

NE = The Quit Signal?

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Definition: Perseverance

- "A determined attitude that makes you continue trying to achieve something difficult"

[Macmillan Dictionary]

- "Steady persistence in adhering to a course of action, a belief, or a purpose; steadfastness"

[American Heritage Dictionary]

Definition: Frustration

- "An annoyed or impatient feeling that you get when you are prevented from doing what you want"

[Macmillan Dictionary]

- "A feeling of disappointment, exasperation, or weariness caused by goals being thwarted or desires unsatisfied"

[Encarta World English Dictionary]

- NE = frustration or just the quit signal?

Definition: Inhibitory Control

- "This ability to dynamically modify or cancel a planned action that is no longer advantageous or appropriate is known as inhibitory control in psychology."

[Shenoy 2011]

- I propose that NE as the Quit Signal operates on a much longer timescale than the inhibitory control mechanism used in the stop signal task

Definition: Contingency

If a consequence does not contingently (reliably, or consistently) follow the target response, its effectiveness upon the response is reduced. But if a consequence follows the response consistently after successive instances, its ability to modify the response is increased. The schedule of reinforcement, when consistent, leads to faster learning. When the schedule is variable the learning is slower. Extinction is more difficult when learning occurs during intermittent reinforcement and more easily extinguished when learning occurs during a highly consistent schedule.

[Wikipedia, "Operant Conditioning", viewed 2011-04-24]

Hypotheses

- The neuromodulator norepinephrine (NE) level rises when cue-predicted events do not occur
- The NE level drops back down to near baseline when a cue-predicted event occurs
- When the NE level exceeds a given threshold, the cue is abandoned as an event predictor
- To prevent premature abandonment, cues with less reliability have higher thresholds
- The neuromodulator acetylcholine (ACh) level determines the cue abandonment threshold

Example 1

High Reliability, Low Threshold

- An experimental subject learns that a cue predicts the future location of a food reward
- The cue is reliable so the ACh threshold is low
- The cue suddenly becomes uncorrelated
- There is a increase in failures to predict the location of the food reward based on the cue
- The NE level rises to exceed the low threshold
- The subject becomes easily discouraged and abandons the cue after just a few trials

Example 2

Low Reliability, High Threshold

- Subject learns to predict location based on a less reliable cue so the ACh threshold is higher
- The cue suddenly becomes uncorrelated
- There is a increase in failures to predict the location of the food reward based on the cue
- The NE level eventually rises to exceed the higher threshold
- The subject perseverates and abandons the cue after many trials, not just a few

Intermittent Reward

- This model captures the idea that behaviors associated with intermittent reward are harder to extinguish than those associated with reliable reward
- If the probability of an event given a cue is 99%, three prediction failures in a row will lead you to believe the game has changed
- If the probability of an event given a cue is 51%, three prediction failures in a row might just be unlucky so keep the faith awhile longer

Yu and Dayan 2005

- $NE > ACh / (0.5 + ACh)$
- "The threshold for NE that determines whether or not the context should be assumed to have changed is set monotonically by the level of ACh. Intuitively, when the estimated cue invalidity is low, a single observation of a mismatch between cue and target could signal a context switch. But when the estimated cue invalidity is high, indicating low correlation between cue and target, then a single mismatch would be more likely to be treated as an invalid trial rather than a context switch."

[Yu and Dayan (2005) Uncertainty, Neuromodulation, and Attention]

Pencil and Paper

- Run an experiment 20 times
- Create a 2 by 2 table and tally how many times
 - Cue 1 is given and food is presented North
 - Cue 1 is given and food is presented South
 - Cue 2 is given and food is presented North
 - Cue 2 is given and food is presented South
- Calculate success for each of four strategies
 - Ignore cue and always choose North or South
 - North for Cue 1, South for Cue 2, or vice versa

Results Tables

	Food North	Food South	Totals
Cue 1	5	6	11
Cue 2	7	2	9
Totals	12	8	20

$P(\text{FN})$	12 / 20	60%
$P(\text{FS})$	8 / 20	40%
$P(\text{C1})$	11 / 20	55%
$P(\text{C2})$	9 / 20	45%
$P(\text{FN} \text{C1})$	5 / 11	45%
$P(\text{FS} \text{C1})$	6 / 11	55%
$P(\text{FN} \text{C2})$	7 / 9	78%
$P(\text{FS} \text{C2})$	2 / 9	22%
$P(\text{C1} \text{FN})$	5 / 12	42%
$P(\text{C2} \text{FN})$	7 / 12	58%
$P(\text{C1} \text{FS})$	6 / 8	75%
$P(\text{C2} \text{FS})$	2 / 8	25%

Ignore Cue, Always Go North	12 / 20	60%
Ignore Cue, Always Go South	8 / 20	40%
Cue 1 North, Cue 2 South	$(5+2) / 20$	35%
Cue 1 South, Cue 2 North	$(6+7) / 20$	65%

Who Moved My Cheese?

- Food presented to the North 60% of the time
- Relying on cues yields rewards 65% of the time
- If the reliability of the cue strategy drops below the 60% threshold, the subject is better off ignoring cues and always going North
- How long of an unlucky streak will subject tolerate before abandoning a cue and switching to the strategy of just always going North?
- What if probability of food to North changes?

Without Paper and Pencil

- Assume I take away paper and pencil and ask subject to choose a strategy based on neuromodulator levels instead
- Subject gets to work with just two neuromodulators, ACh and NE, which seem to have some relationship with each other
- Somehow top-down cortical versus bottom-up sensory gating might be involved, so keep that in mind

Possible Rules:

For Picking a Favorite Location

- Increase the ACh level associated with a location each time food is not presented there
- Decrease the ACh level associated with a location each time food is presented there
- ACh levels rise and fall incrementally on some sort of squashing function logarithmic scale
- Favor the location with the lowest ACh level and use this as the primary target location for choosing cues

Possible Rules:

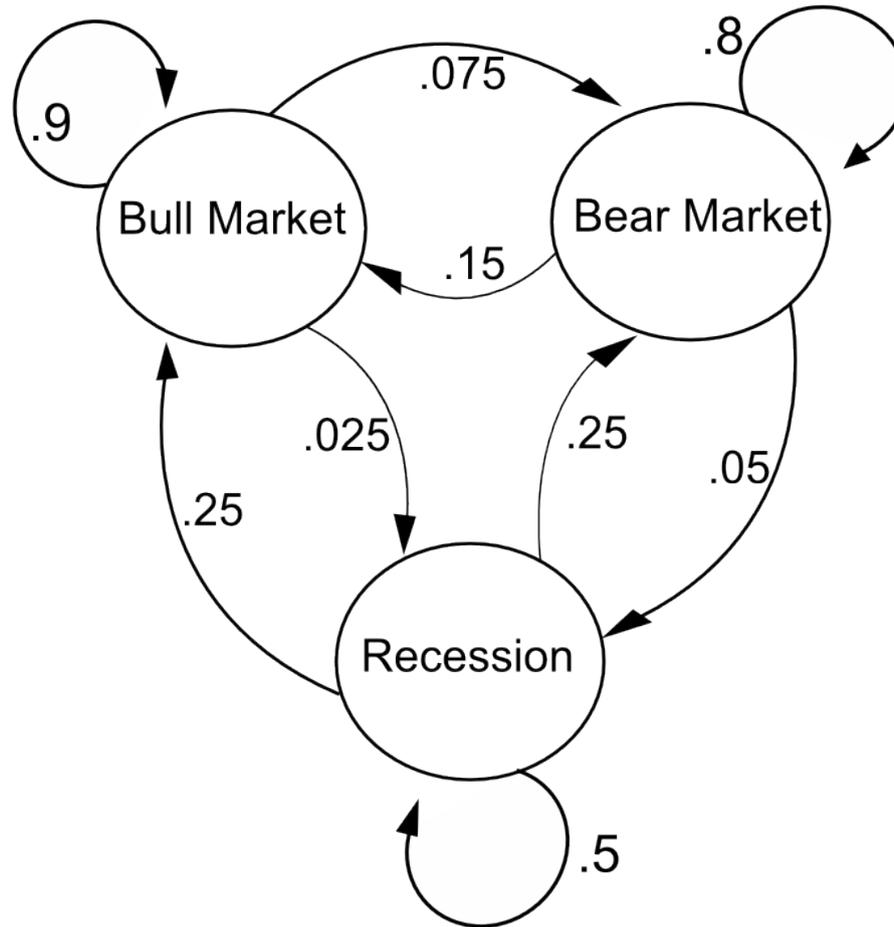
For Picking a Favorite Cue

- Increase the NE level associated with a cue strategy each time it fails
- Drop the NE level associated with a cue strategy back down to near baseline each time it succeeds
- If NE level exceeds the ACh determined threshold, abandon the cue and choose another

Why Drop to Near Baseline?

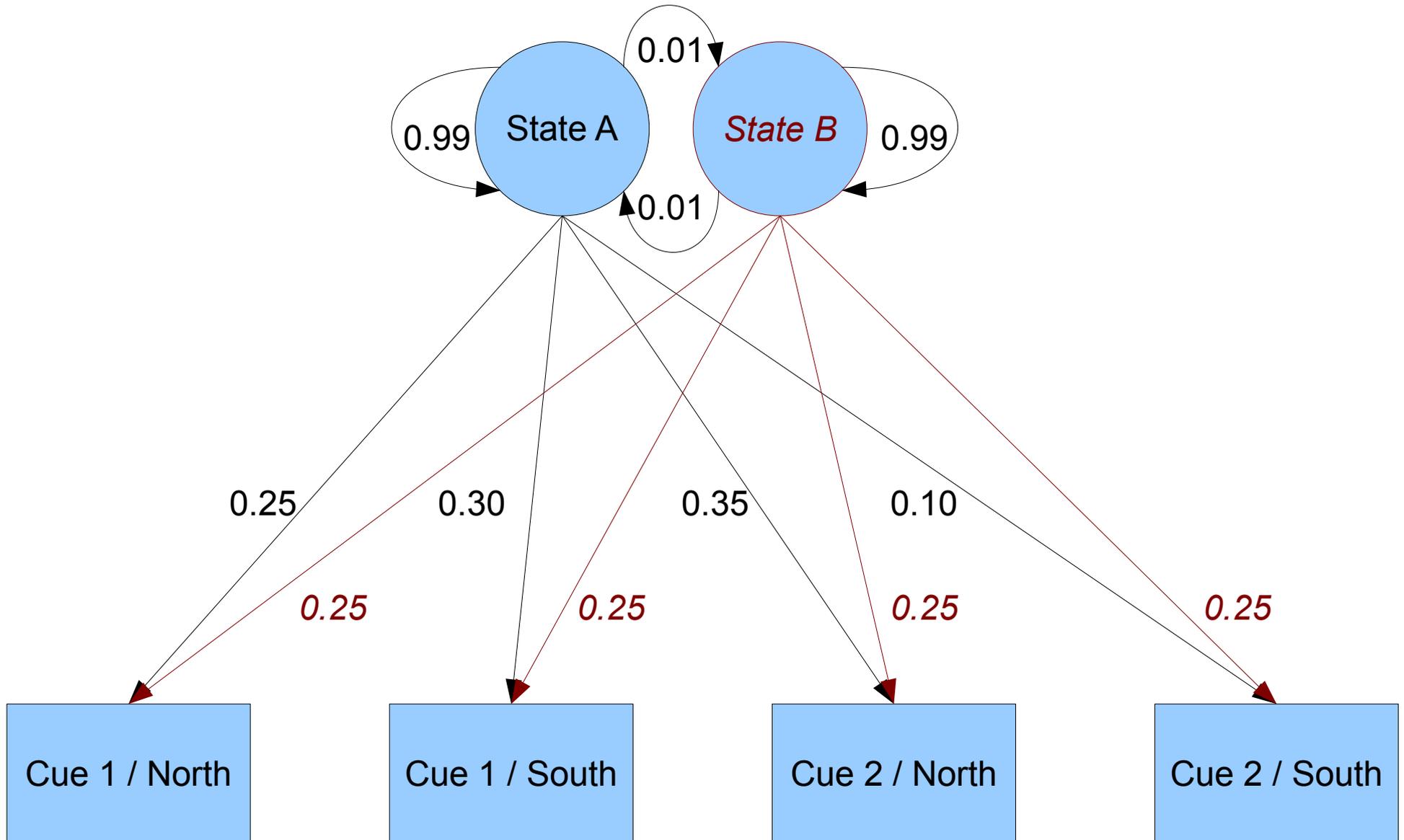
- ACh levels rise and fall incrementally on some sort of logarithmic scale related to unreliability
- I predict that NE levels rise incrementally then plummet back to near baseline with each cue-prediction success. Why?
- Relate to feeling gradual rising frustration and then finally sudden relief as you have a success
- Mathematically it relates to the probability of a long unlucky streak for a given cue reliability

Markov Chain



<http://en.wikipedia.org/wiki/File:MarkovChain1.png>

Hidden Markov Model



When Did It Switch States?

--+ - + - + + + + + - + + - - + + + + - + - + + - - - + - - - + + - - + - - +

- State changes from A to B halfway through
- Adopted strategy payoff drops from 65% to 50%
- How many observations before we know?
- State switch more obvious if reliability high

+ - + + + + + + + - - + + + + + + + - + - + + - - - + - - - + + - - + - - +

- Explains intermittent reward perseverance
- Bayesian filtering vs. quitting on unlucky streak

Top-down vs. Bottom-up

"Yu and Dayan describe a model of the role of acetylcholine and norepinephrine in balancing top-down expectation and bottom-up sensory input in guiding behavior. The model builds from data on physiological effects of modulators regulating the balance of cortical feedback and thalamic input." [Hasselmo 2005]

- Bayesian filtering estimates state given observations
- Uses conditional probabilities to infer from noisy data
- Anticipated versus perceived
- Seeing and hearing what you expect
- Schizophrenics who smoke regulating nicotinic ACh?

Definition: Idazoxan

"[A] drug which is used in scientific research. It acts as both a selective α_2 adrenergic receptor antagonist, and an antagonist for the imidazoline receptor. Idazoxan has been under investigation as an antidepressant, but it did not reach the market as such. More recently, it is under investigation as an adjunctive treatment in schizophrenia. Due to its alpha-2 receptor antagonism it is capable of enhancing therapeutic effects of antipsychotics, possibly by enhancing dopamine neurotransmission in the prefrontal cortex of the brain, a brain area thought to be involved in the pathogenesis of schizophrenia."

[Wikipedia, viewed 2011-04-24]

Regulation Effects

| | Upregulating (+) | Downregulating (-) |
|---------------------------------|--|--|
| Norepinephrine (NE) | Less perseverance | More perseverance |
| Muscarinic Acetylcholine (mACh) | Decreases cue validity effect (reduces top-down influence)

Increases "presynaptic inhibition of excitatory glutamateric feedback synapses from higher cortical areas" [Hasselmo 2005] | Increases cue validity effect

scopolamine |
| Nicotinic Acetylcholine (nACh) | Decreases cue validity effect (increases bottom-up influence)

"[E]nhances the influence of afferent sensory input (the target) on pyramidal cells, due to nicotinic receptors enhancing thalamocortical transmission" [Hasselmo 2005] | |

DA vs. NE

- Substantia Nigra
 - Black substance
 - Dopamine
 - Reward signal
- Locus Coeruleus
 - Blue spot
 - Norepinephrine (Noradrenaline)
 - Quit signal?

References

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