Modeling the Effect of Norepinephrine Levels on Working Memory through α1 and α2 Receptors

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Outline

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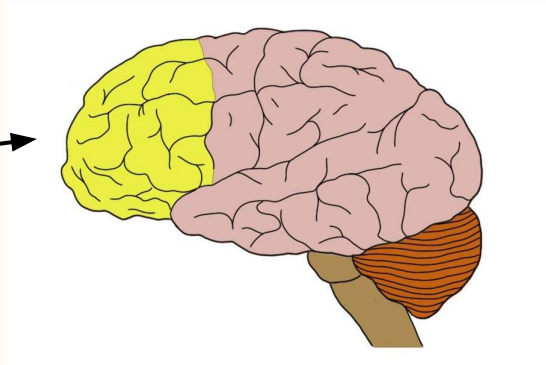
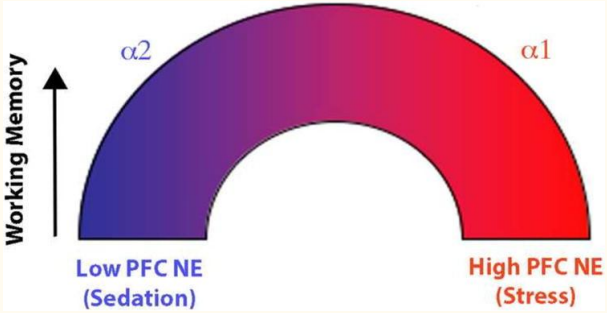
Intro to Norepinephrine and Working Memory

- **Working Memory (WM):**
  - Short term memory
  - **Prefrontal Cortex (PFC)**



- **Norepinephrine (NE) (aka noradrenaline):**
  - NT released during stress
  - **Memory storage**, attention/focus, emotions, sleep-wake cycle
- **Effect depends on amount**
  - **Low** Levels of NE → **Improve** WM
  - **High** Levels of NE → **Impair** WM

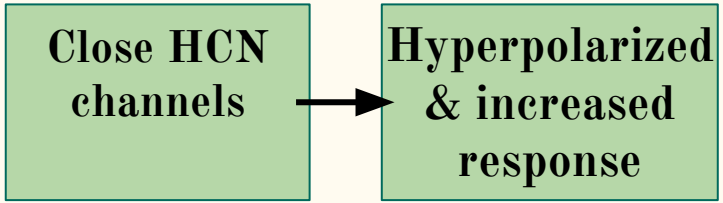


NE Receptors in PFC

- **Alpha-receptors:**
  - **Alpha-1 Receptor**
    - Higher concentrations of NE
    - Impairs WM
  - **Alpha-2 Receptor**
    - Lower concentrations of NE
    - Improves WM
- **Beta-Receptors**
  - Inconsistent findings
  - Blocking receptors doesn't affect WM

Alpha-1 Effects

Alpha-2 Effects



Methods: How the Model Works

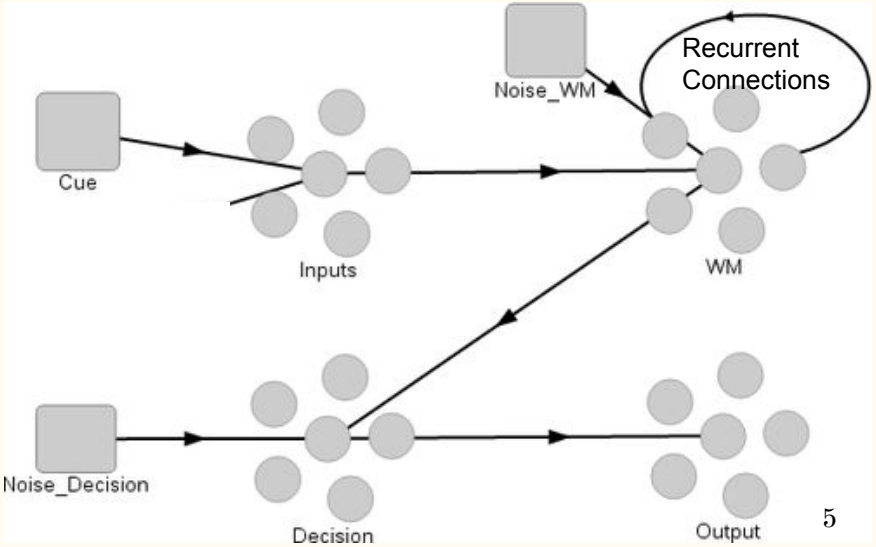
- 100-neuron spiking neural network model of PFC
  - ➢ **DFT (Spatial Delayed Response Task)**
- Cue vector (-1 or 1)
  - ➢ Causes pattern of neuron firing **(x)**
    - Based on the neurons' **preferred direction**
- Must maintain pattern of firing with recurrent connections
- Similarity between **x** and **output vector**→ determines performance of WM

Study/Original Model:

The Effects of Guanfacine and Phenylephrine on a Spiking Neuron Model of Working Memory

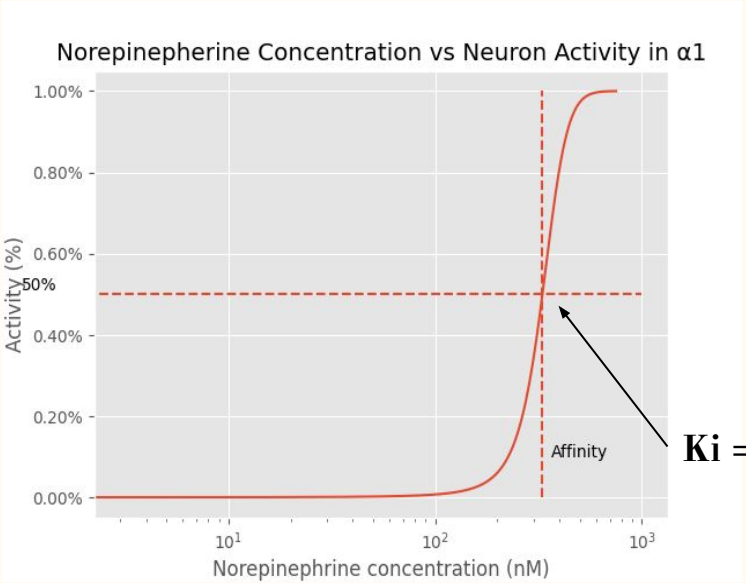
Peter Duggins ✉,Terrence C. Stewart,Xuan Choo,Chris Eliasmith

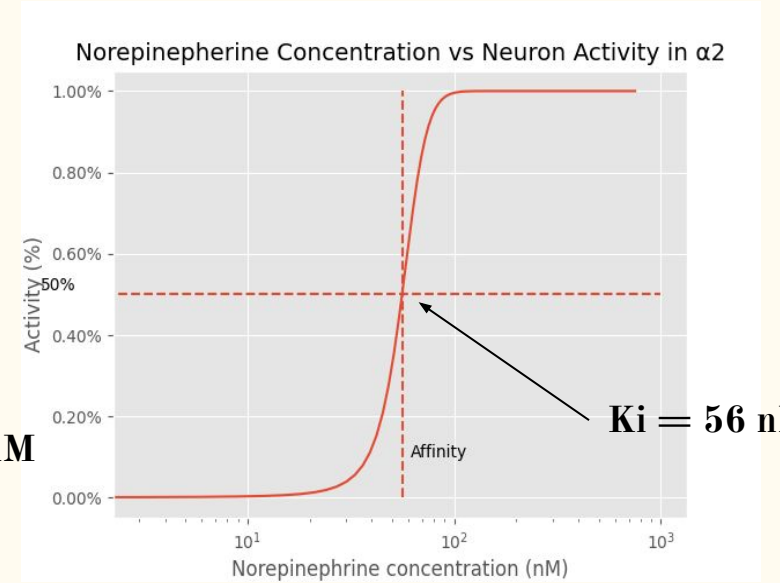
First published: 21 December 2016
https://doi.org/10.1111/tops.12247
Citations: 3



Methods: Modeling Effects of Alpha receptors

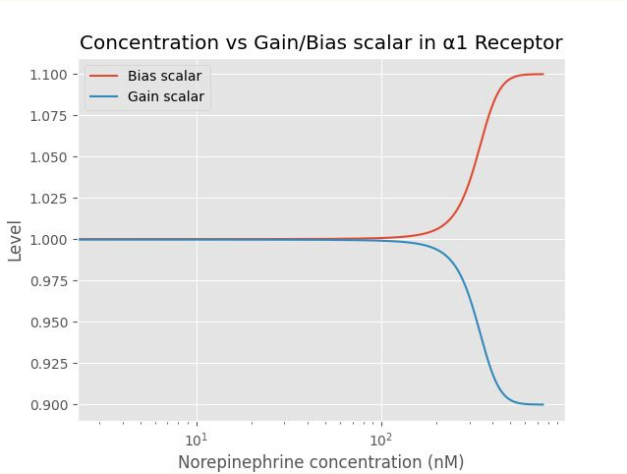
- Altered the gains and biases
- Little numerical data → estimated changes to α and β
  - **Ki value:** Concentration w/ 50% total receptor activity
    - Concentration vs. receptors activity → **Sigmoidal curve**

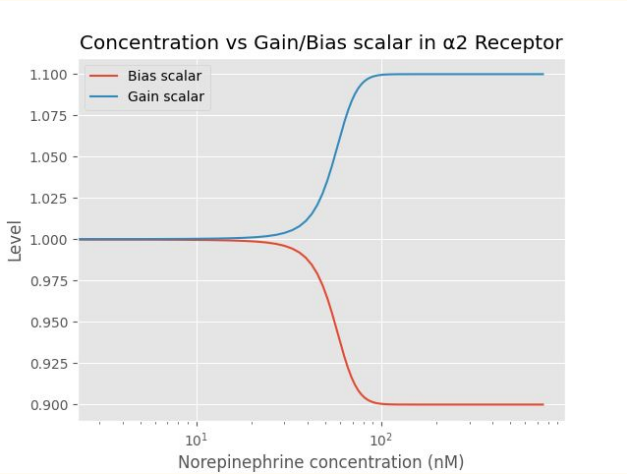




Methods: Modeling Effects of Alpha receptors (cont.)

- Multiplied by scalar
  - At 100% activity:
    - **α-2:** α=1.1 (1+0.1), β=0.9
    - **α-1:** α=0.9, β= 1.1
  - Ex: Gain at **50%** activity of alpha-2 = $1 + 0.1(0.5) \rightarrow \underline{1.05}$

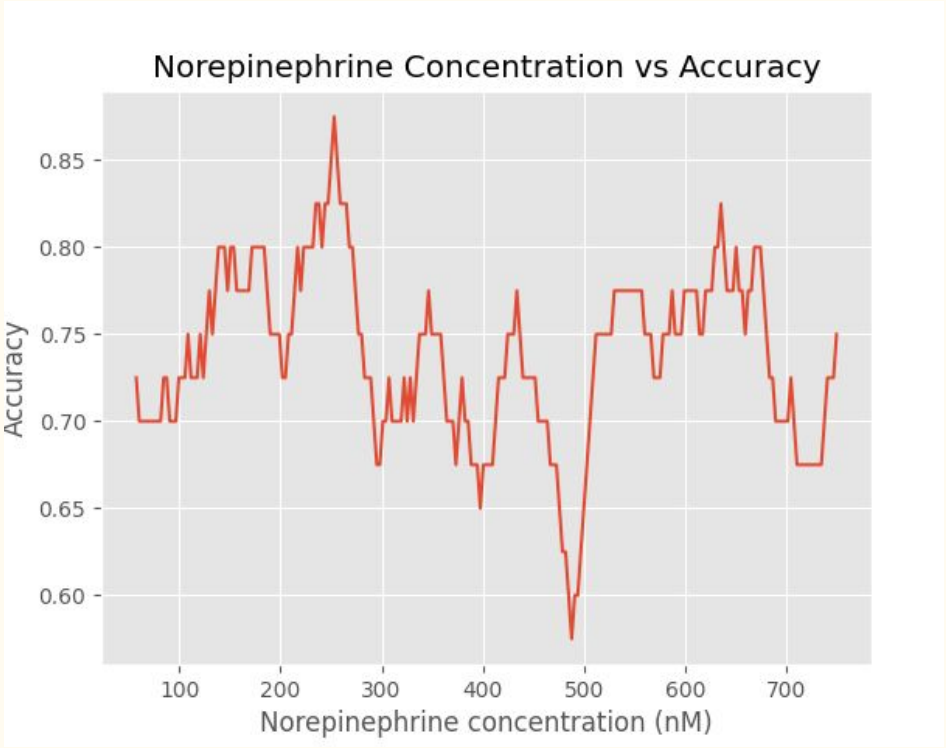


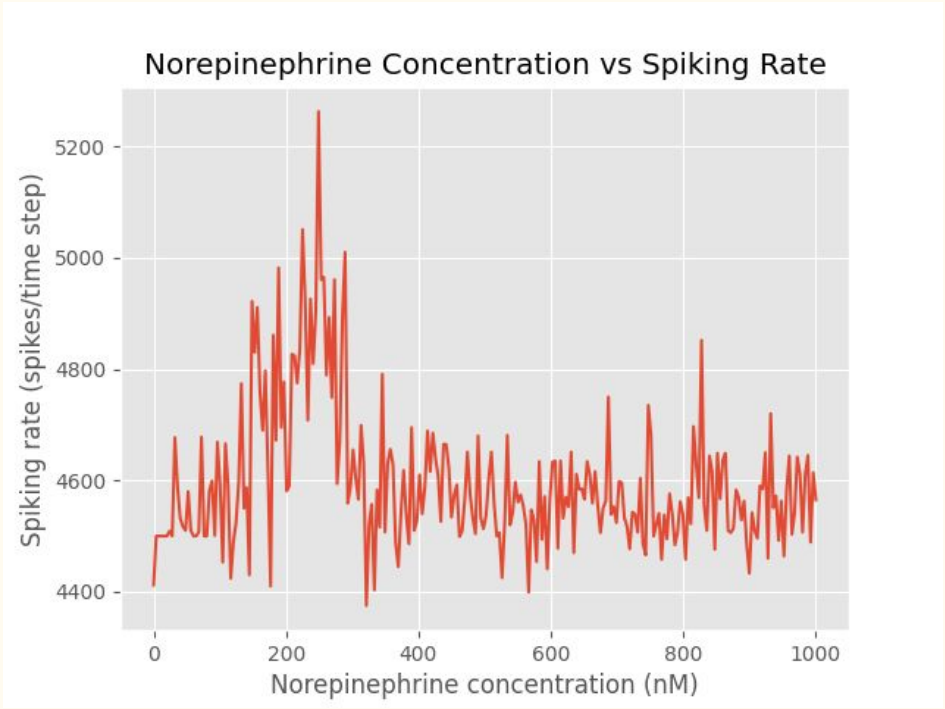


Methods/Results: Running the Model

- Modeled NE concentrations from **0 nM to 750 nM**
  - **3 nM** steps
- **3 trials** run for each step
  - Results were averaged
- DFT accuracy & Firing Rates after 8 secs were graphed

Results


Norepinephrine Concentration vs Accuracy
Accuracy
0.85
0.80
0.75
0.70
0.65
0.60
100
200
300
400
500
600
700
Norepinephrine concentration (nM)


Norepinephrine Concentration vs Spiking Rate
Spiking rate (spikes/time step)
5200
5000
4800
4600
4400
0
200
400
600
800
1000
Norepinephrine concentration (nM)

Limitations/Potential for Development

- Lots of estimations
  - More data → more accurate model
- Add details
  - $\beta 1$ and $\beta 2$ receptors
  - NT that affects WM (epinephrine, dopamine, etc.)

Significance of Model

- Studying diseases
  - ADHD, PD, PTSD, Depression, Anxiety, etc.
- Treating Diseases
  - Simulate potential treatments / effects
- Researching Cognitive Functions

Summary

- Modeled effects of NE on WM performance w/ alpha-1 and alpha-2 receptors
- Altered gains/biases in PFC neural network model
- Results consistent w/ predictions
- Applications in research of diseases, drugs, and cognitive function

Acknowledgements

- Dr. Marianne Bezaire, Nitsueh Kebere and the other TFs
  - Taught how to construct computational models
  - Guided us through our projects
- Ms. Kaitlyn Dorst
  - Taught us neuroscience knowledge
- Our parents and other family members
  - Emotional and financial support

Questions?

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Source code is available from https://ftp.armaanb.net/research/norepinephrine_wm/