Global neuromodulatory signal fluctuation and the stability of the neural code

CARL CORRENS FOUNDATION FOR MATHEMATICAL BIOLOGY

ICM, Paris, Sept 16th-17th, 2026

Gabriele Scheler[1] and Johann Schumann[2]

[1]Carl Correns Foundation for Mathematical Biology

Introduction

Neuromodulatory signals which originate from central brain regions like dopamine, serotonin, or noradrenaline affect synaptic connectivity and neural transfer functions. This raises a fundamental question: **how can neural representations of patterns, the neural code, remain stable when the network undergoes fluctuations of the global NM signal?**

Purpose and Hypothesis

Neuromodulatory recptors when activated distort neural representations of input patterns. We demonstrate this effect with random distributions of NM receptors and show that pattern recognition is impaired, destroying the neural code. This could mean that NM receptor activation is incompatible with neural code stability. Our hypothesis was that distributions for NM receptors exist, which keep a core pattern intact and allow for robust classification.

Materials and Methods

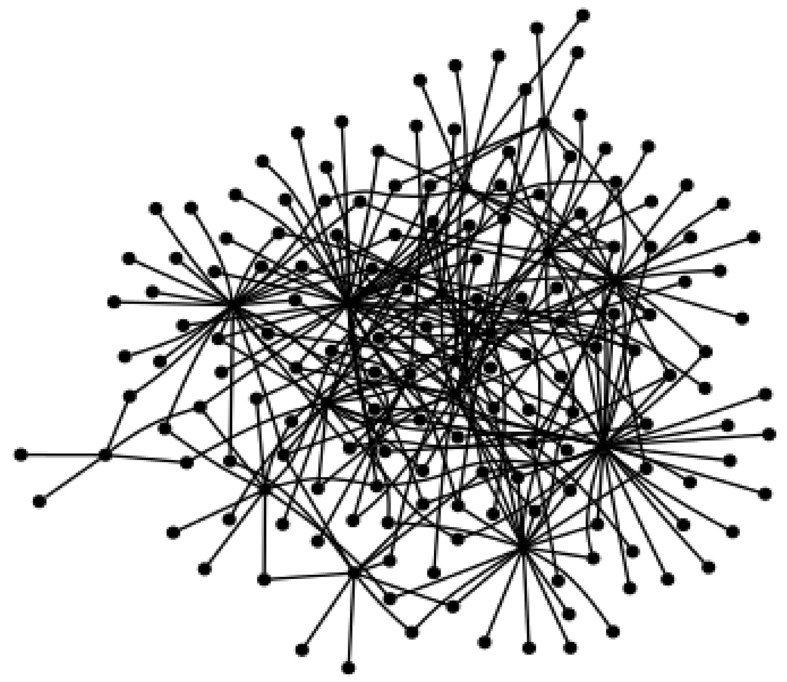
We use a cortical model of pattern learning for stable pattern recognition of 250 MNIST digit patterns, by a reservoir-like network with 1000 E/200 I neurons. The network was a SW graph with lognormal distribution of neuron strength. Both labeled and unlabeled input patterns were successfully classified, about 80-90% correct. Distributions of D2 receptors on 30% of synaptic sites and D1 receptors on about 20% of neurons, with the capacity to reduce synaptic strength (D2) and increase neuron strength (D1) led to unclassifiable activation patterns proportional to NM signal strength κ, a global, fluctuating parameter. Specifically, some classes were unrecognized and falsely classified (e.g. all "3" and "5" classified as "4").

Pattern classification for random NM positioning, typical results

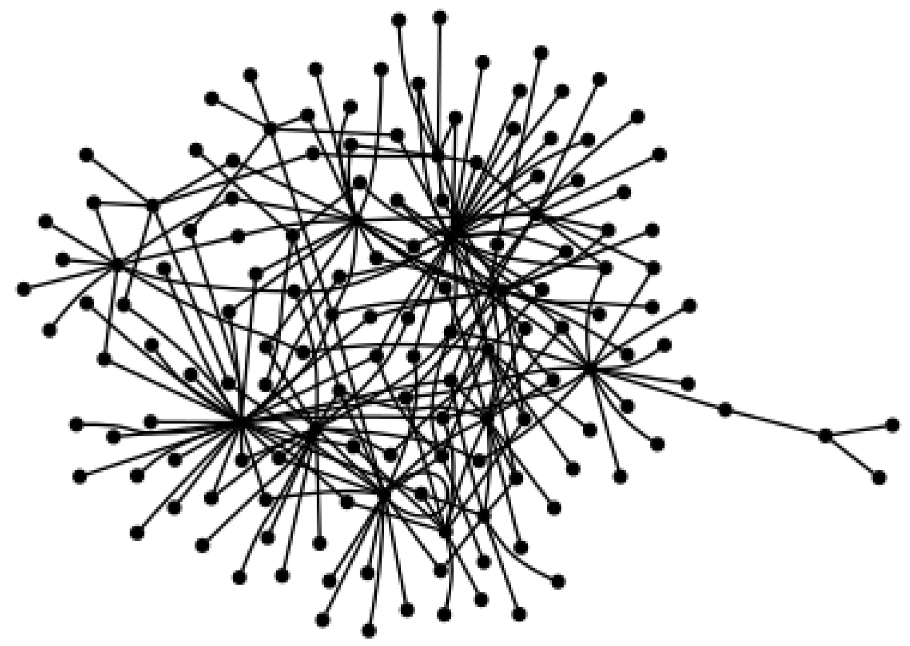
class	%patterns correct, k=0	%patterns correct, k=2
"1"	90%	88%
"2"	90%	54%
"3"	98%	0%
"4"	80%	92%
"5"	90%	0%
"overall"	89,6%	46,7%

Global NM signal k
k = 0 low signal, low receptor occupancy
K = 2 high signal, high receptor occupancy

Graph structure of sample network NE=1000, NI=200 Ke=18600 (SW Graph) , Ki=180,000 (fully connected), top-level connectivity Ke, N=50



Graph structure with NM signal (k=2) after (random/selective) D2 based cuts of 6000 Ke connections, top-level connectivity Ke, N=50

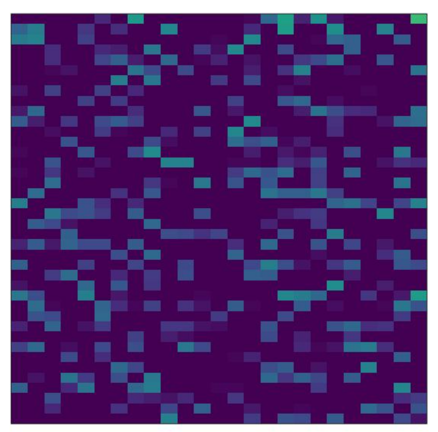


Further Methodology

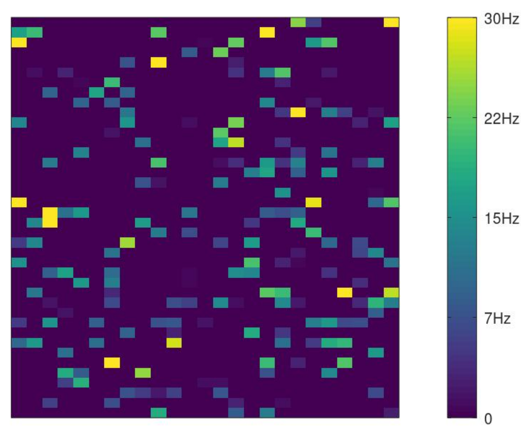
These results could mean that NM receptor activation by a global signal is ***incompatible*** with neural code stability. But we hypothesized that NM distributions could be found which preserve classification and the neural code under NM signaling. We implemented a simple Monte Carlo search procedure for receptor positioning at k=2 under an objective function of keeping recognition stable. About 20% of NM distributions were successful with a classification rate above 80%. The unmodulated network (k=0) exhibited a stable 'core' representation over all 50 variations of a pattern. These core representations were smaller under k=2, in all cases. We did not find a systematic correlation between activity patterns or D1/D2 placement with classification success, but neural code stability was always restricted to a ***subset*** of modulated (k=2) networks.

Network activations for random NM positioning

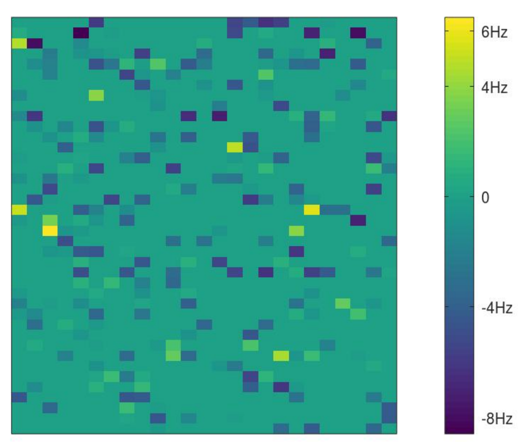
Activation for "2", 50 variations, k=0, difference to baseline (absolute)



Activation for "2", 50 variations, k=2, difference to baseline (absolute)



Difference in activation value under NM signal (for k=0 → k=2)

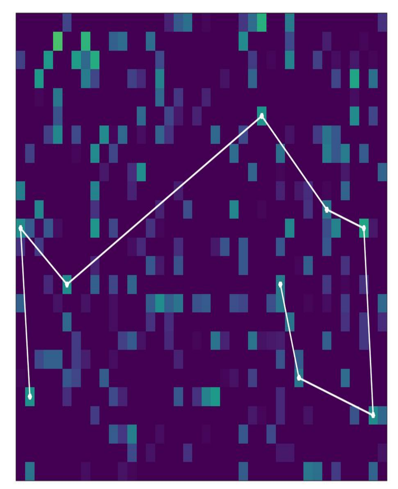


Results

When activating NM receptors by a global signal, underlying networks change their architecture and firing strength. They respond differently to an identical input pattern. However, classification and **stability of the neural code** can be achieved with **selected** receptor configurations. A simple search+optimization identified numerous receptor configurations that maintained stable pattern recognition. The 'degeneracy'of the solution space suggests that local receptor plasticity can be reconciled with network-level coding stability.

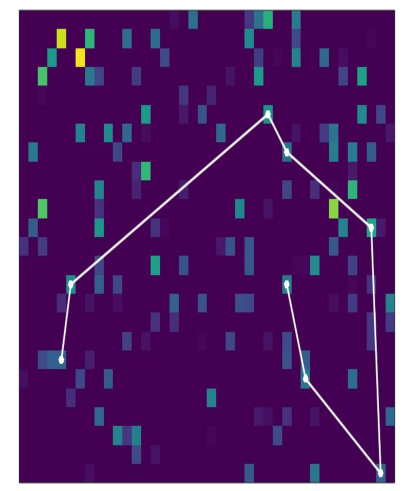
Code stability under NM signal fluctuation for selective NM positioning

Core pattern for "5" - K=0 over 50 variations – classification correct (>80%)



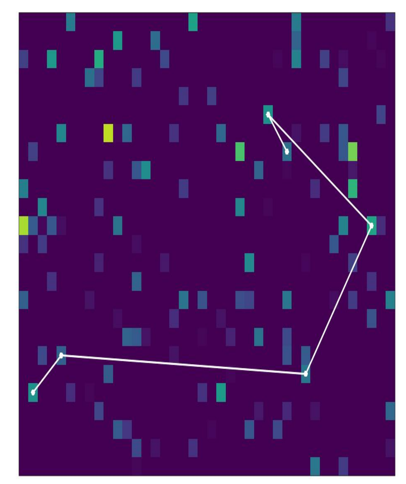
Core activation

Core pattern for "5" - K=2 over 50 variations, selective positioning – 86% classification



Core activation- code stability

Core pattern for "5" - K=2 over 50 variations, random positioning – 25% classification



Core activation- code destroyed

Conclusions

The model shows that plasticity of NM receptors is compatible with neural code stability, when it is provided with an 'outer loop' of optimization for coordination over the whole network. The results point to a possible principle in which degenerate parameter spaces and optimization loops allow biological networks to reconcile neuron-specific information-carrying plasticity with preservation of functionally important representations.

Acknowledgments

Bibliography

- LeCun, Y. and Cortes, C., The MNIST database of handwritten digits, 1998.
- G. Scheler, M.L. Schumann, and J. Schumann. Localist neural plasticity identified by mutual information. J Comp Neuroscience 53(2):321-331, 2025
- G. Scheler, M. L. Schumann, and Johann Schumann. Non-standard memory models with indexed retrieval. Complex Networks 2026. https://arxiv.org/abs/2608.27479
- G. Scheler. Regulation of neuromodulator receptor efficacy-implications for whole-neuron and synaptic plasticity. Prog Neurobiol. 2004 72(6):399-415

Further Information

gscheler@gmail.com; contact@theoretical-biology.org;
URL: www. theoretical-biology.org