heavily regulated by behavior; for example, running and enrichment increase, stress and aging decrease.
- Maturation process extends over months, excitatory and inhibitory pathways develop in parallel
- Young neurons are more "excitable" than mature counterparts due to distinct physiological and connectivity



Aimone et al., Nature Neuroscience 2006

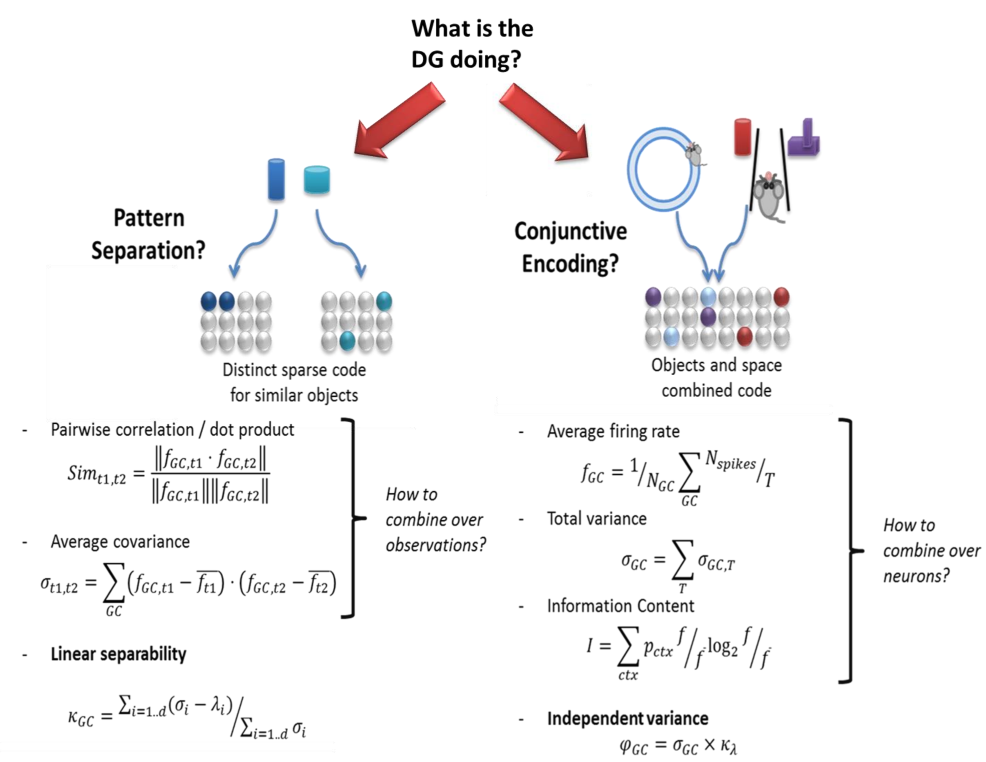


Aimone, Deng and Gage Neuron; 2011



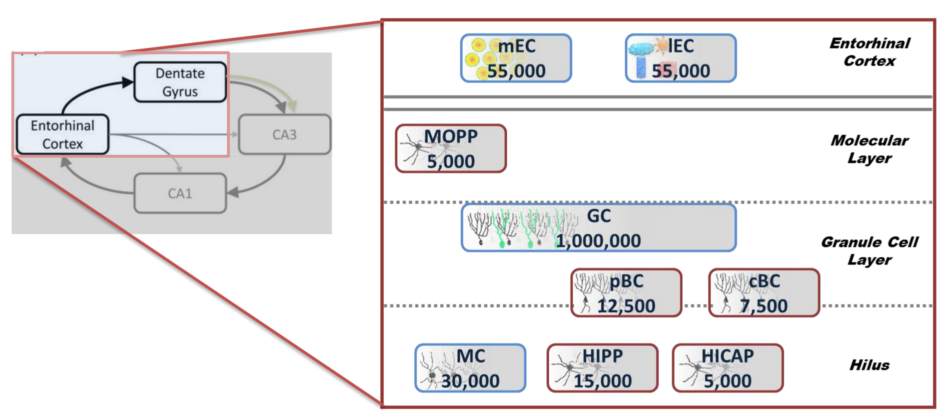
Aimone, Deng and Gage Neuron; 2011

What is Pattern Separation



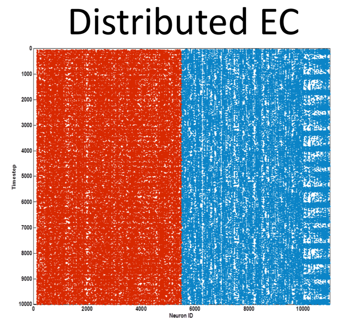
Overview of Modeling Approach

- Nine layer model of DG and entorhinal cortex inputs
- Oscillating modulatory inputs
- Feed-forward and feedback inhibitory and excitatory pathways
- Biologically realistic neuron numbers and ratios

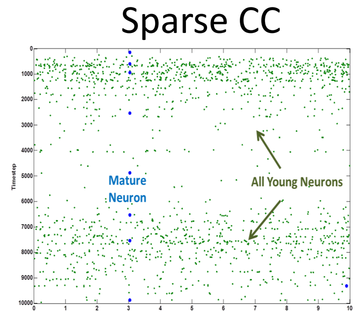


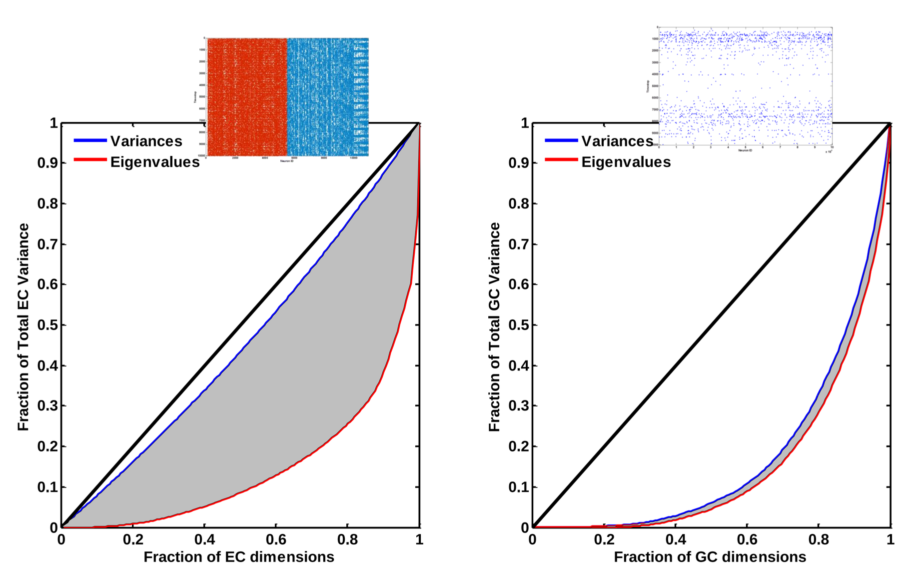
- Multi-day simulation to capture acute and long-term effects of neurogenesis
- Each day has novel contexts and (after initial day) familiar contexts
- Contexts can vary by which objects, object locations, and broader features

Distributed EC



Sparse CC





Analysis Methods

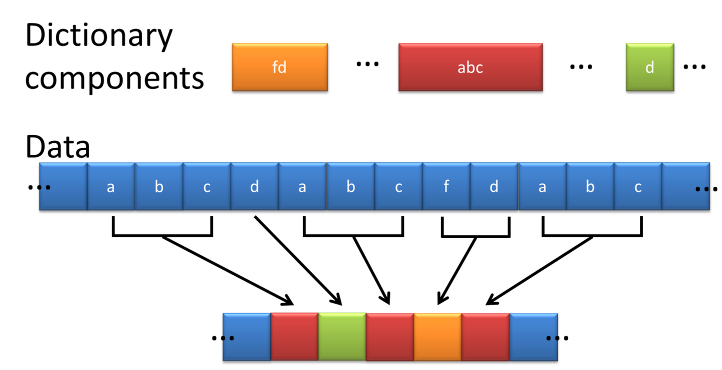
- Information theory provides entropy of a discrete random variable as a quantitative measure of information

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

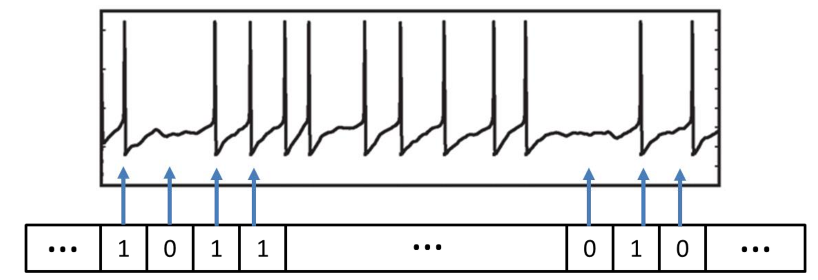
- Can be applied to neuroscience to quantitatively measure the information content of firing neurons
- And it has been with various methods such as (not a complete list):
  - Plug-in Entropy
  - Jackknife debiased
  - Asymptotically debiased
  - Ma bound
  - Bayesian/Dirichlet prior
  - Coverage-adjusted
  - Best upper bound
- 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.



- 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.

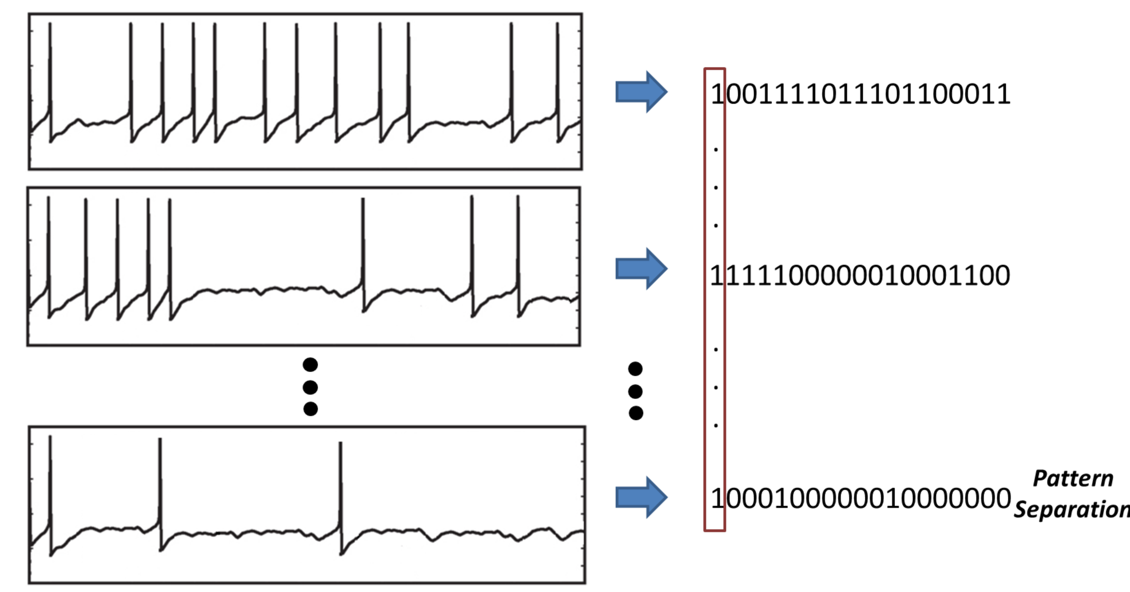


- Once the spike signal is converted into a binary signal, where an action potential is encoded as a one and the absence of activity by a zero, the normalized complexity may then be computed as follows:

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

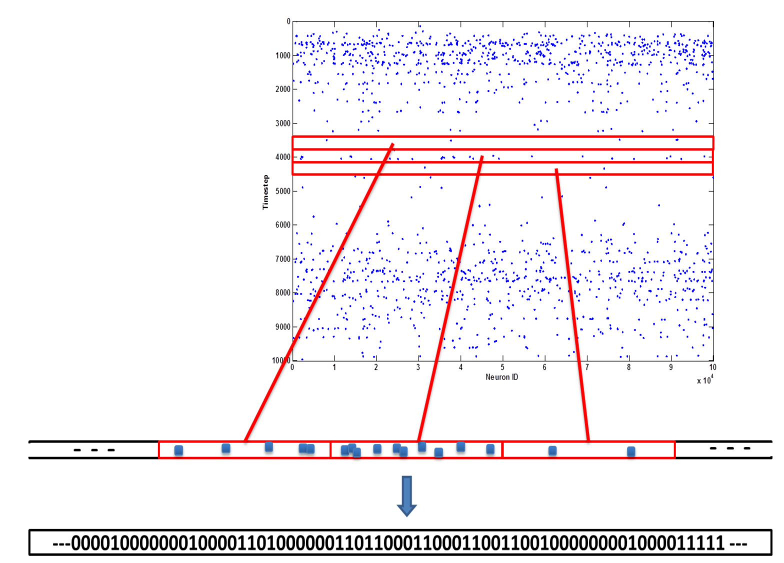
- Normalized complexity measures the generation rate of new patterns along a word of length n with letters from an alphabet of size α (in this case two).

- 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.



- 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:

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



Results

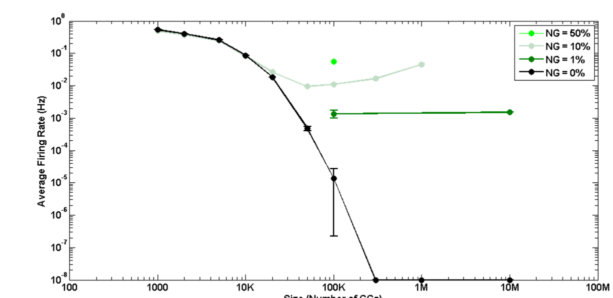
Entropy (Information) Estimates

- EC shows higher overall entropy than GC layer
- EC-GC weight increase marginally increases representation complexity
- NG substantially increases GC complexity

	EC (5,500)	GC (50,000)
No NG	Context 1: 0.025883 2: 0.026099 3: 0.025258	Context 1: 0.000003 2: 0.000003 3: 0.000003
No NG EC – GC x 1.3	Context 1: 0.027590 2: 0.027745 3: 0.027310	Context 1: 0.000021 2: 0.000016 3: 0.000014
10% NG	Context 1: 0.025876 2: 0.025795 3: 0.026334	Context 1: 0.000032 2: 0.000031 3: 0.000031
10% NG EC – GC x 1.3	Context 1: 0.025895 2: 0.025961 3: 0.025169	Context 1: 0.000044 2: 0.000041 3: 0.000041

	EC (11,000)	GC (100,000)
No NG	Context 1: 0.026020 2: 0.025982 3: 0.026502	Context 1: 0.000001 2: 0.000001 3: 0.000001
No NG EC - GC x 1.3	Context 1: 0.025728 2: 0.025824 3: 0.025312	Context 1: 0.000003 2: 0.000002 3: 0.000002
10% NG	Context 1: 0.025957 2: 0.025965 3: 0.026172	Context 1: 0.000034 2: 0.000034 3: 0.000033
10% NG EC - GC x 1.3	Context 1: 0.026320 2: 0.026402 3: 0.026389	Context 1: 0.000034 2: 0.000033 3: 0.000032

Lack of neurogenesis in large networks correlates with much lower activity

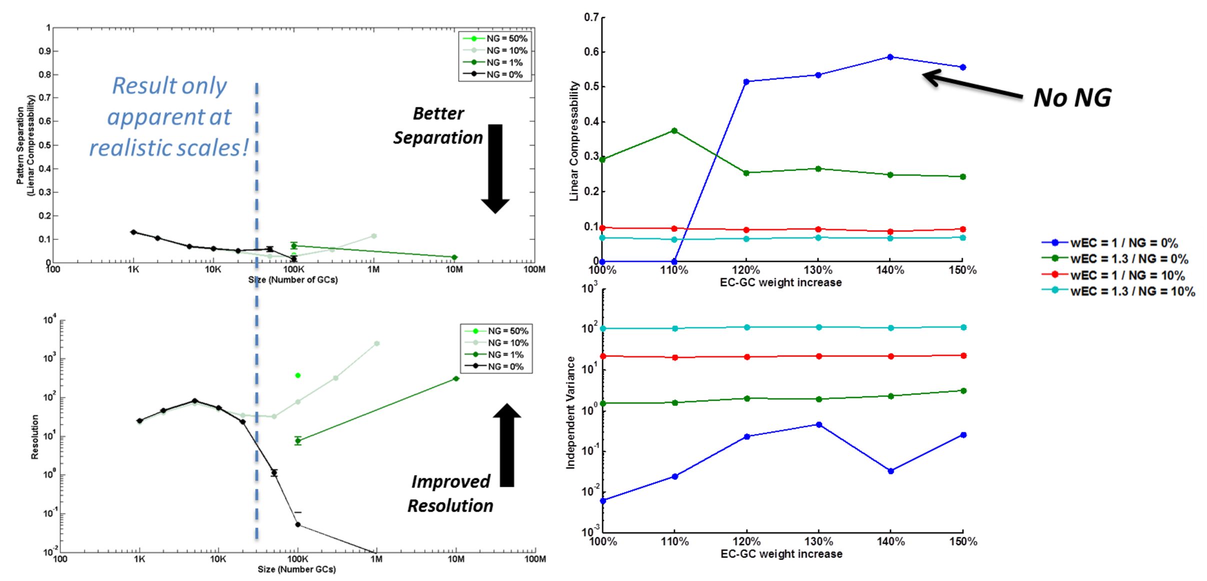


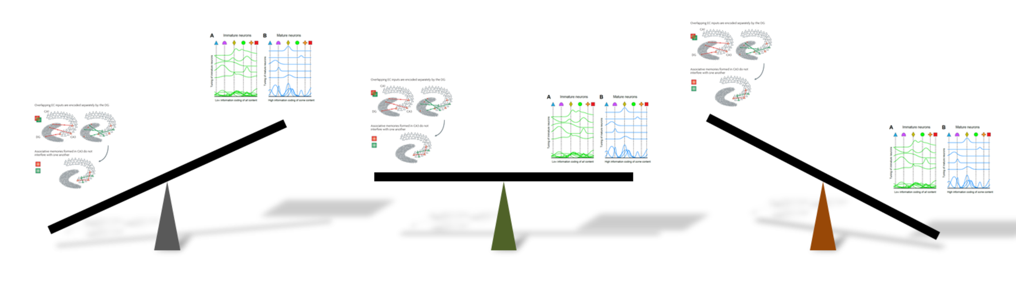
- Neurogenesis networks show activity to novel information at much higher scales
- As we approach human scales, mature neurons appear essentially silent in response to novel information

- Signal (immature) to noise (mature) is amplified in larger networks

Neurogenesis maintains compressibility and increases total representation

Increasing EC-GC weights impairs separation without improving coding





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

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