Microcircuit Flexibility: 35 Years Post-Connectome in the Crab STG

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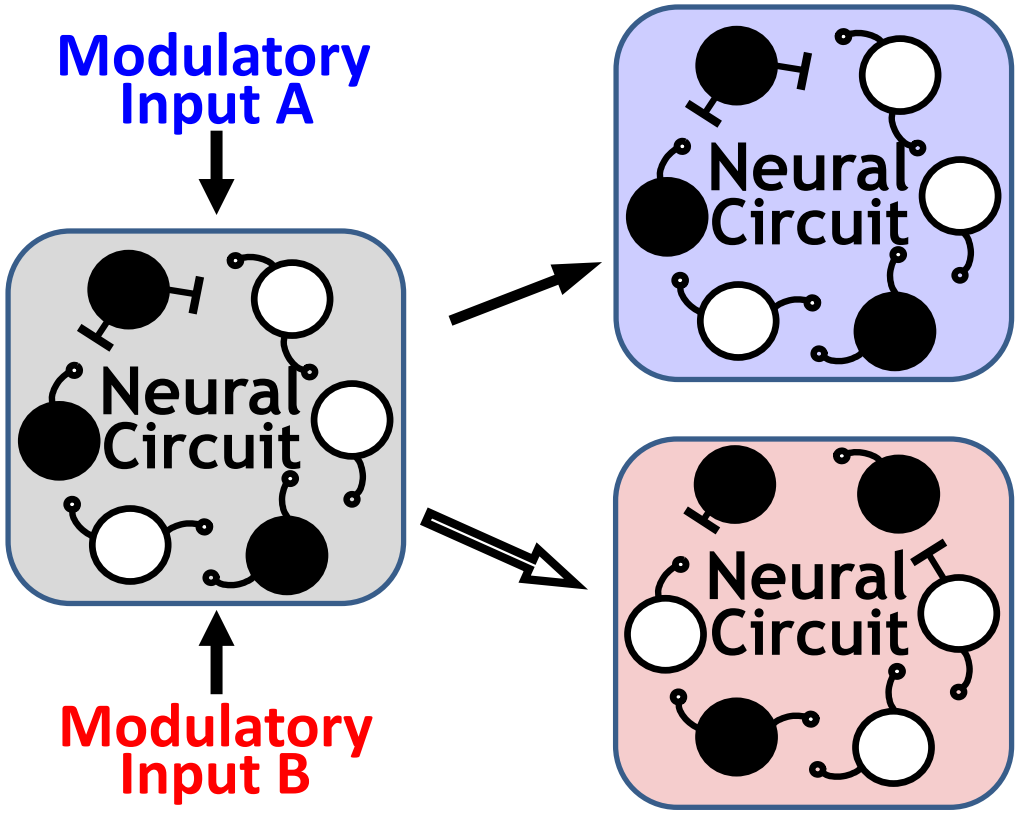
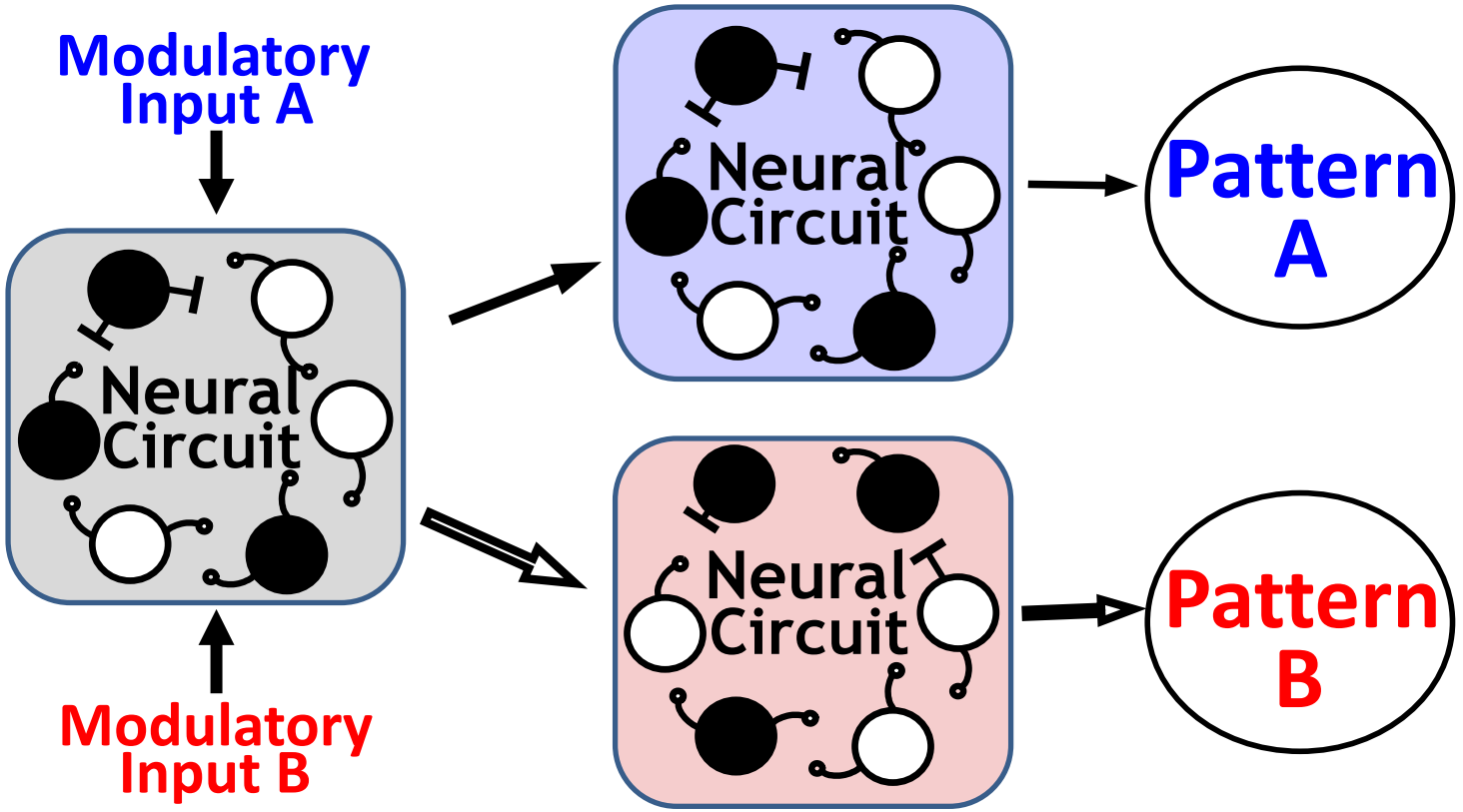
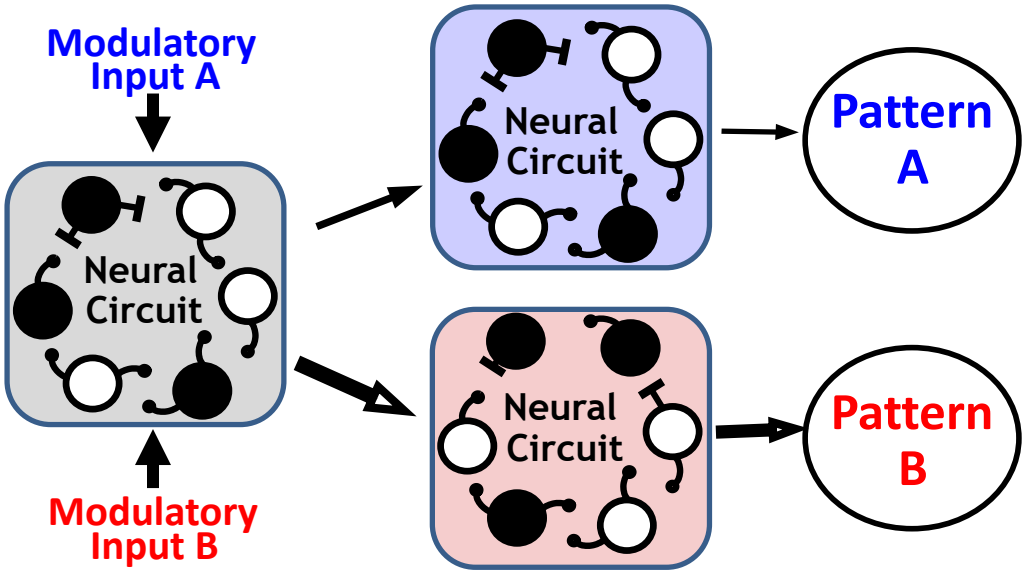
Multi-Functional Circuits: Circuit Modulation Elicits Distinct Circuit States



Multi-Functional Circuits: Circuit Modulation Elicits Distinct Circuit States/Activity Patterns

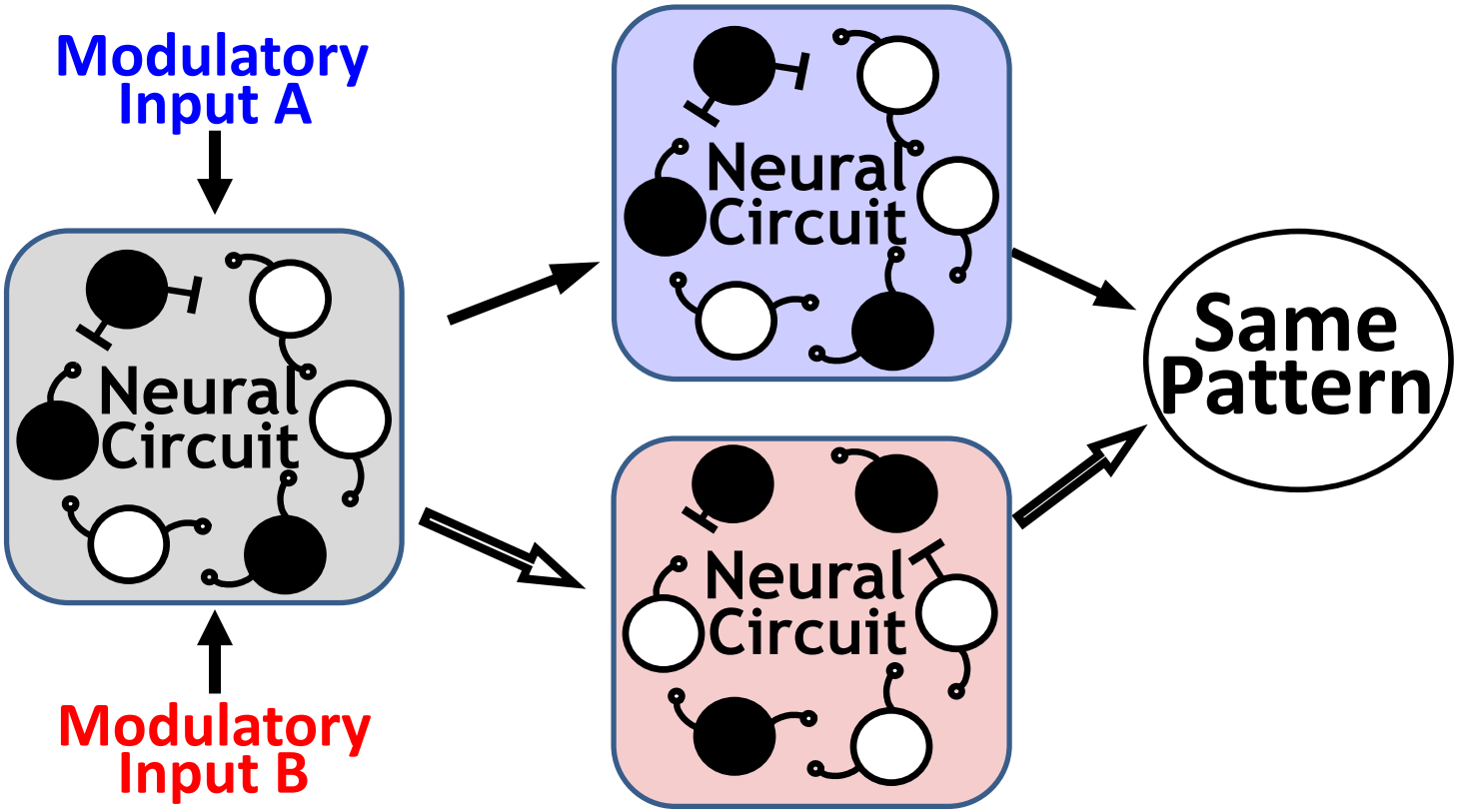


Neural Circuit Flexibility

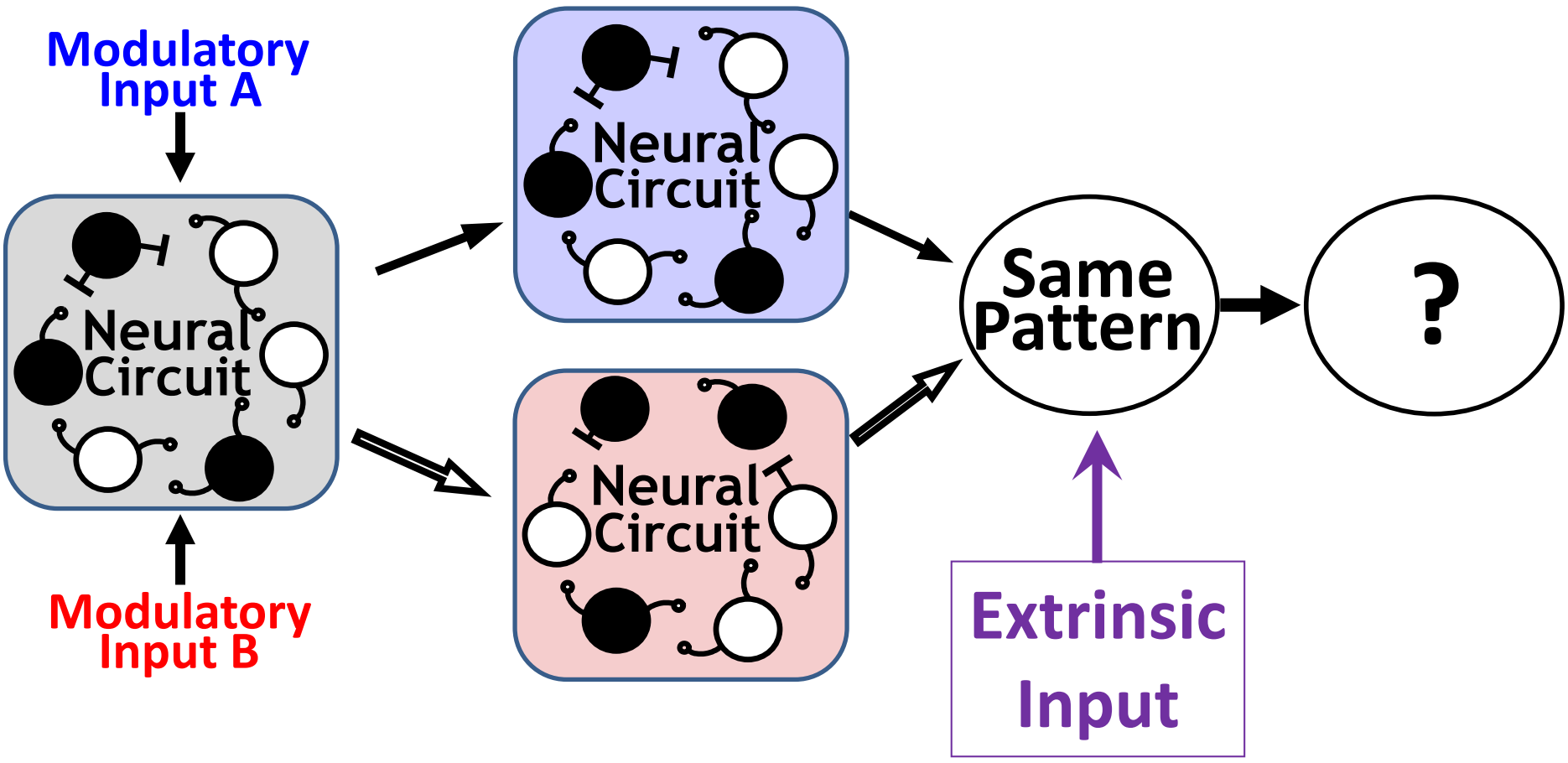


- **Establishing a connectome is necessary but not sufficient for understanding neural circuit operation.**

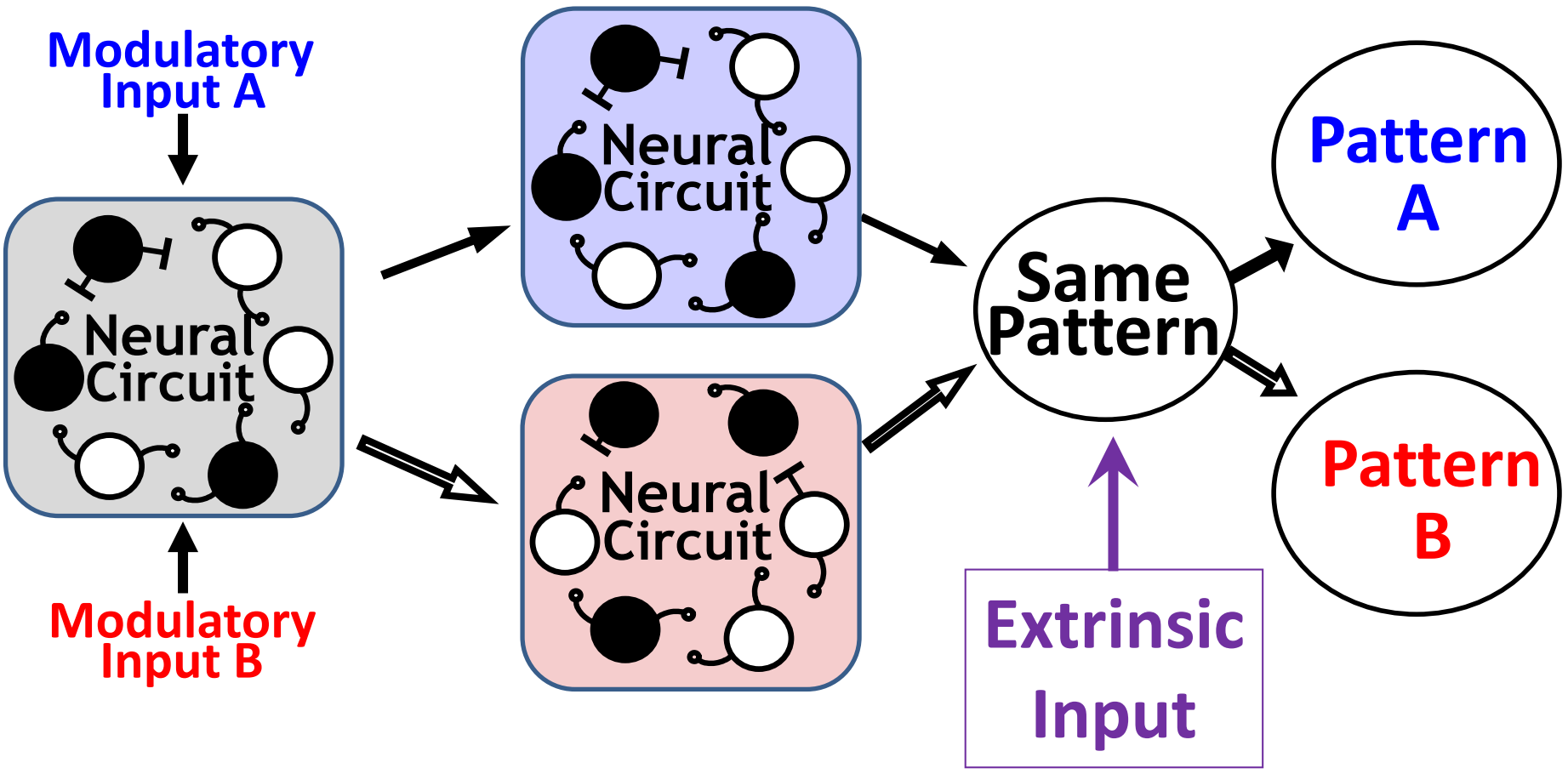
Multi-Functional Circuits: Different Circuit States Can Generate the Same Output



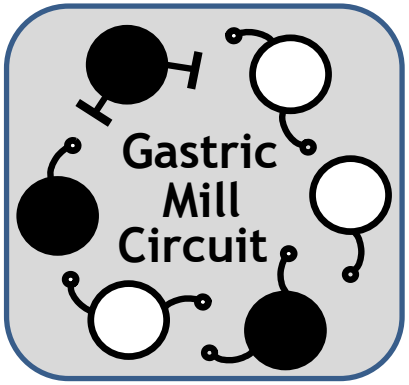
Impact of an Unchanging Input on Different Circuit States



Hypothesis: Different Circuit States Respond Differently to an Unchanging Input



Impact of the Same Input on Different Circuit States in the Crab Stomatogastric Ganglion



(Saideman et al., 2007 J Neurosci)

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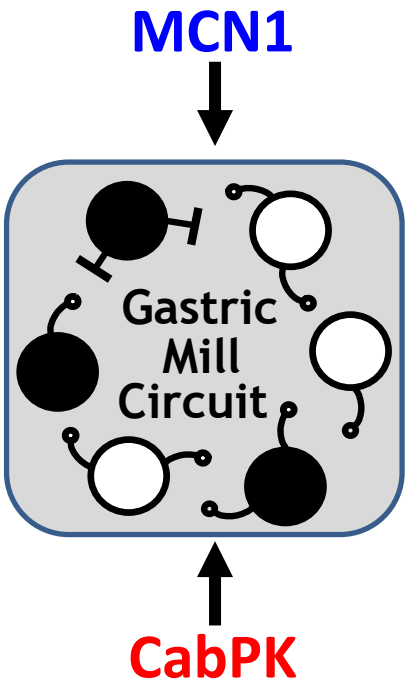

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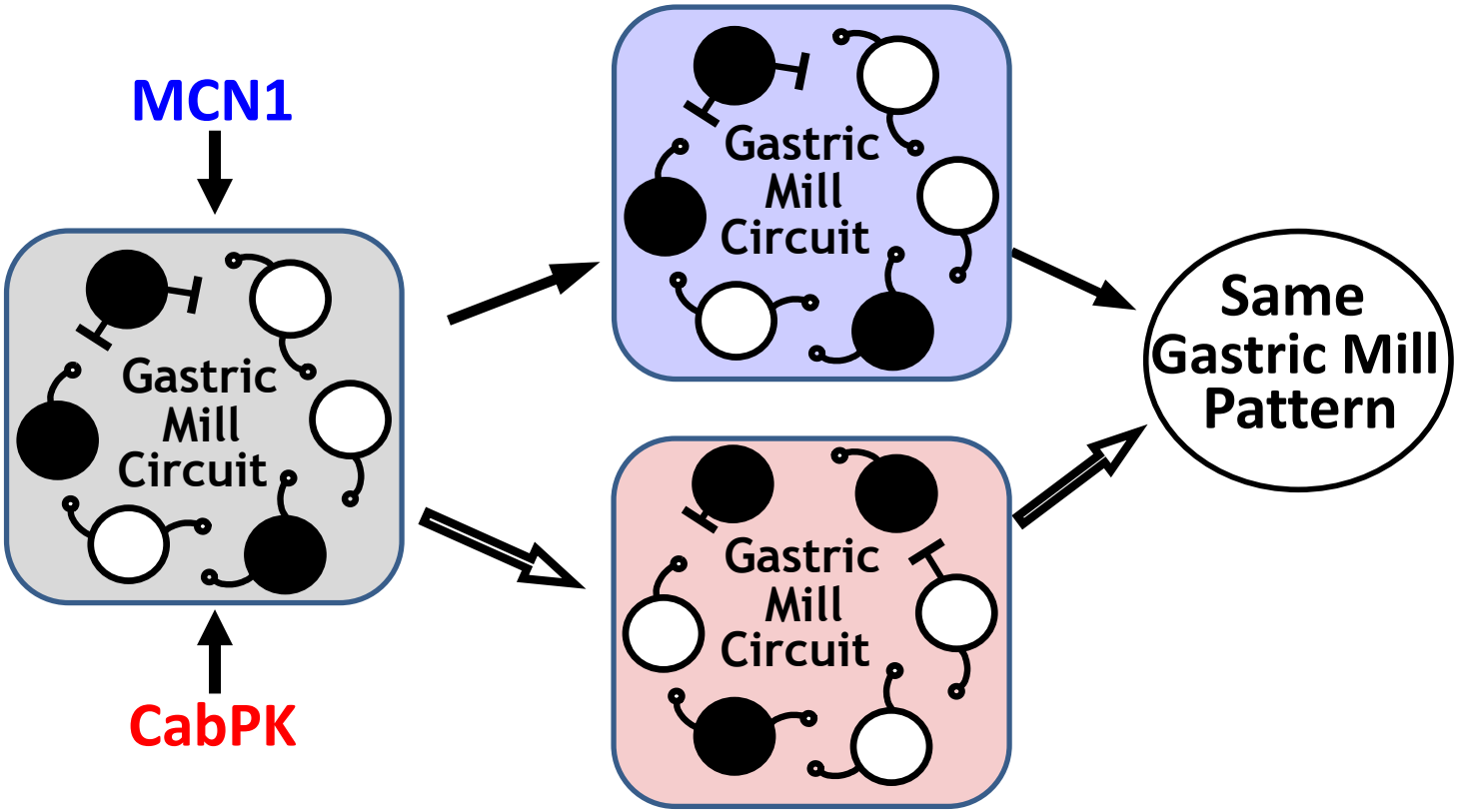

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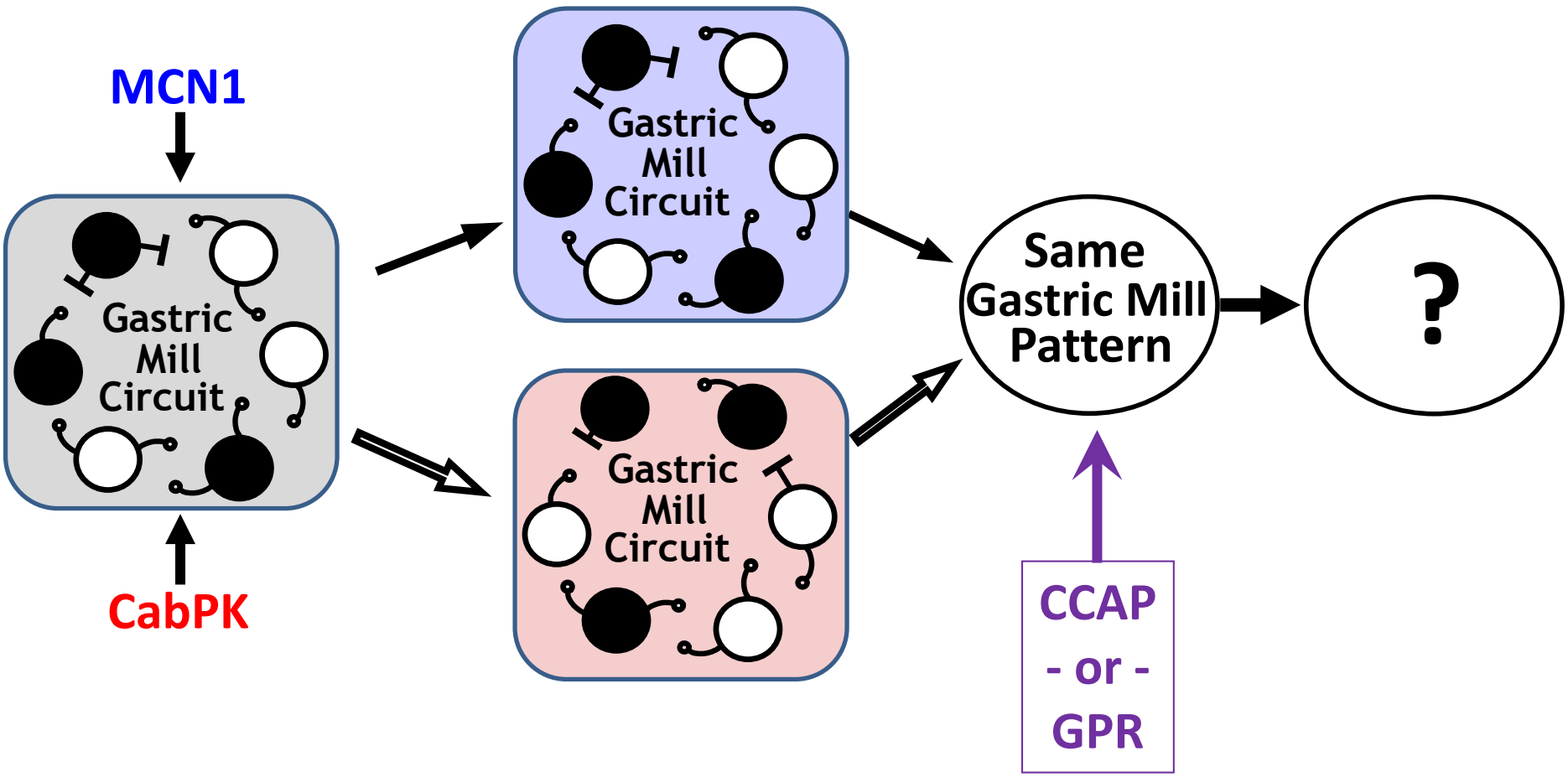
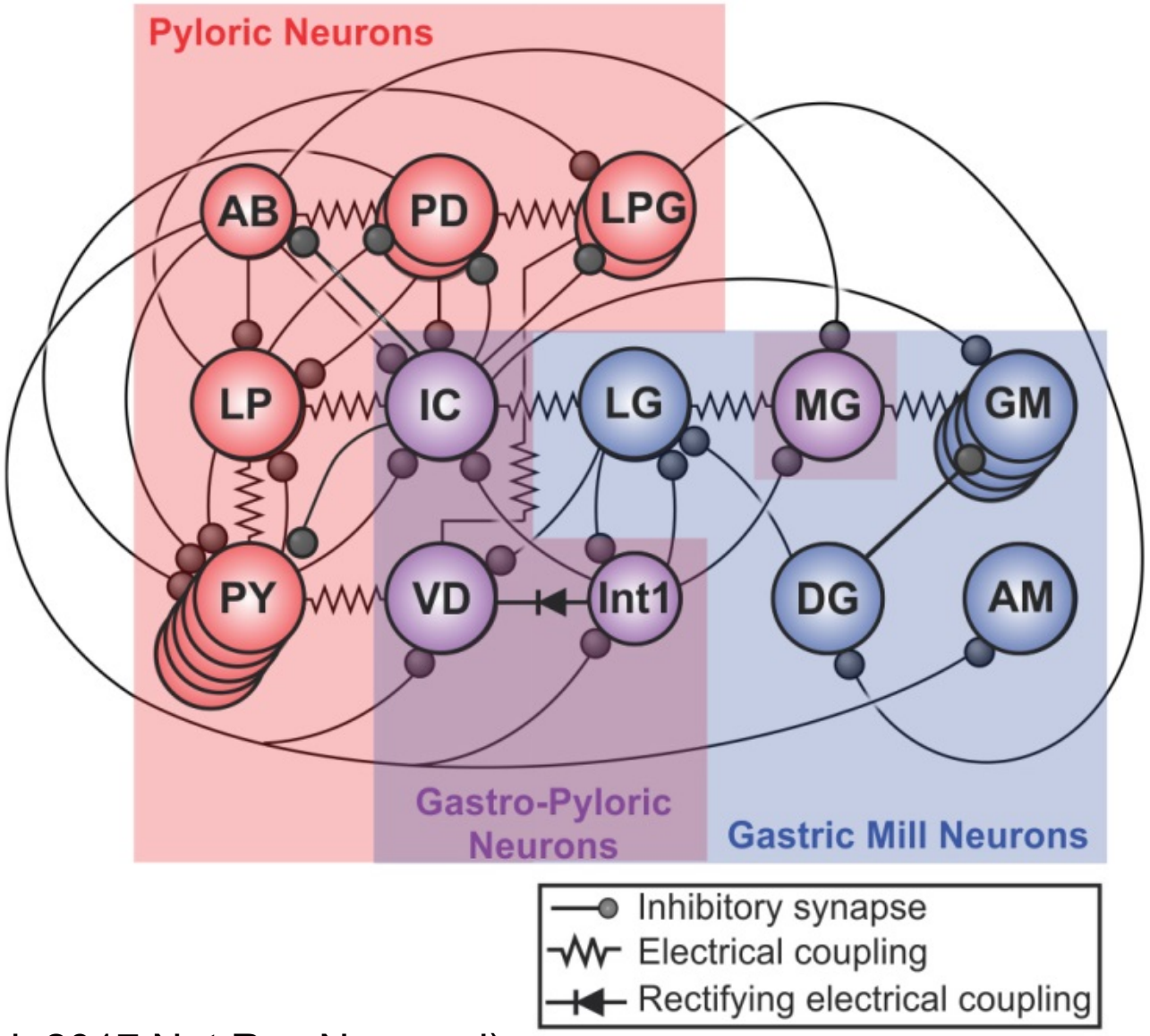


The Gastric Mill/Pyloric Connectome in the Crab (*Cancer borealis)* Stomatogastric Ganglion



(Nusbaum et al, 2017 Nat Rev Neurosci)

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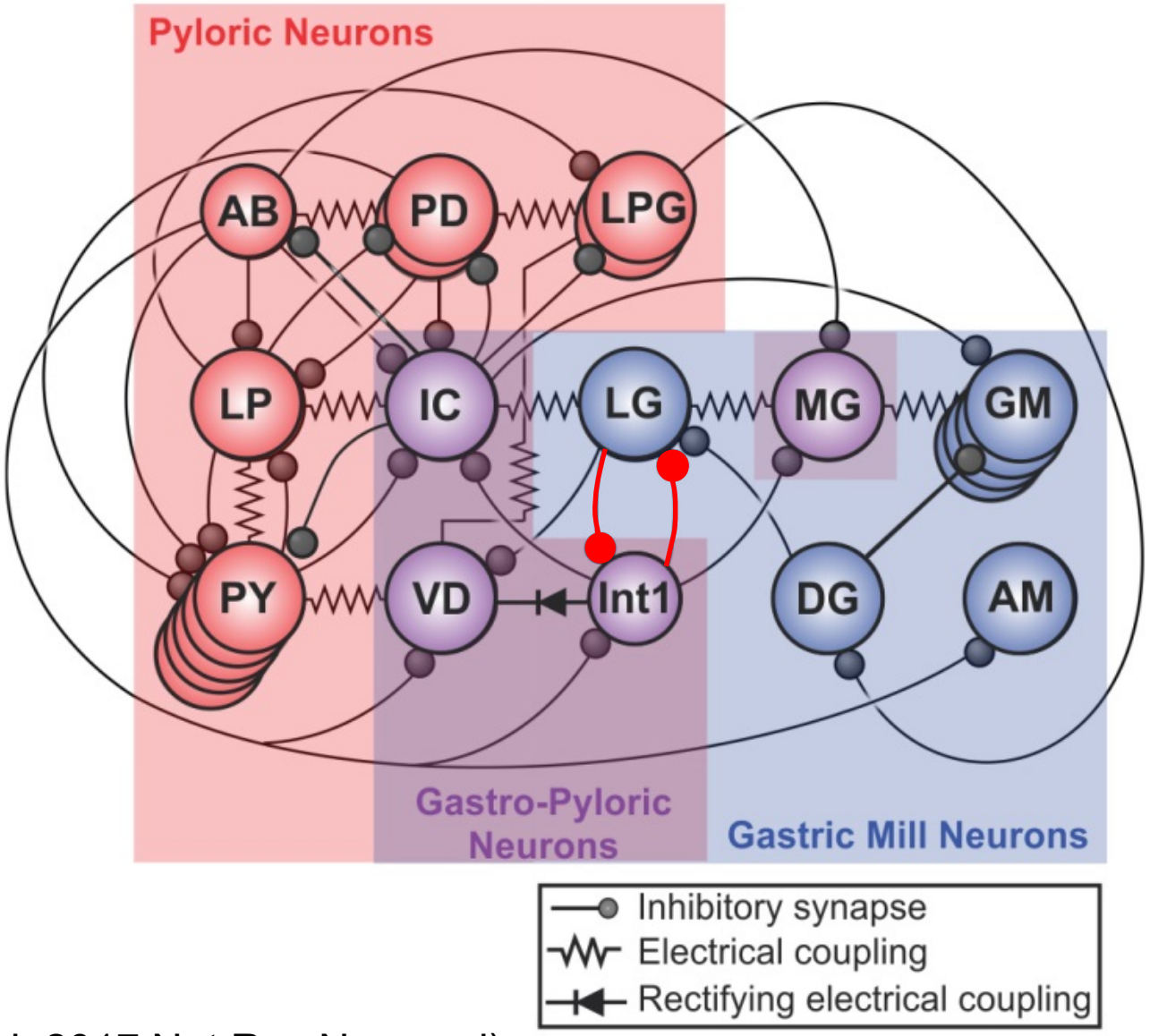

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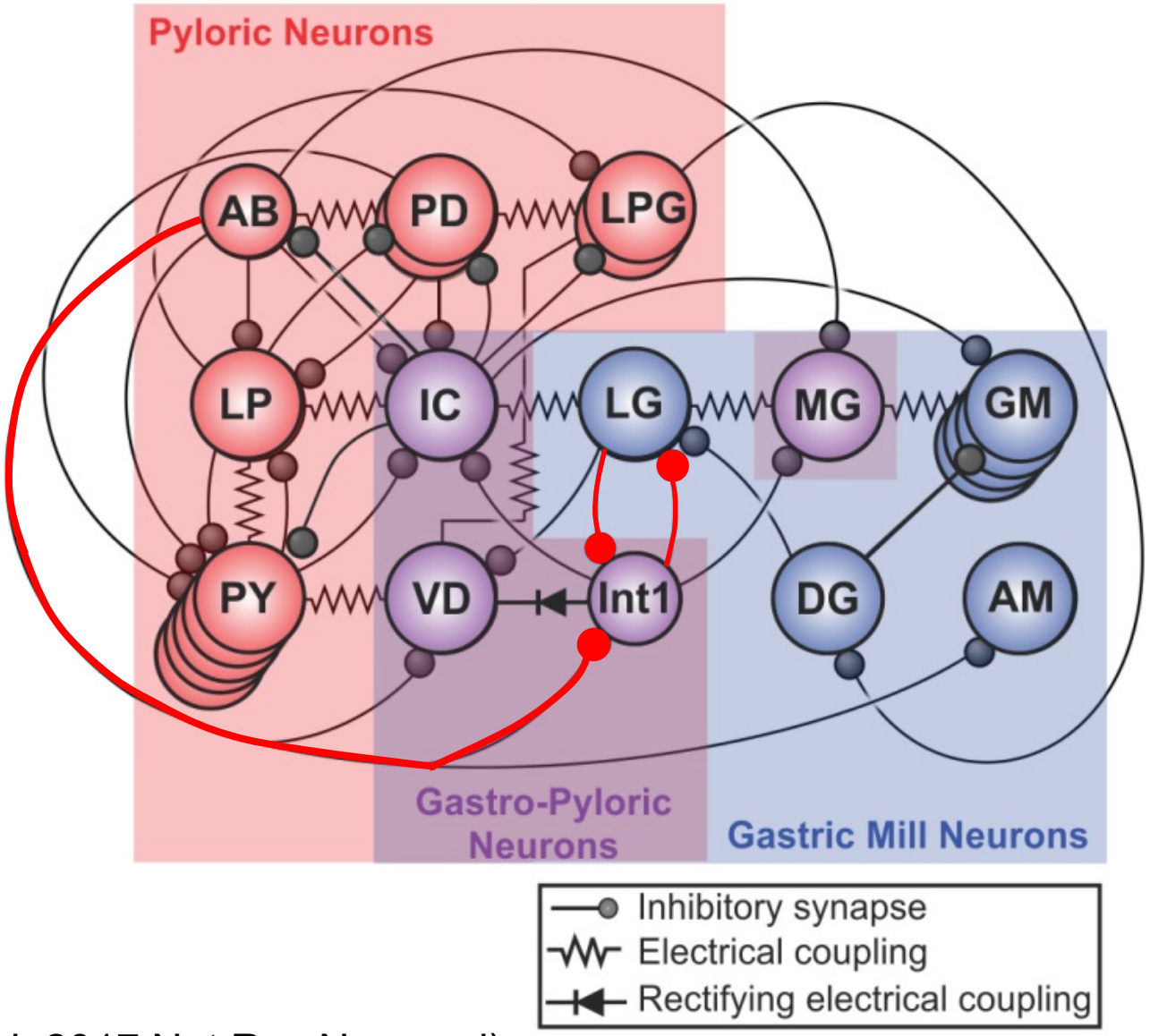

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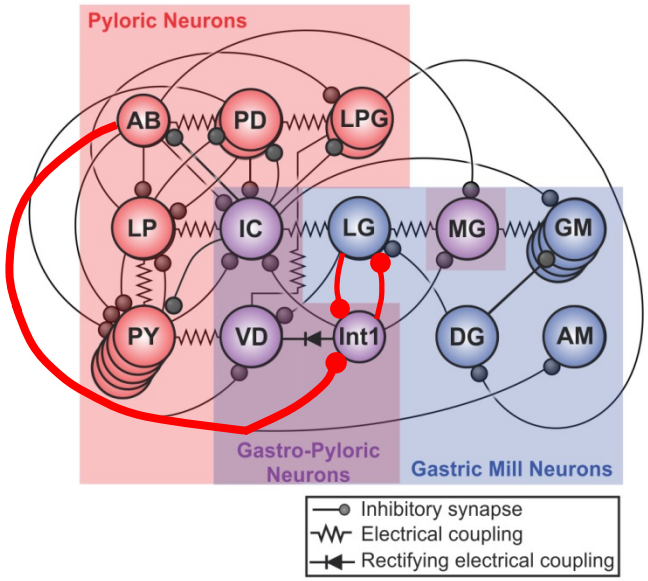
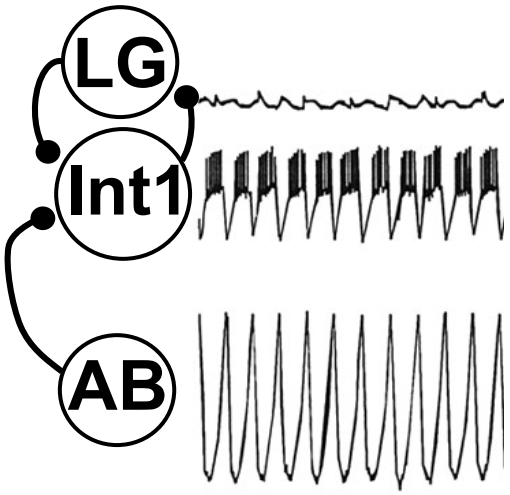
The Gastric Mill & Pyloric Rhythms in the Crab (*Cancer borealis)* Stomatogastric Ganglion





Inhibition

LG: 15mV
Int1: 18mV
AB: 10mV
6 sec

(Coleman et al, Nature 1995)

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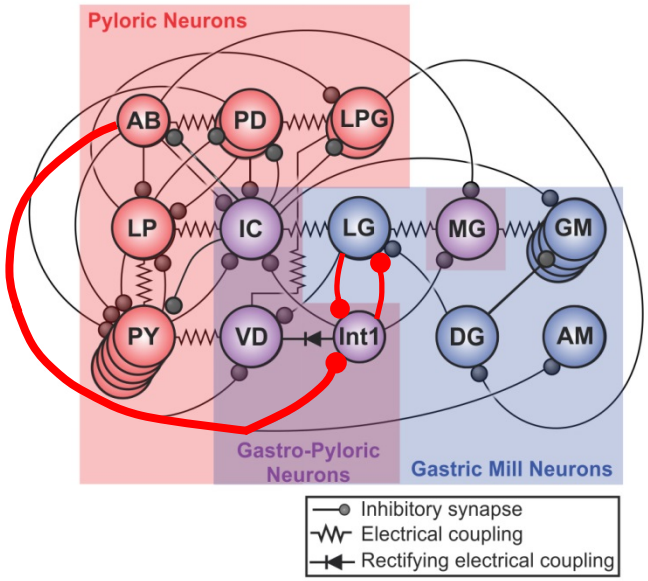

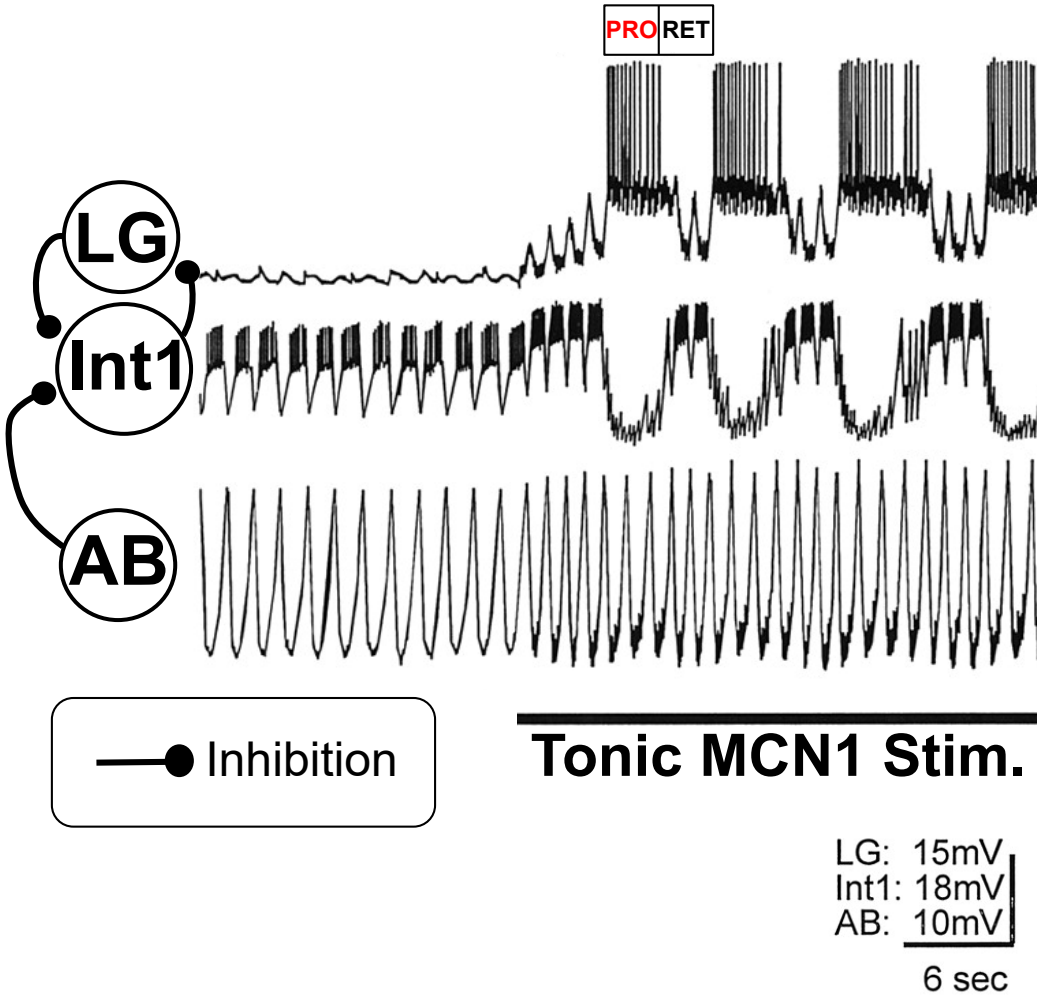

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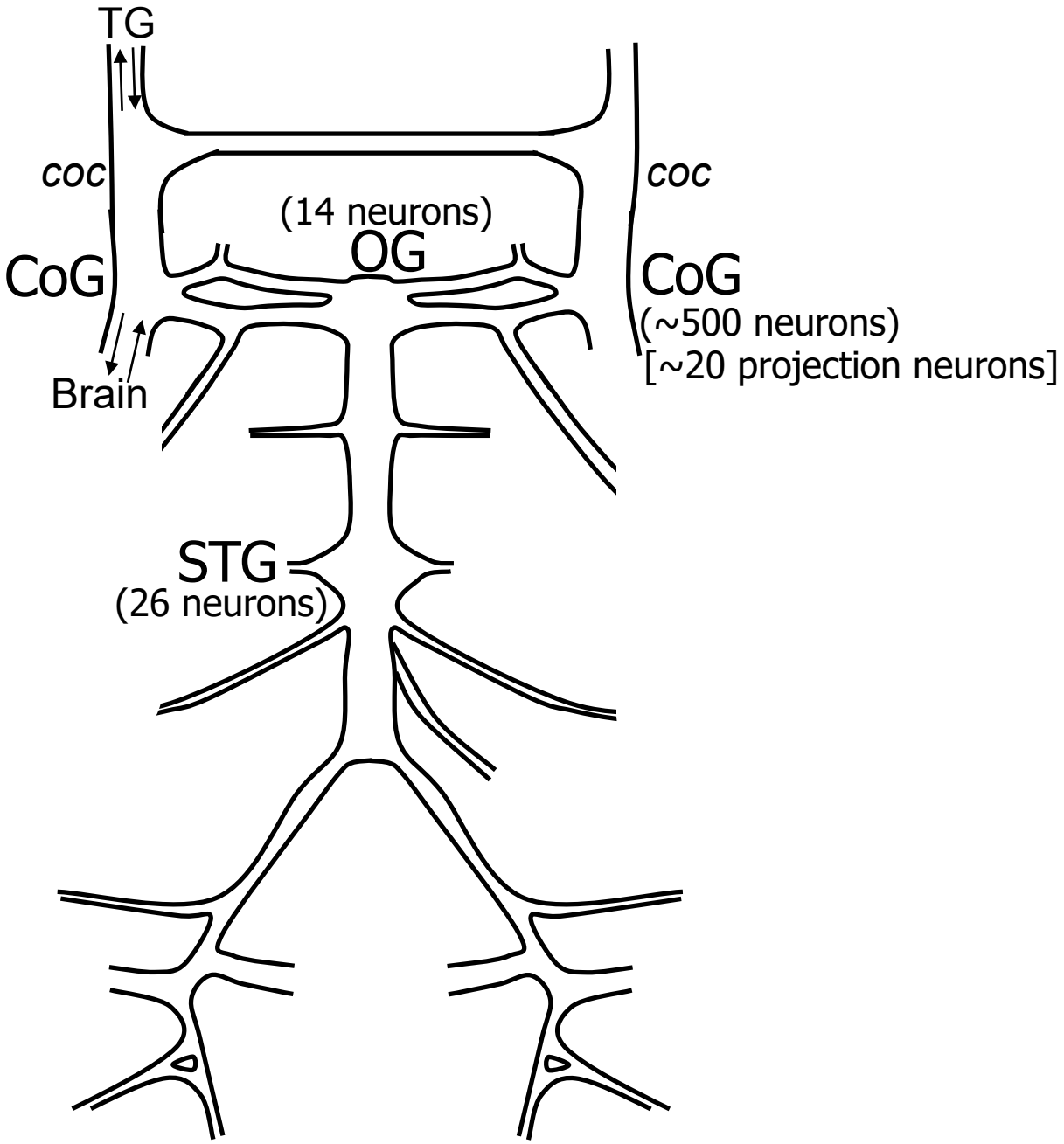
The Crab Stomatogastric Nervous System



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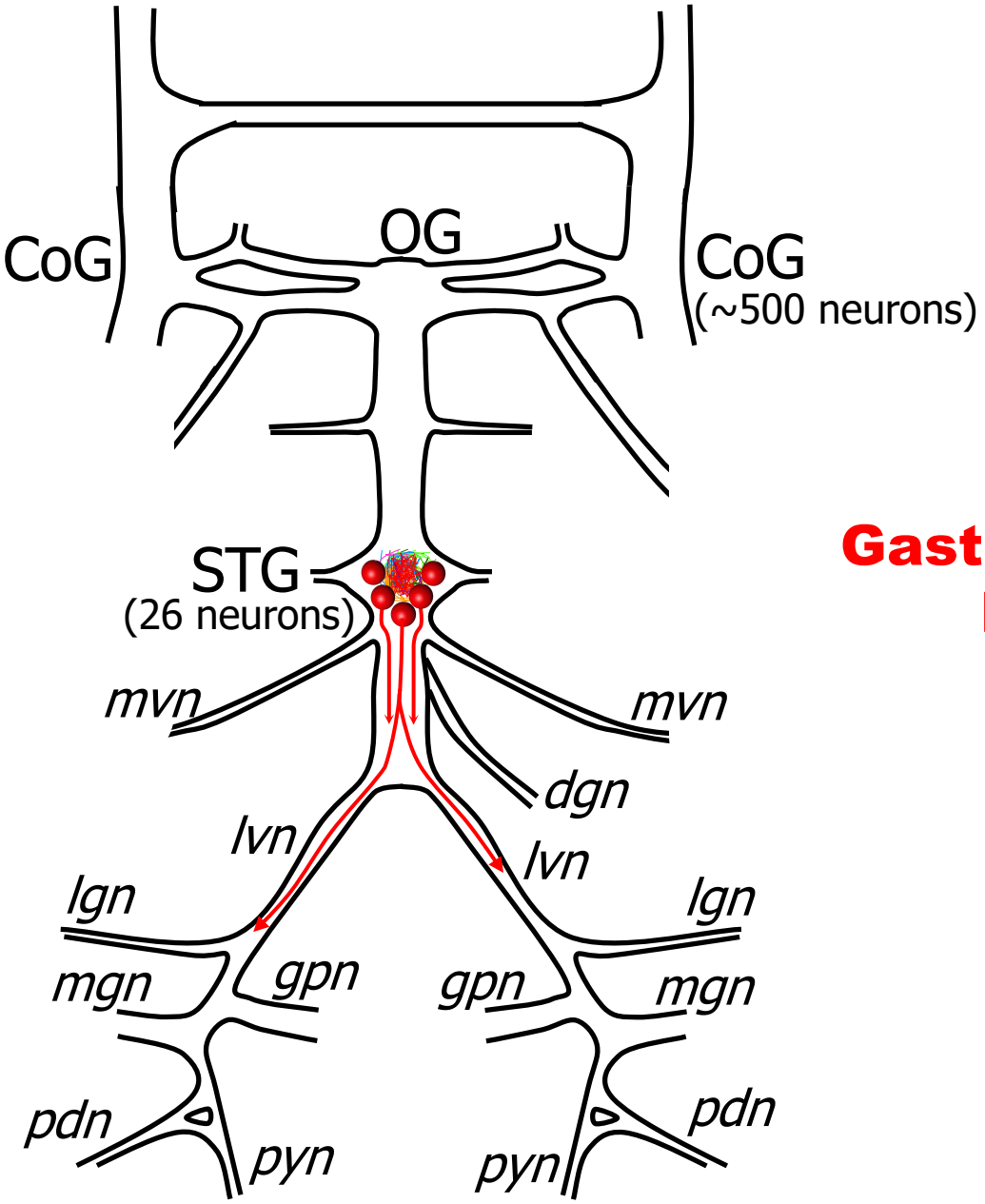

Gastric Mill CPG: Chewing
Pyloric CPG: Filtering

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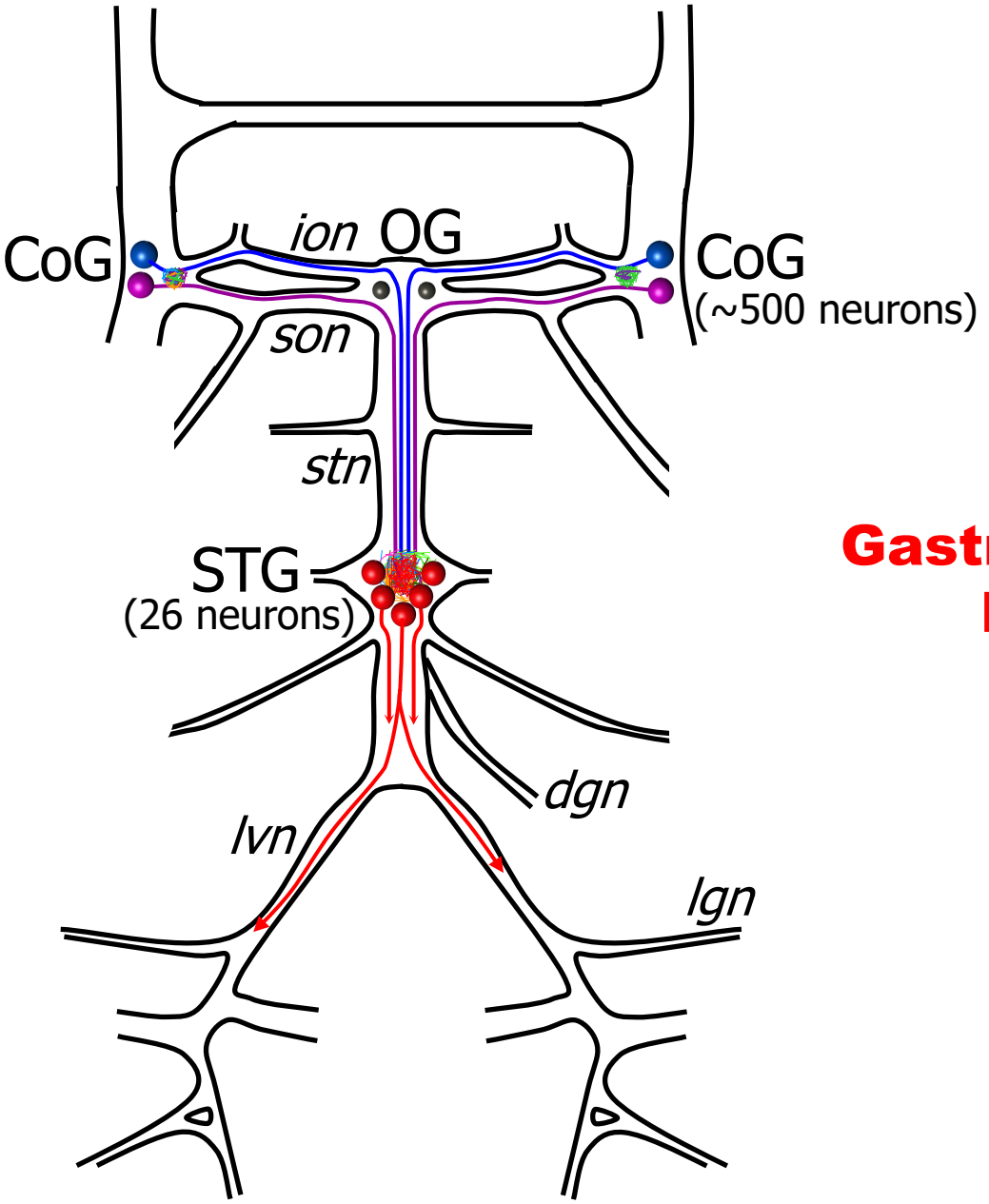

Projection Neurons

Gastric Mill CPG: Chewing
Pyloric CPG: Filtering

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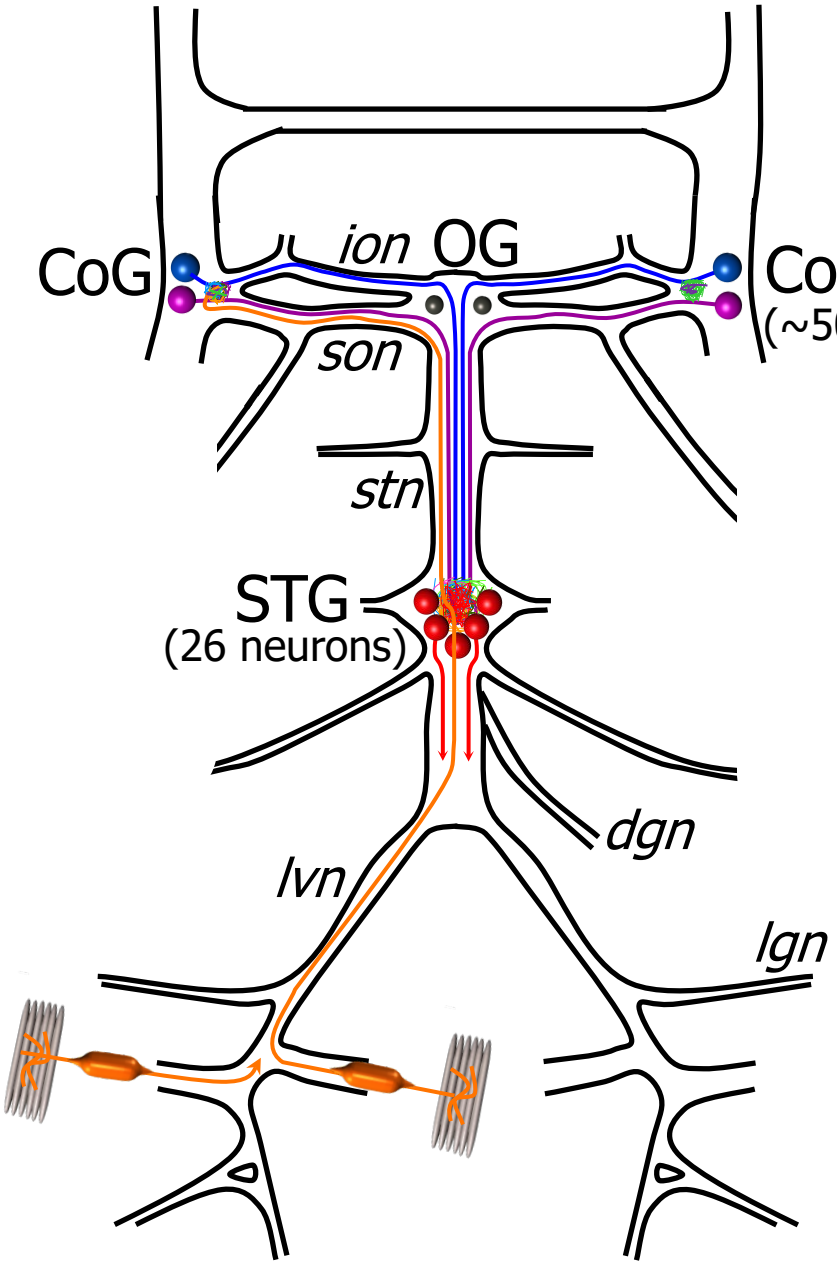
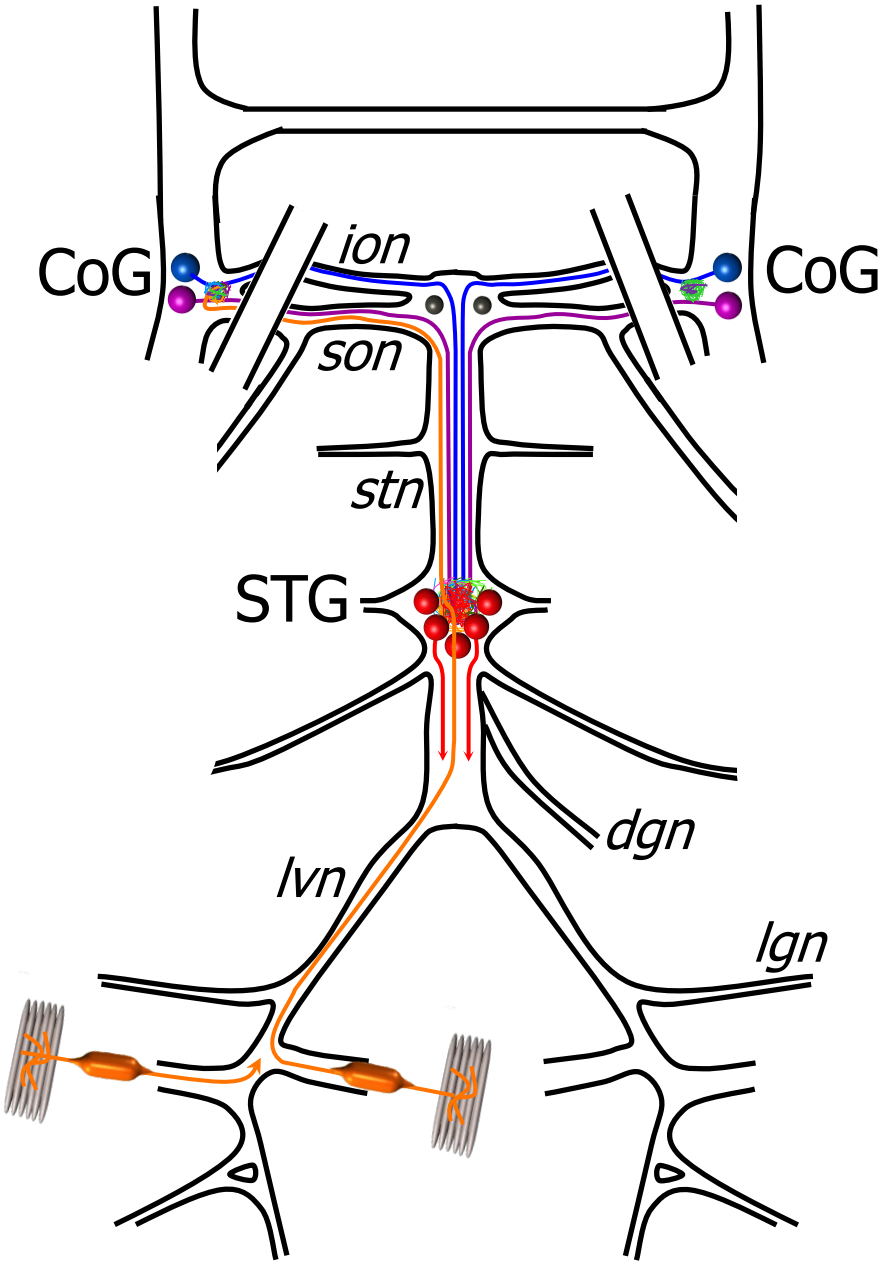


Projection Neurons

Gastric Mill CPG: Chewing
Pyloric CPG: Filtering

Muscle Sensory Neurons

The Crab Stomatogastric Nervous System



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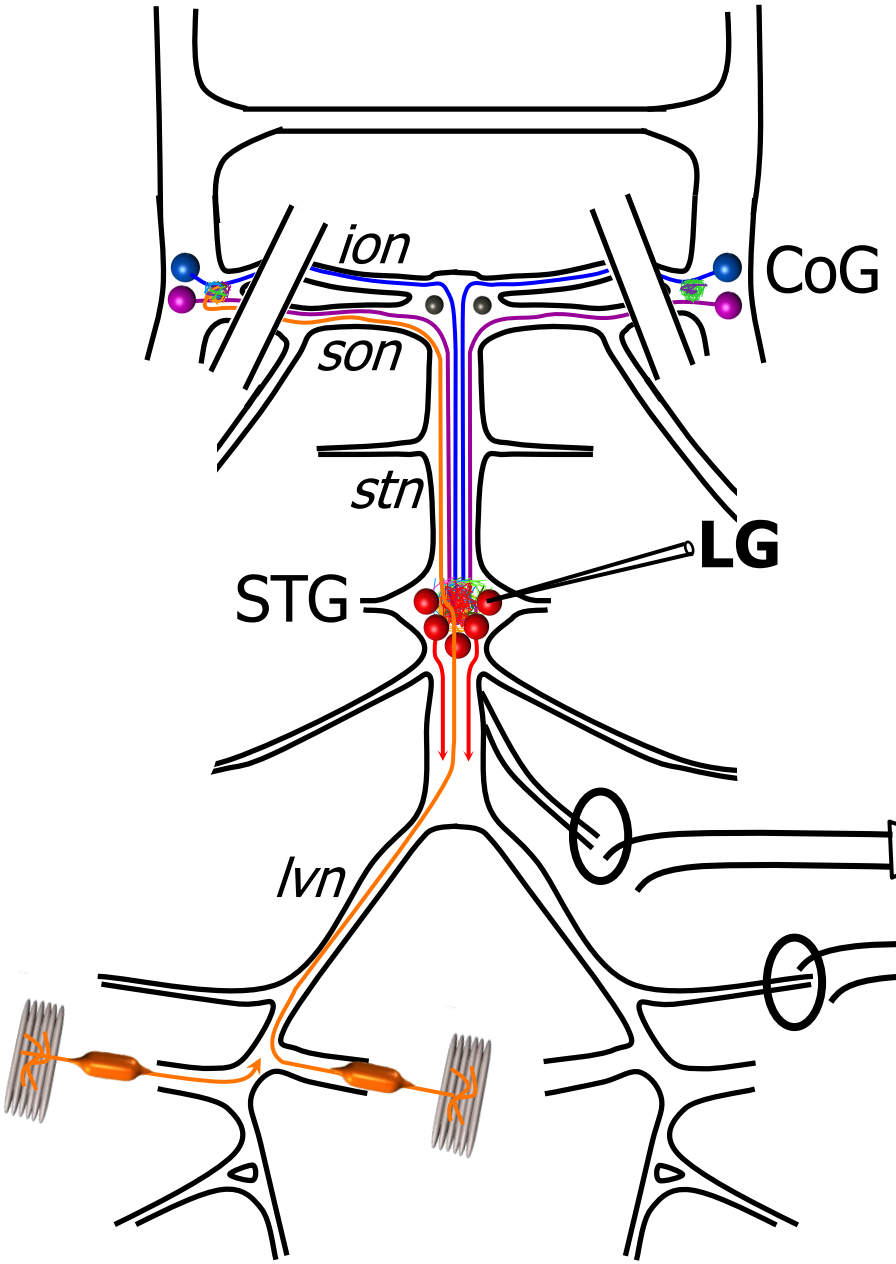
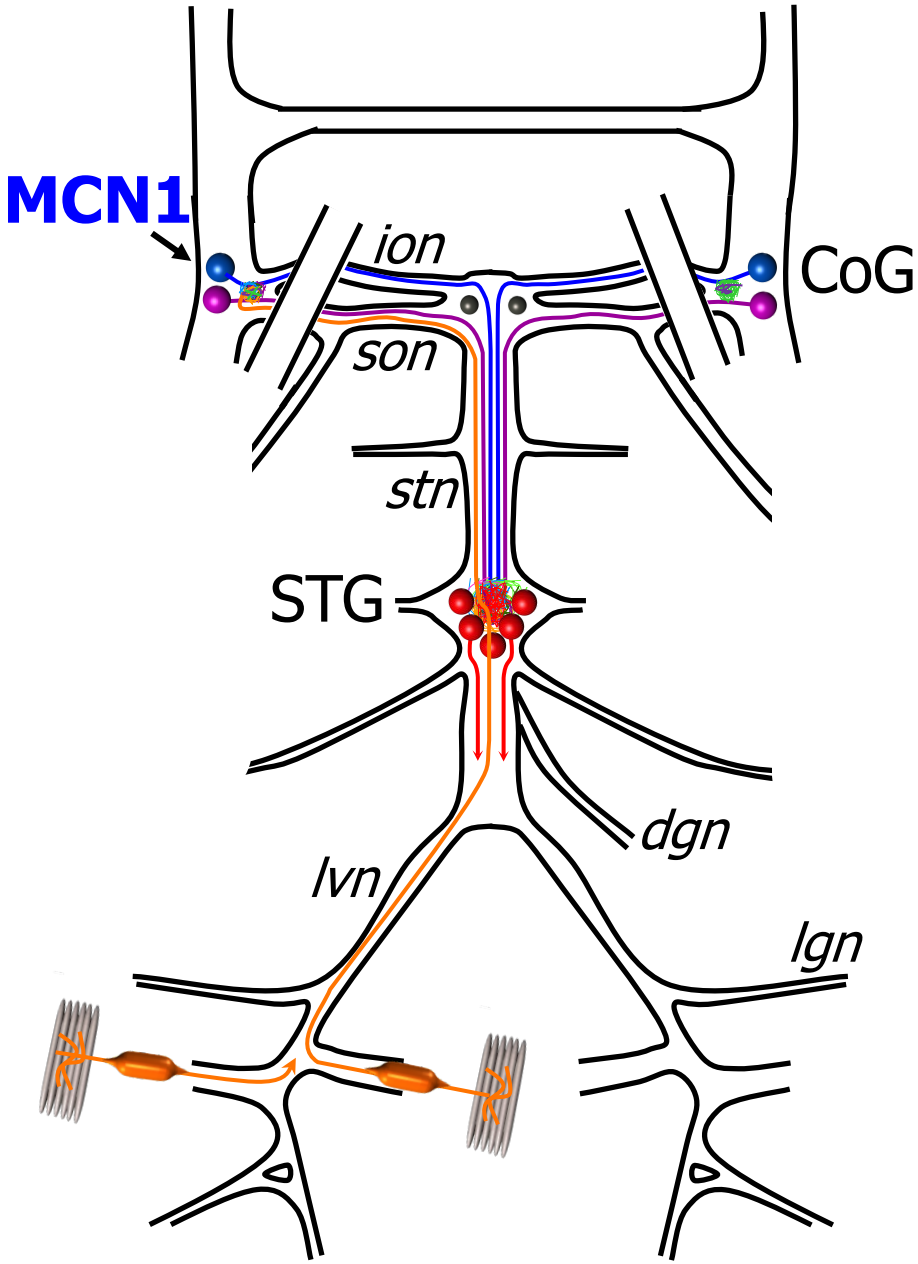


Gastric Mill Rhythm
LG: Protraction
DG: Retraction

The Crab Stomatogastric Nervous System



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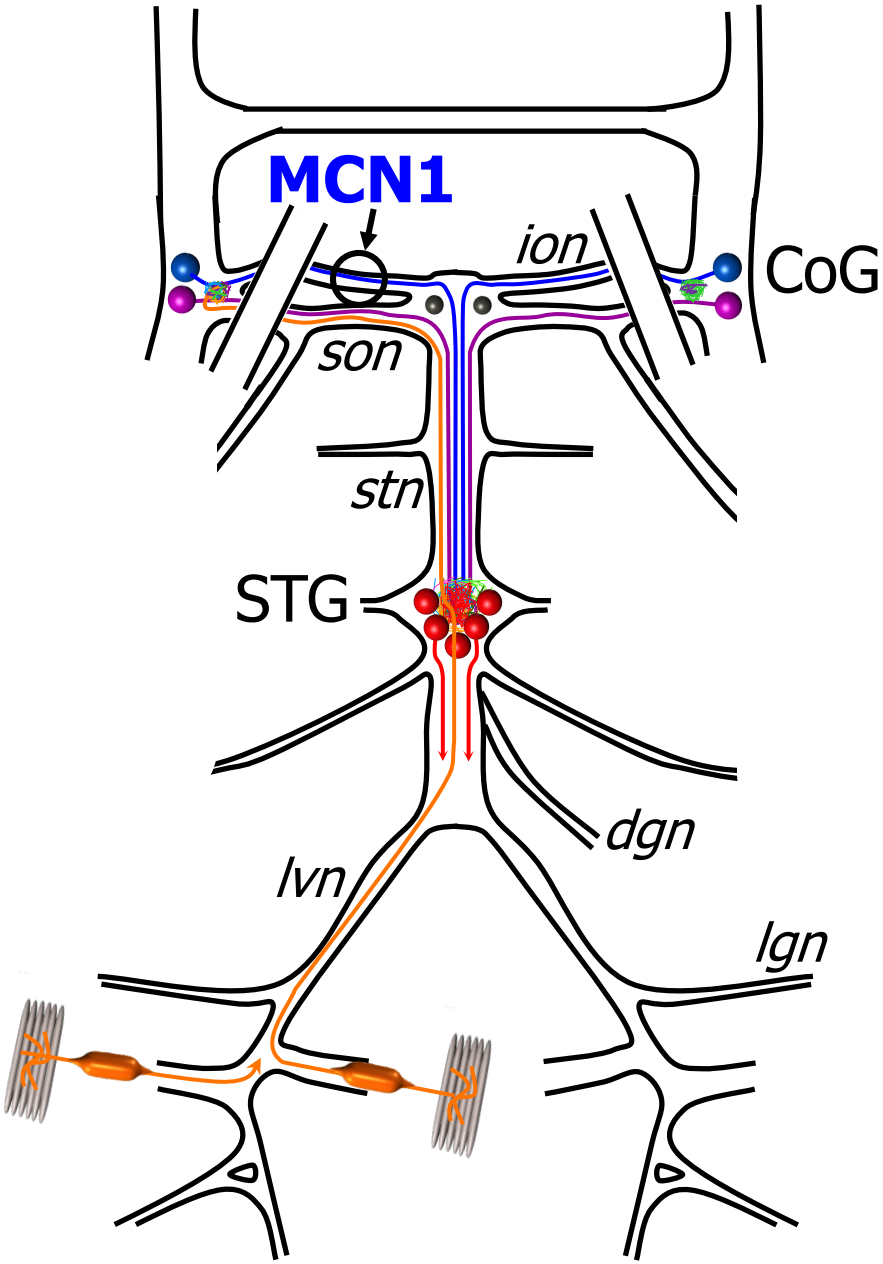

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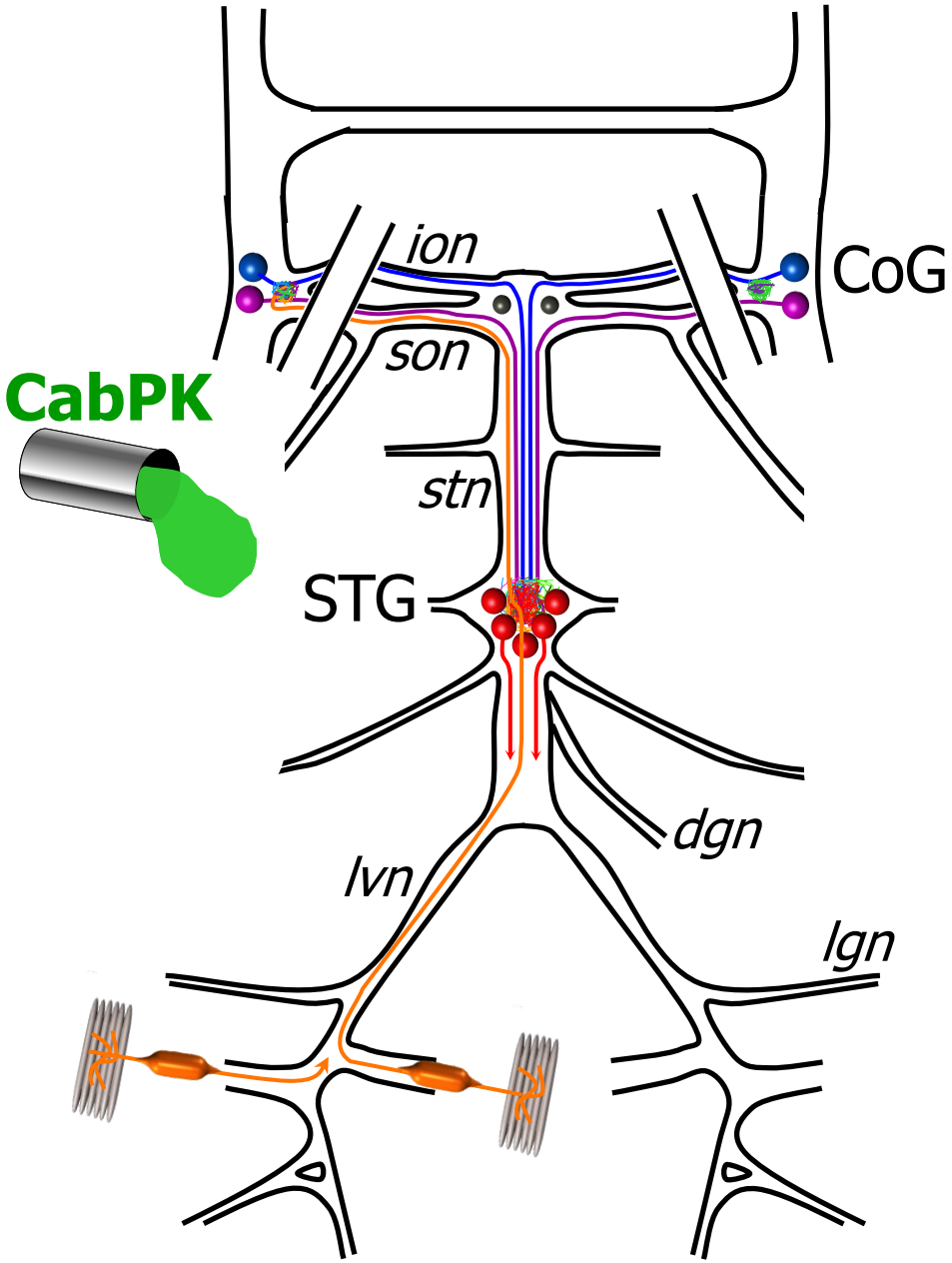

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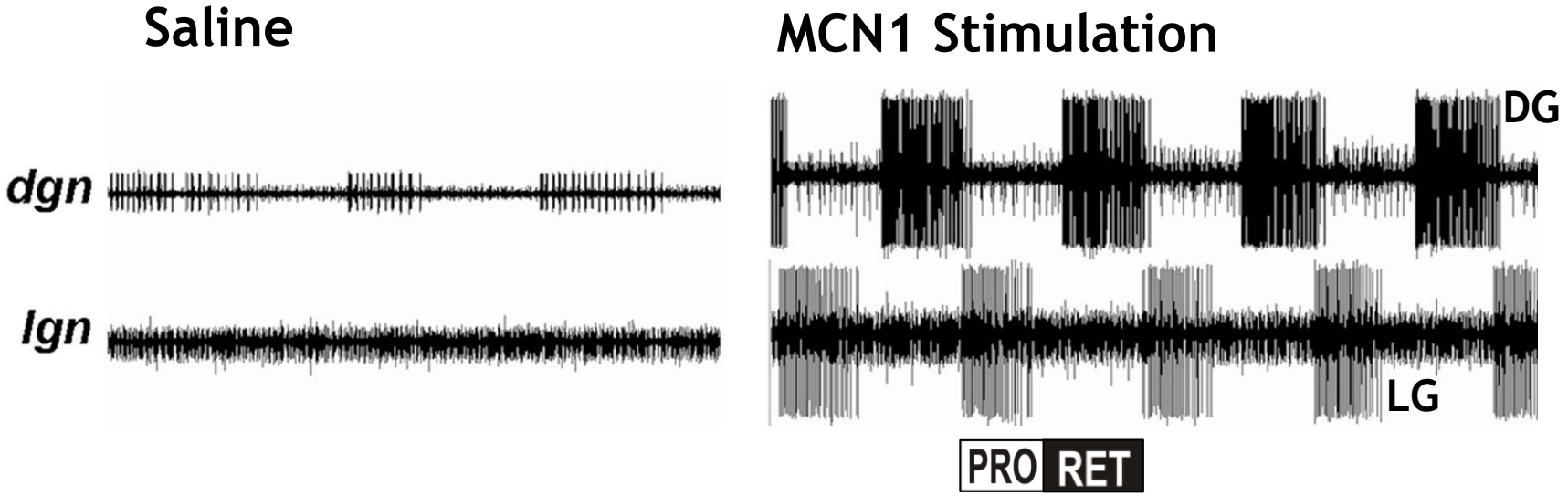
Distinct Modulatory Inputs Elicit the Same Motor Pattern



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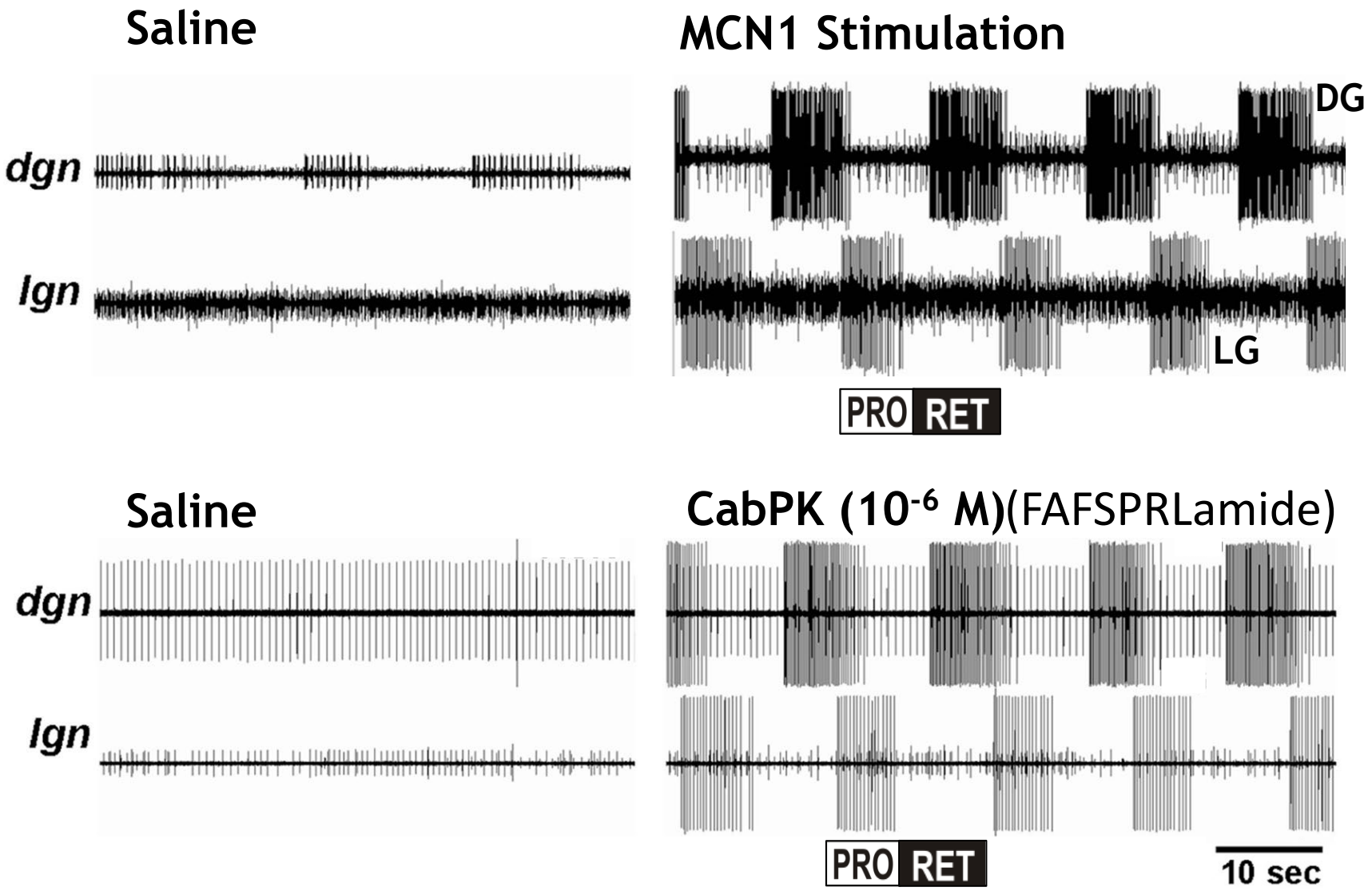

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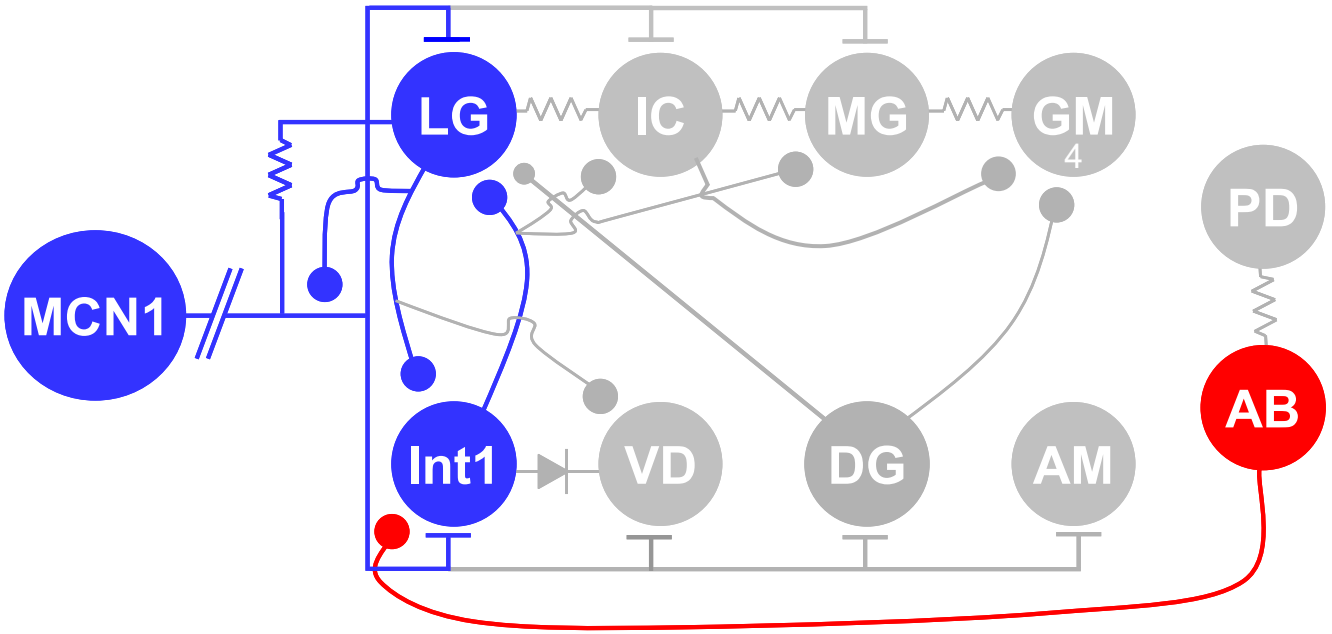
Same Motor Pattern, Different Circuit States



Rhythm Generation

- necessary
- regulates, but not necessary

- Excitation
- Inhibition
- Elect. Coupling

(Saideman et al, J Neurosci 2007)

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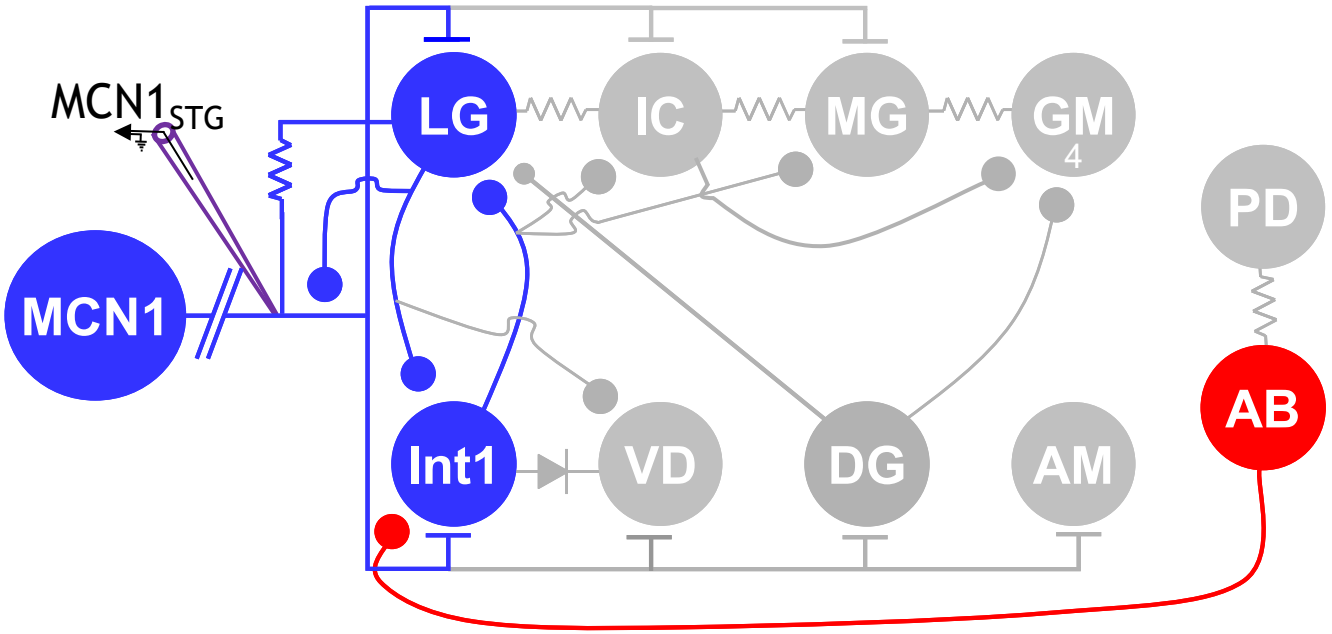

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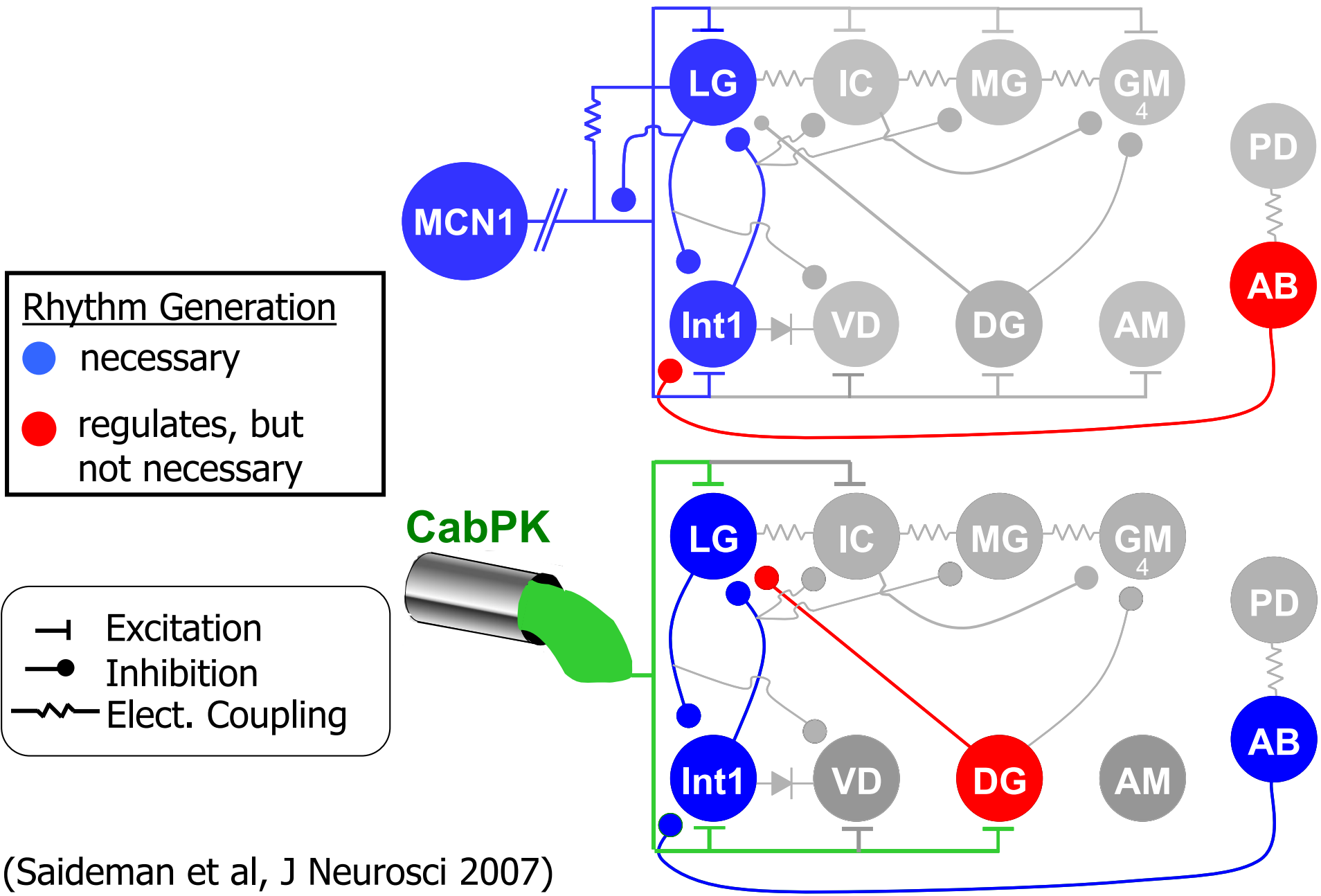

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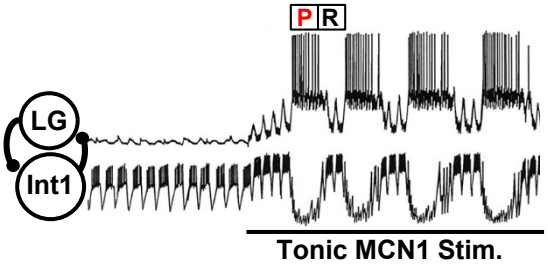
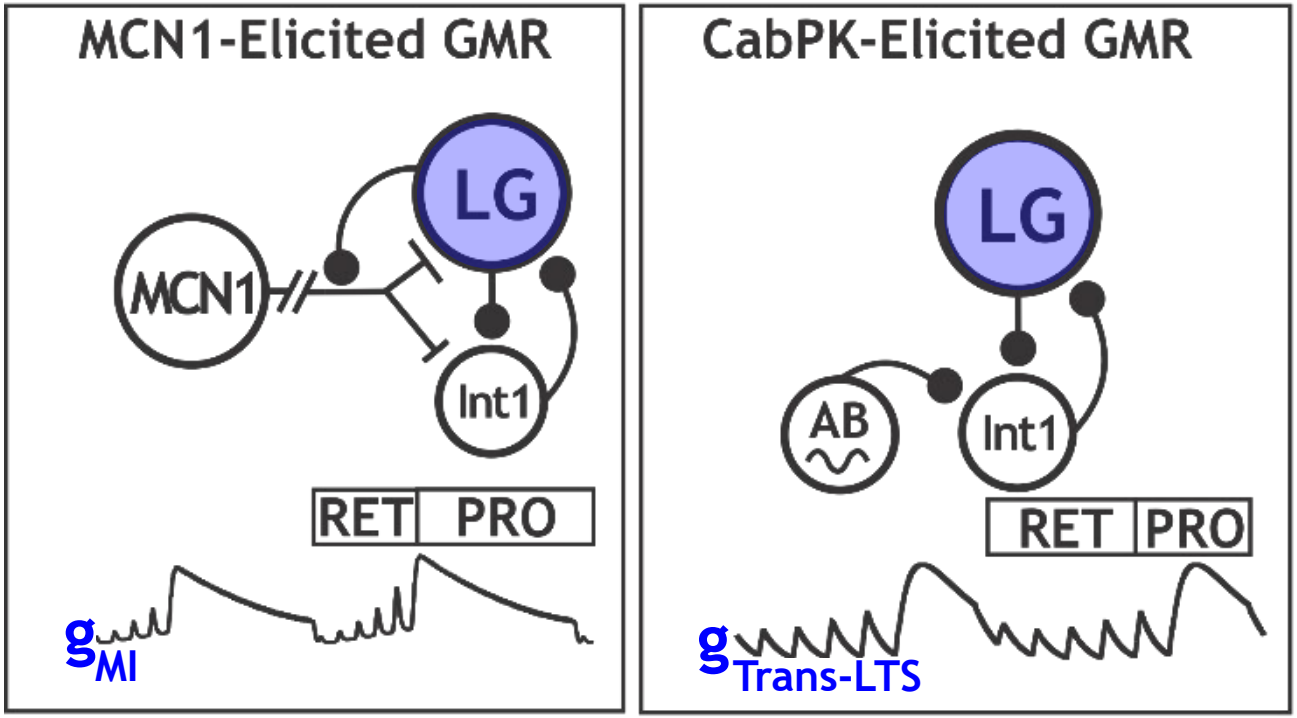


Different Currents, Same Role



(Rodriguez et al, J Neurosci 2013)

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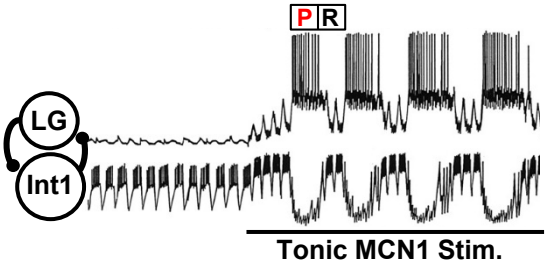

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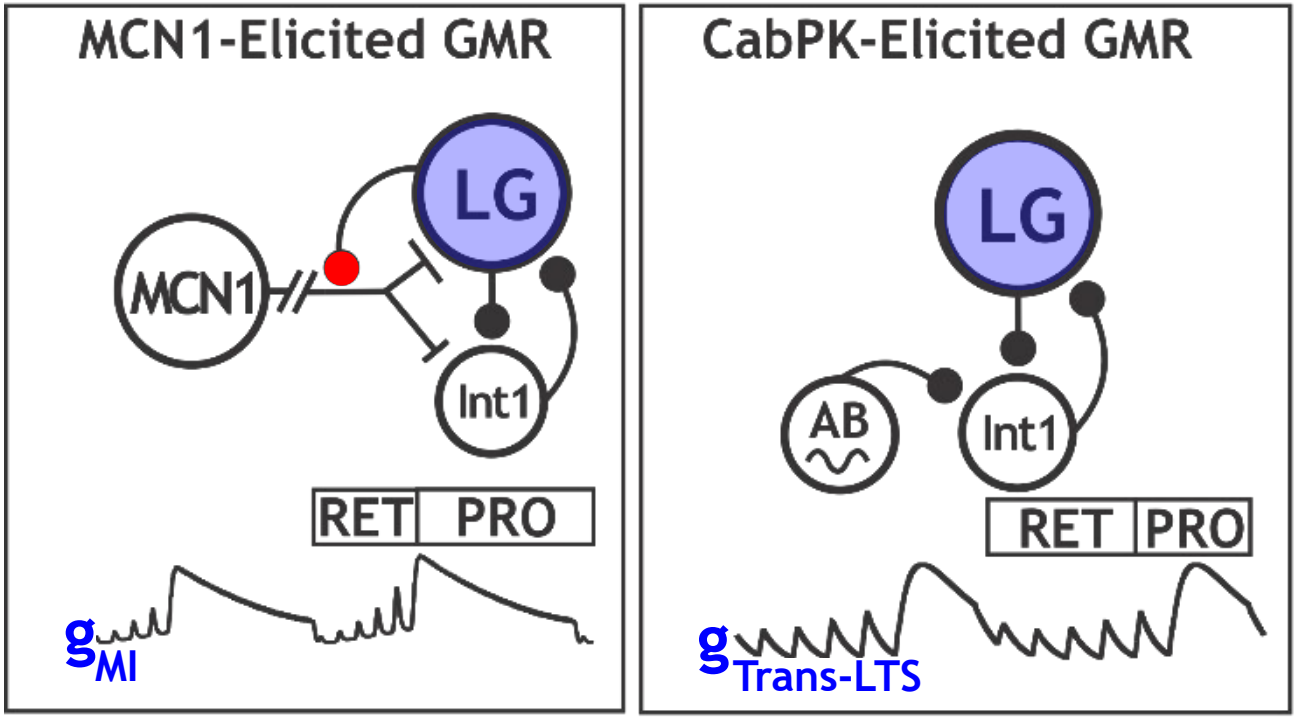

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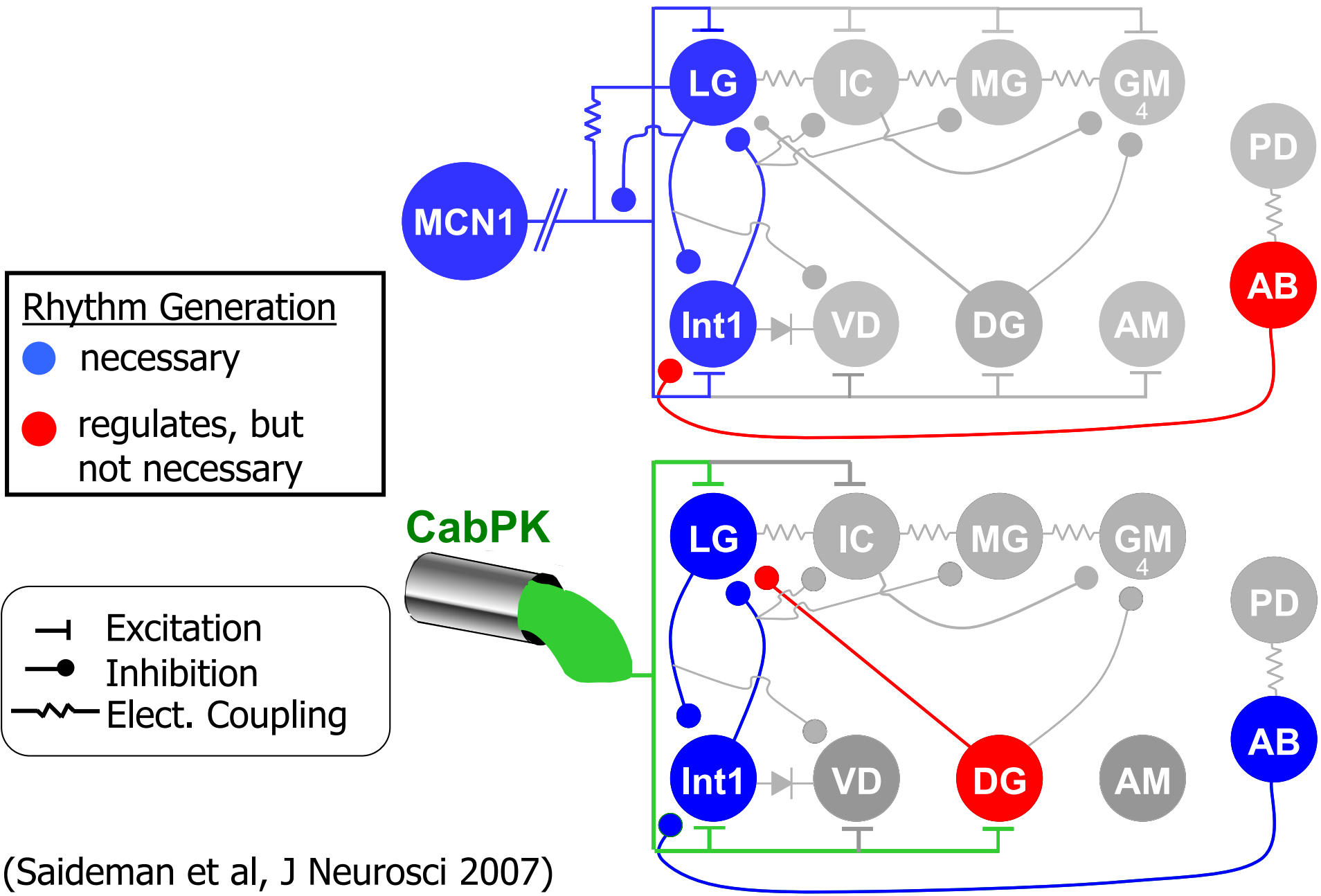

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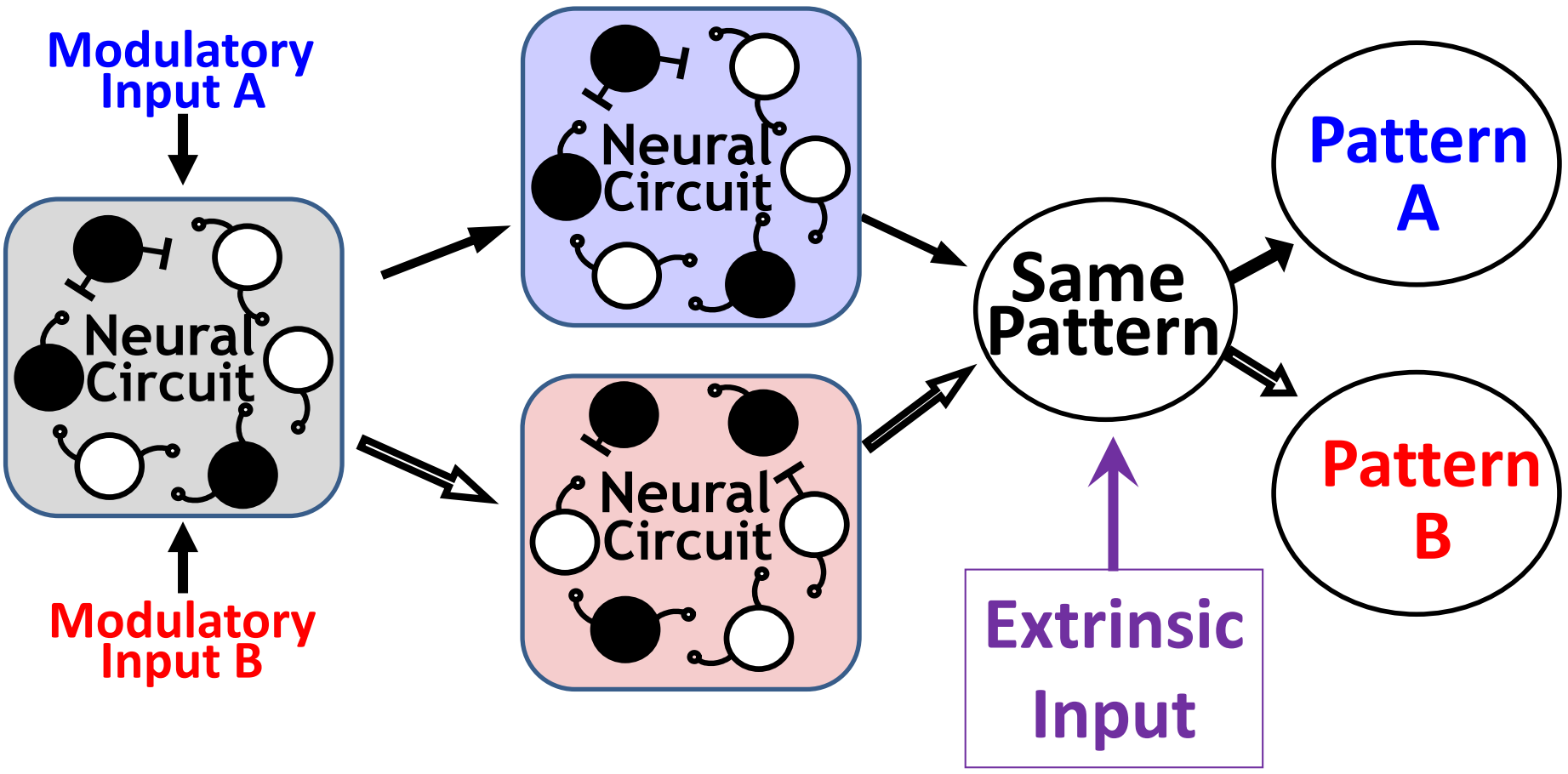

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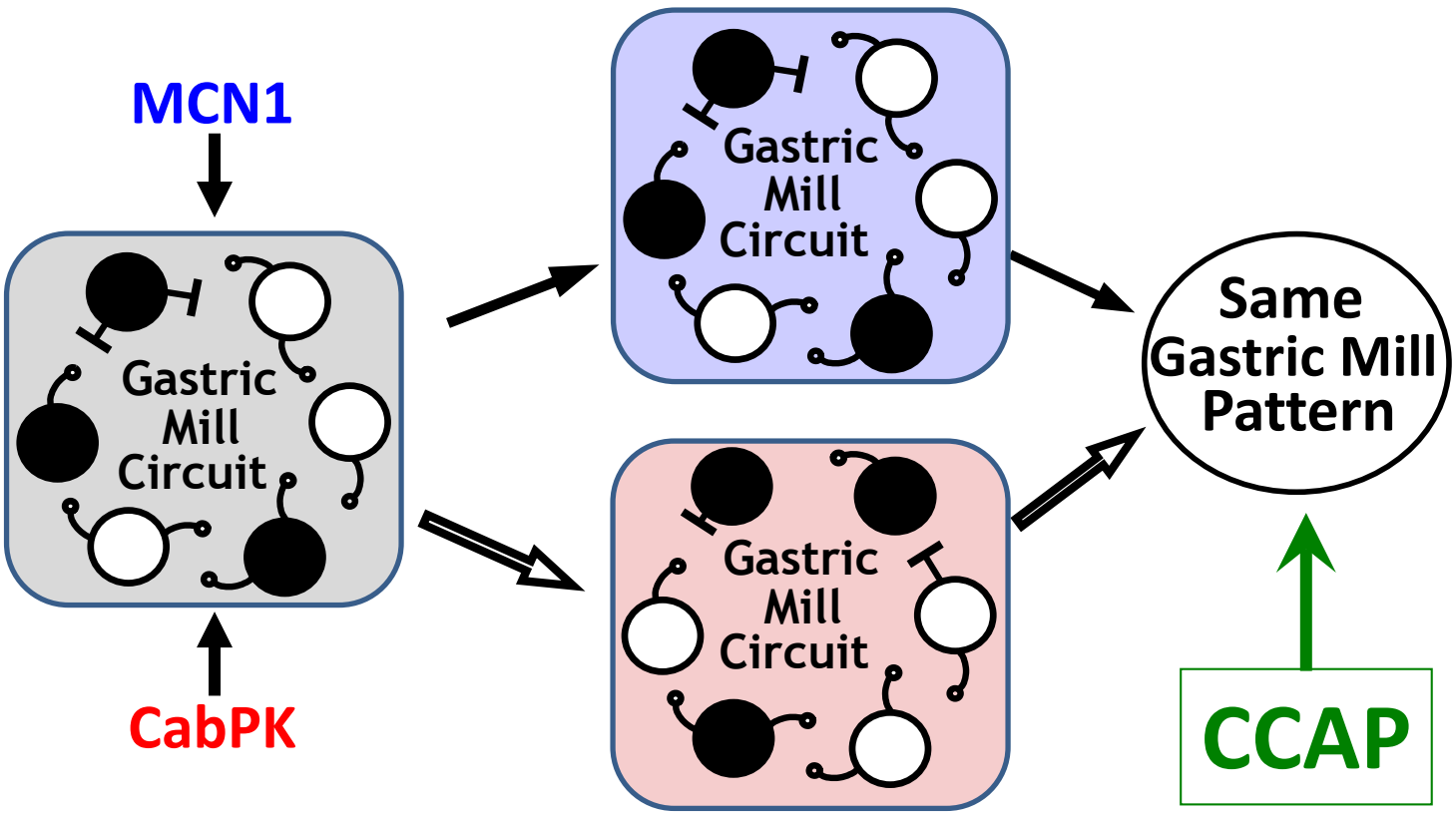
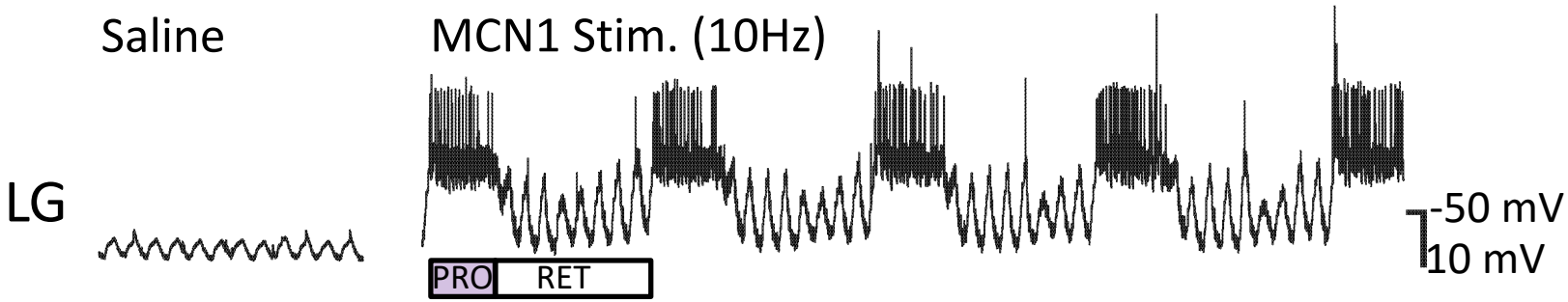


A Slower MCN1-GMR With CCAP



(MCN1: Kirby and Nusbaum, 2007 J Neurophysiol)

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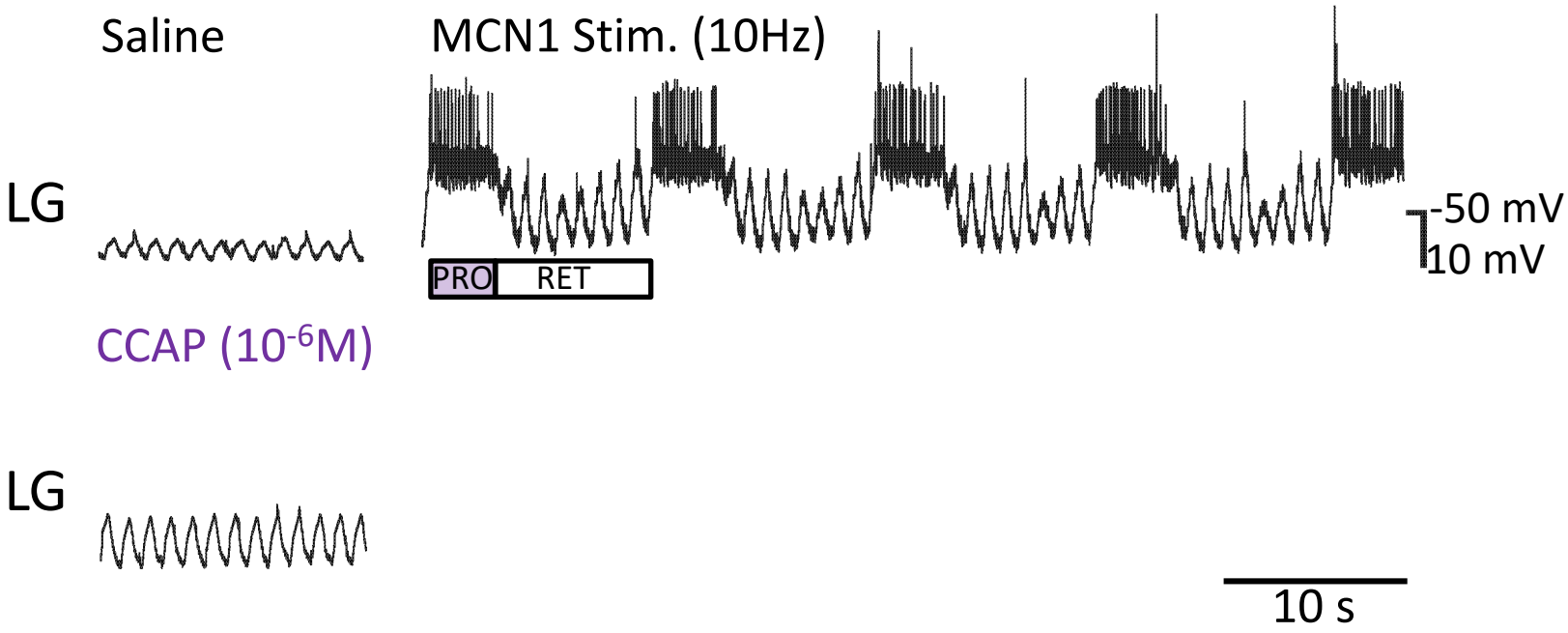

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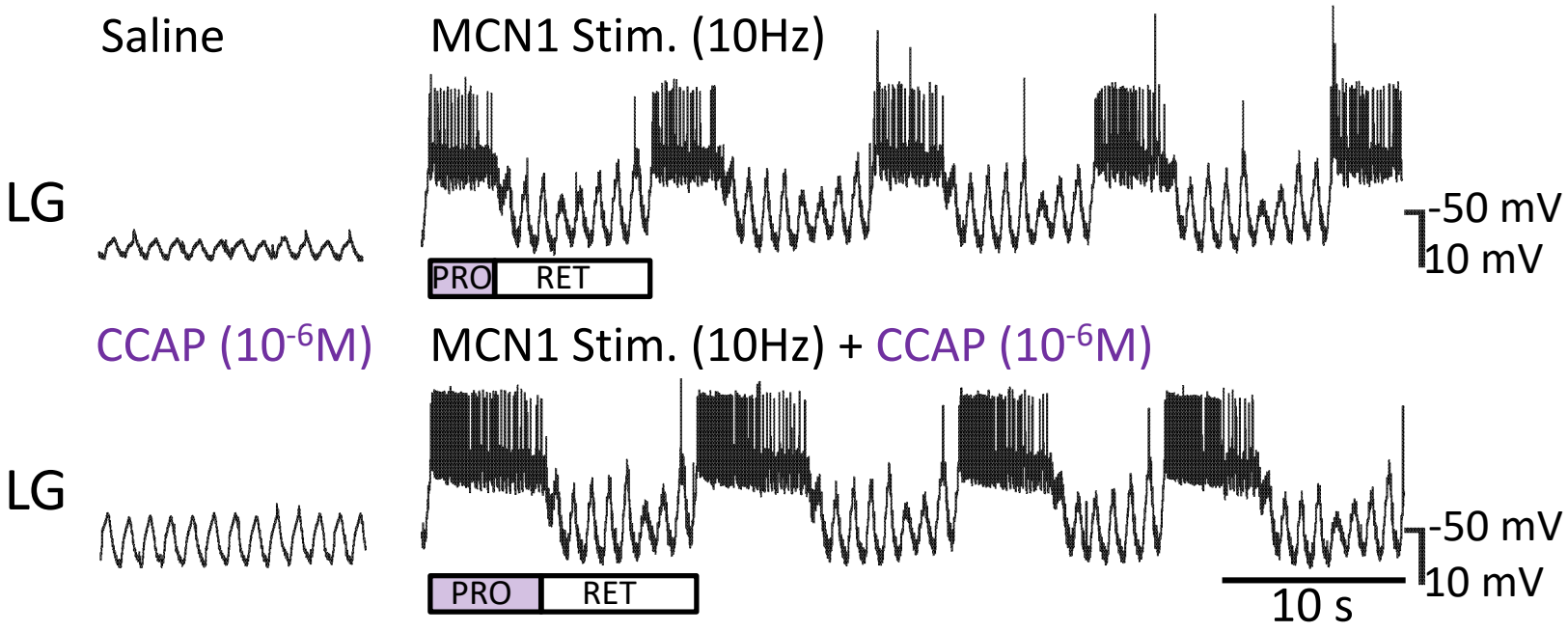

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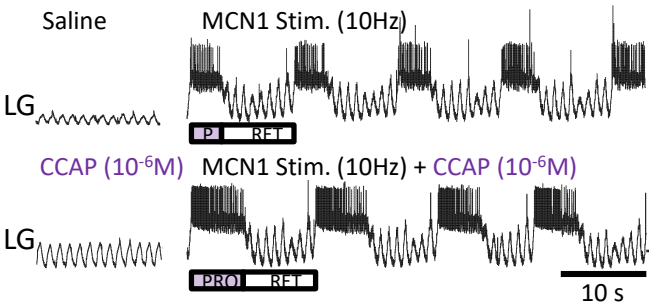
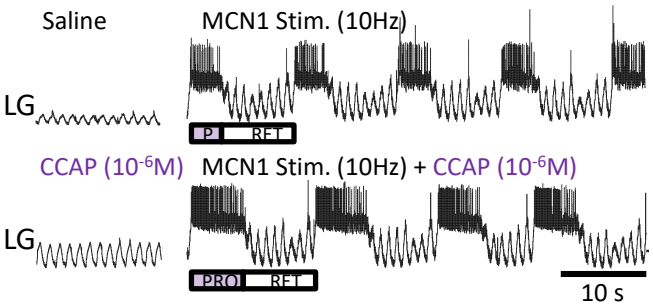
CCAP Influence on the CabPK-GMR

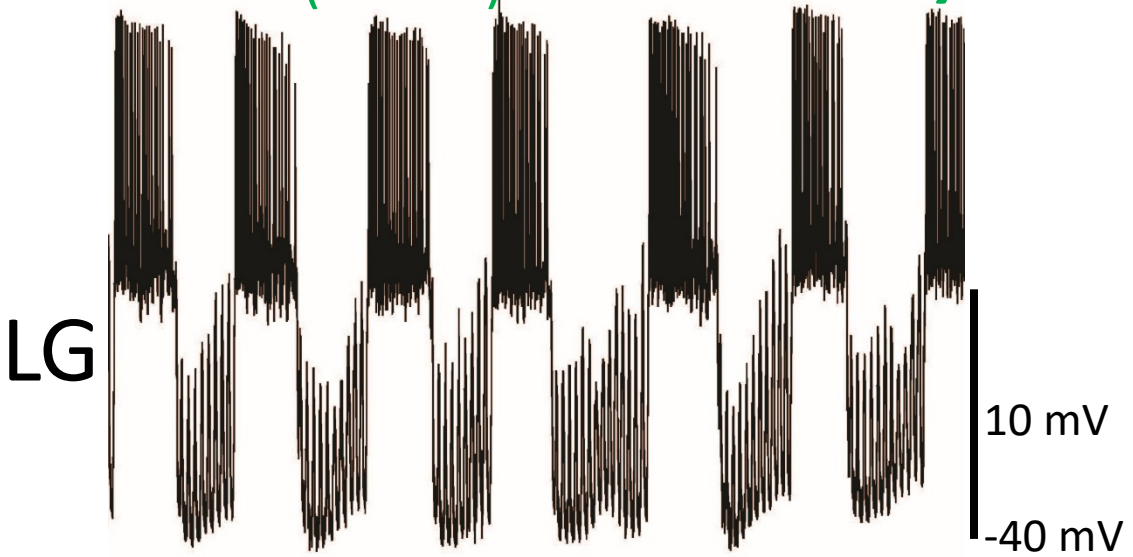


(CabPK: Powell, Marder & Nusbaum, In Prep.)

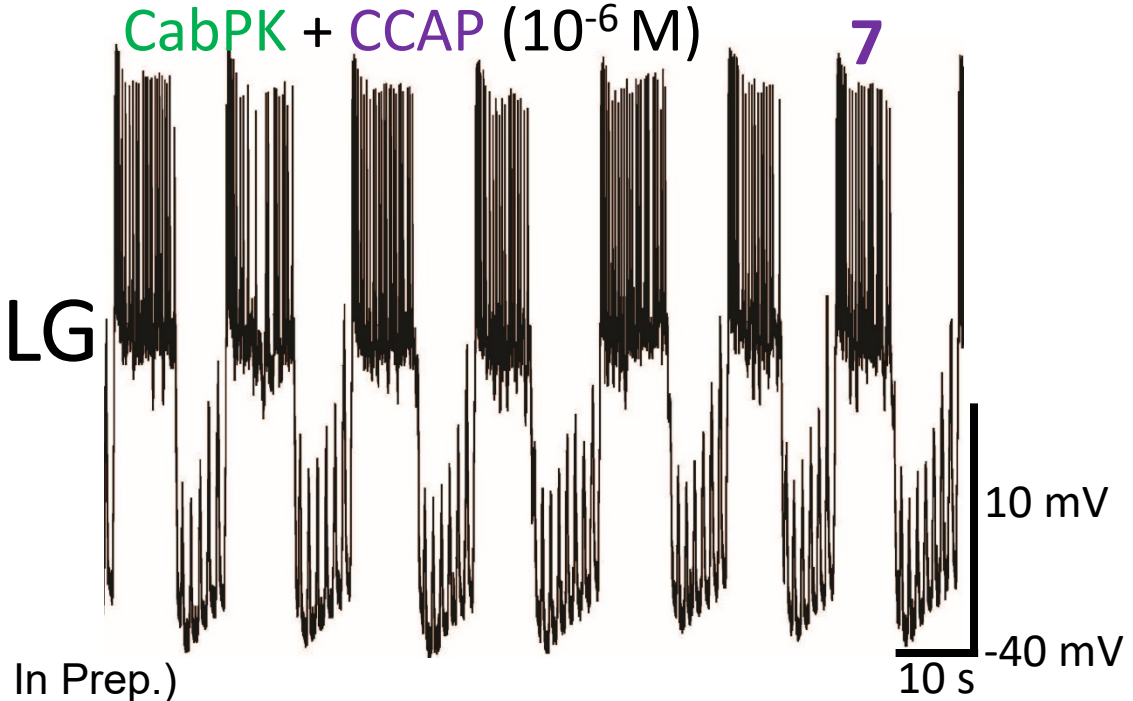
A Faster CabPK-GMR With CCAP



CabPK (10^{-6} M) **7**



CabPK + CCAP (10^{-6} M) **7**



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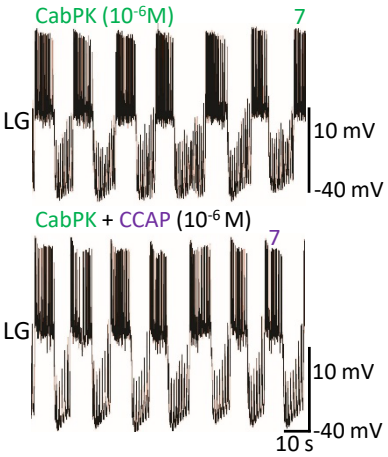

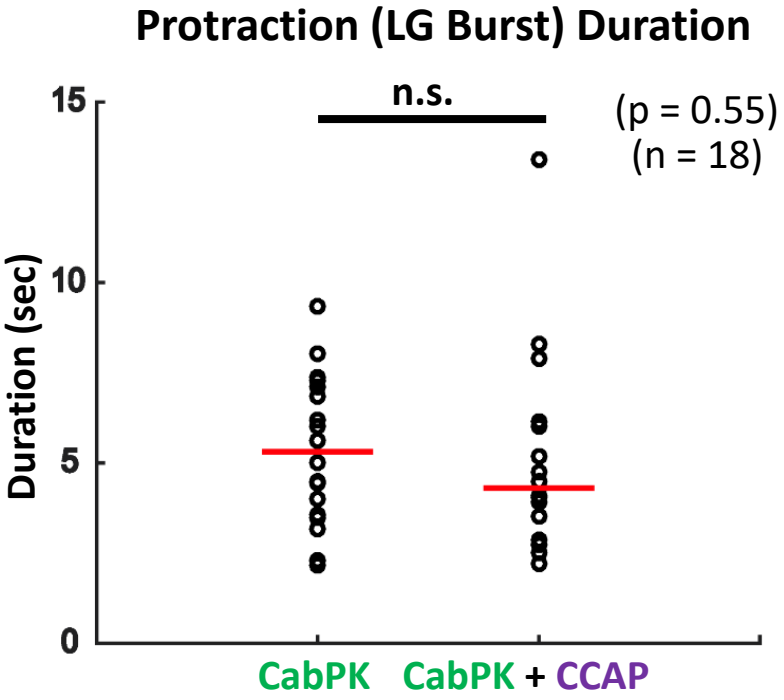

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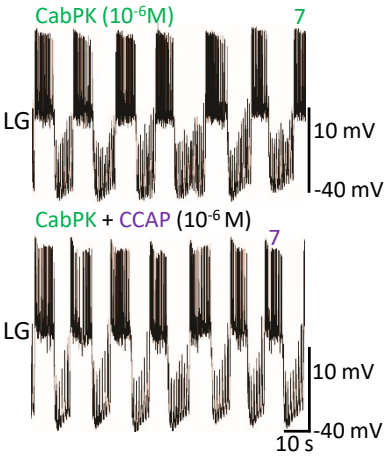

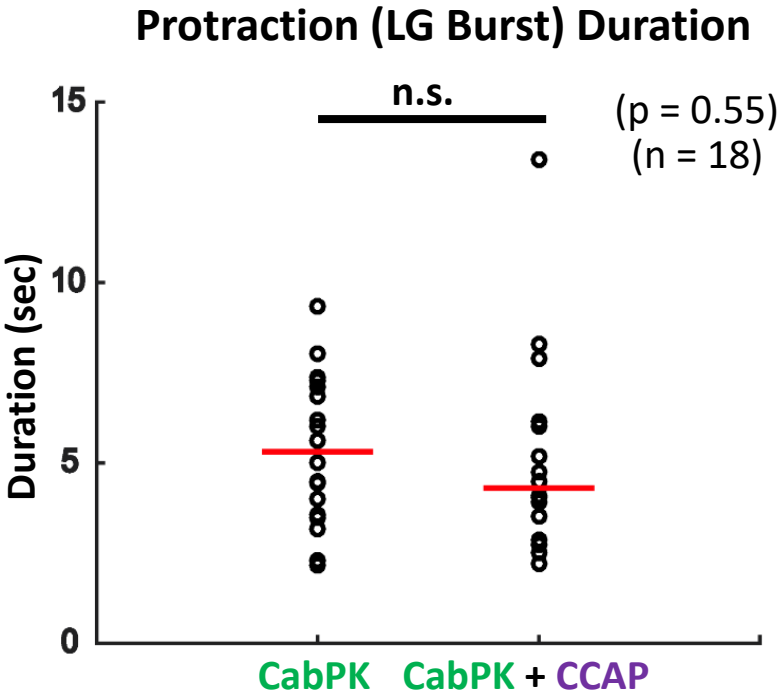

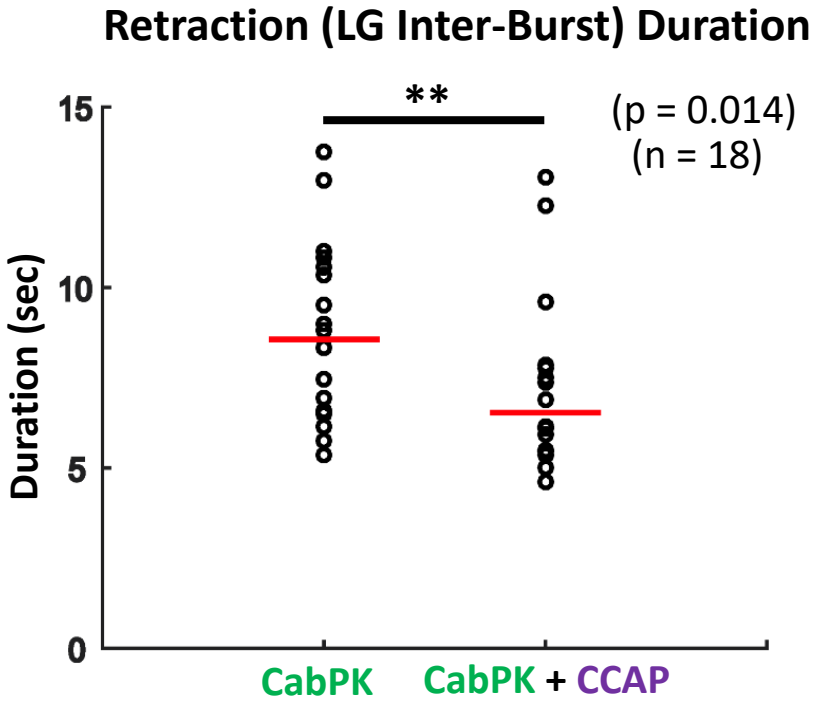

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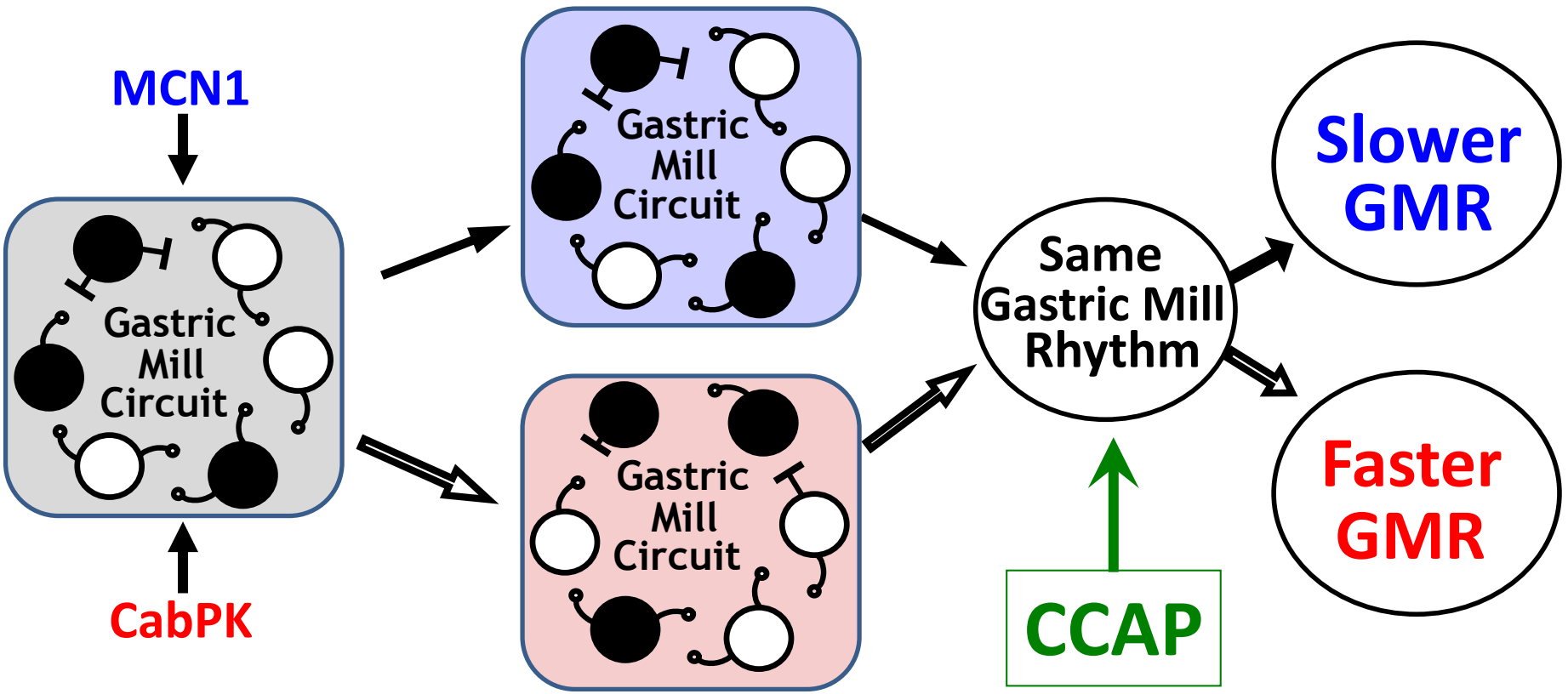
Distinct Peptide Hormone Actions on Different Circuit States



(Kirby et al., 2007 J Neurophysiol)
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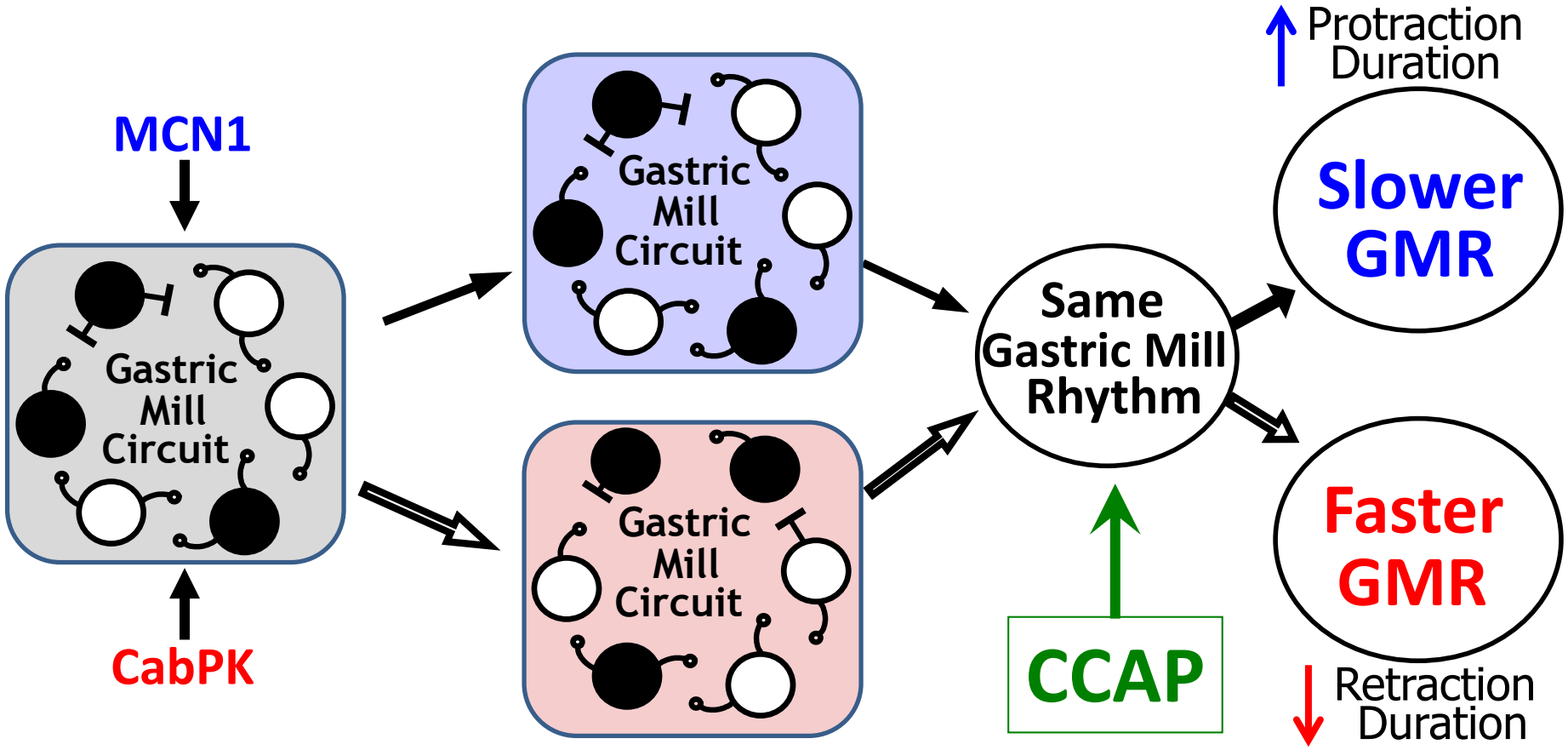

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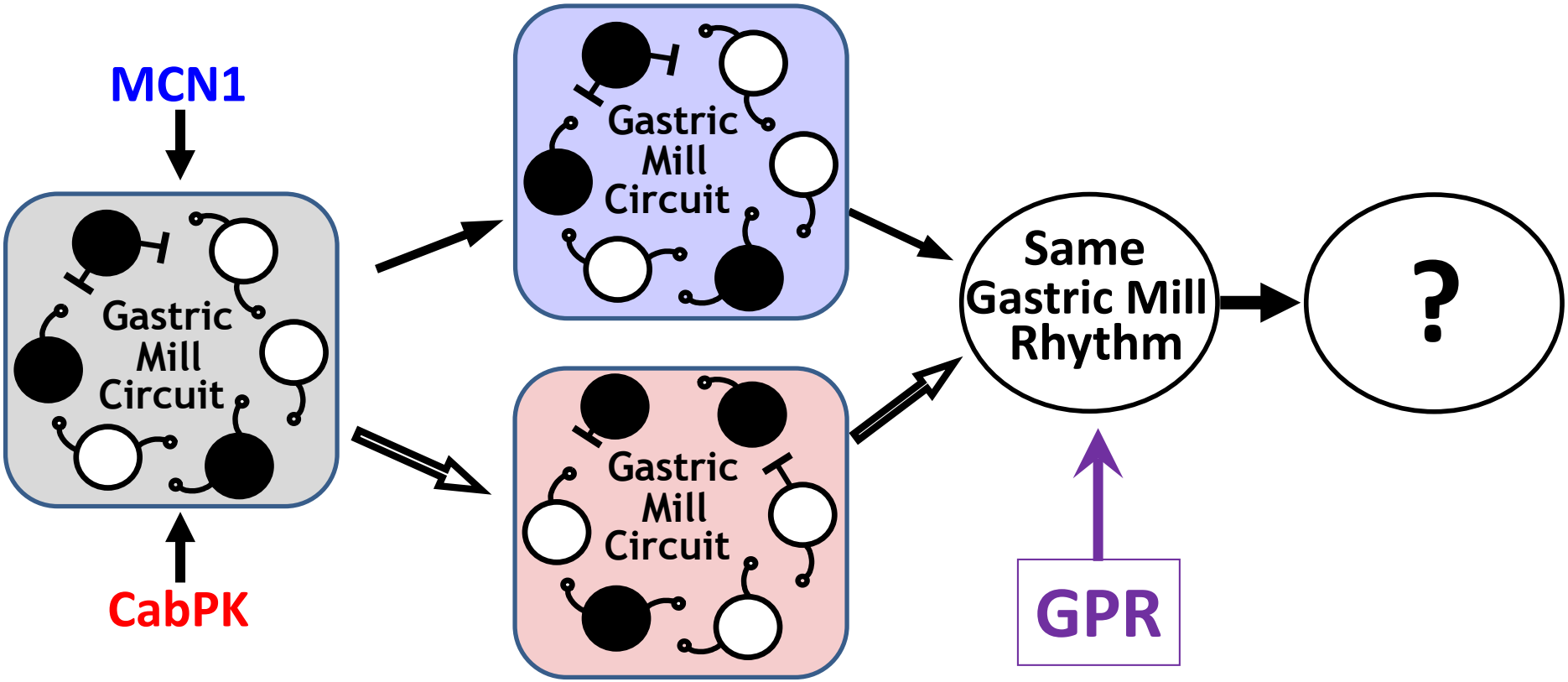
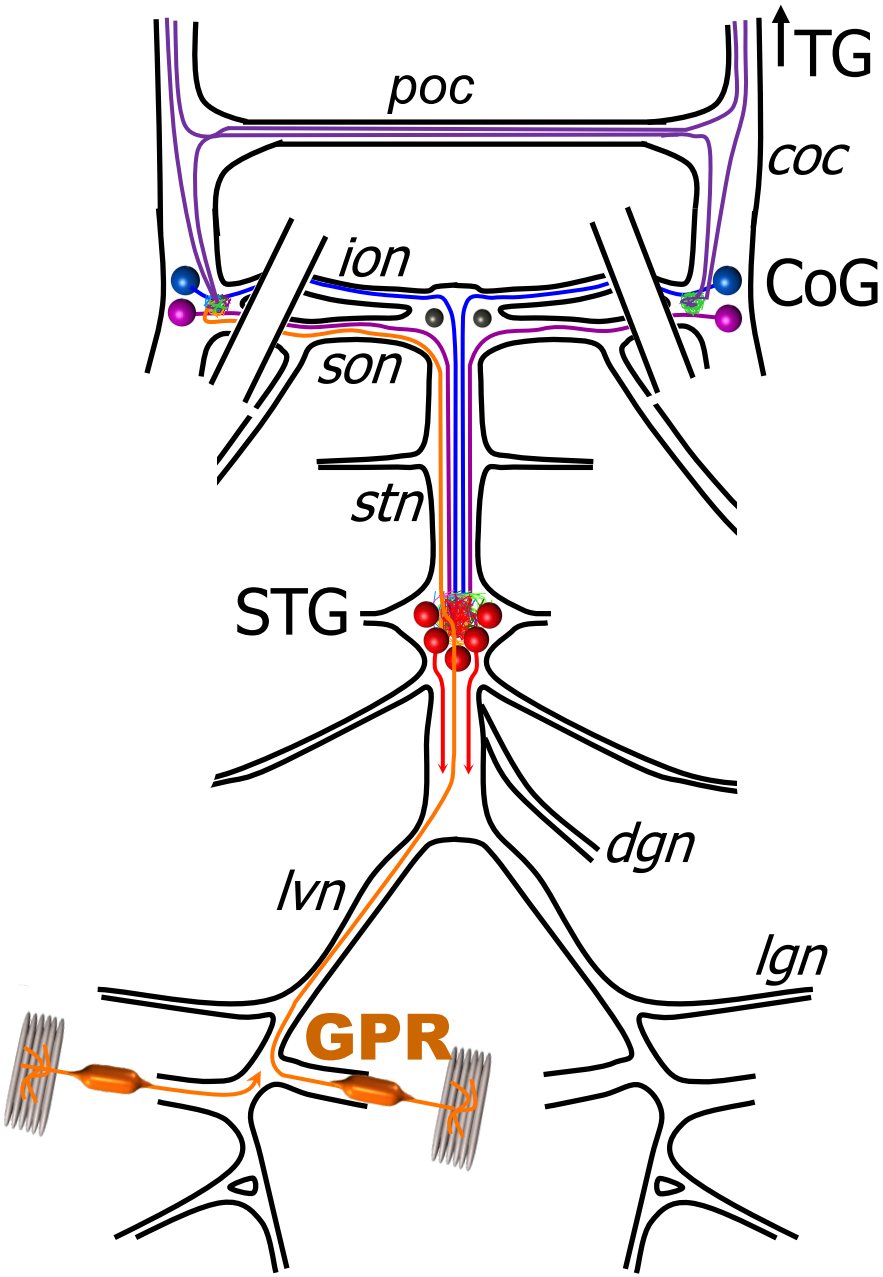
(Powell, Marder, Nusbaum, In Prep.)

Sensory Feedback During Different Circuit States



Sensory Feedback During Different Circuit States



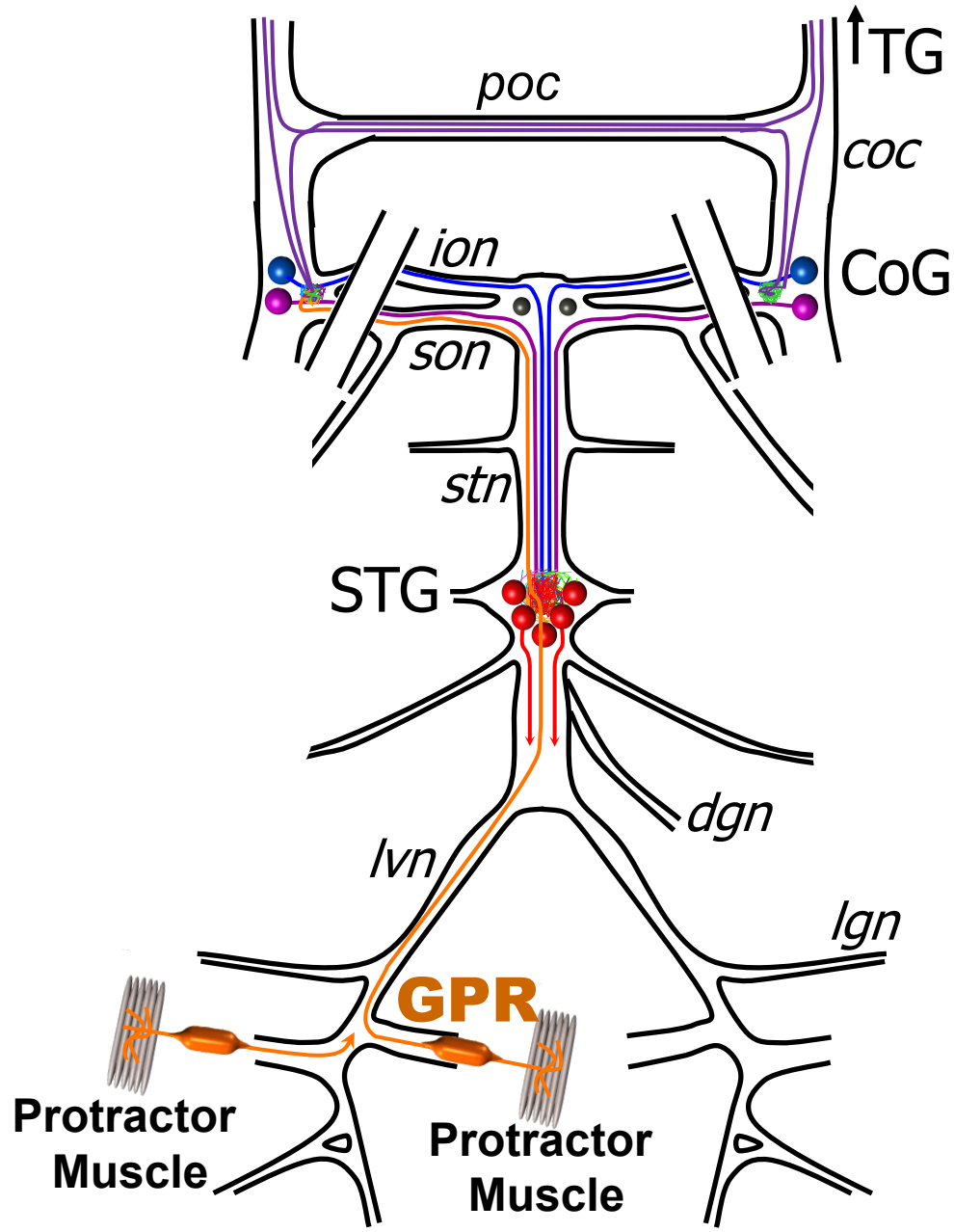
Projection Neurons

Gastric Mill CPG: Chewing

Pyloric CPG: Filtering

Muscle Stretch-Sensitive Sensory Neurons

Sensory Feedback During Different Circuit States



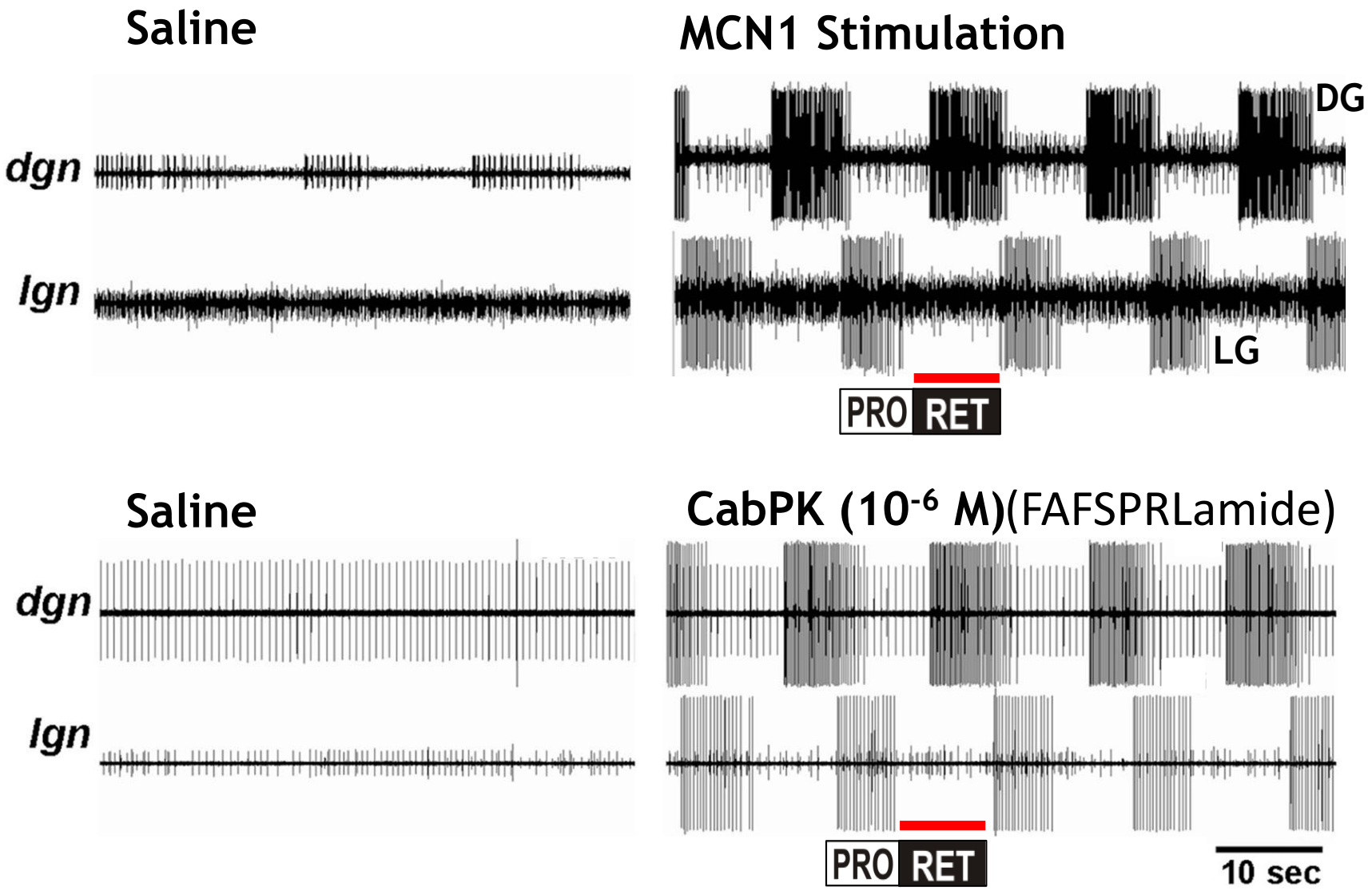
Projection Neurons

Gastric Mill CPG: Chewing

Pyloric CPG: Filtering

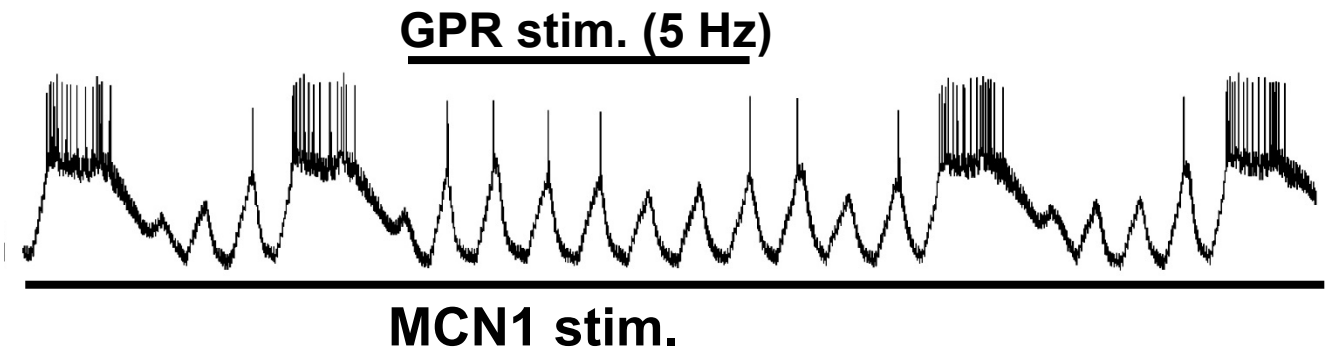
Muscle Stretch-Sensitive Sensory Neurons

GPR Stimulation During Retraction



GPR Regulates the MCN1-Gastric Mill Rhythm

MCN1-Elicited GMR:



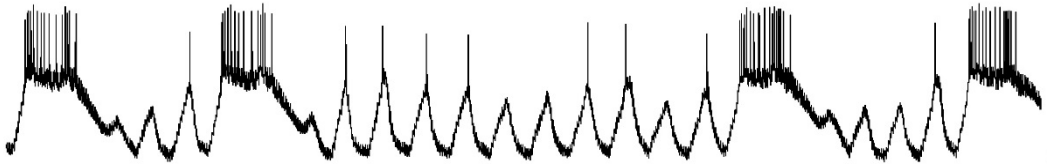
(Beenhakker et al, 2005 J Neurosci)

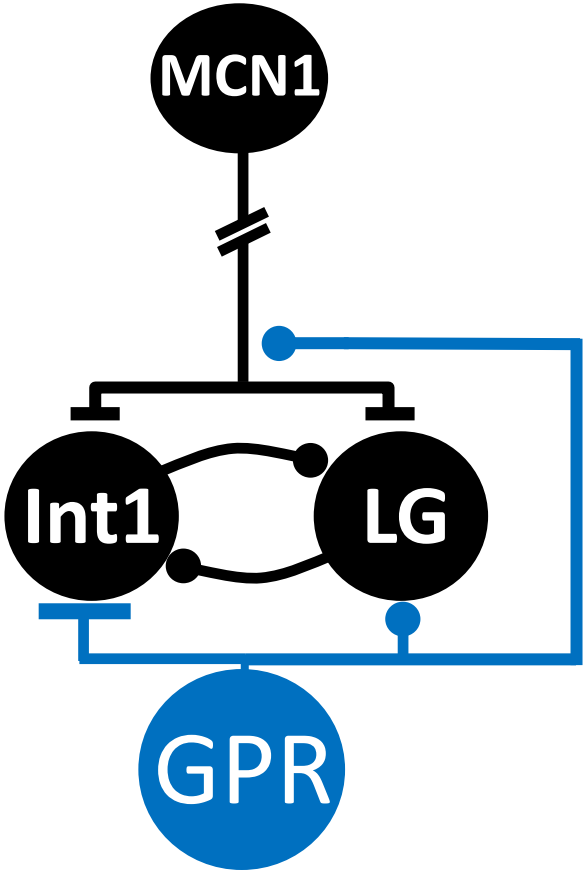
GPR Regulates the MCN1-Gastric Mill Rhythm

MCN1-Elicited GMR:

GPR stim. (5 Hz)

LG



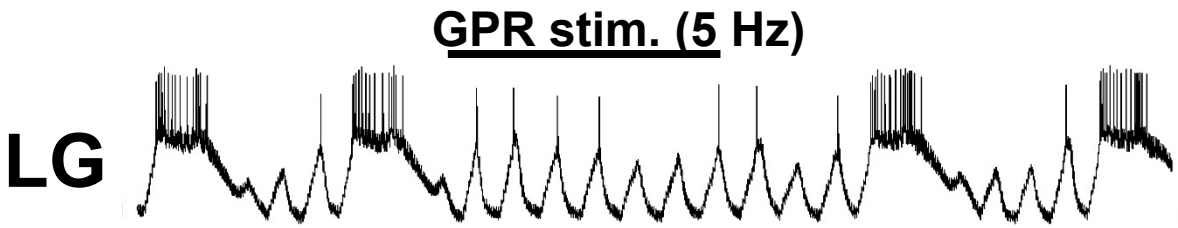


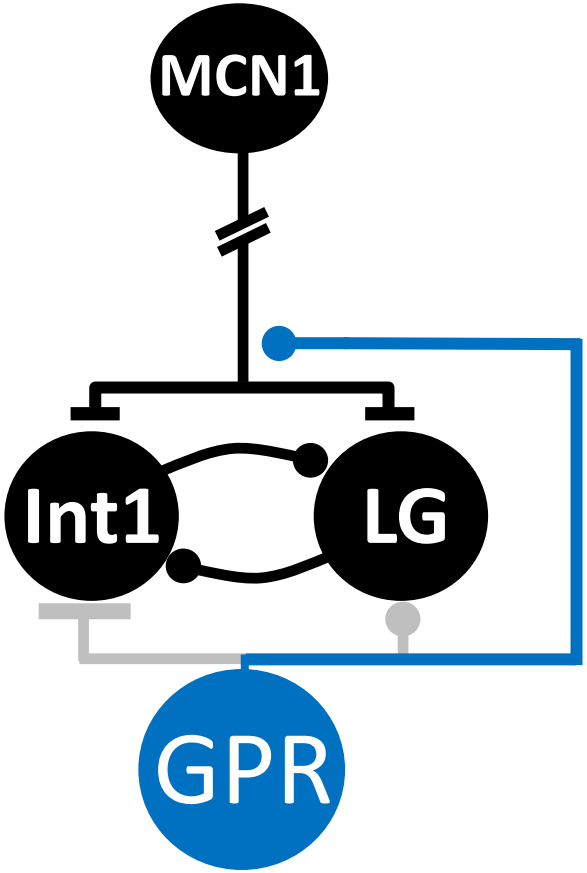
(Beenhakker et al, 2005 J Neurosci)

Excitation
Inhibition

GPR Regulates the MCN1-Gastric Mill Rhythm: Selective Presynaptic Inhibition of MCN1

MCN1-Elicited GMR:





(Beenhakker et al, 2005 J Neurosci)
(DeLong et al, 2009 J Neurophysiol)

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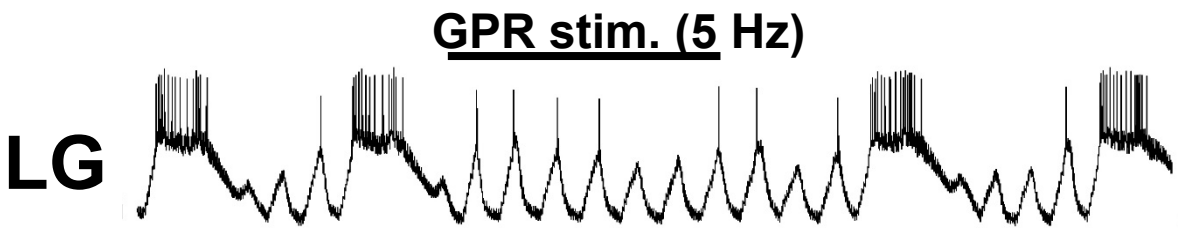
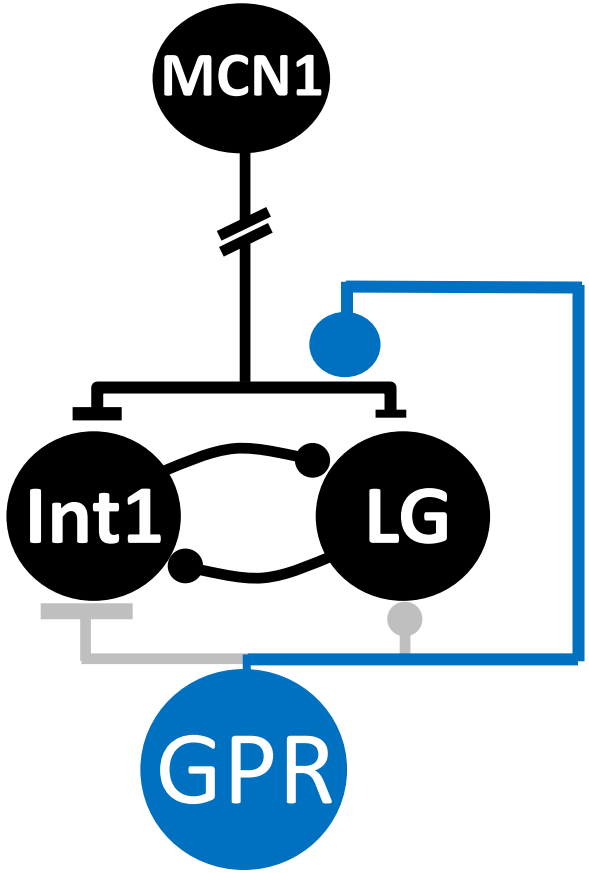
Inhibition

GPR Regulates the MCN1-Gastric Mill Rhythm: Selective Presynaptic Inhibition of MCN1

MCN1-Elicited GMR:





(Beenhakker et al, 2005 J Neurosci)
(DeLong et al, 2009 J Neurophysiol)

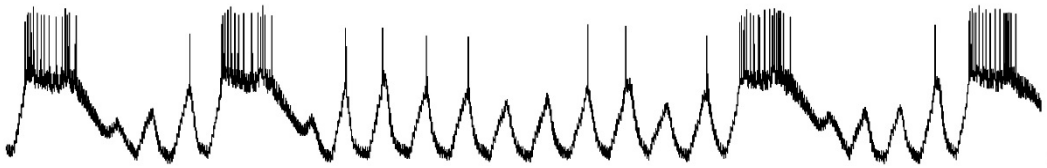
Excitation
Inhibition

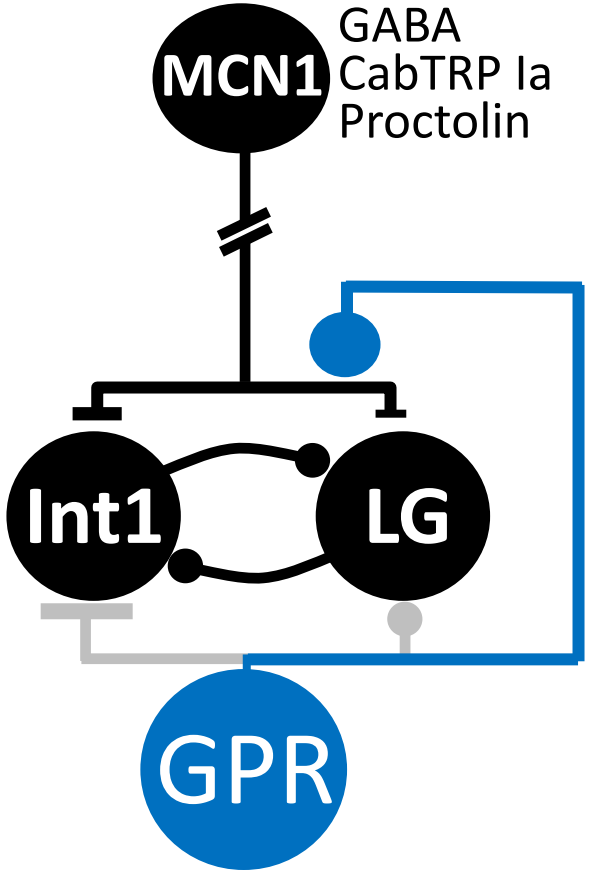
GPR Regulates the MCN1-Gastric Mill Rhythm: Divergent Co-transmission

MCN1-Elicited GMR:

GPR stim. (5 Hz)

LG



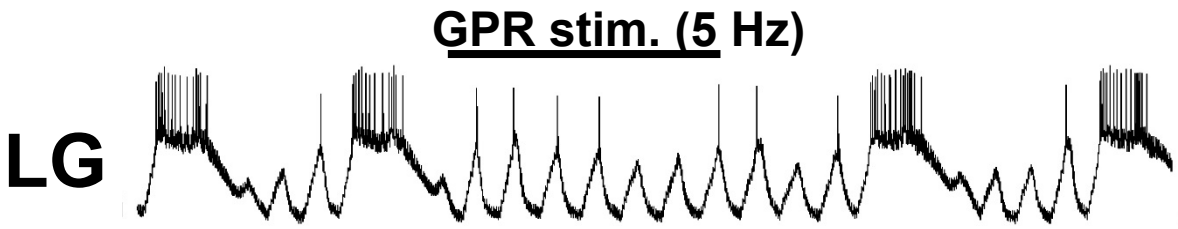


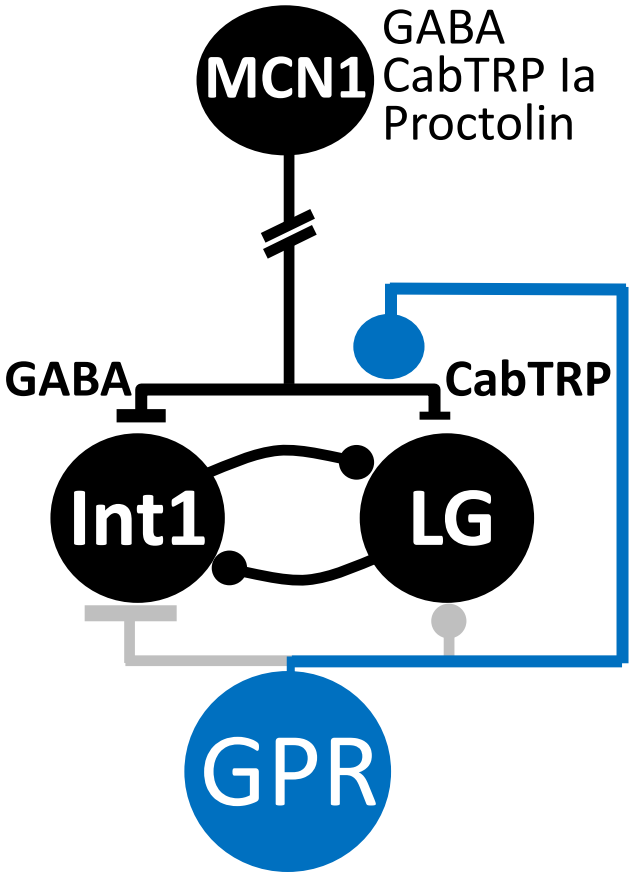
(Beenhakker et al, 2005 J Neurosci)
(DeLong et al, 2009 J Neurophysiol)

Excitation
Inhibition

GPR Regulates the MCN1-Gastric Mill Rhythm: Divergent Co-transmission

MCN1-Elicited GMR:





(Beenhakker et al, 2005 J Neurosci)
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Inhibition

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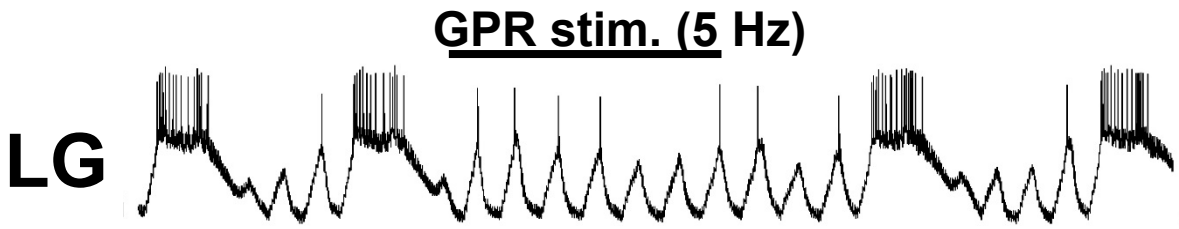
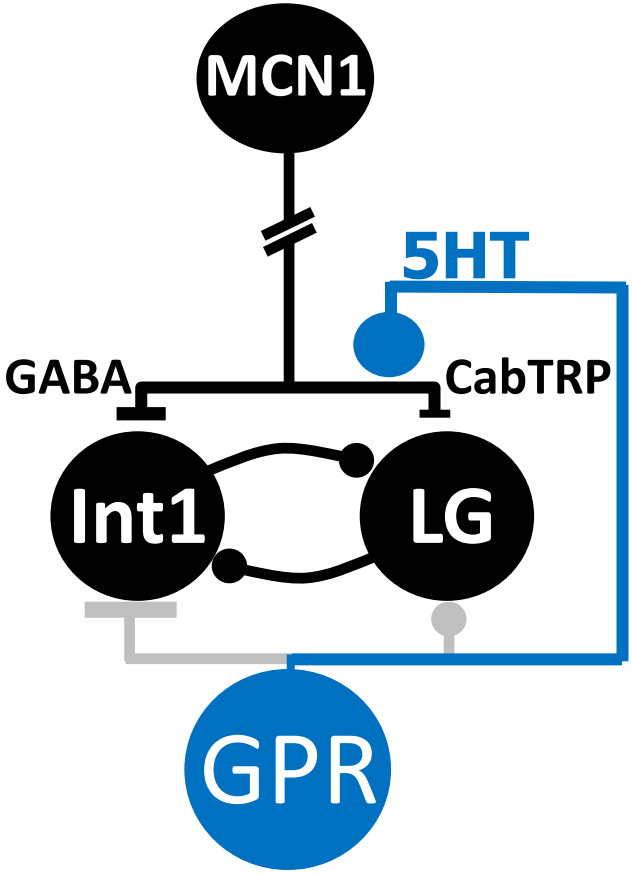
MCN1-Elicited GMR:



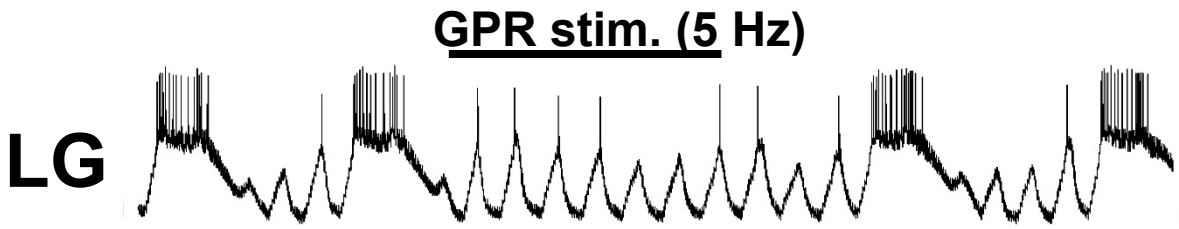


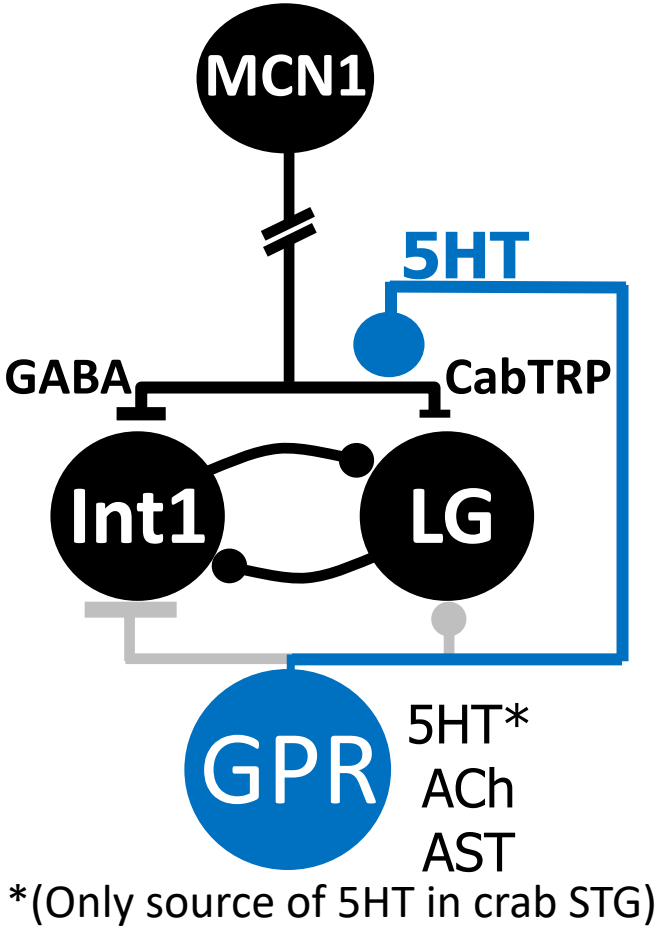
(Beenhakker et al, 2005 J Neurosci)
(DeLong et al, 2009 J Neurophysiol)

Excitation
Inhibition

GPR Regulates the MCN1-Gastric Mill Rhythm: Divergent Co-transmission

MCN1-Elicited GMR:

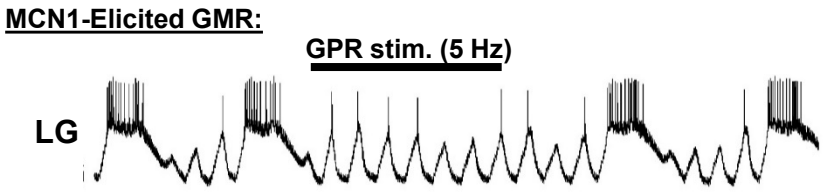


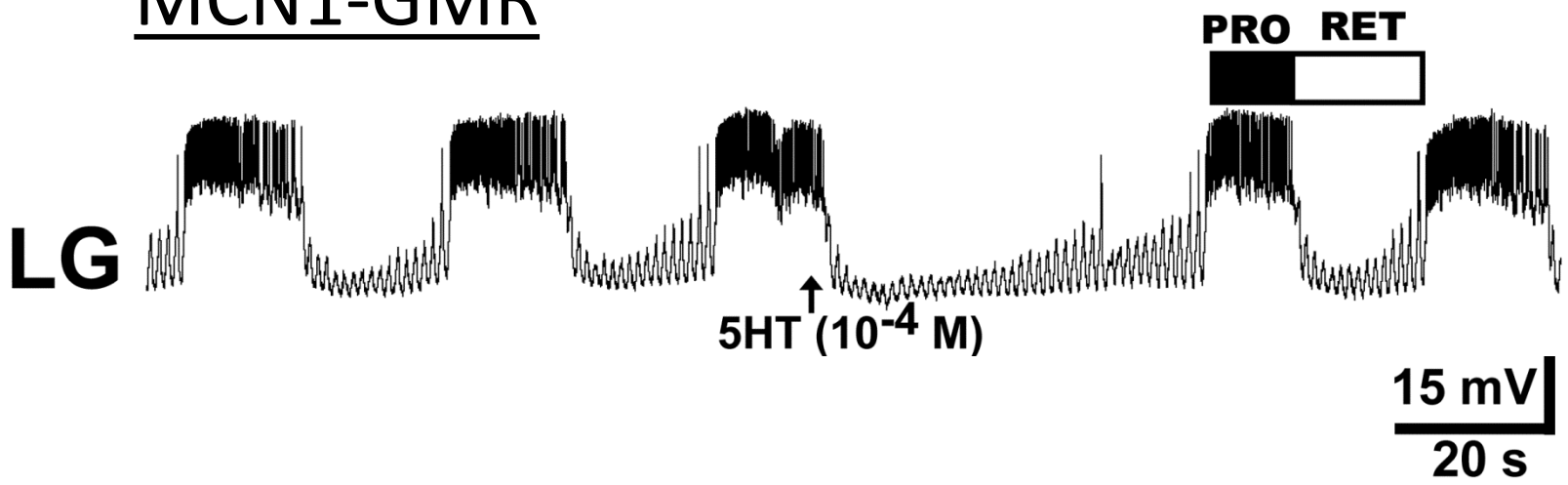


(Beenhakker et al, 2005 J Neurosci)
(DeLong et al, 2009 J Neurophysiol)

Excitation
Inhibition

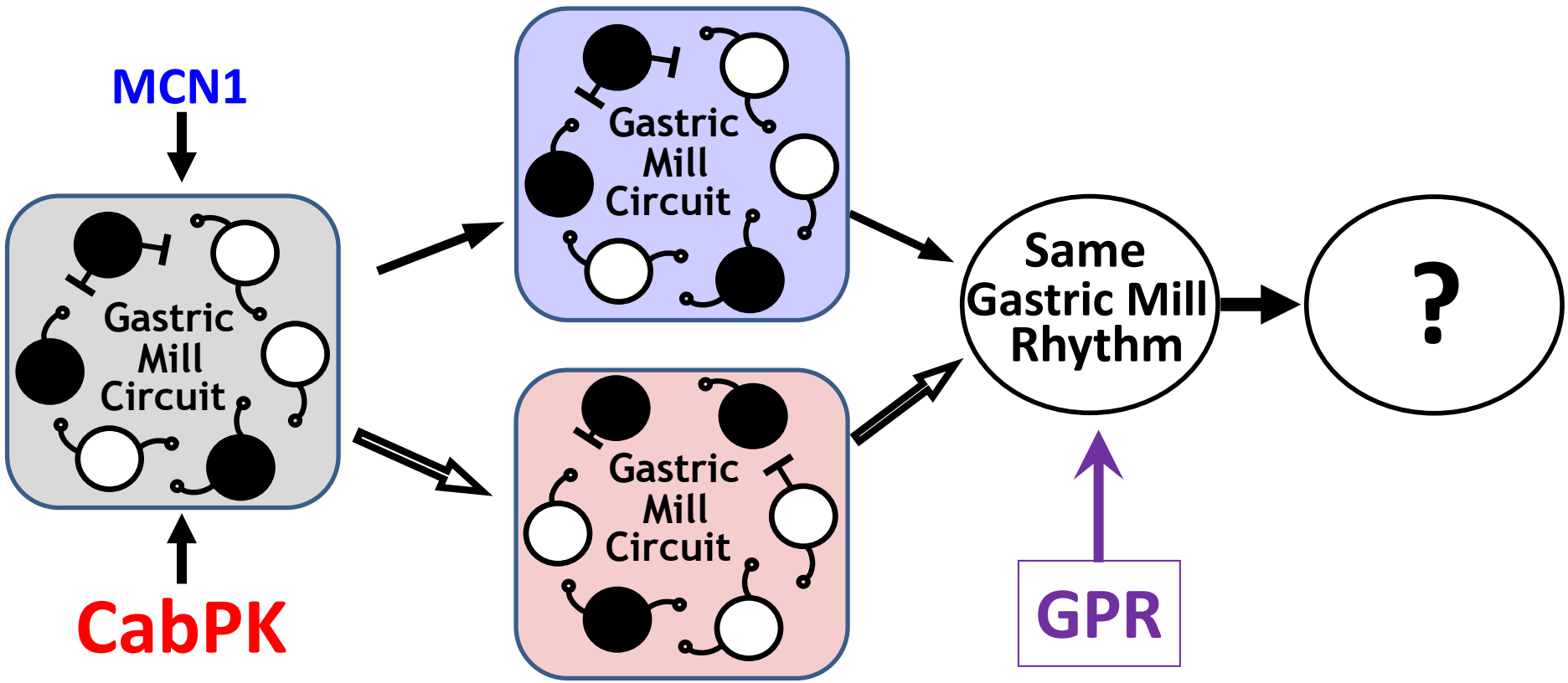
5HT Prolongs the MCN1-GMR Retraction Phase



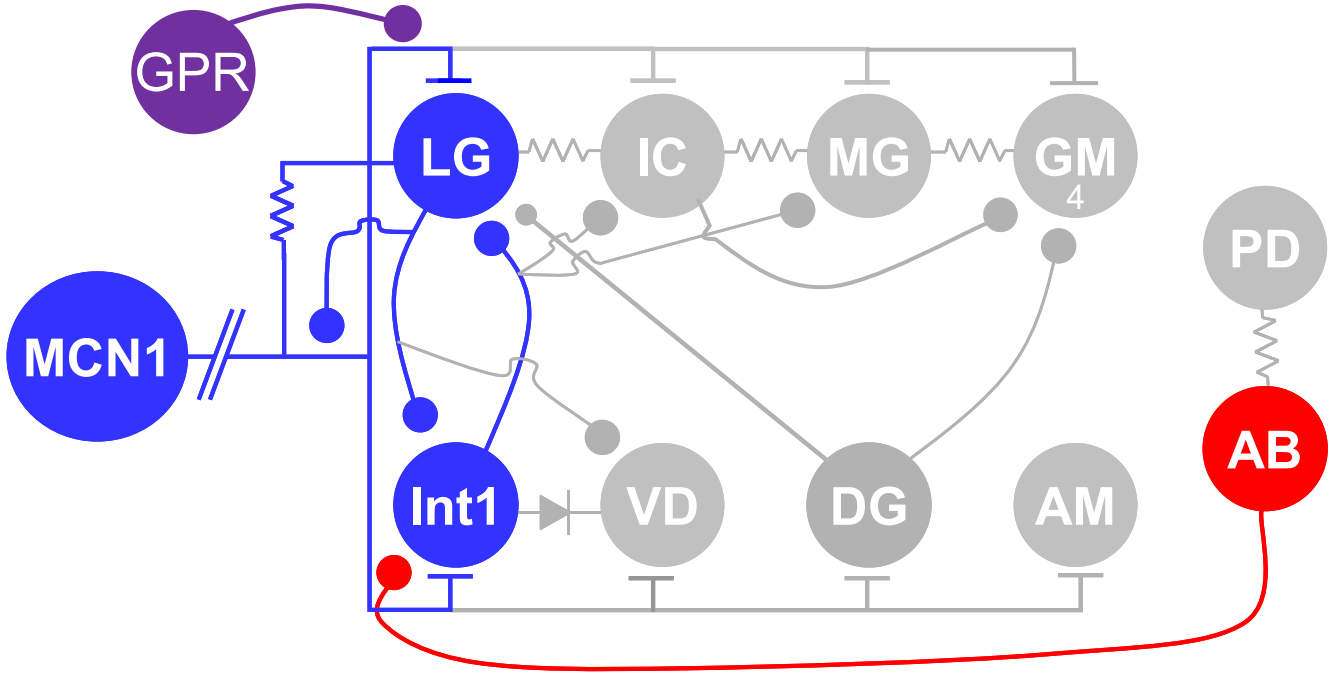


(DeLong et al, 2009 J Neurophysiol)

Sensory Feedback During Different Circuit States



Sensory Feedback During Different Circuit States



Rhythm Generation

necessary

regulates, but not necessary

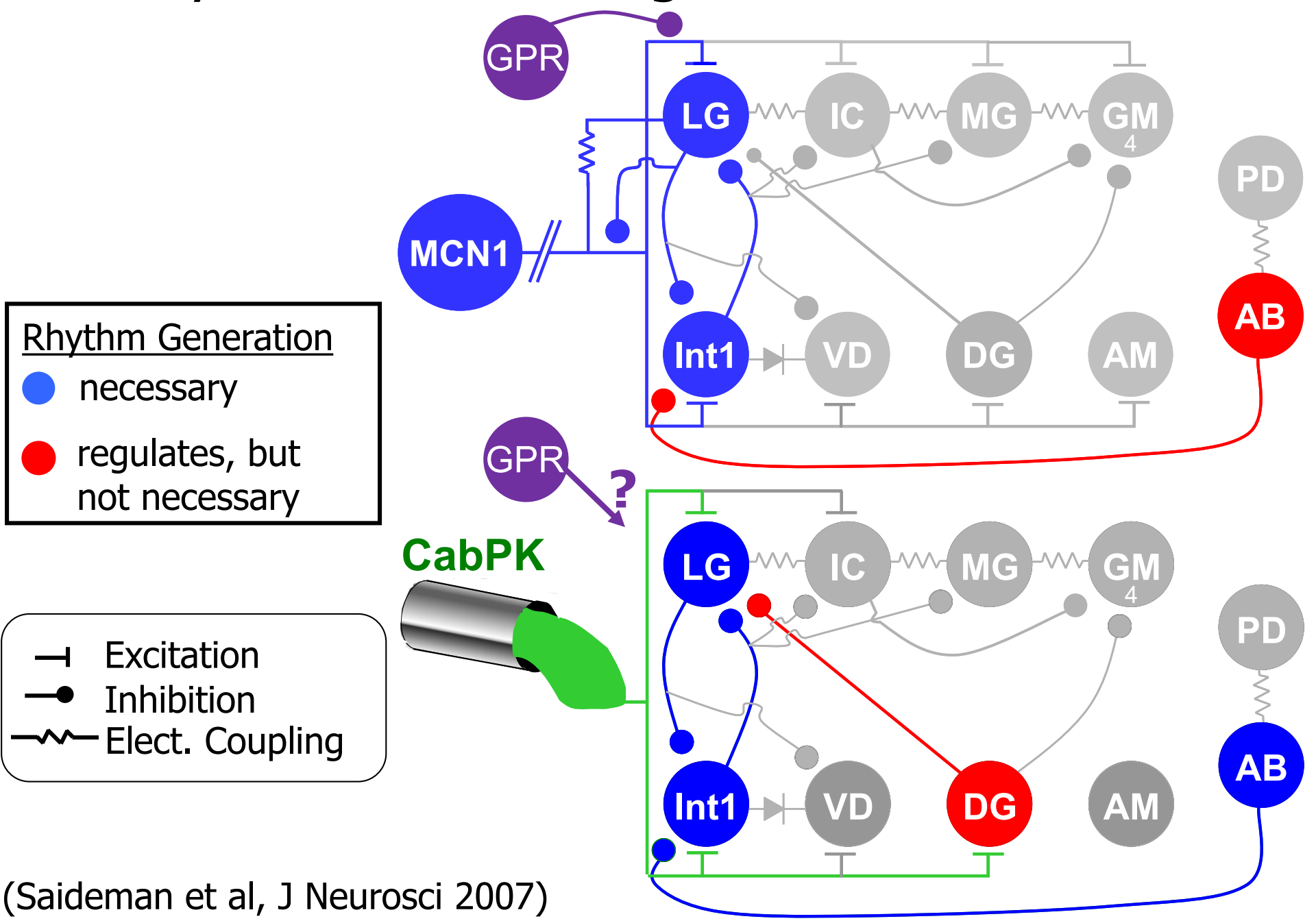
Excitation

Inhibition

Elect. Coupling

(Saideman et al, J Neurosci 2007)

Sensory Feedback During Different Circuit States



Rhythm Generation

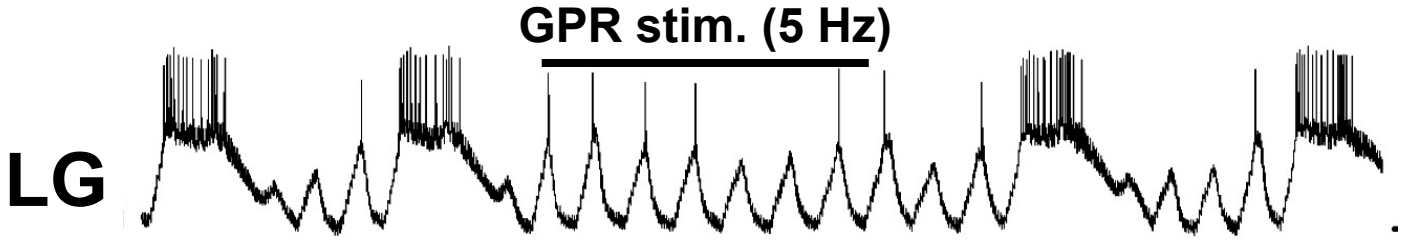
- necessary
- regulates, but not necessary

- Excitation
- Inhibition
- Elect. Coupling

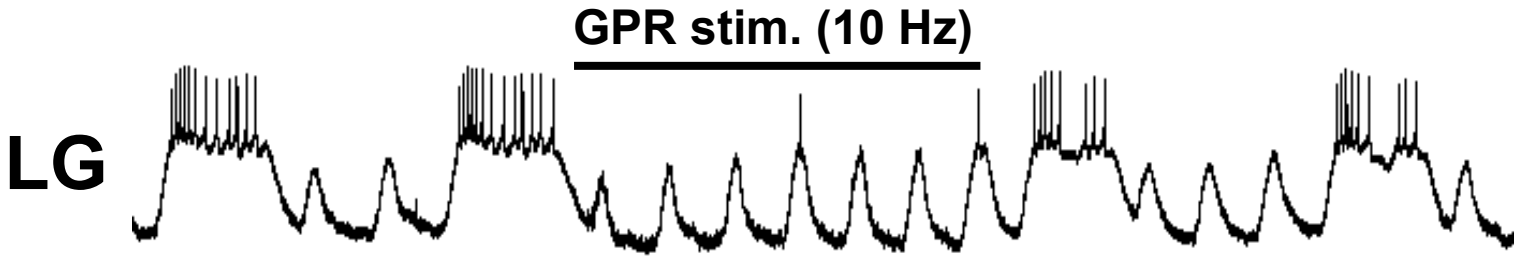
(Saideman et al, J Neurosci 2007)

GPR Has an Equivalent Action on the MCN1- and CabPK-GMRs

MCN1-Elicited Rhythm:



CabPK-Elicited Rhythm:

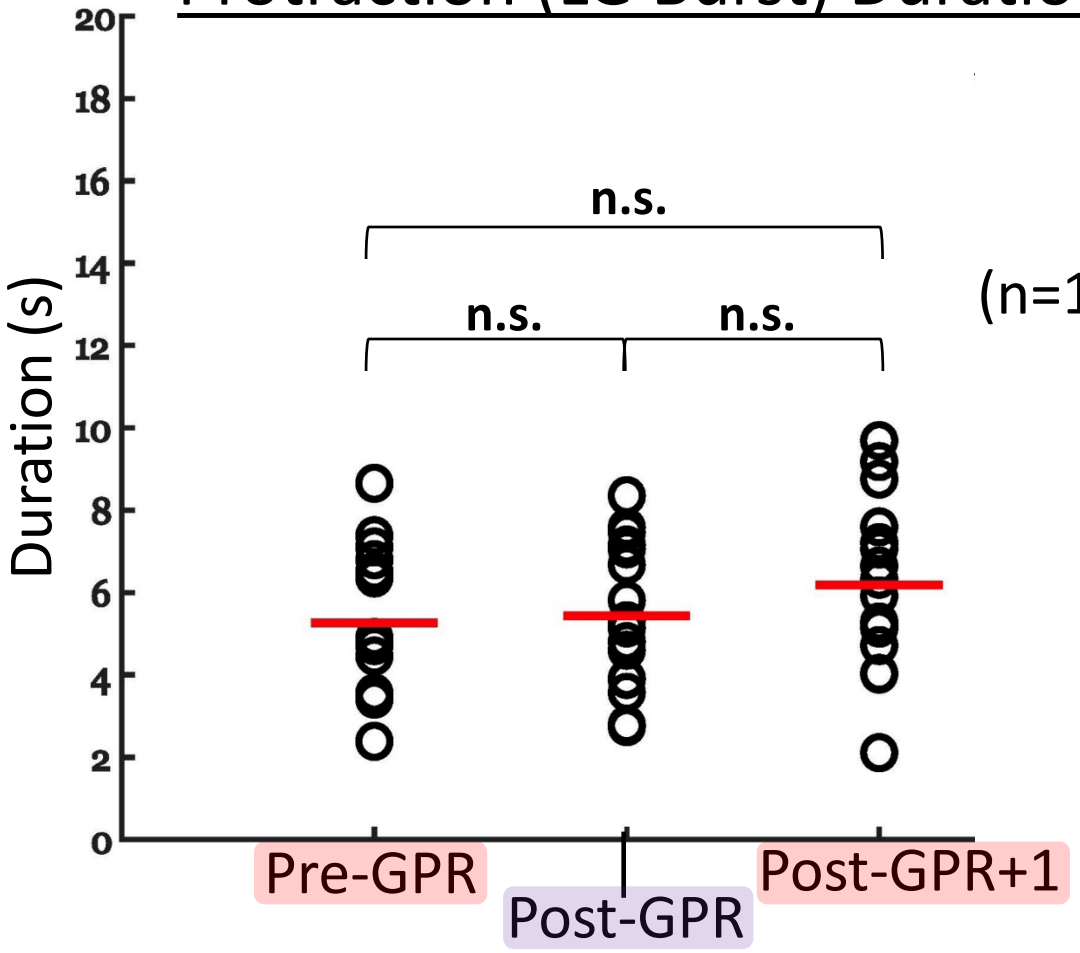


(Powell, Marder, Nusbaum, In Prep.)

GPR Selectively Prolongs the CabPK-GMR Retraction Phase

CabPK-Elicited Rhythm:

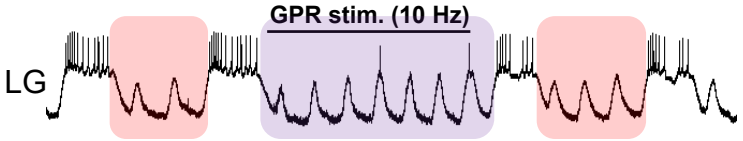
Protraction (LG Burst) Duration



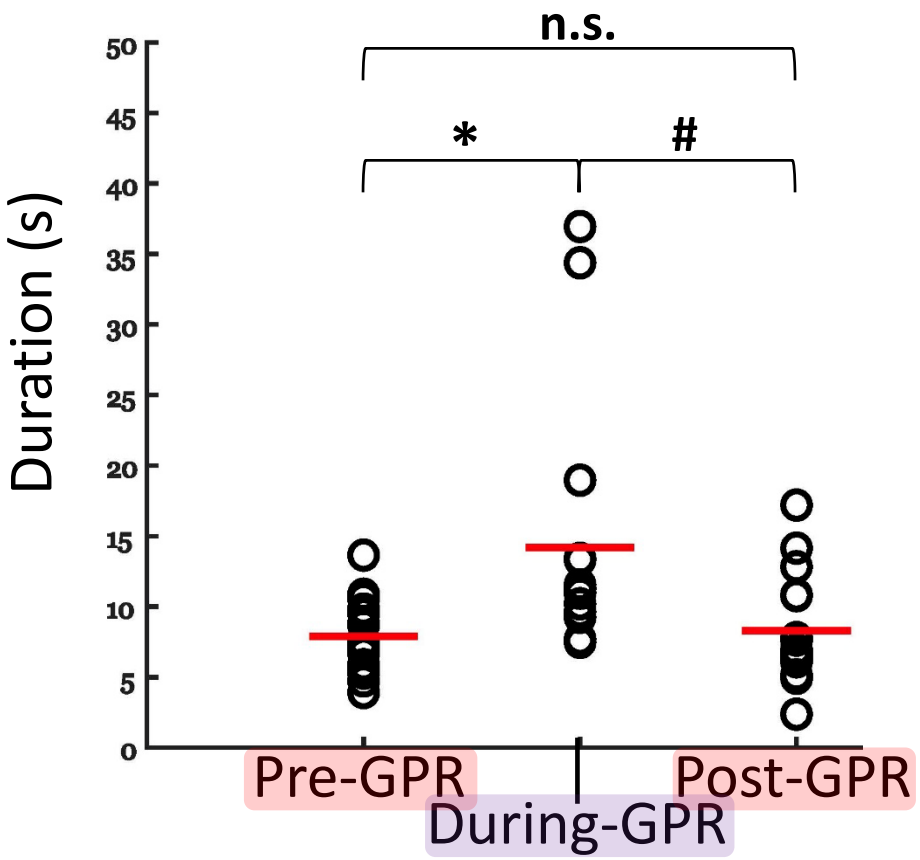
(CabPK: Powell, Marder & Nusbaum, In Prep.)

GPR Selectively Prolongs the CabPK-GMR Retraction Phase

CabPK-Elicited Rhythm:



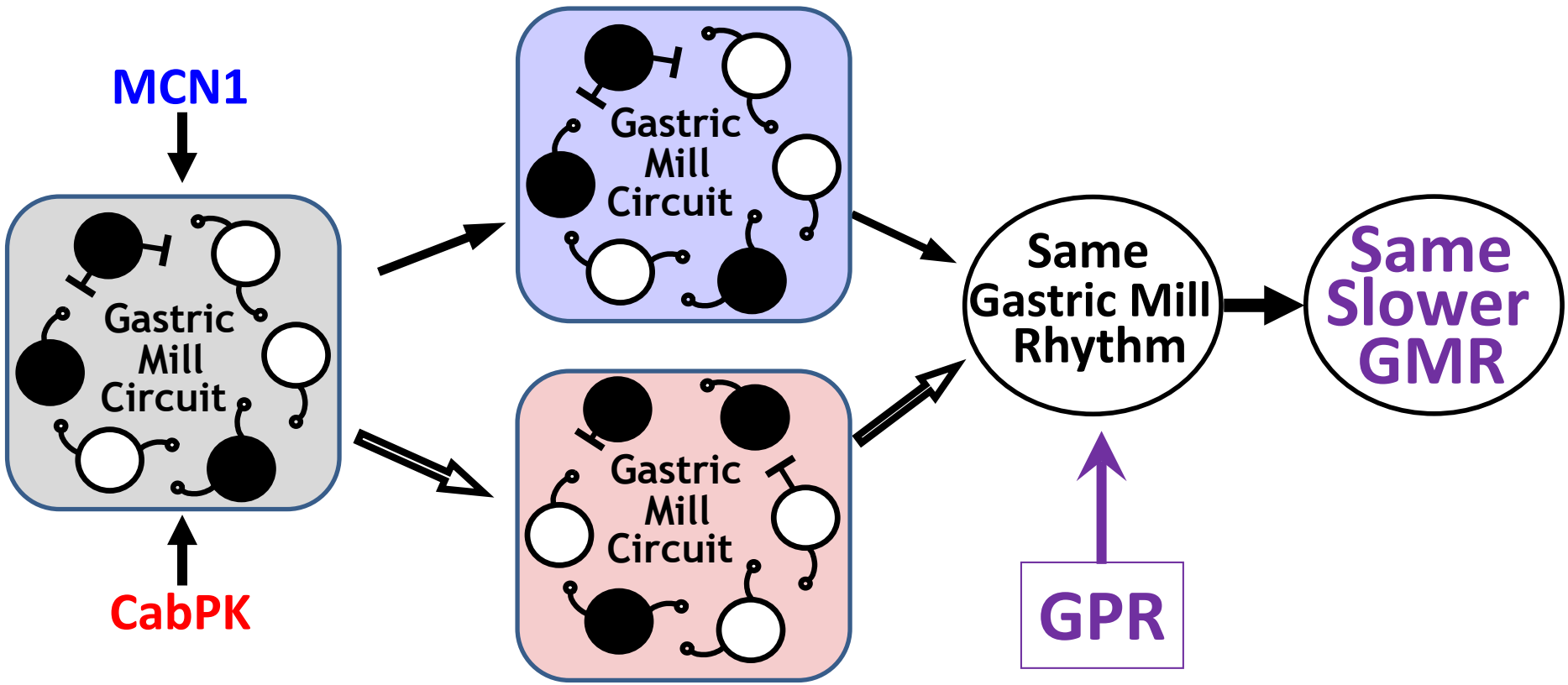
Retraction (LG Inter-Burst) Duration



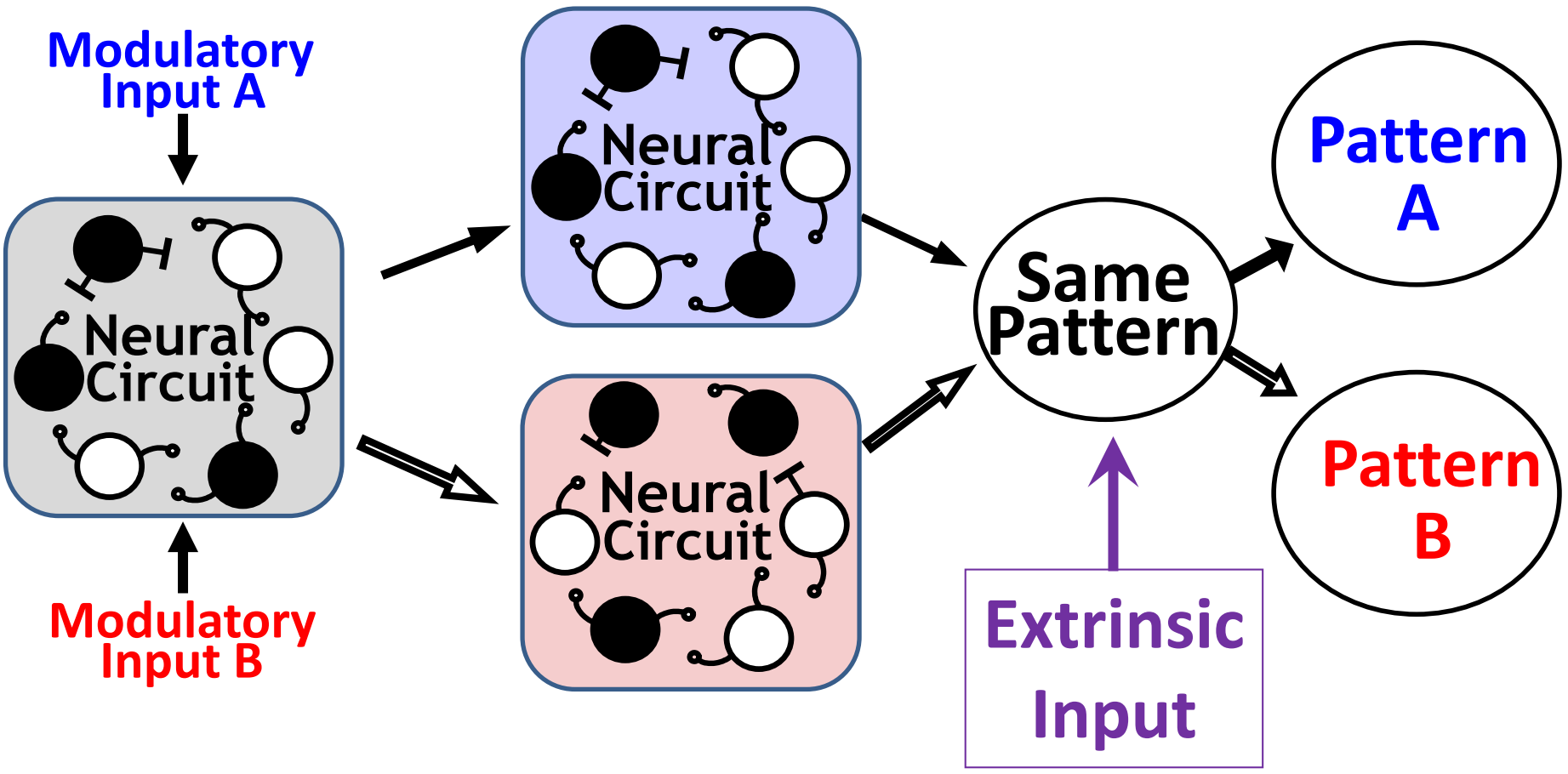
(n=16)
*p = 0.005
#p = 0.002

(CabPK: Powell, Marder & Nusbaum, In Prep.)

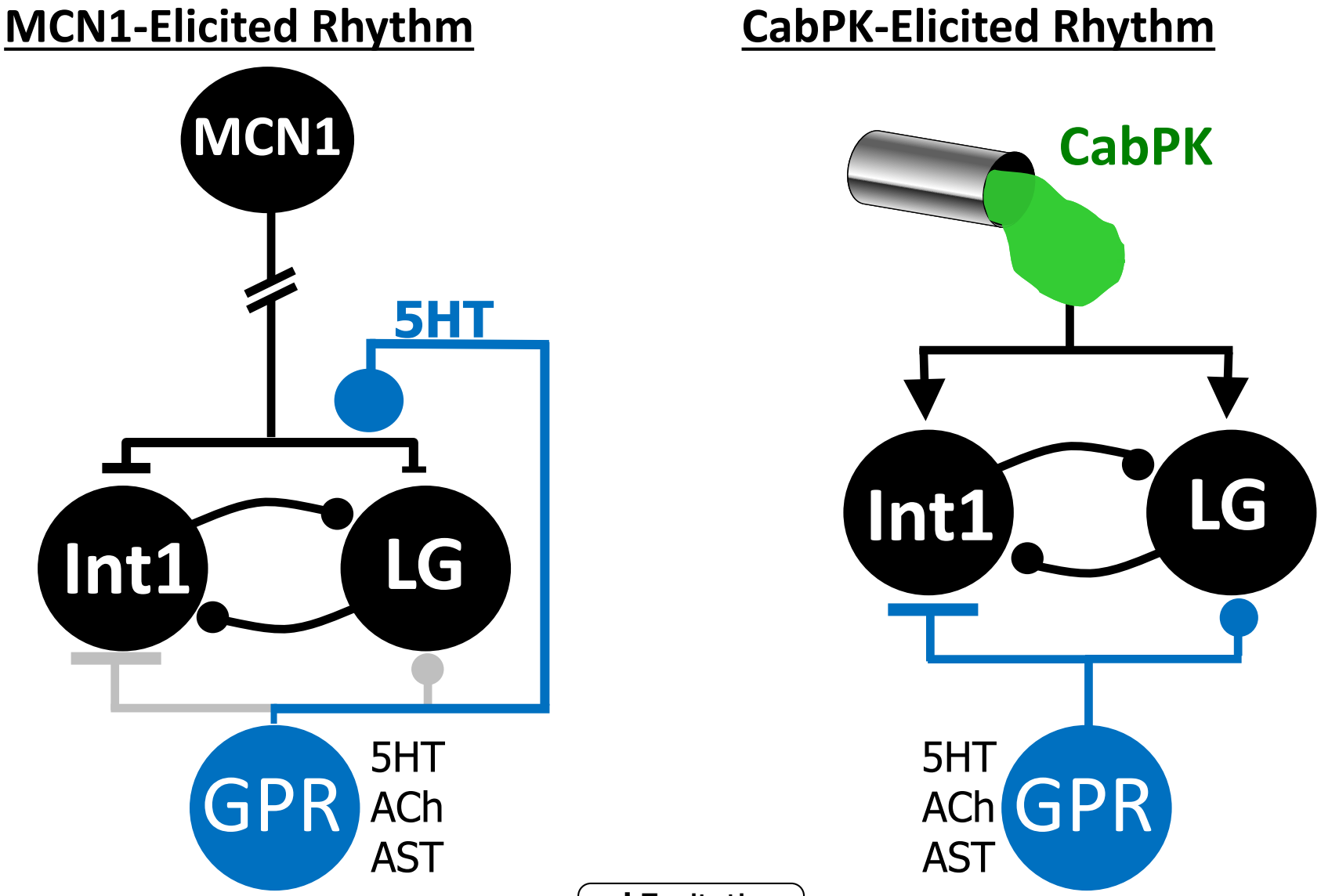
Conserved Response to Sensory Feedback by Different Circuit States



Hypothesis: Different Circuit States Respond Differently to an Unchanging Input

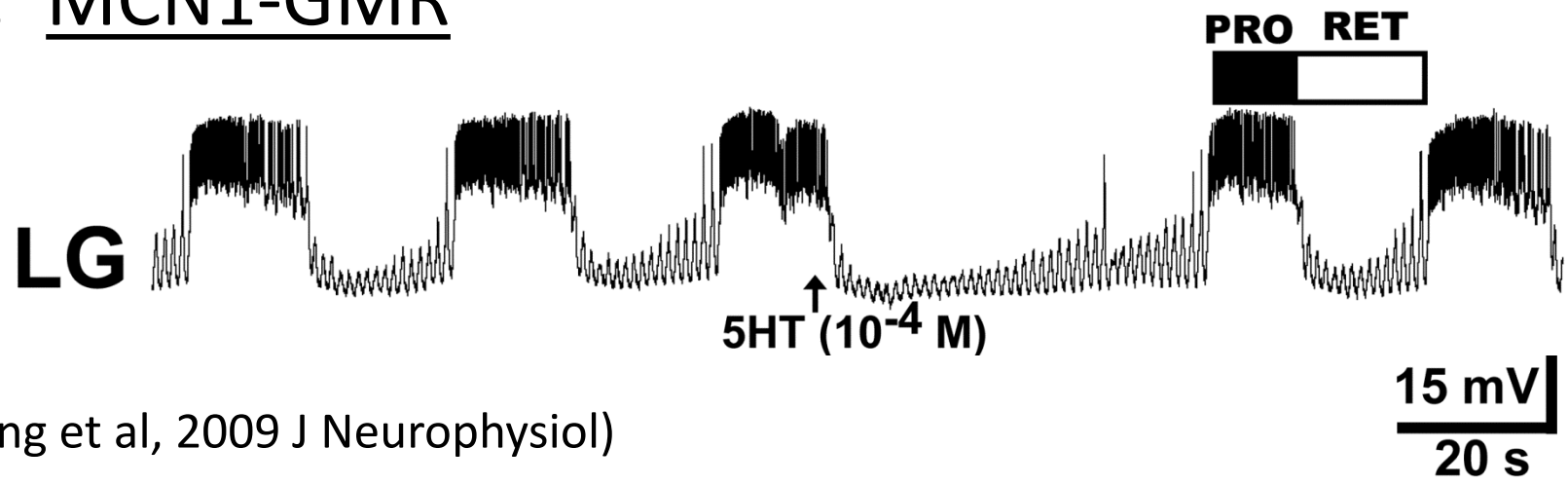


GPR Transmitter Action on the CabPK-GMR



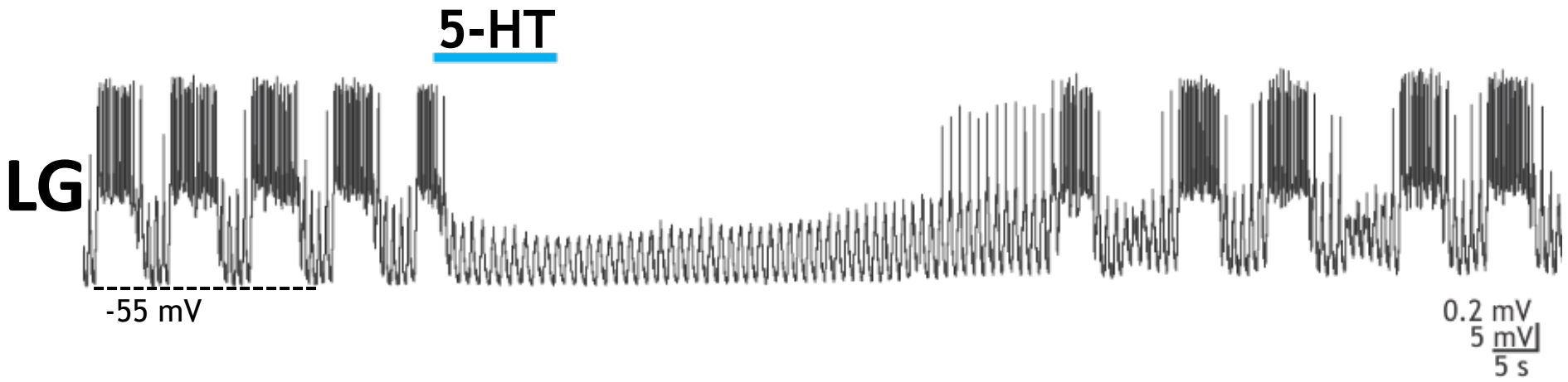
5HT Prolongs Retraction During Both GMRs

A. MCN1-GMR



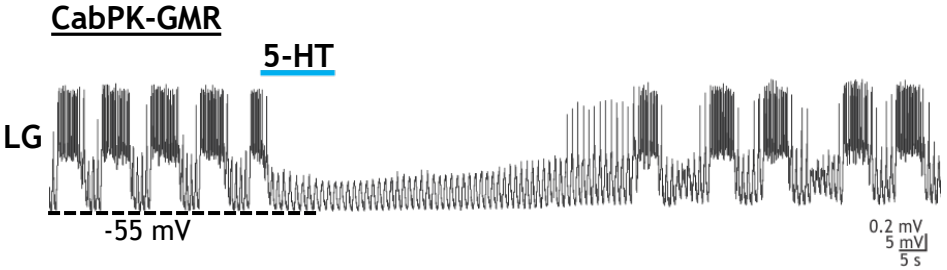
(DeLong et al, 2009 J Neurophysiol)

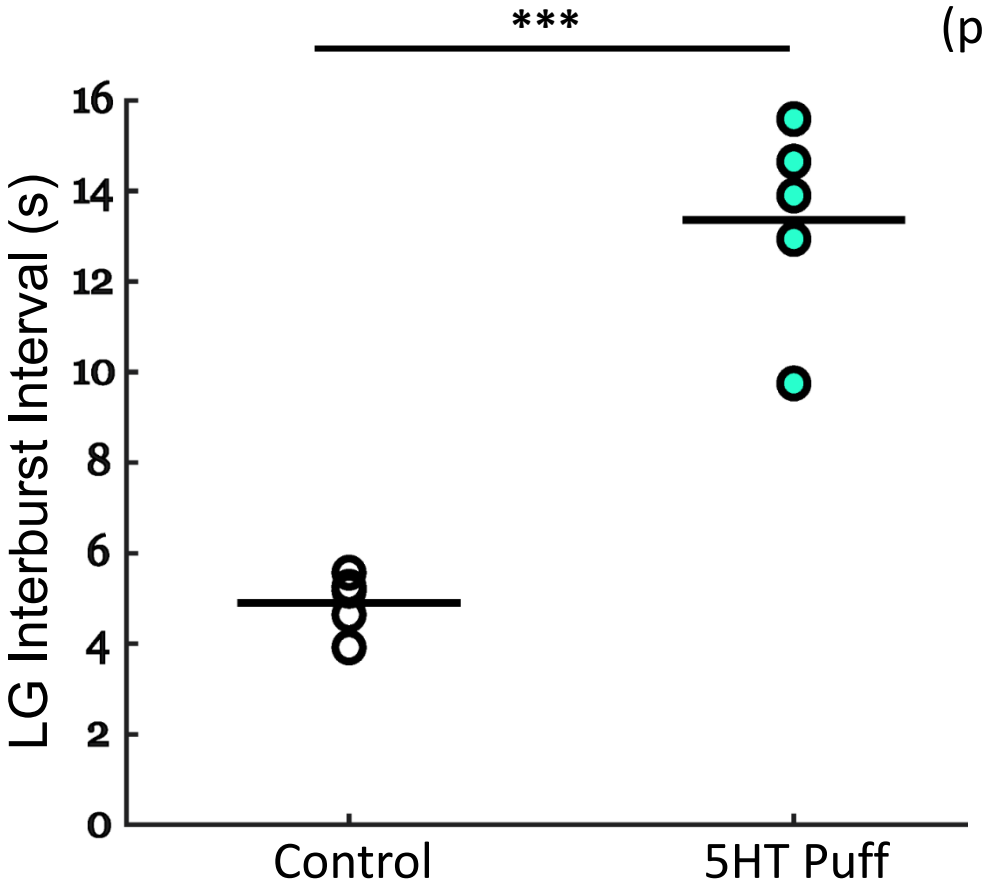
B. CabPK-GMR



(Powell, Marder, Nusbaum, In Prep.)

5HT Prolongs the CabPK-GMR Retraction Phase

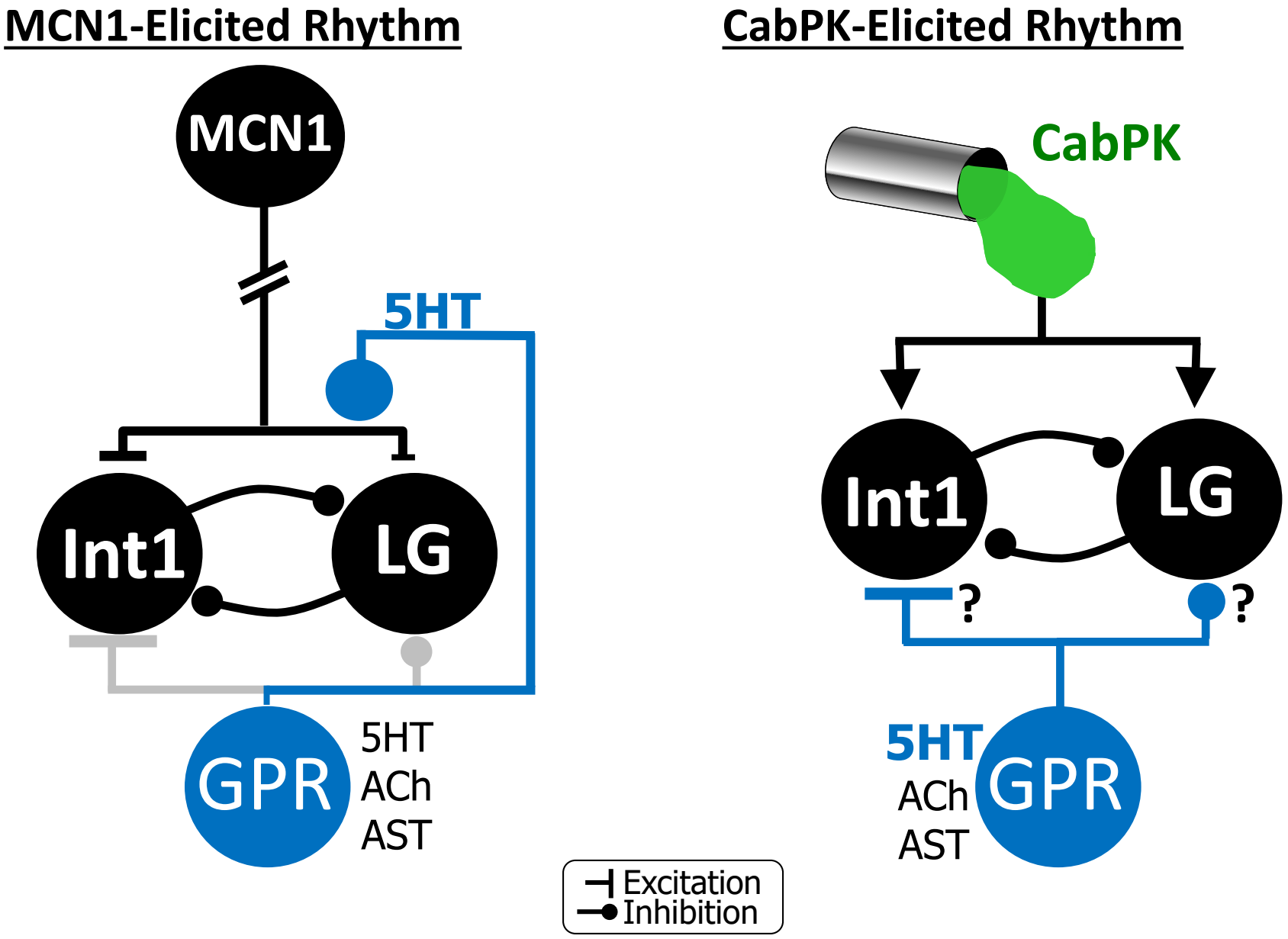




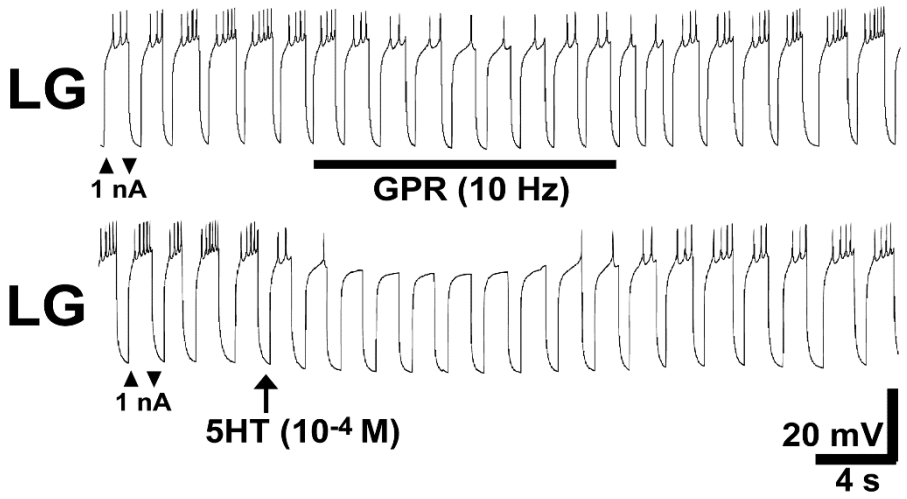
(p = 0.002)
(n = 5)

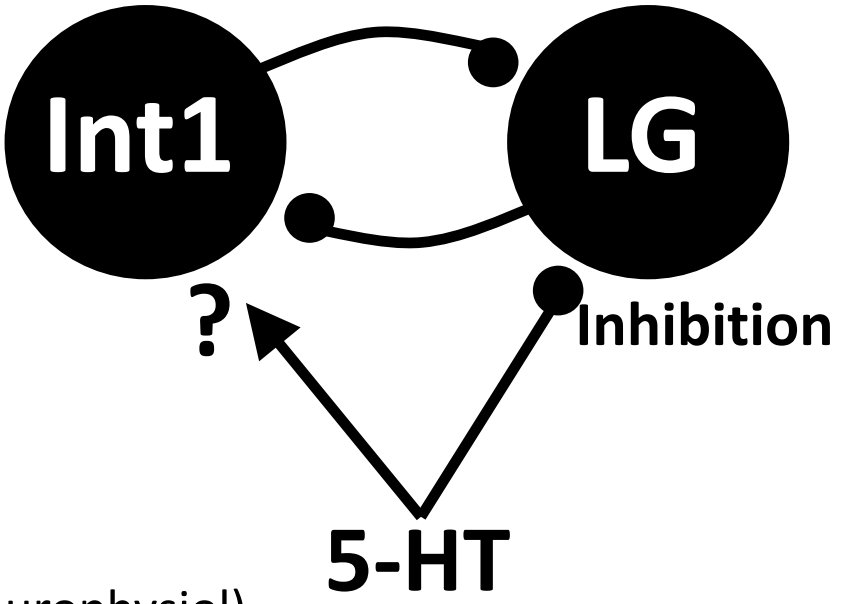
(Powell, Marder, Nusbaum, In Prep.)

Same Sensory Action via Different Synapses



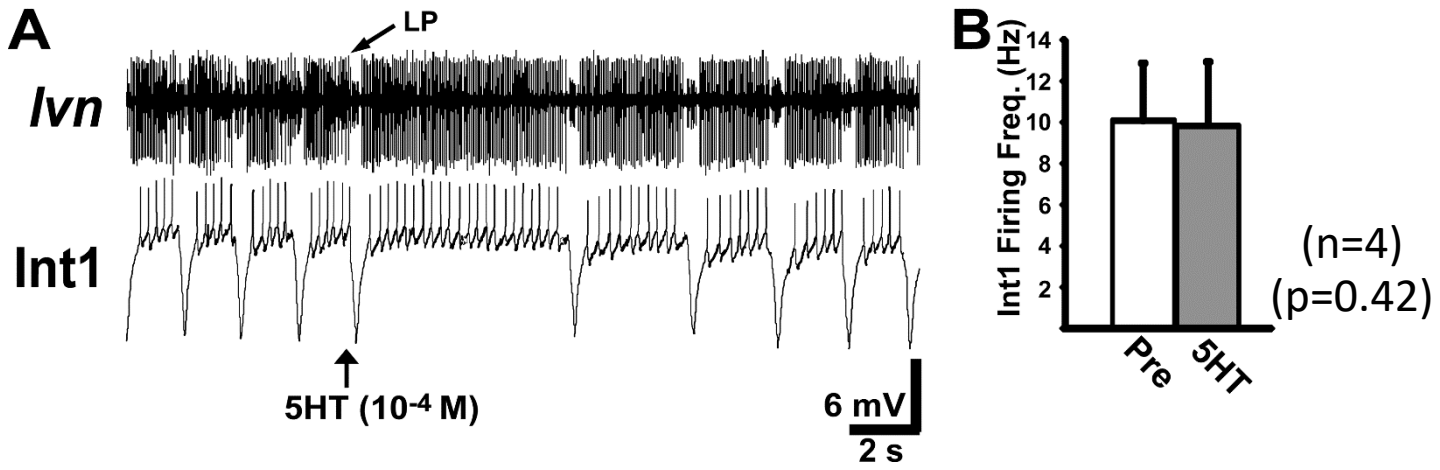
5HT Mimics GPR Inhibition of LG Neuron

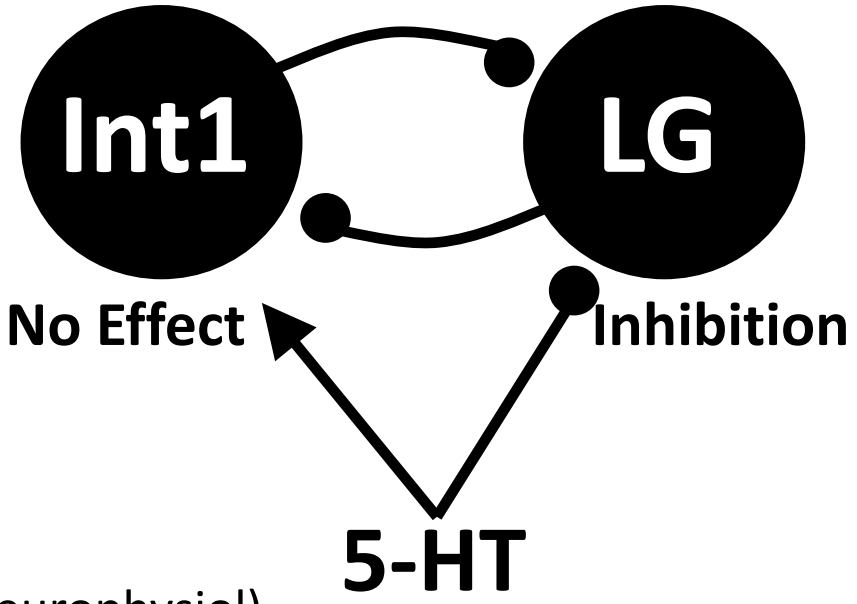




(DeLong et al, 2009 J Neurophysiol)

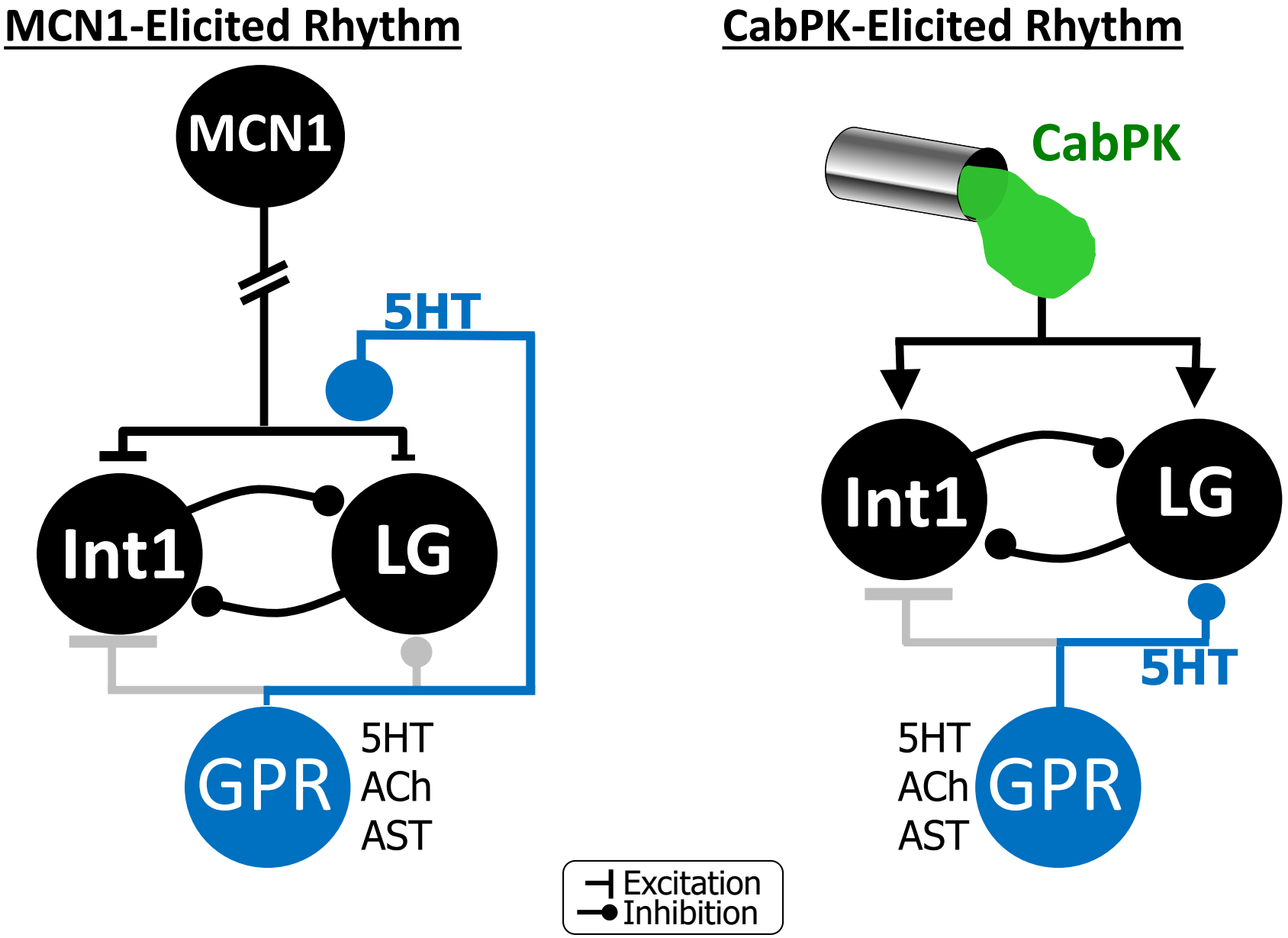
5HT Does Not Alter Int1 Activity



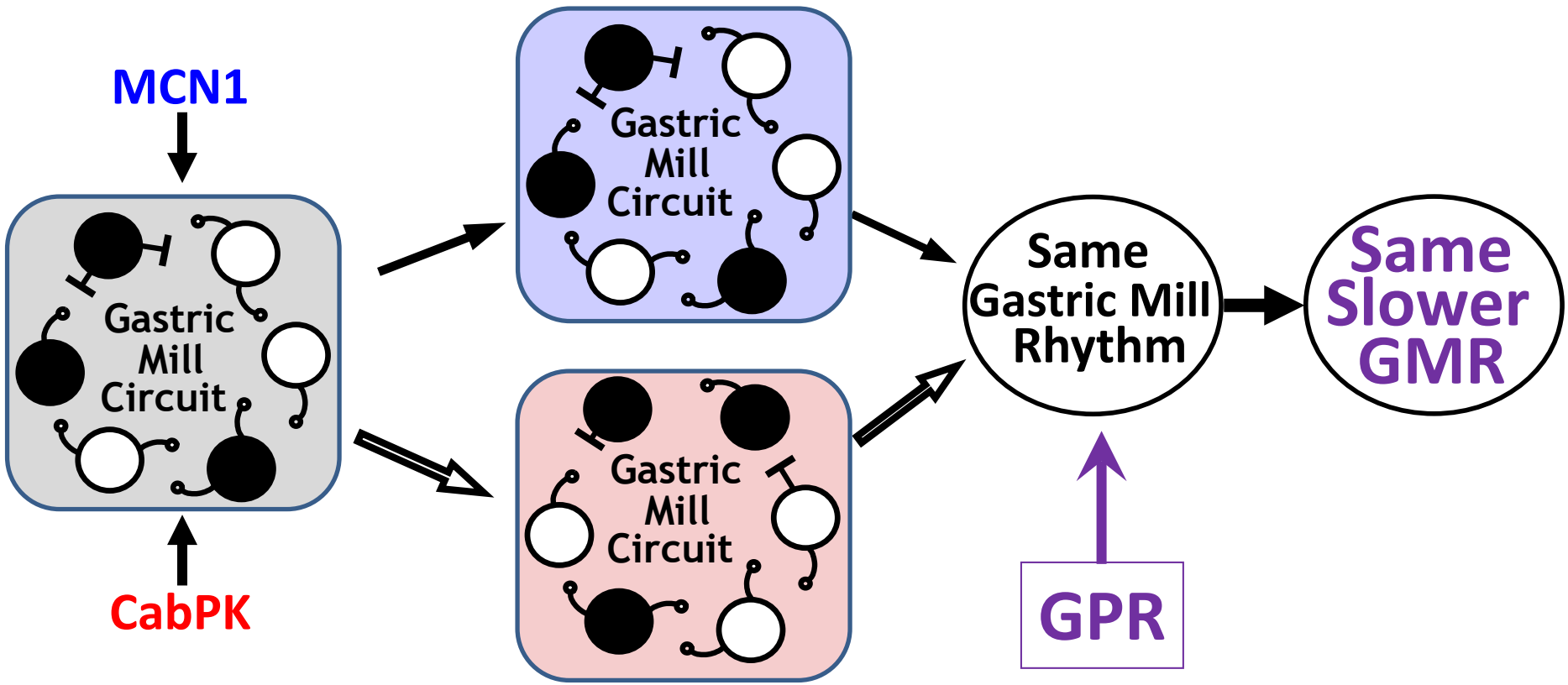


(DeLong et al, 2009 J Neurophysiol)

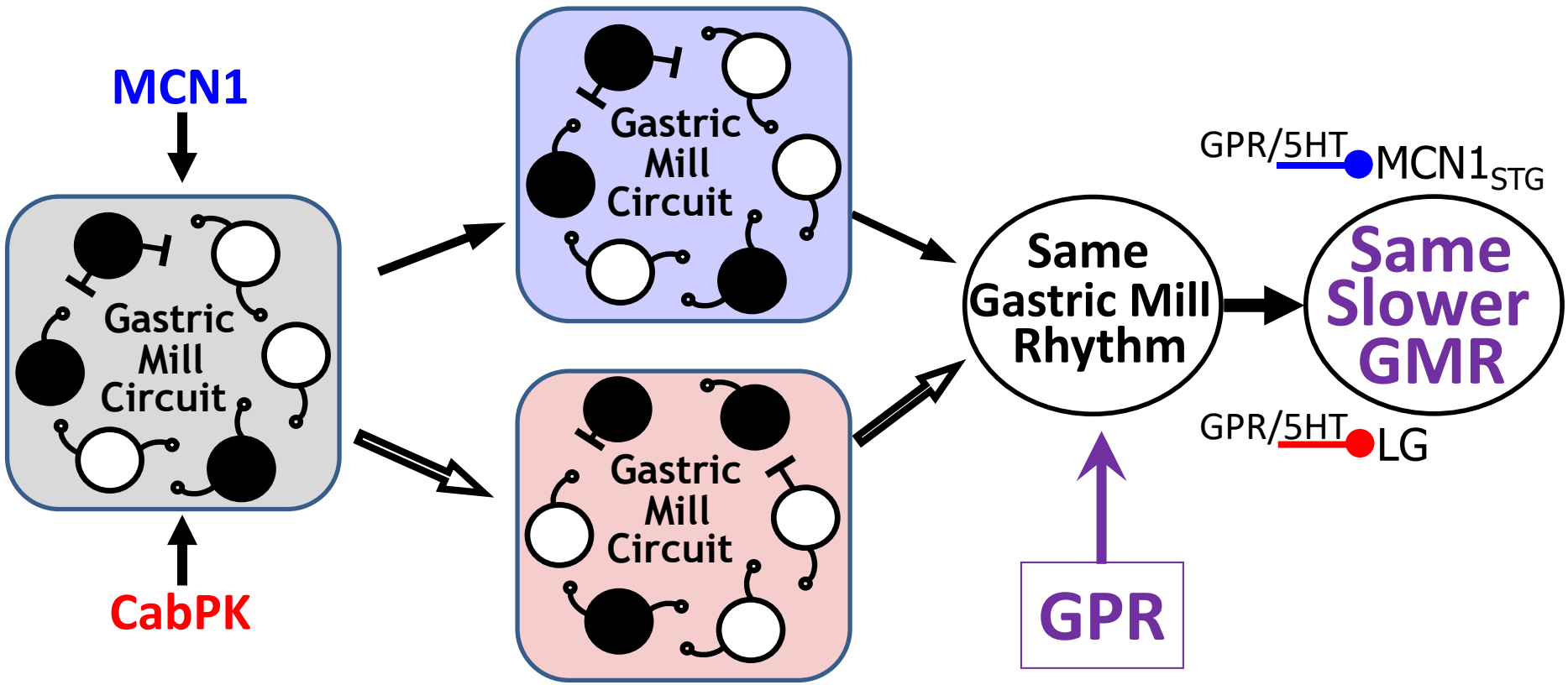
Same Sensory Action via Different Synapses



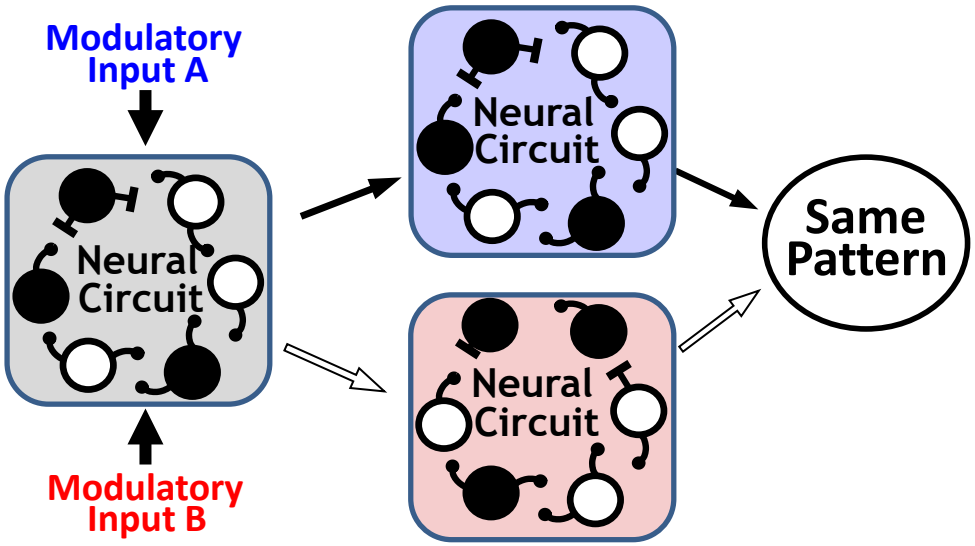
Conserved Response to Sensory Feedback by Different Circuit States via Different Synapses



Conserved Response to Sensory Feedback by Different Circuit States via Different Synapses

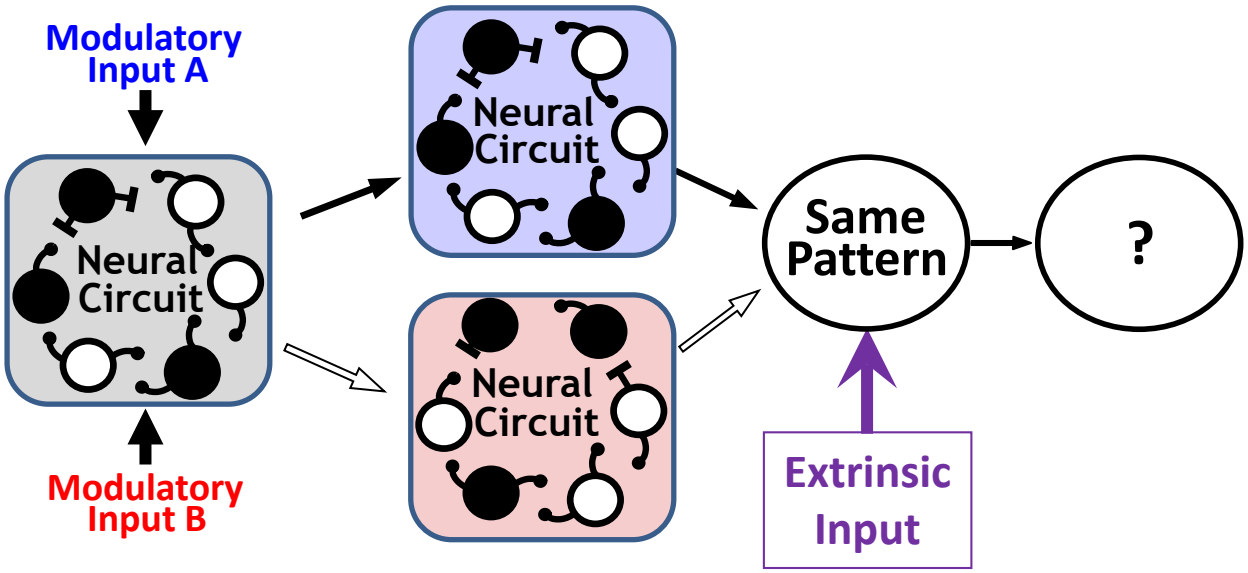


Neural Circuit Flexibility



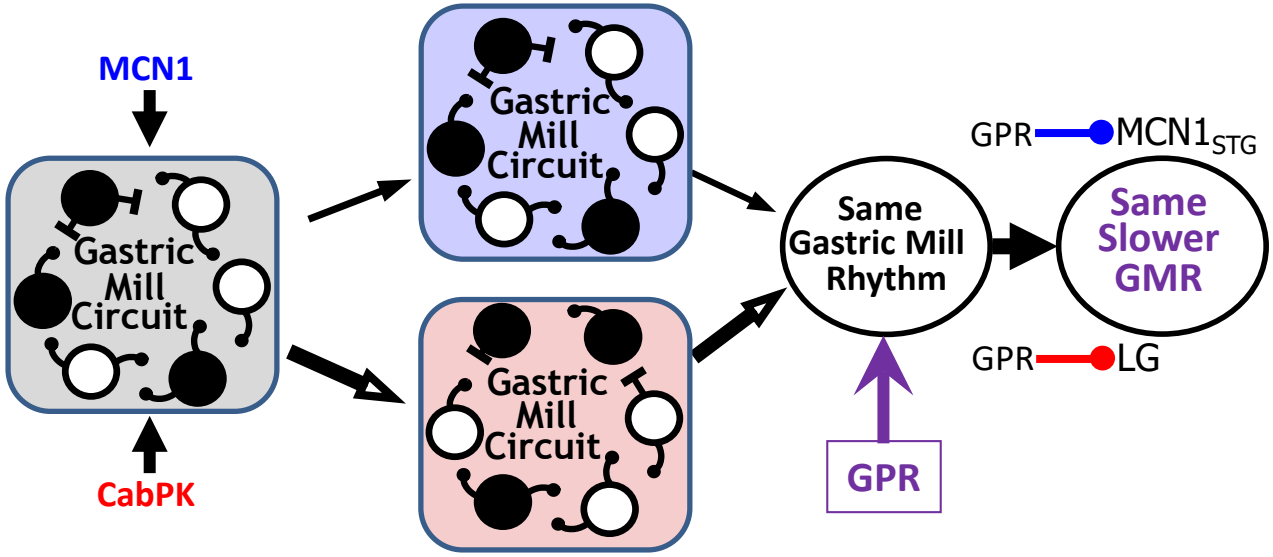
- **Different circuit states can generate the same neural activity pattern.**

Neural Circuit Flexibility



- **An extrinsic input can have divergent (CCAP) or convergent (GPR) action on different circuit states.**

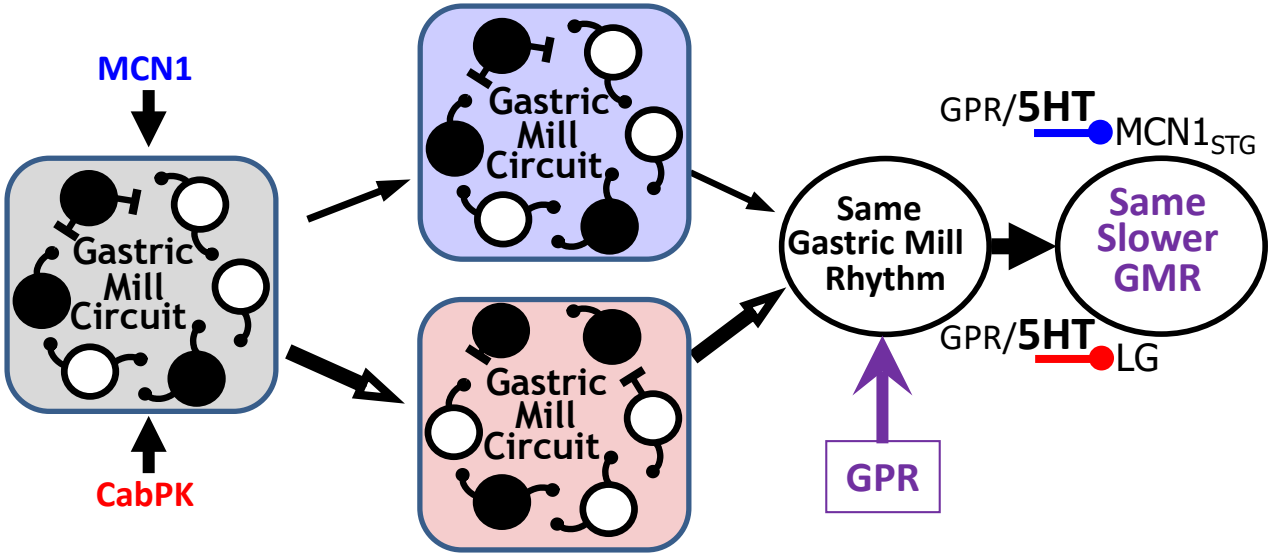
Neural Circuit Flexibility



- **Convergent actions on different circuit states can result from different synaptic pathways.**

- **Conserved action of applied modulator is not sufficient to establish conserved mechanism.**

Neural Circuit Flexibility



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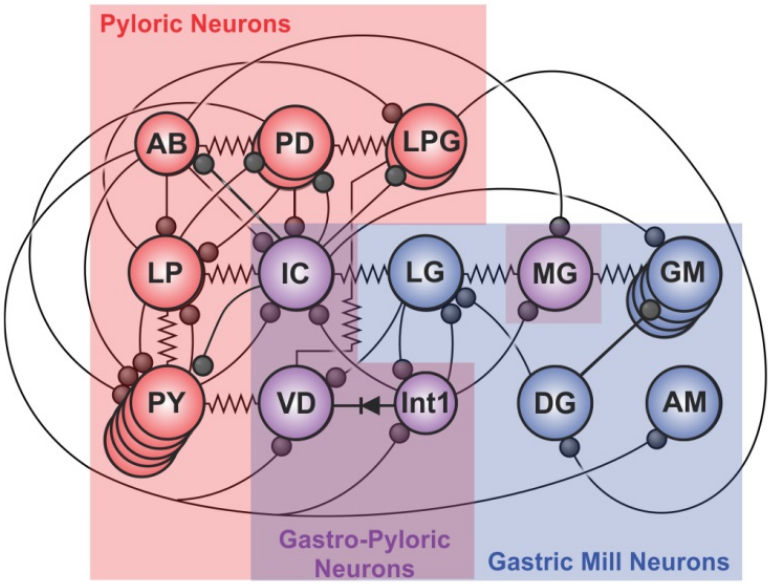
Neural Circuit Flexibility



- **Establishing a connectome is necessary but not sufficient for understanding neural circuit operation.**

Acknowledgments

Nusbaum Lab

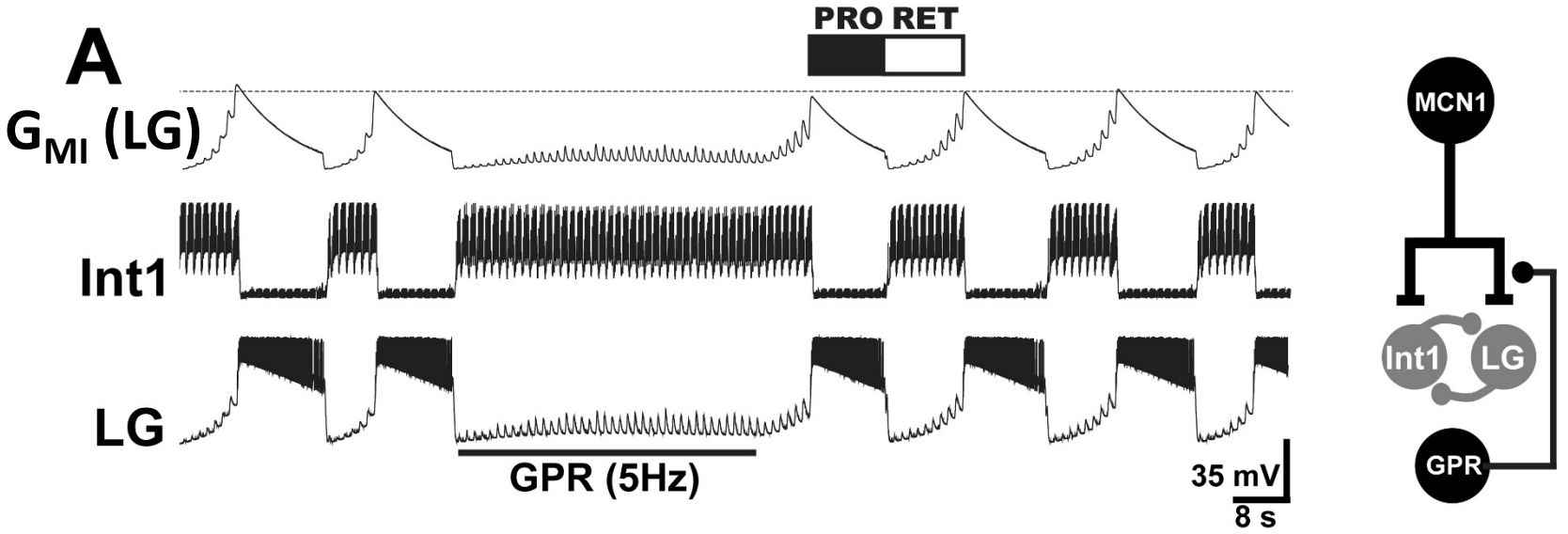
Mark Beenhakker **Dawn Blitz**
Aaron Cook **Melissa Coleman**
Nick DeLong **Matt Kirby**
Jason Rodriguez **Shari Saideman**

Eve Marder Lab
(Brandeis Univ.)
Daniel Powell

Support: NIH-NINDS

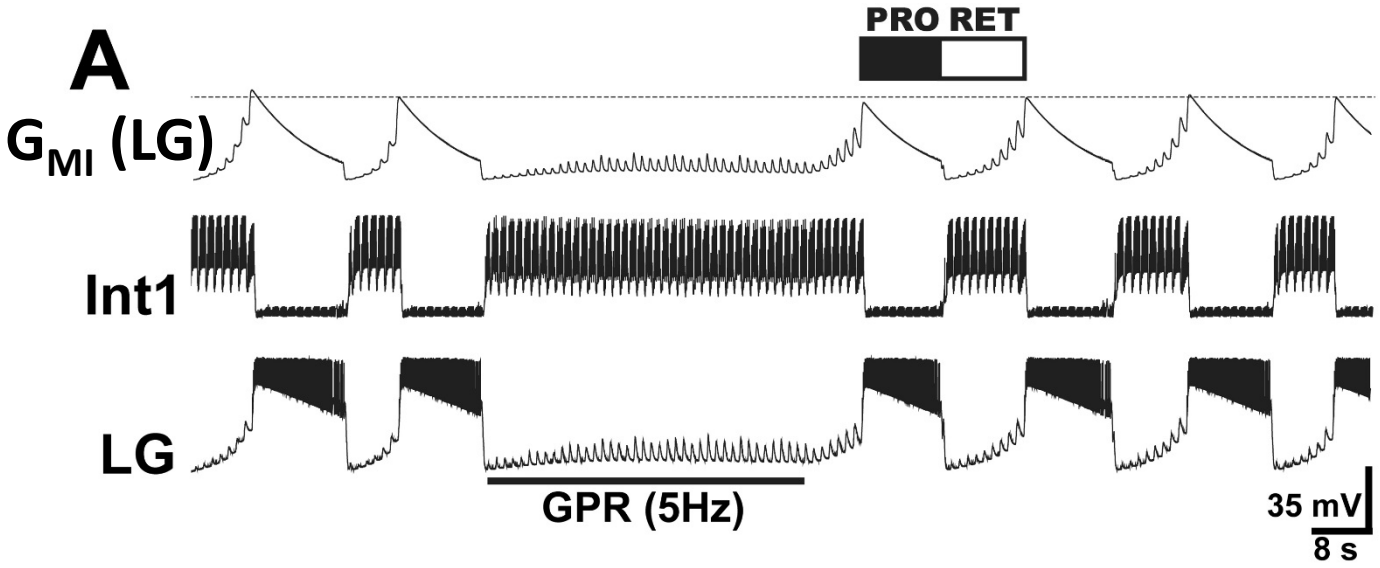

THANX

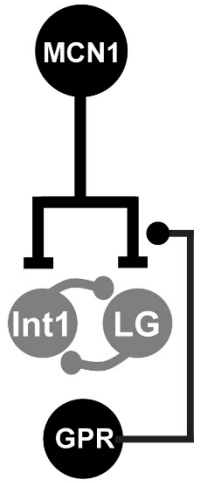
GPR Regulates the MCN1-Gastric Mill Rhythm: Selective Presynaptic Inhibition of MCN1

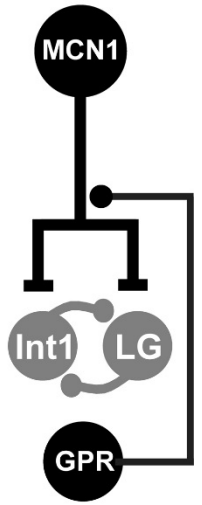


(DeLong et al, 2009 J Neurophysiol)

GPR Regulates the MCN1-Gastric Mill Rhythm: Selective Presynaptic Inhibition of MCN1







(DeLong et al, 2009 J Neurophysiol)

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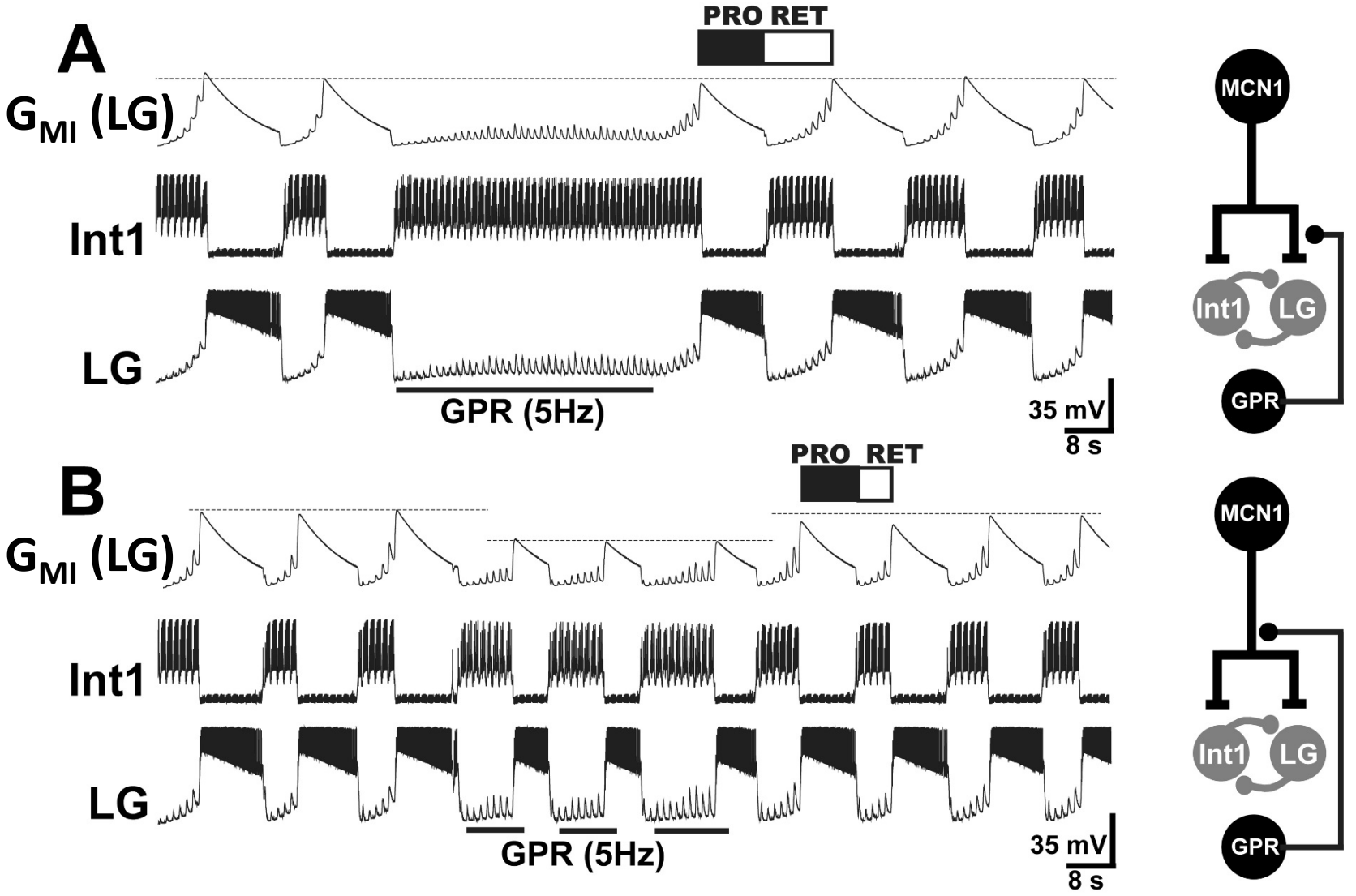

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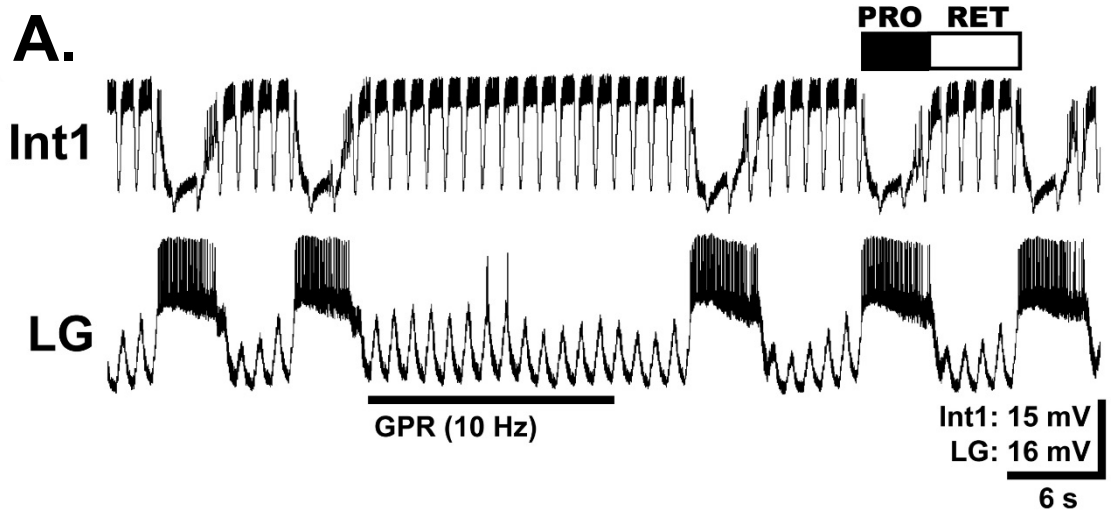

(DeLong et al, 2009 J Neurophysiol)

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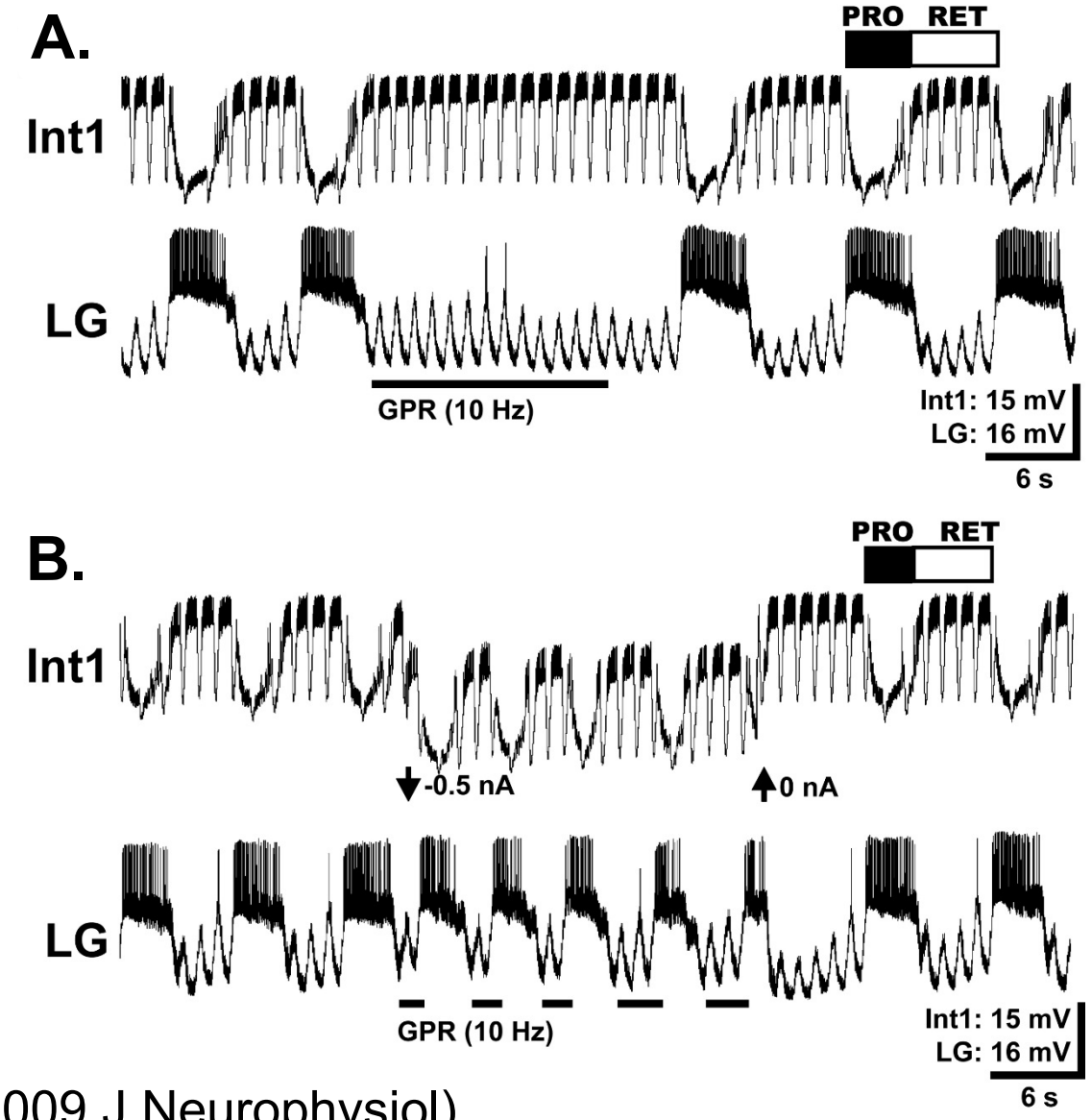
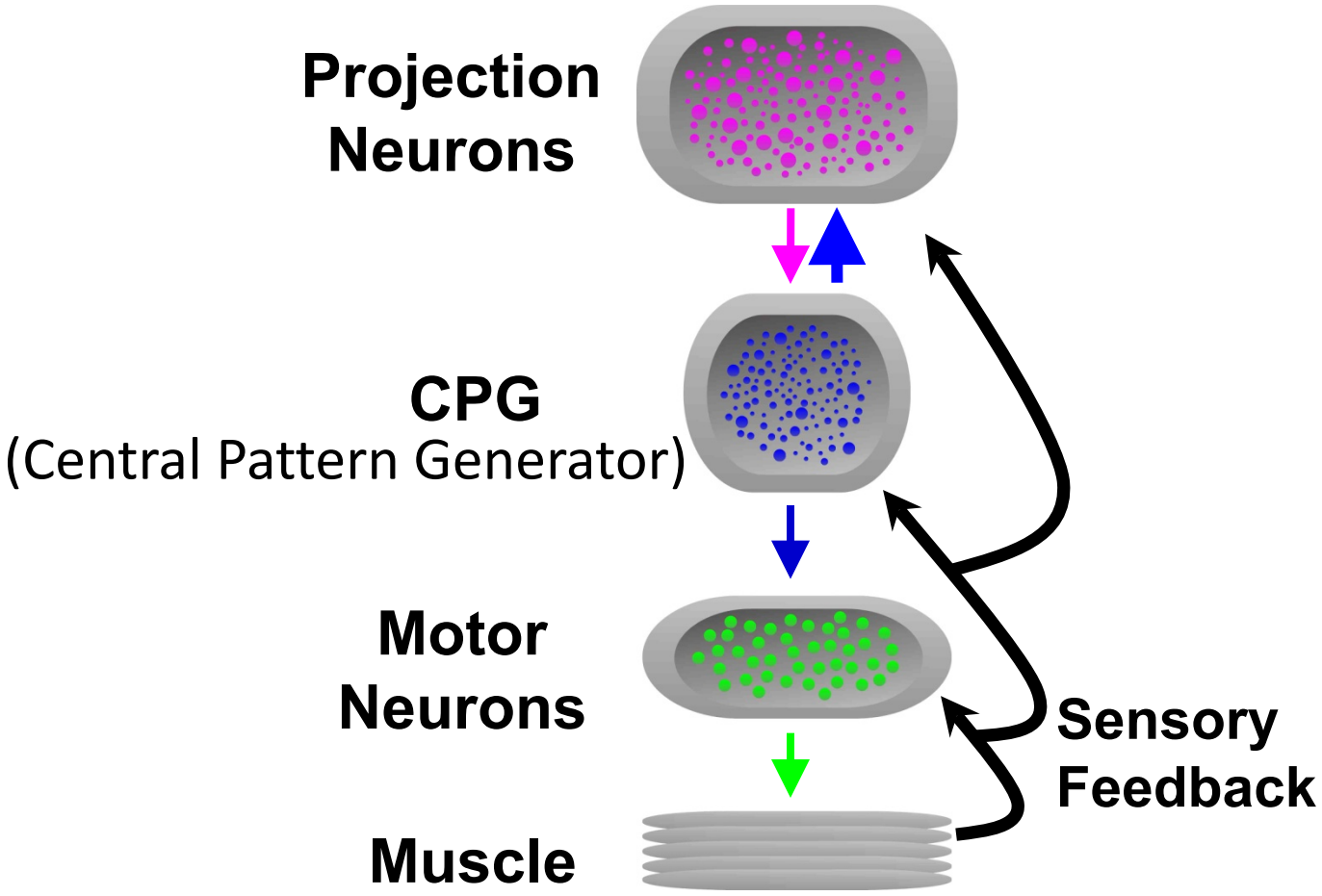


(DeLong et al, 2009 J Neurophysiol)

Rhythmic Motor Systems

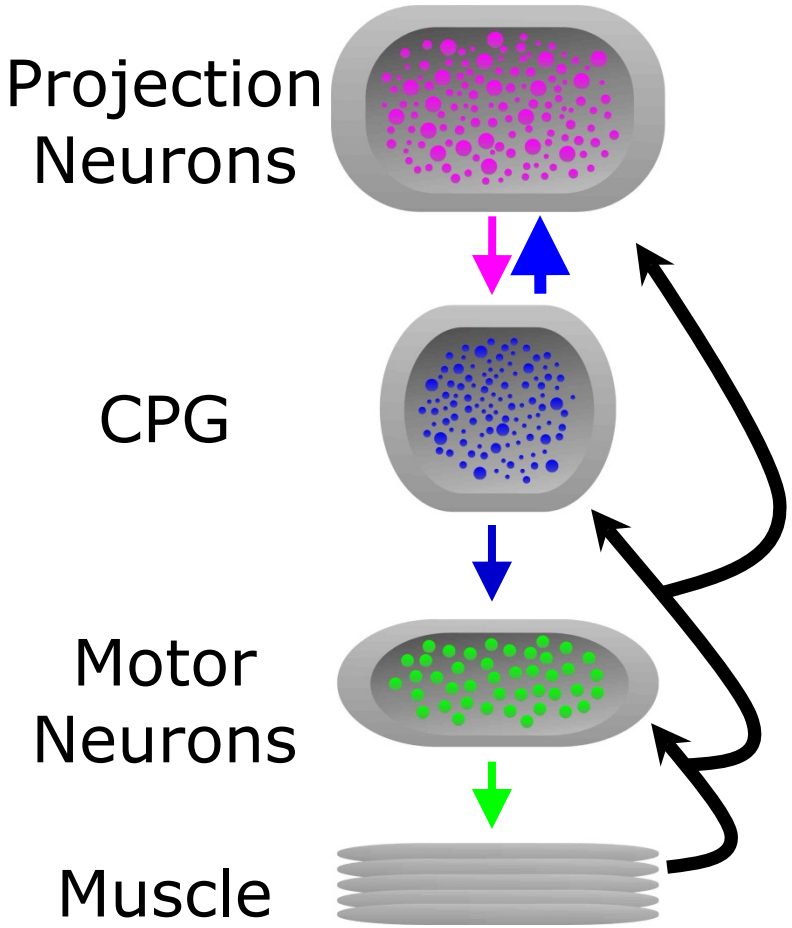
Basic Organization

("Top Down" *and* "Bottom Up")

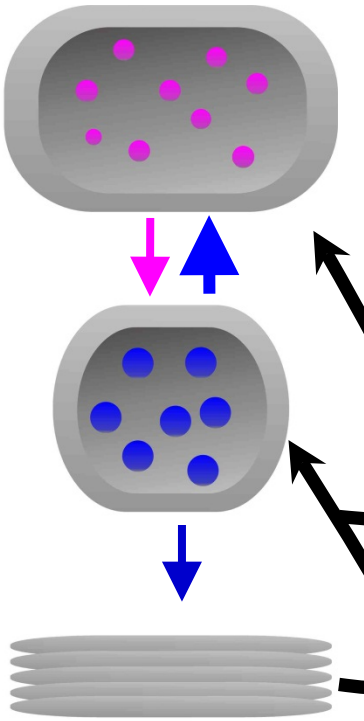


Rhythmic Motor Systems

Basic Organization



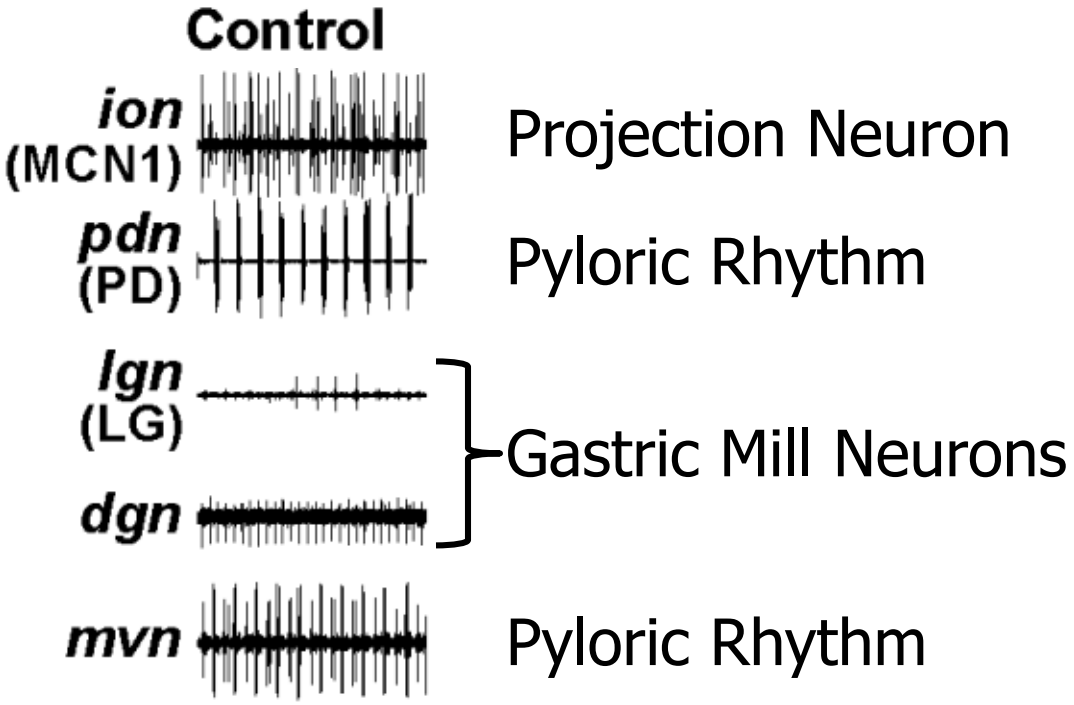
Small Model System



Cancer borealis

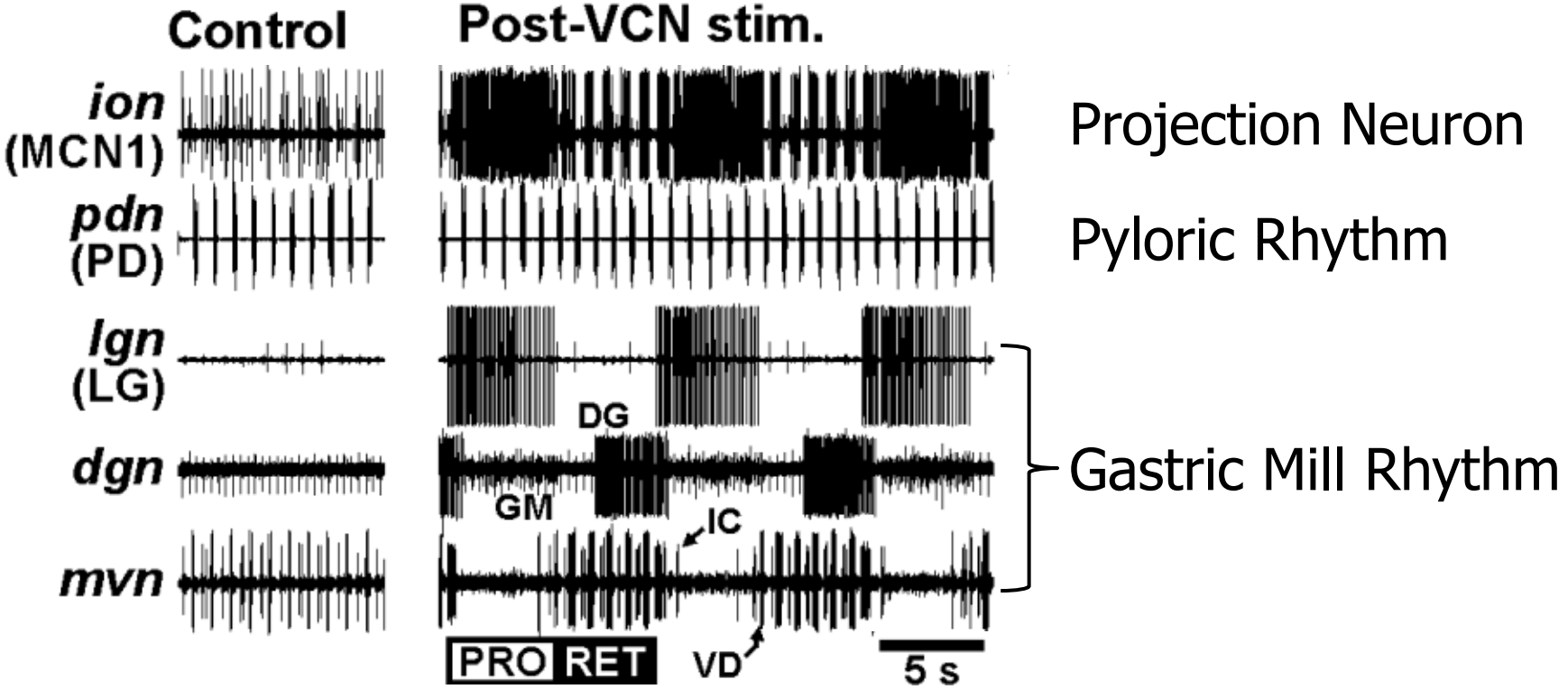
1. **Same general principles.**
2. **Neurons are:**
   Fewer.
   Small copy #.
   Larger.
3. **Projection- & CPG neurons and synapses are identified.**

Distinct Gastric Mill Rhythms



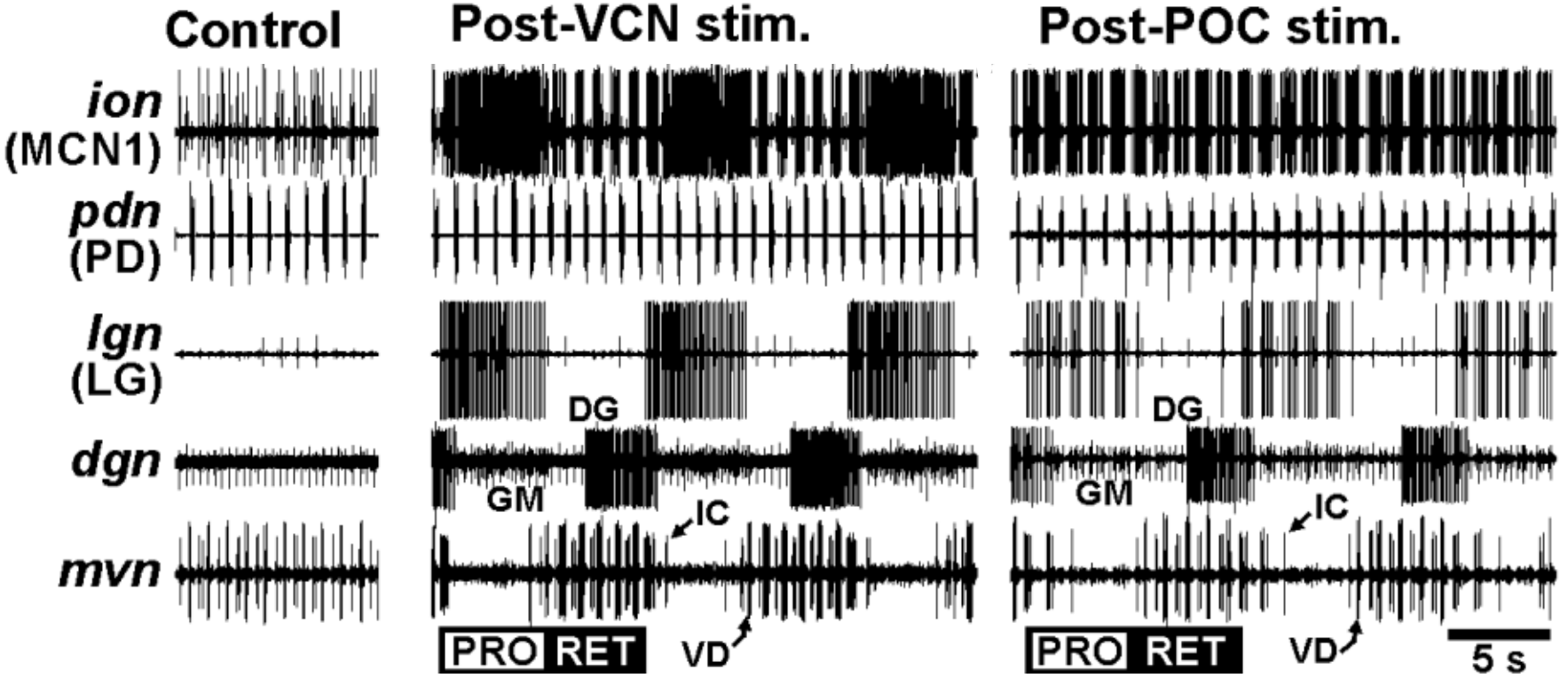
(White and Nusbaum, 2011 J Neurosci)

Distinct Gastric Mill Rhythms



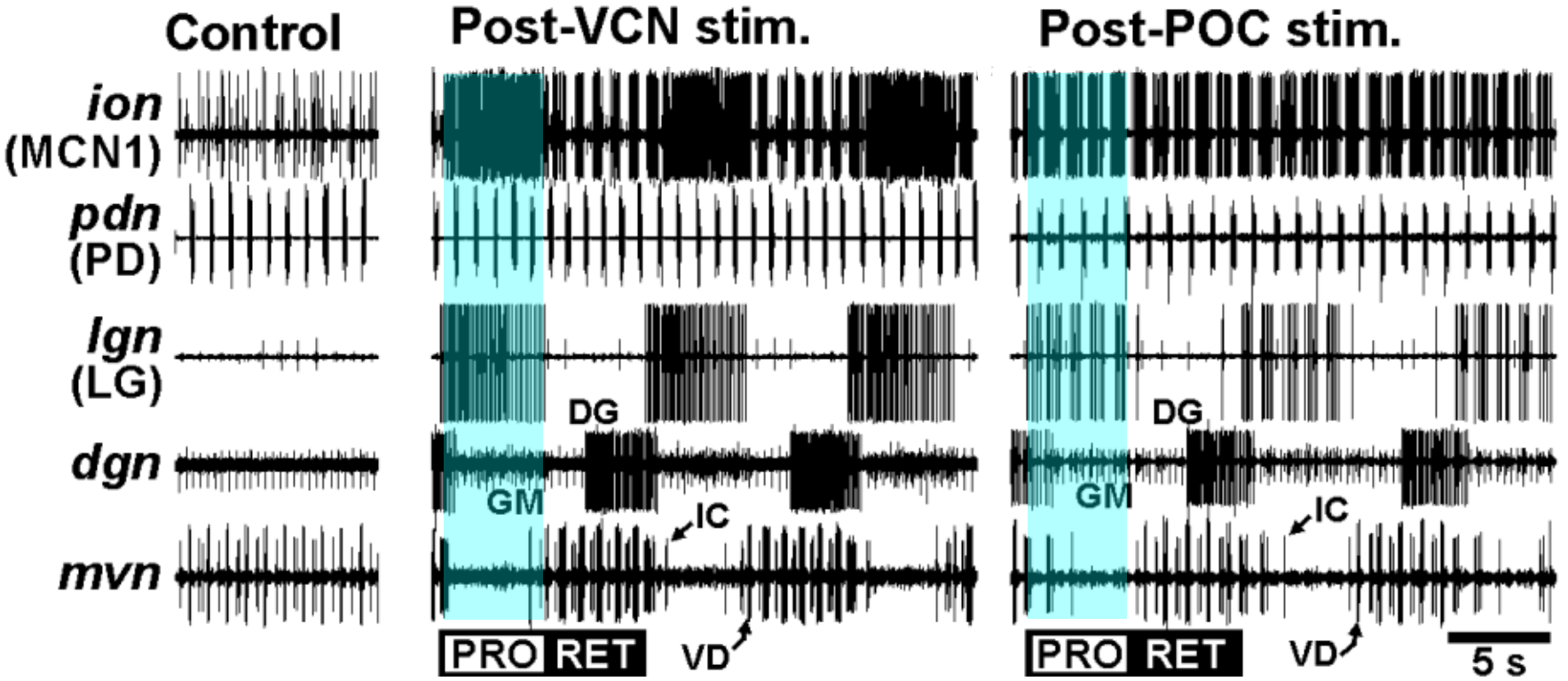
(White and Nusbaum, 2011 J Neurosci)

Distinct Gastric Mill Rhythms



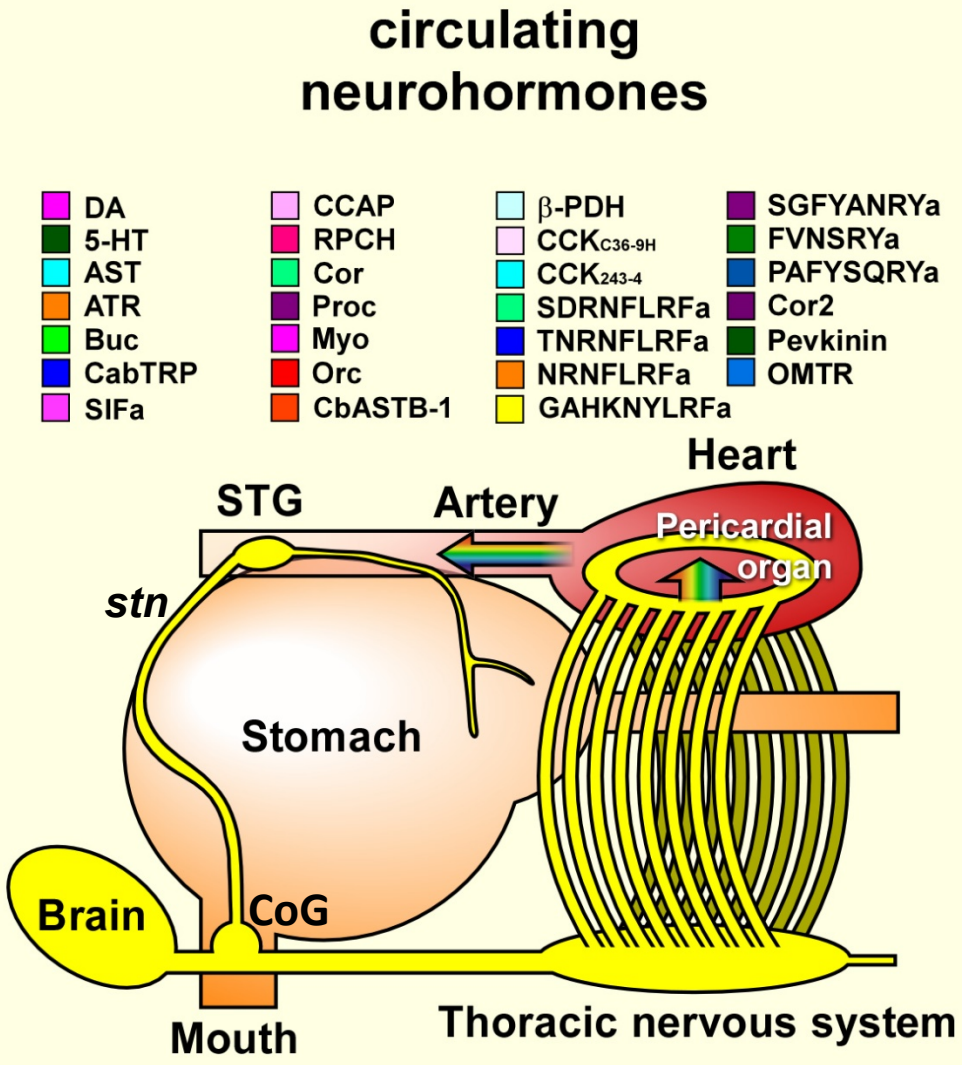
(White and Nusbaum, 2011 J Neurosci)

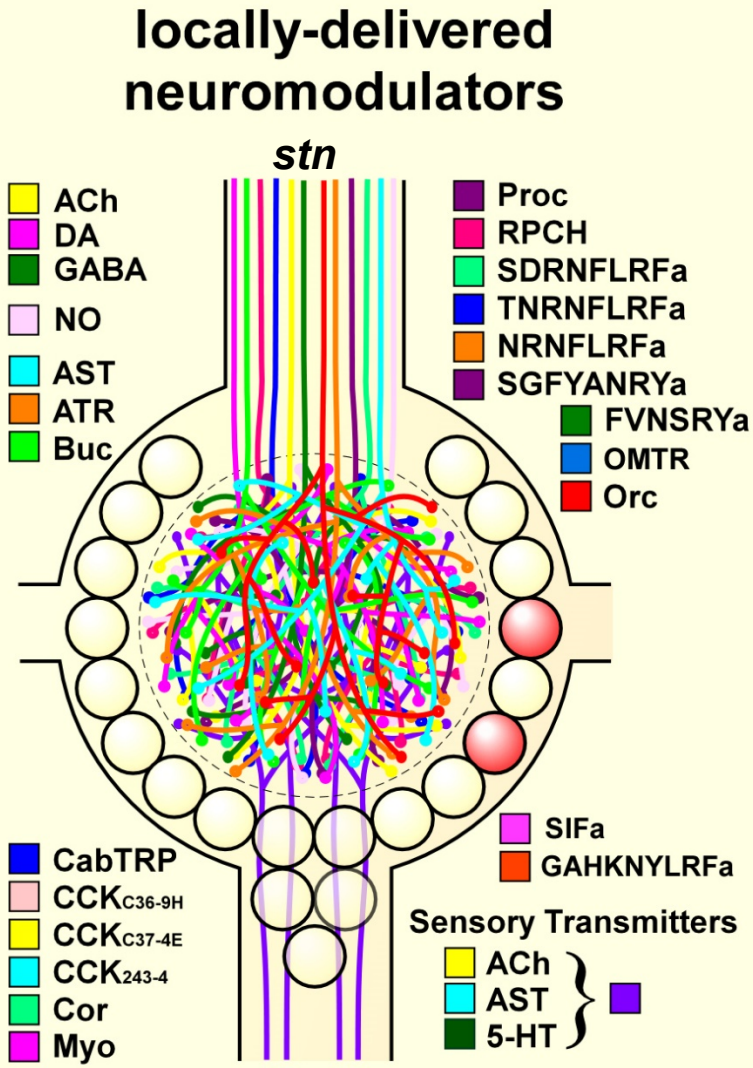
Distinct Gastric Mill Rhythms



(White and Nusbaum, 2011 J Neurosci)

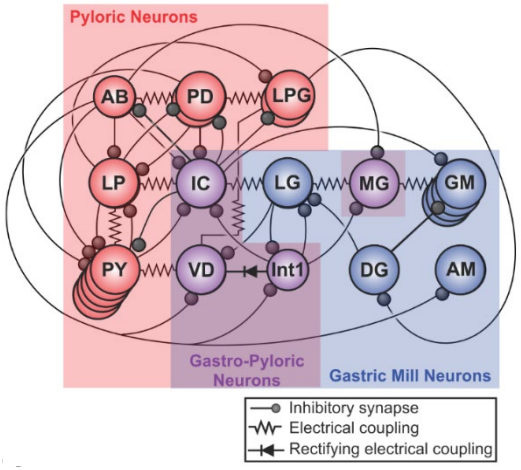
Neuromodulators in the Crab Stomatogastric System

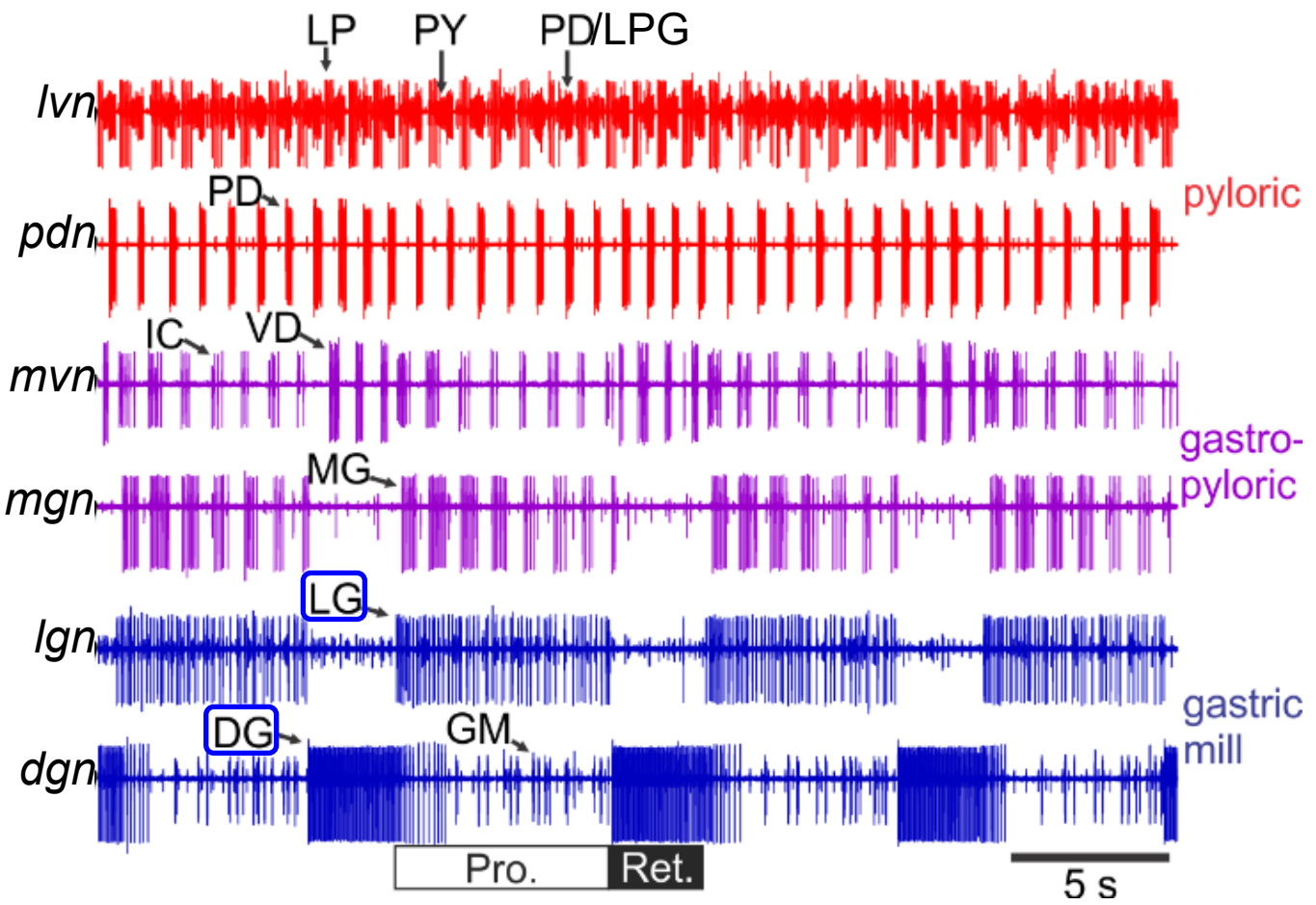




(Marder E, Lab Website)
(Updated From: Marder, 2012 Neuron)

The Gastric Mill & Pyloric Rhythms in the Crab (*Cancer borealis)* Stomatogastric Ganglion





(Nusbaum et al, 2017 Nat Rev Neurosci)