



University of
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Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

ZNZ Advanced Course in Neuroscience
Mon 27.04.2015

Limbic System II

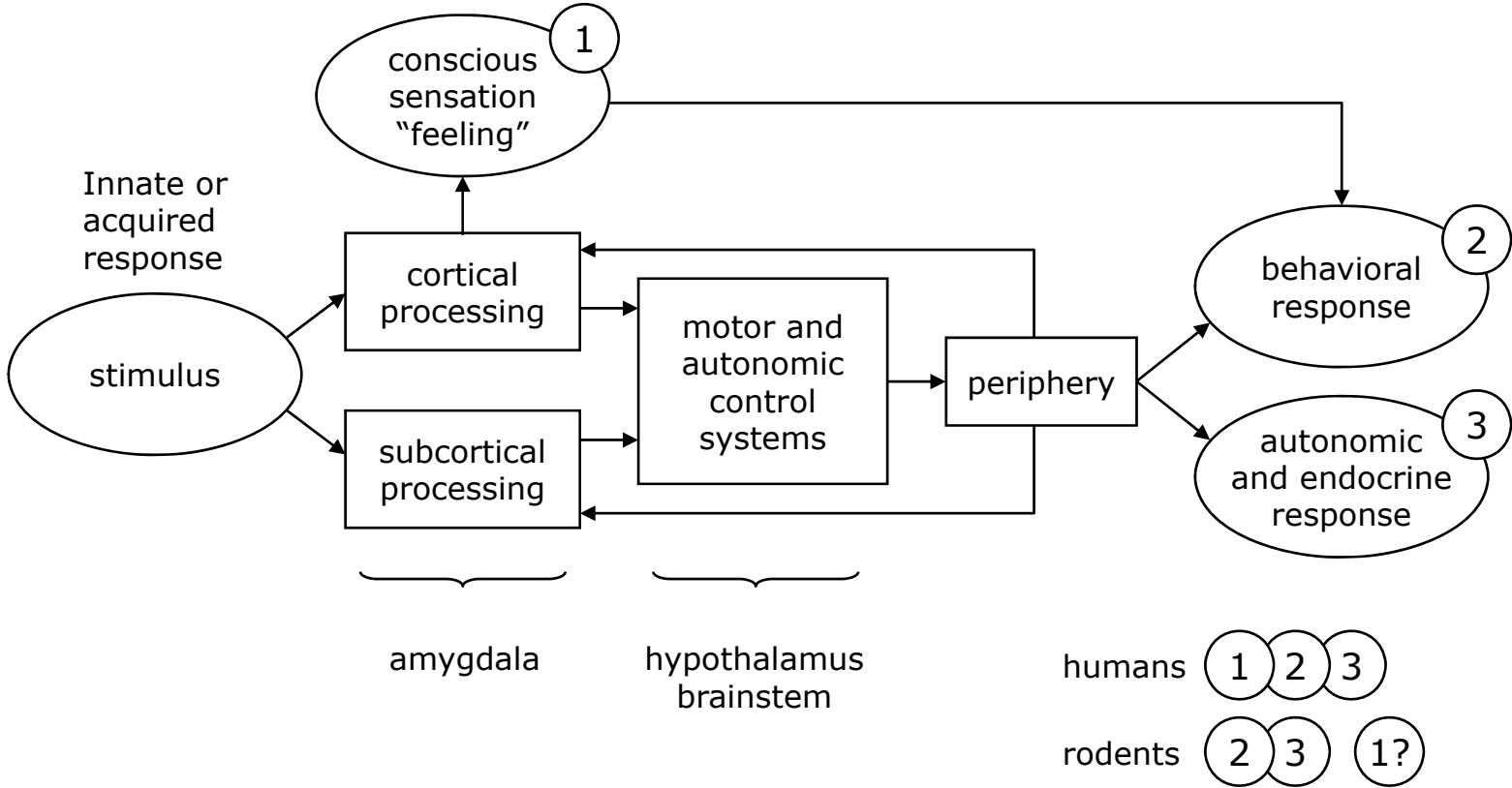
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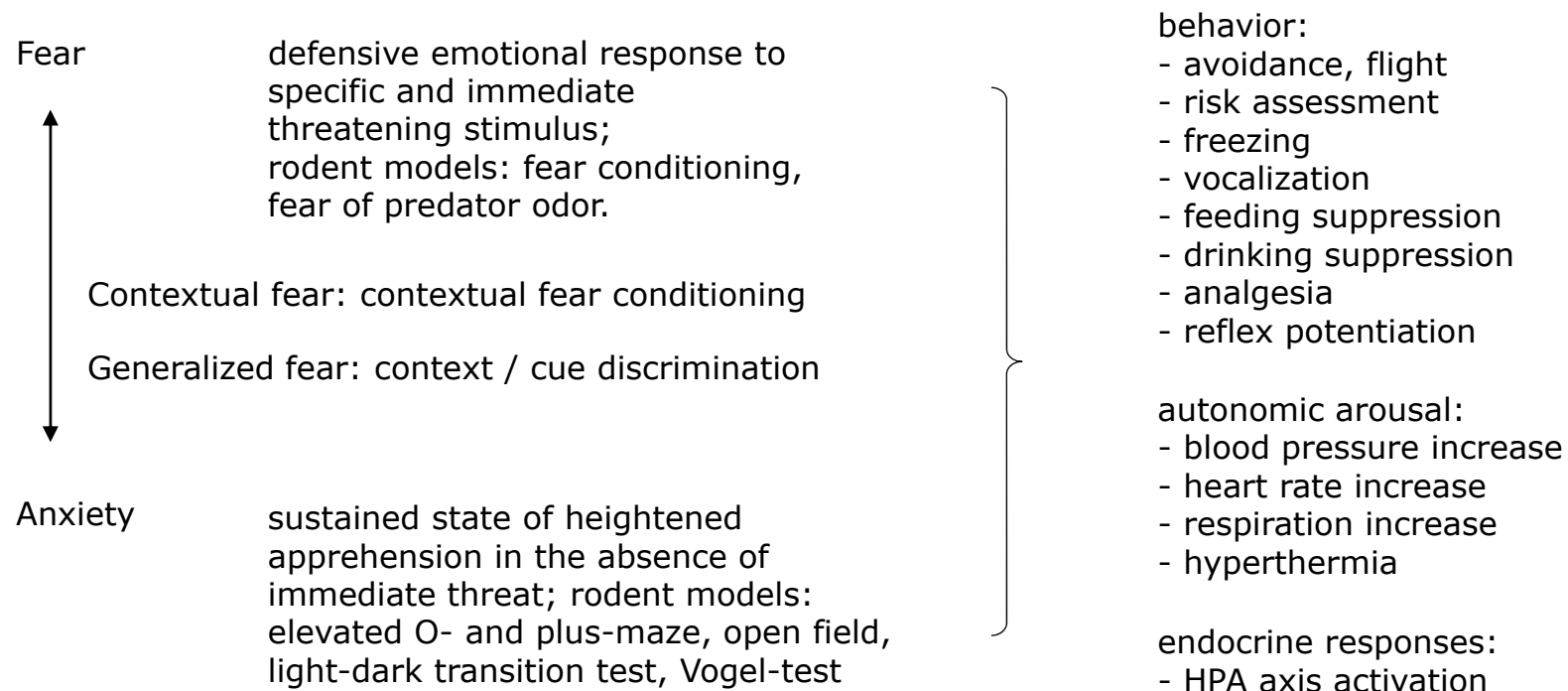
Limbic system – outline

- ① *Introduction*
 - history
 - definition
- ② *Theories of hippocampal Function – rodent tests*
 - declarative memory
 - episodic memory
 - cognitive map
 - relational memory
- ③ *The hippocampus beyond memory*
 - exploratory behavior and anxiety
 - species typical behaviors
 - home cage behavior
- ④ *Emotions*
 - general properties
 - rodent models: fear and anxiety
- ⑤ *Anatomy of the Amygdala*
 - components
 - extended amygdala
- ⑥ *Amygdala and fear conditioning*
 - behavioral model
 - brain circuits
- ⑦ *Amygdala and anxiety*
 - behavioral model
 - brain circuits

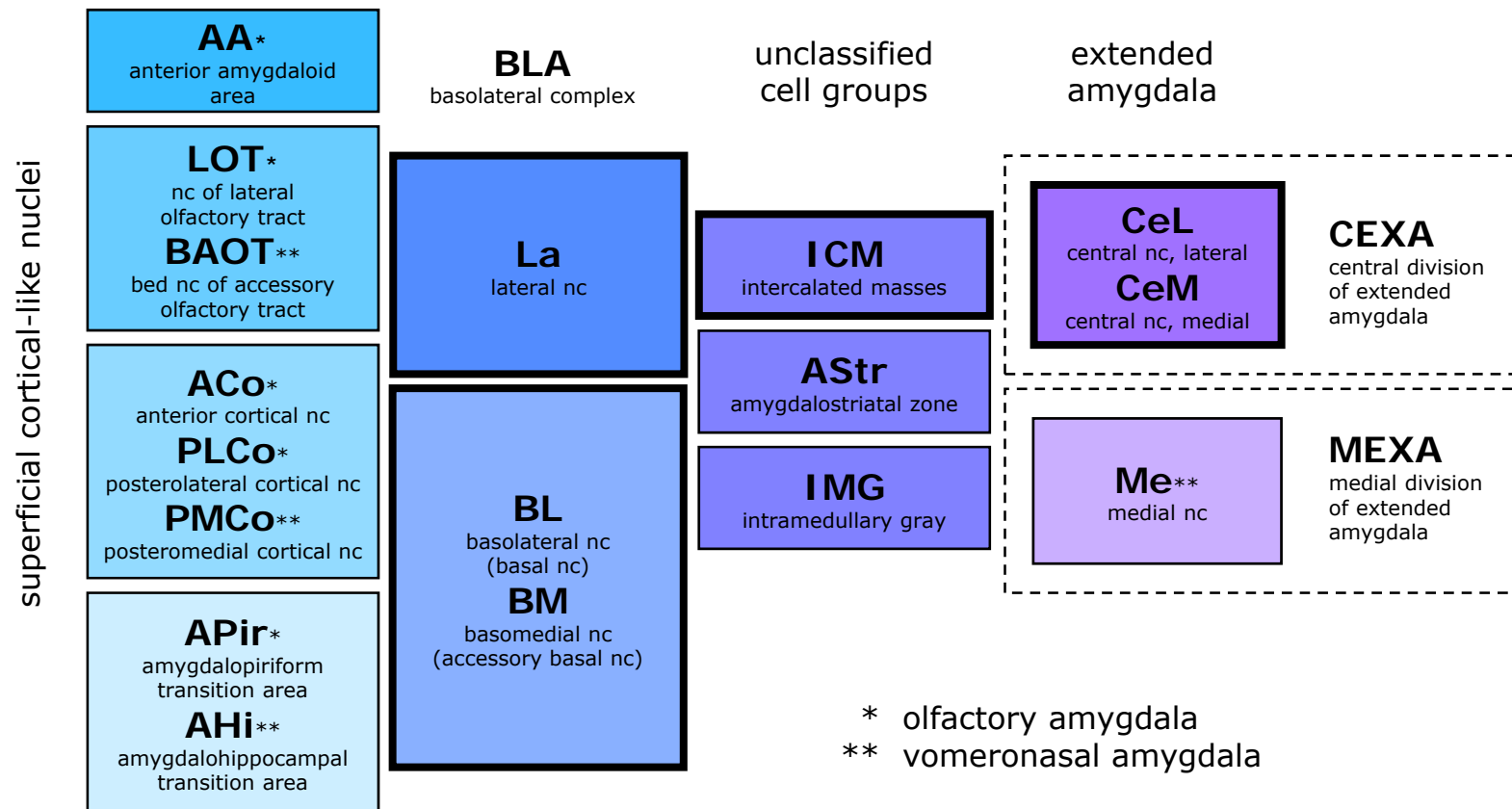
Emotions



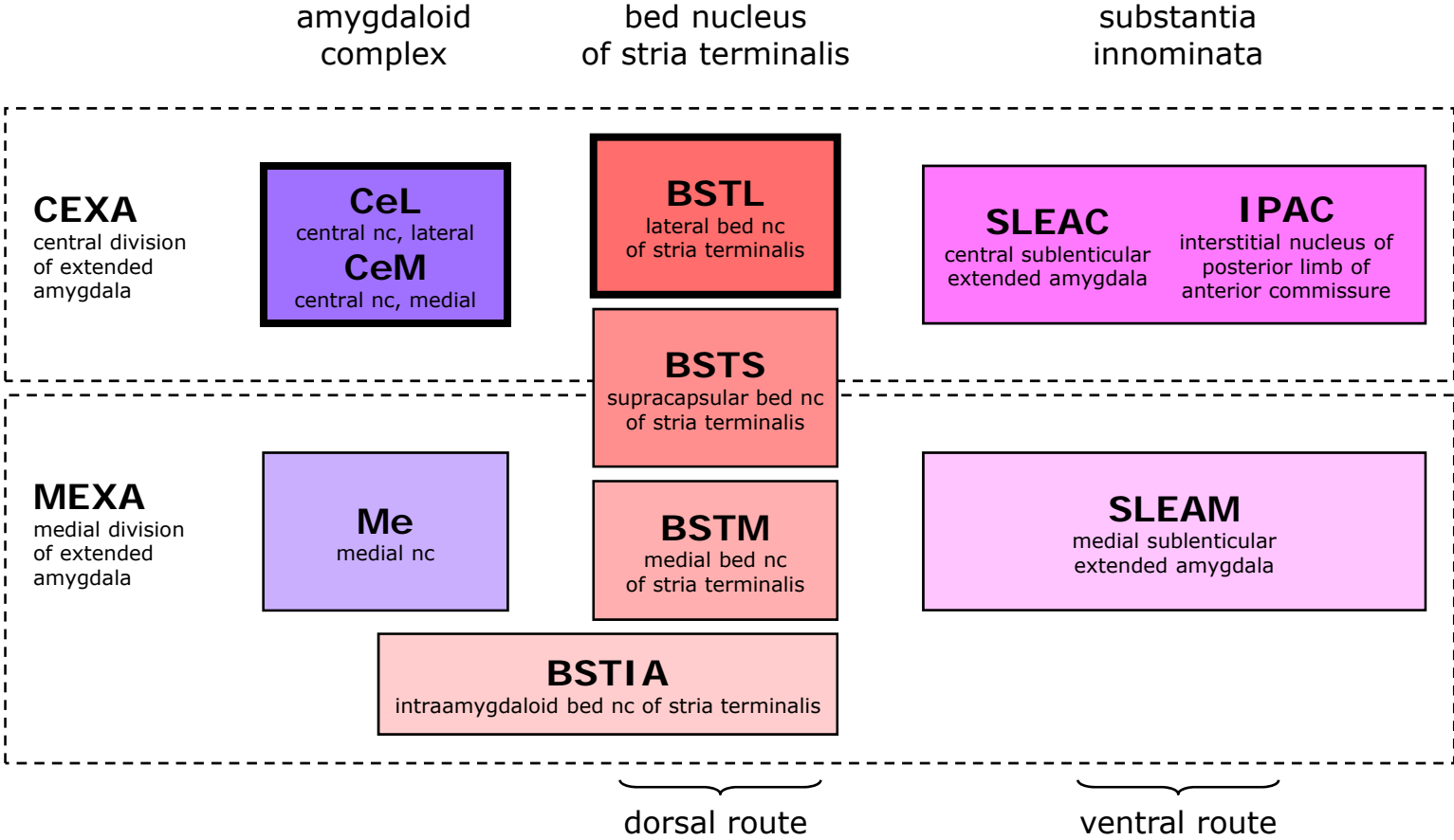
Fear and anxiety in rodents



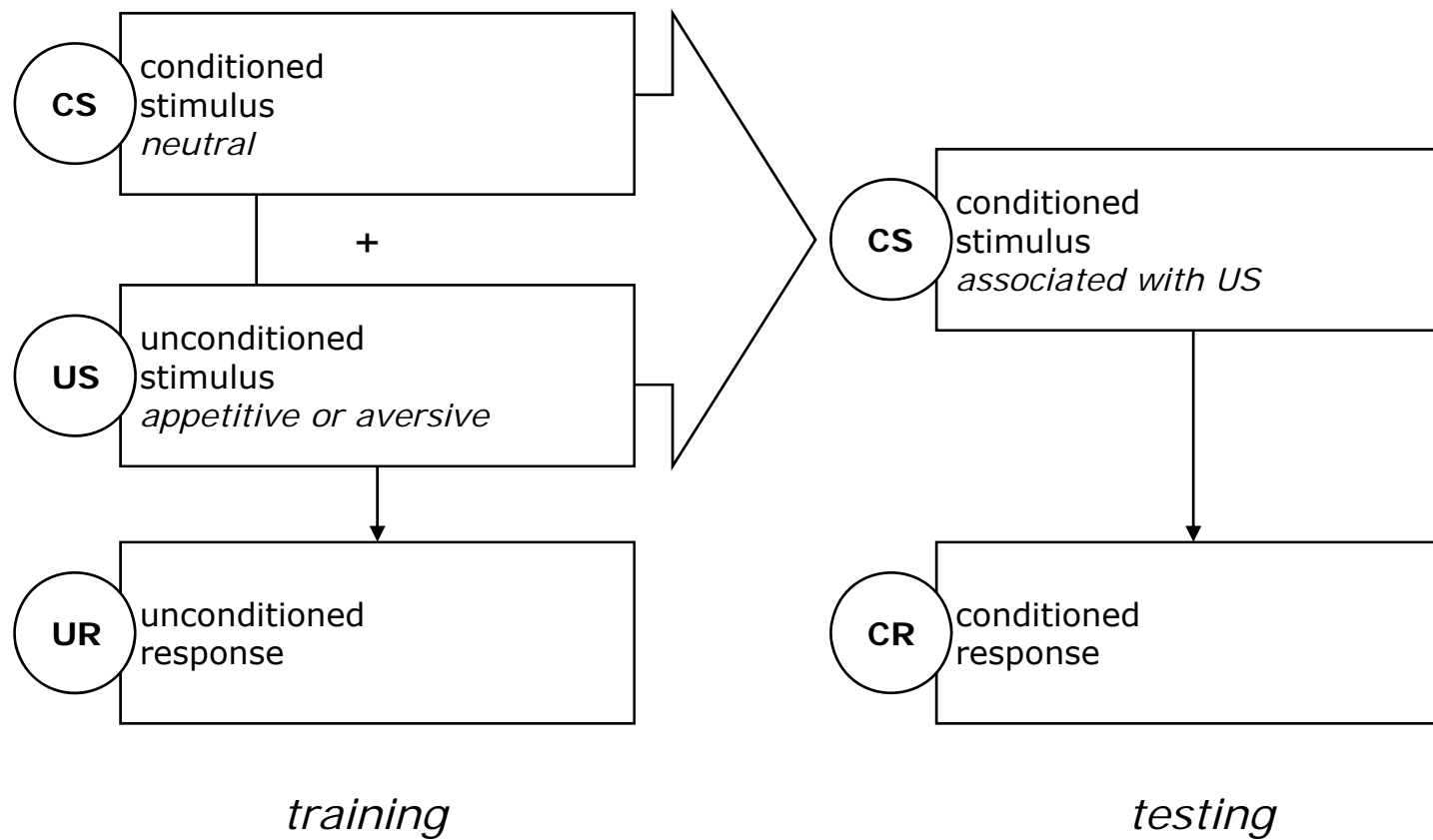
Amygdaloid complex - components



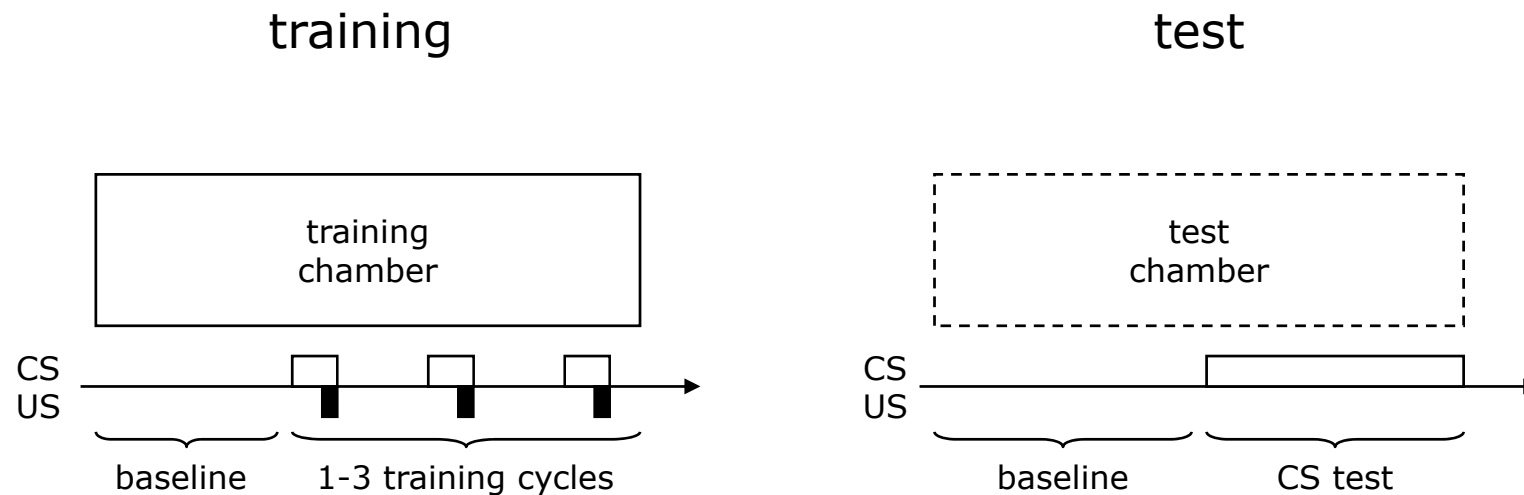
Extended amygdala



Classical (Pavlovian) conditioning

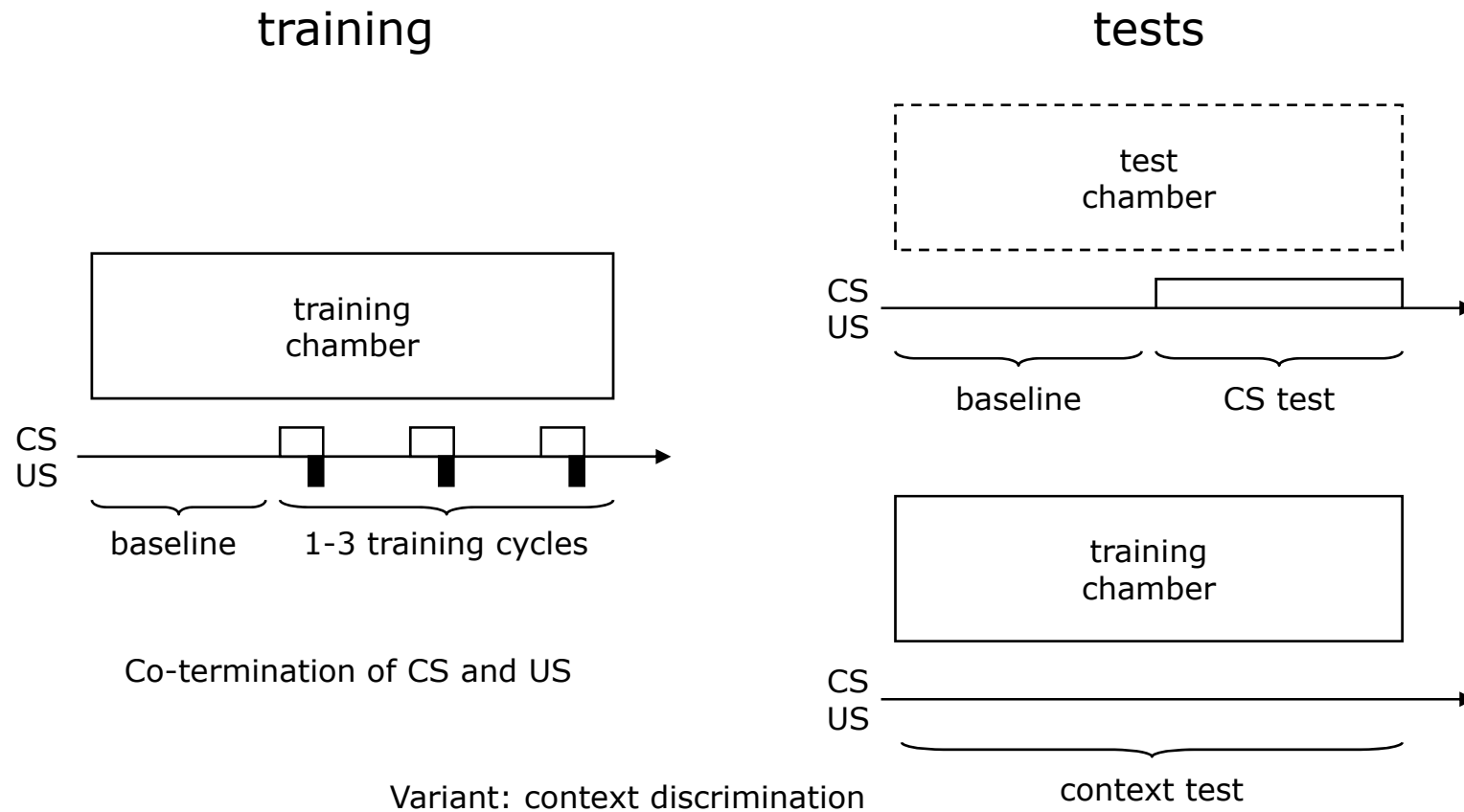


Pavlovian (cued) fear conditioning

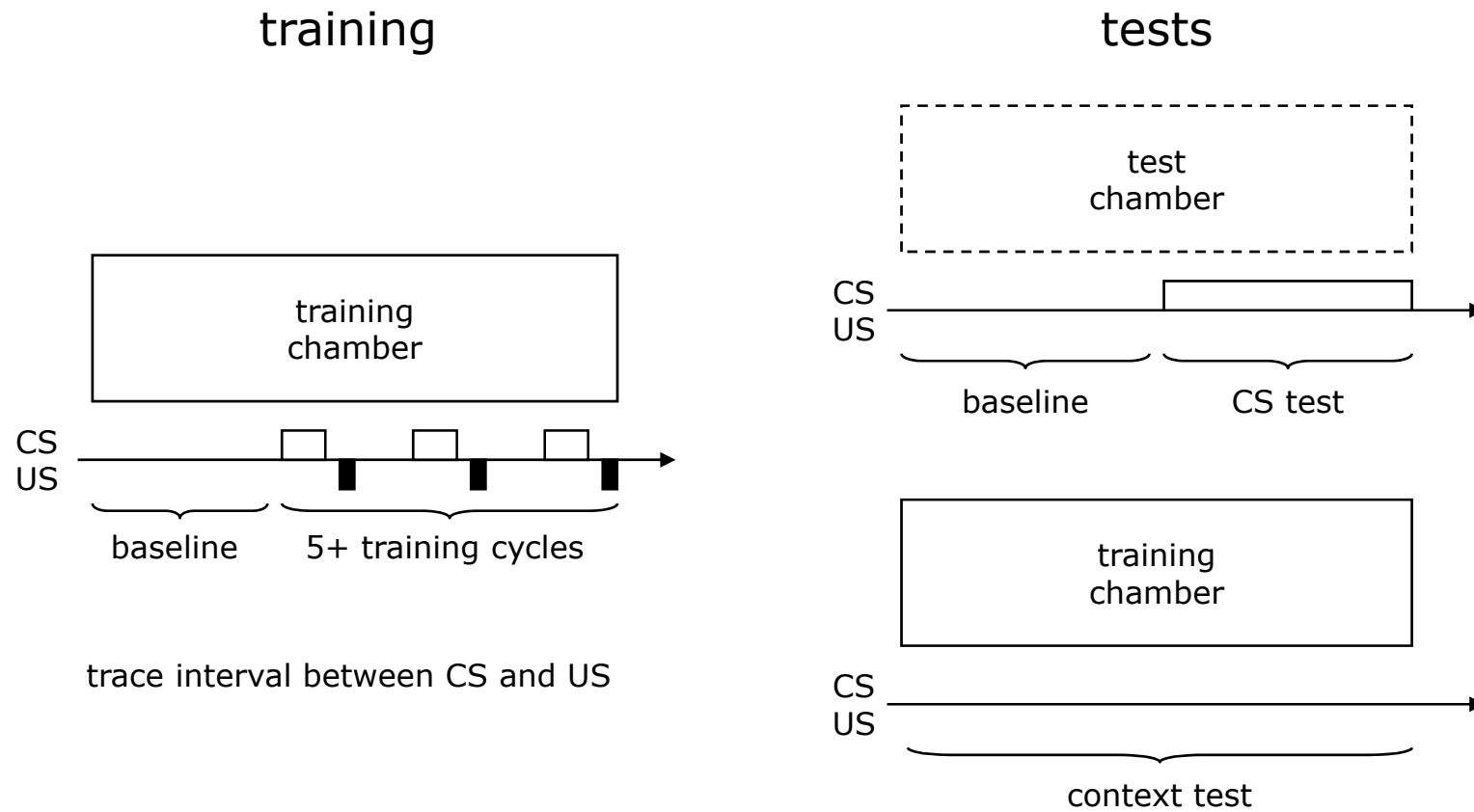


- measured response
- defensive behavior (freezing, vocalization, flight)
 - reflex potentiation (startle)
 - hypoalgesia
 - autonomic arousal (blood pressure, heart rate)
 - HPA axis stimulation

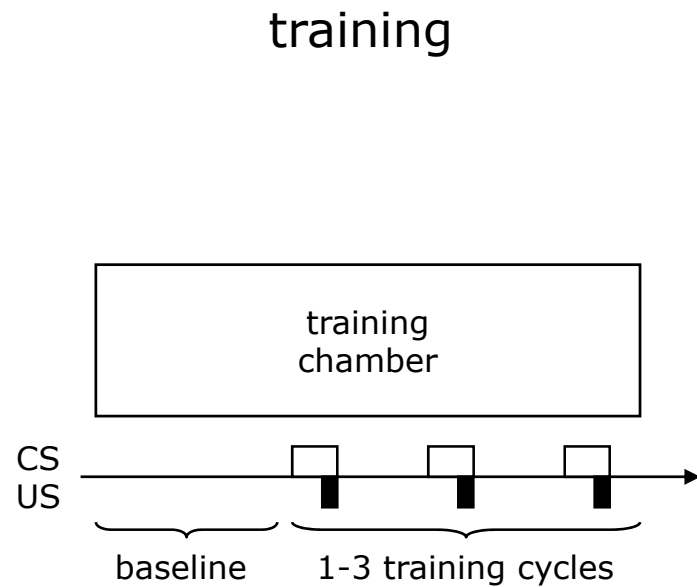
Cued and contextual fear conditioning



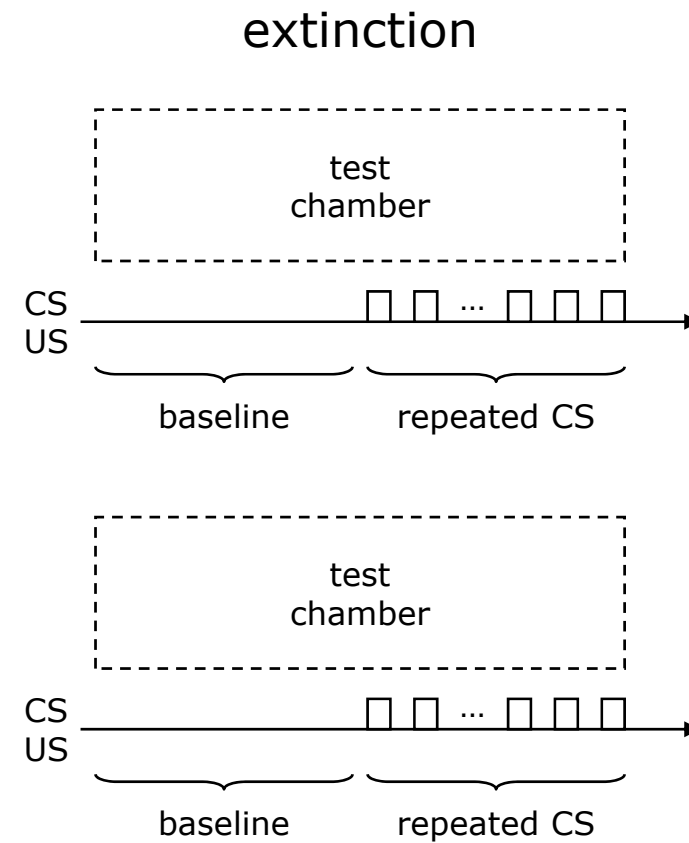
Trace fear conditioning



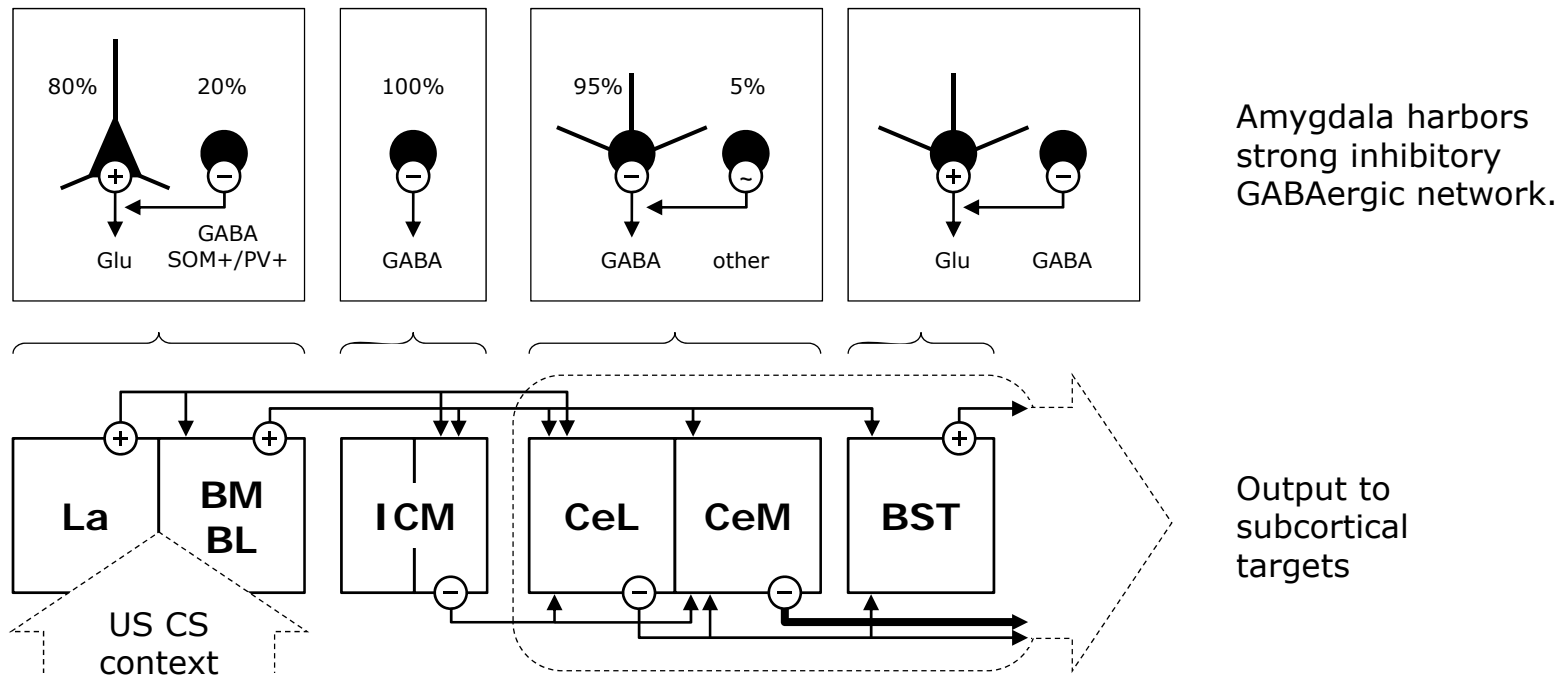
Extinction of conditioned fear



- reappearance of CR after extinction:
- recovery (with time)
 - reinstatement (US exposure)
 - renewal (new context)

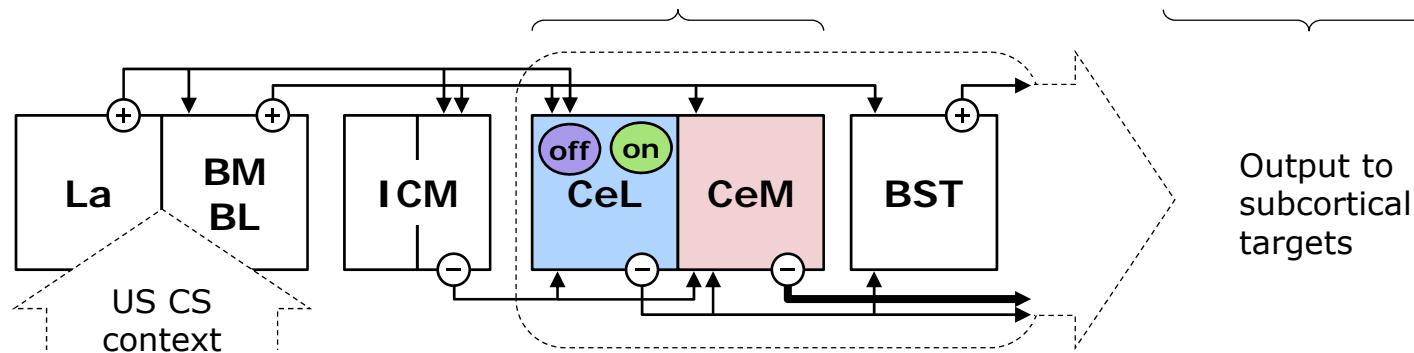
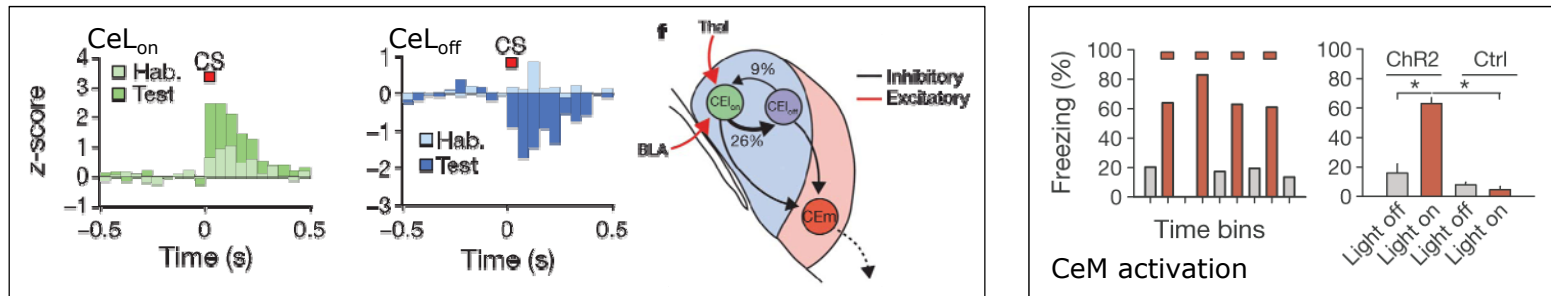


Amygdala: cytoarchitecture and flow of information



- La, BM/BL share cortex-like cytoarchitecture with 80% excitatory principal neurons
- Ce has striatum-like cytoarchitecture with 95% medium spiny-like projection neurons
- Ce (inhibitory!) and BST (mostly excitatory) are the principal output structures
- overall information flow is from laterobasal complex (La, BM/BL) to extended amygdala
- CS-US associations formed and stored in La, lesion disrupts acquisition and retrieval

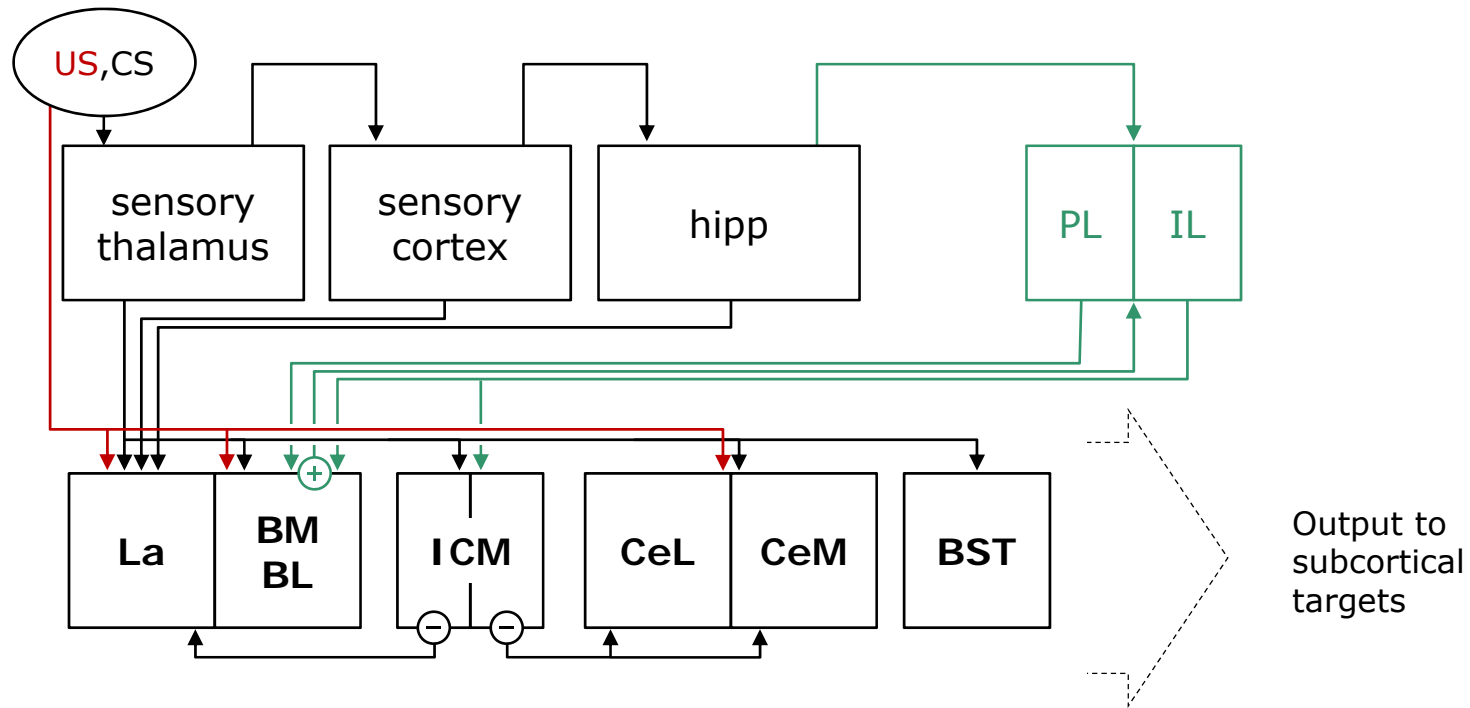
CS-on and CS-off cells as a fear gate in the CeL



- CS-on cells in the CeL acquire positive response to CS with learning
- CS-off cells in the CeL acquire negative response to CS with learning
- cell-type specific plasticity in the CeL to CeM pathway may gate fear expression
- conditioned fear responses are driven by activity of CeM output neurons

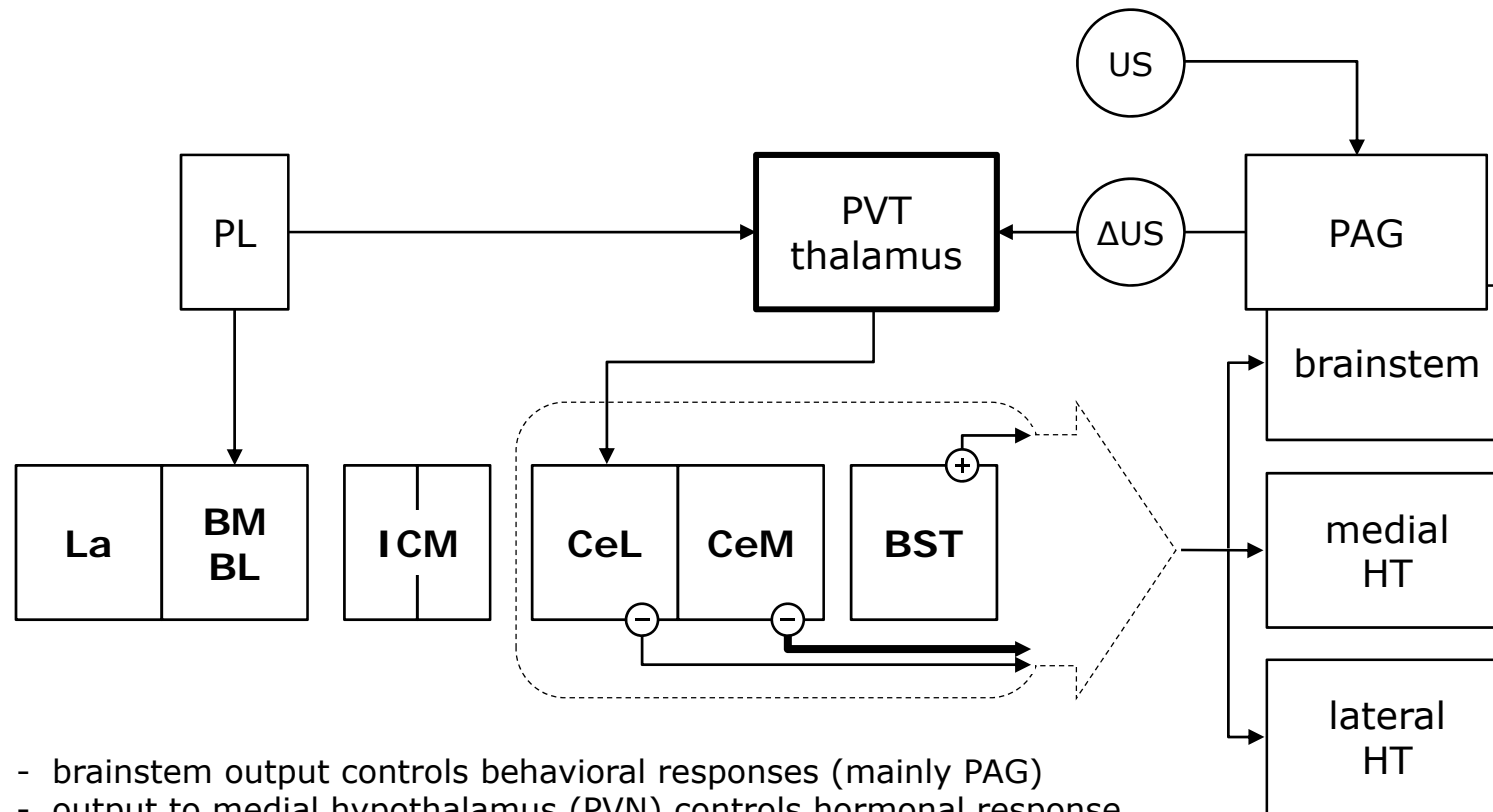
Ciocchi S et al. Nature 468:277,2010

Amygdala: sensory and cortical inputs



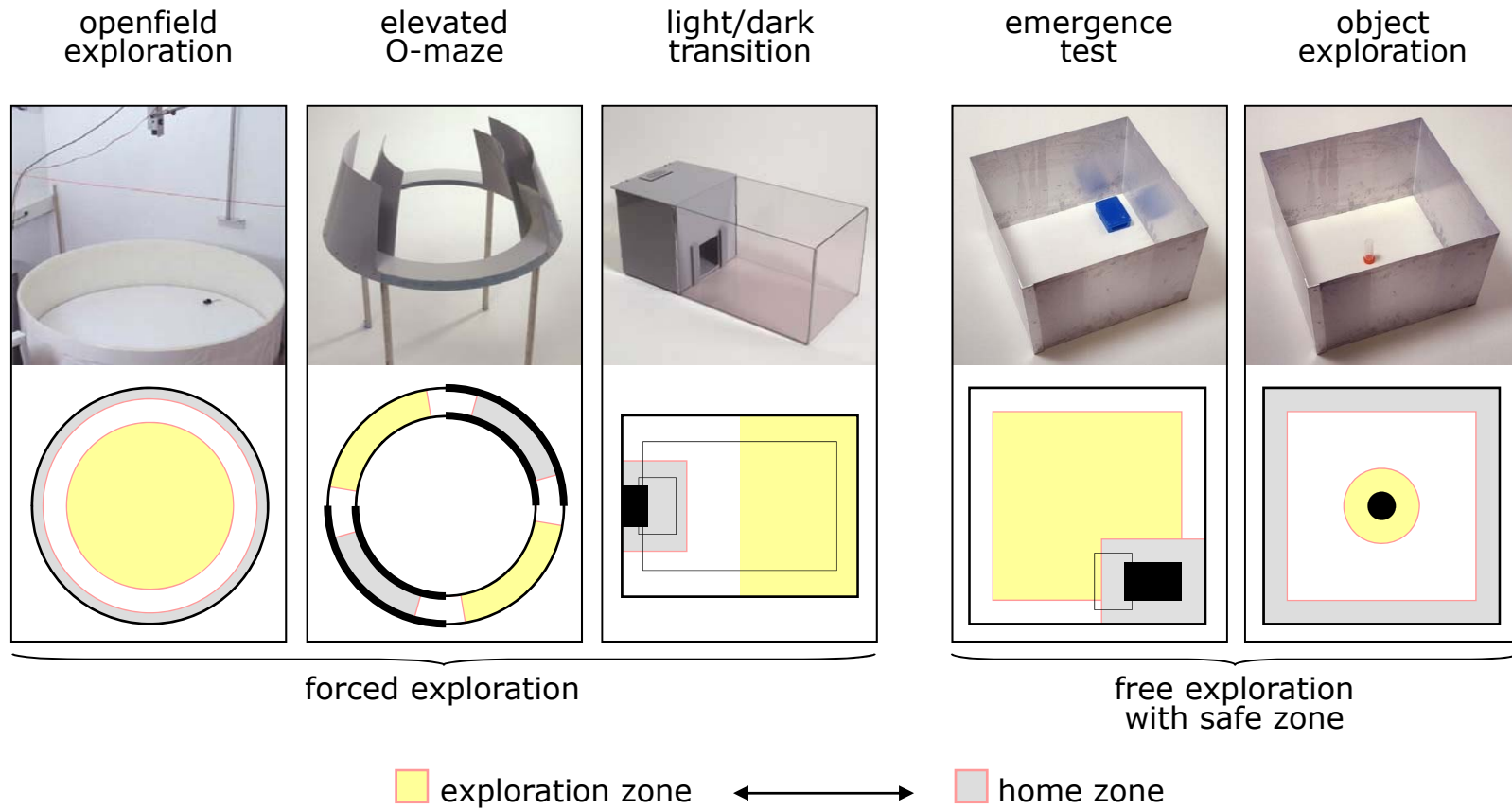
- quick and dirty **pre-thalamic (especially nociceptive)** and thalamic sensory input
- slower and more precise input from sensory cortex to basal and extended amygdala
- multimodal and contextual input from hippocampus
- **bidirectional modulation by medial prefrontal cortex (IL, PL)**
- **extinction signal mediated by IL prefrontal cortex via intercalated cells**

Amygdala: output and control by thalamus

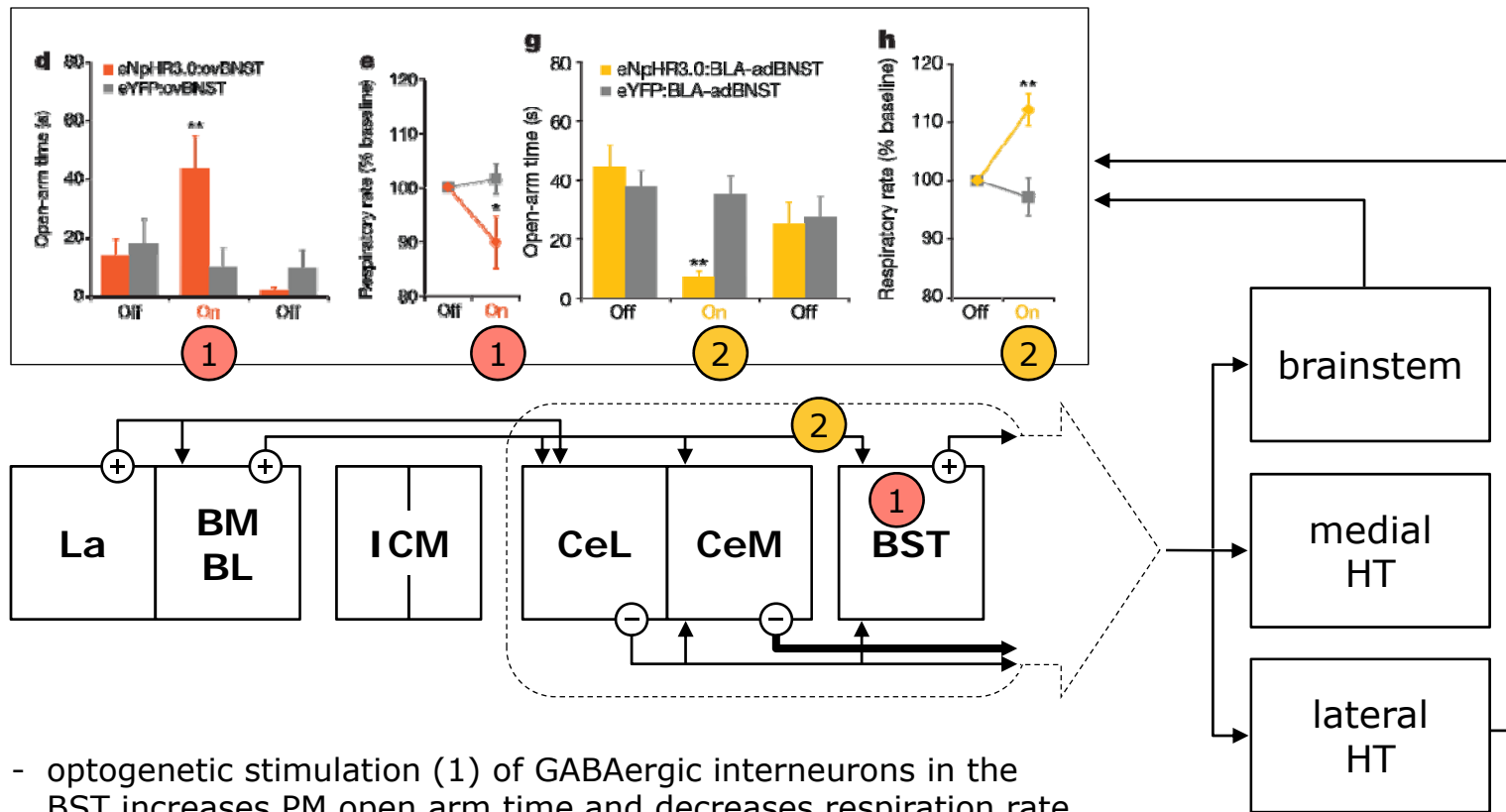


- brainstem output controls behavioral responses (mainly PAG)
- output to medial hypothalamus (PVN) controls hormonal response
- output to lateral hypothalamus controls autonomic and behavioral responses
- PVT required for acquisition and long-term retrieval of fear memories
- convergence of US and US prediction signals in PAG permits calculation of prediction error

Rodent tests of anxiety-related responses



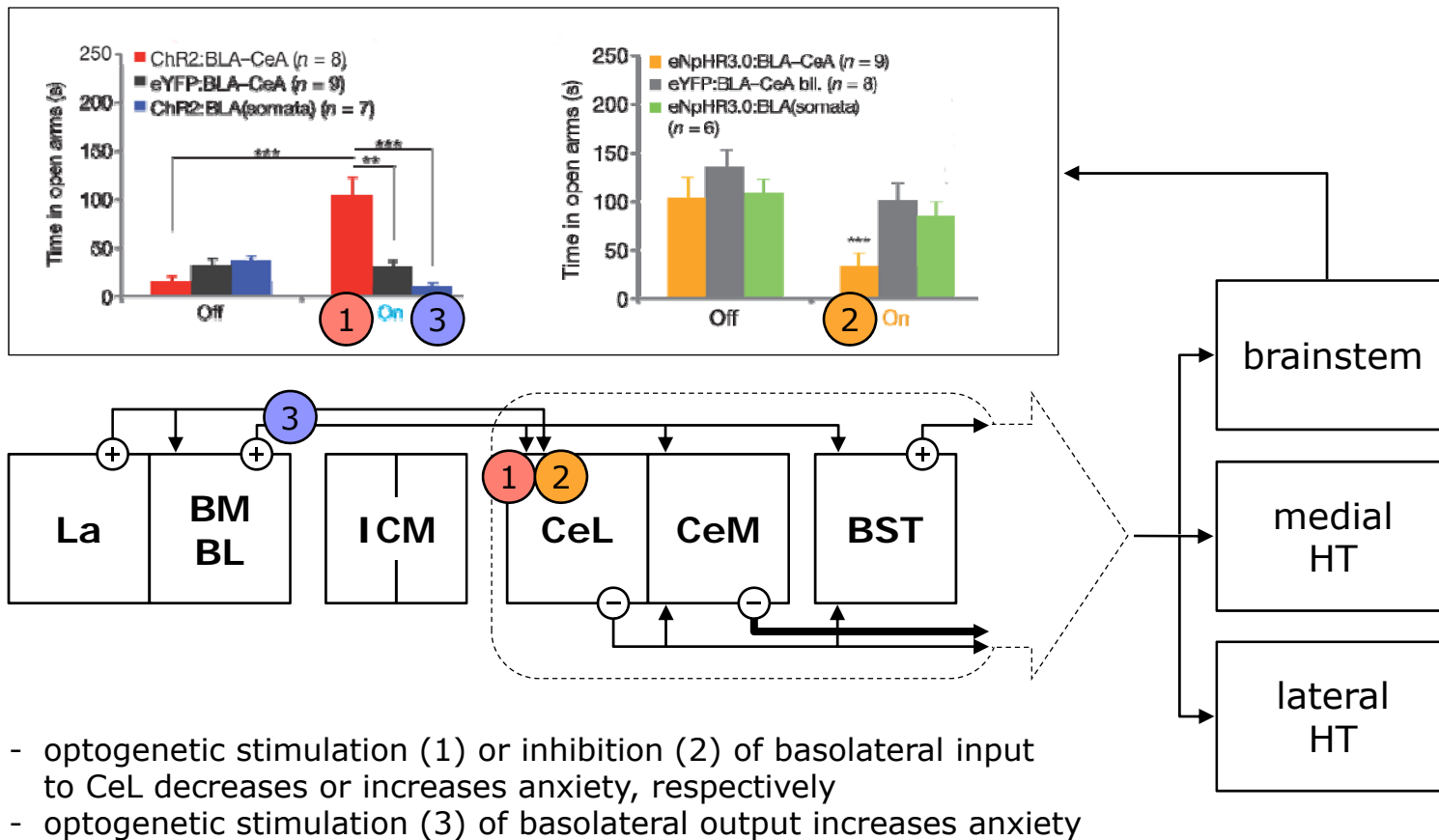
Bidirectional control of anxiety through the BST



- optogenetic stimulation (1) of GABAergic interneurons in the BST increases PM open arm time and decreases respiration rate
- optogenetic stimulation (2) of basolateral input to BST decreases PM open arm time and increases respiration rate

Kim SY et al. Nature 496:219,2013

Bidirectional control of anxiety by the amygdala



Tye KM et al. Nature 471:358,2011