Using computation to translate across species

A. David Redish
Department of Neuroscience
University of Minnesota

redish@umn.edu
@adredish

Redish Lab at the University of Minnesota

redishlab.umn.edu
No conflicts of interest to declare.

Funded by NIMH, NIDA.
Behavior depends on computation

This suggests a new view of psychiatry as neurophysiological computational dysfunctions in decision making.
Are the circuits the same?

Comparing circuits across species requires that both species are doing the same computations, not necessarily the same tasks.

van der Meer, Kurth-Nelson, Redish (2012) *The Neuroscientist*
Redish (2016) *Nature Reviews Neuroscience*
It helps to get the ethology right.

Rats on the Mazur adjusting delay discounting task are not locally differentiable from random. *Cardinal, Daw, Robbins, Everitt 2002 Neural Networks.*
It helps to get the ethology right

This isn’t just true for rats or mice. Human behavior depends on framing as well.

A vowel on one side implies an odd number on the other.

Which cards do you have to flip over to check this statement?

Wason and Johnson-Laird 1972
It helps to get the ethology right

This isn’t just true for rats or mice. Human behavior depends on framing as well.

What do you have to do to check that no one underage is drinking alcohol?

Wason and Johnson-Laird 1972
Starting points...

• Computation is the key to cross-species translation

• Framing matters
  (it’s important to get the ethology right)
Two case studies

I Deliberation and Automation

II Restaurant Row
I Deliberation and Automation

Henry Molaison (HM)

[WikiCommons]

pbs.org
I Deliberation and Automation

There was a sequence: 1 3 2 4 5
We are not unitary decision-makers

Rats use cognitive maps to navigate. (1932, 1948)

Training 4x/day, 7 days

Rats learn stimulus-response action-chains. (1943)

Place-strategy (return to same location by taking a different action)

Response-strategy (turn in same direction but reach a different goal)

Dependent on hippocampal function

Dependent on dorsolateral striatal function

The left-right-alternate (LRA) task
The left-right-alternate (LRA) task

Version 1: *Strategy changes from day to day (2000-2010)*
The left-right-alternate (LRA) task

**Version 1:** Strategy changes from day to day (2000-2010)

**Version 2:** One strategy change midway through a session on probe days (2010-2015)
The left-right-alternate (LRA) task

**Version 1:** Strategy changes from day to day (2000-2010)

**Version 2:** One strategy change midway through a session on probe days (2010-2016)

**Version 3:** Multiple strategy changes within each day (2017-present)
Result 1: VTE laps
A marker of deliberation

When rats come to choice-points, they sometimes pause and look back and forth.

(Meunzinger and Gentry 1931, Meunzinger 1938, Tolman 1938, 1939, 1946, 1948, ...)

Tolman suggested that this allows the animal to consider “future possibilities”.
Result 1: VTE laps
A marker of deliberation

When rats come to choice-points, they sometimes pause and look back and forth.

(Meunzinger and Gentry 1931, Meunzinger 1938, Tolman 1938, 1939, 1946, 1948, ...)

Tolman suggested that this allows the animal to consider “future possibilities”.
Result 1: VTE laps
A marker of deliberation

Anoopum Gupta, van der Meer, Touretzky, Redish (2012) Nat Nsci
Seiichiro Amemiya, Redish (2016) J Neurosci
Andy Papale, Zielinski, Frank, Jadhav, Redish (2016) Neuron
Hippocampal representations sweep ahead of the animal

During vicarious trial and error (VTE) events, decoding reveals coherent sequences running ahead of the animal alternating between goals.

Hippocampal sequences go to the next goal


1 segment trajectory

2 segment trajectory

3 segment trajectory

1 segment trajectory

2 segment trajectory

3 segment trajectory

Look ahead dist. (cm)
Theta sequences

Every theta cycle consists of a “you are there” component, followed by a “what’s next” component.
Theta sequences

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Theta sequences

Every theta cycle consists of a “you are there” component, followed by a “what’s next” component.

When faced with a delay to a goal, the second half (sweep portion) of the theta cycle lengthens.
We are not unitary decision-makers.

Rats use cognitive maps to navigate. (1932, 1948)

Training 4x/day, 7 days

Place-strategy (return to same location by taking a different action)

Response-strategy (turn in same direction but reach a different goal)

Dependent on hippocampal function

Dependent on dorsolateral striatal function

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One week of training

Many weeks of training

Result 2:
Rats develop automation (flow)
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Procedural actions

Predictions:
1. We should see cells represent key situation parameters.
2. No sweeps to a goal
3. Represent the beginning of each action sequence
Procedural actions

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Smith & Graybiel 2013
Procedural actions

Predictions:
1. We should see cells represent key situation parameters.
2. No sweeps to a goal.
3. Represent the beginning of each action sequence.
Result 1: Rats deliberate over choices (prefrontal – hippocampal interactions; sweeps to the goal).

Result 2: Rats develop a flow as they automate their behavior (dorsolateral striatal interactions; task-initiation bursts).

Result 3: Ventral striatum (and orbitofrontal cortex) represent reward during deliberation and value during automation.

Result 4: Prelimbic cortex encodes strategy and reflects strategy changes.
Two case studies

I Deliberation and Automation

II Restaurant Row
Two case studies

II Restaurant Row
Rats run around a circular track for food reward. On each encounter, they are offered reward only after a delay. The delay is completely cued with an auditory tone that counts down. (pitch=delay)

Because they have a **limited time on the track**, waiting for one reward must be balanced against waiting for another.
Because they have a limited time on the track, waiting for one reward must be balanced against waiting for another.

This means we can talk about good deals and bad deals.
From rats and mice to humans

What do humans forage for?
From rats and mice to humans

What do humans forage for?
From rats and mice to humans

What do humans forage for?
Cross-species studies
Cross-species studies
Rodents show different behaviors in the offer and wait zones.

**DELIBERATION**
Rats and mice show re-orientation behaviors in the offer zone.

**RE-EVALUATION**
And quit behaviors in the wait zone.
Manipulations separately affect the offer and wait zones.

Optogenetic manipulations of infralimbic cortex to nucleus accumbens shell synaptic efficacy affects wait zone but not offer zone.

Cocaine affects offer zone decisions. Morphine affects wait zone decisions.

DREADD manipulations of prelimbic cortex affects offer zone but not wait zone.
The sunk cost fallacy

Sensitivity to sunk costs arises when decisions are made based on past expenses rather than future expectations.

Brisn Sweis, Samantha Abram, Brandy Schmidt, Kelsey Seeland, Angus MacDonald, Mark Thomas, Redish (2018) Science
Sunk costs in the wait zone

Brian Sweis, Samantha Abram, Brandy Schmidt, Kelsey Seeland, Angus MacDonald, Mark Thomas, Redish (2018) *Science*
Sunk costs in the offer zone?

We can make the same measurement based on time spent in the offer zone.
Sunk costs only start to accrue after **investment** in a choice.

No sunk costs in the offer zone
<table>
<thead>
<tr>
<th></th>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
<th>Cohort 5</th>
<th>Cohort 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
<td>Spring 2014</td>
<td>Spring 2014</td>
<td>Fall 2016</td>
<td>Spring 2017</td>
<td>Spring 2017</td>
<td>Fall 2017</td>
</tr>
<tr>
<td>Species</td>
<td>Rat</td>
<td>Human</td>
<td>Mouse</td>
<td>Rat</td>
<td>Human</td>
<td>Mouse</td>
</tr>
<tr>
<td>Breed</td>
<td>Brown-Norway</td>
<td>undergraduates</td>
<td>C57BL6J</td>
<td>Fisher Brown-Norway</td>
<td>undergraduates</td>
<td>C57BL6J</td>
</tr>
<tr>
<td>Sample Size &amp; Sex</td>
<td>22 (M) &amp; 0 (F)</td>
<td>4 (M) &amp; 13 (F)</td>
<td>32 (M) &amp; 0 (F)</td>
<td>4 (M) &amp; 6 (F)</td>
<td>24 (M) &amp; 41 (F)</td>
<td>32 (M) &amp; 0 (F)</td>
</tr>
<tr>
<td>Age</td>
<td>8-12 months</td>
<td>19.63 years (mean)</td>
<td>13 weeks</td>
<td>6-10 months</td>
<td>20.23 years (mean)</td>
<td>13 weeks</td>
</tr>
<tr>
<td>Task Variant</td>
<td>wait zone only</td>
<td>wait phase only</td>
<td>offer zone + wait zone</td>
<td>offer zone + wait zone</td>
<td>offer phase + wait phase</td>
<td>offer zone + wait zone</td>
</tr>
<tr>
<td>Experimenters &amp; Gender</td>
<td>1 (M) &amp; 1 (F)</td>
<td>3 (M) &amp; 5 (F)</td>
<td>2 (M) &amp; 3 (F)</td>
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<td>3 (M) &amp; 3 (F)</td>
</tr>
<tr>
<td>Length of Training</td>
<td>20+ days</td>
<td>5 minutes</td>
<td>70+ days</td>
<td>20+ days</td>
<td>5 minutes</td>
<td>70+ days</td>
</tr>
<tr>
<td>Food Deprivation</td>
<td>&gt;80% free weight</td>
<td>N / A</td>
<td>&gt;80% free weight</td>
<td>&gt;85% free weight</td>
<td>N / A</td>
<td>&gt;90% free weight</td>
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Sunk costs – human replications

*N = 280 (after Bot removal)*

Rebecca Kazinka, Angus MacDonald, Redish (work in progress)
Sunk costs – human replications

$N = 280$ (after Bot removal)

Rebecca Kazinka, Angus MacDonald, Redish (work in progress)
Sunk costs – human replications

$N = 259 \text{ (after Bot removal)}$

Rebecca Kazinka, Angus MacDonald, Redish (work in progress)
Sunk costs –
human replications

In an mTurk sample, sunk costs depend on the ability to attend to the delay.

$N = 259$ (after Bot removal)
### Cross-species translation takes time

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<th>mTurk</th>
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</tr>
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<td>Rat</td>
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<td>Mouse</td>
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<td>18-60</td>
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<td>offer zone + wait zone</td>
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<td>OZ + WZ Attention &amp; not</td>
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Two case studies

- Foraging and deliberation access different decision systems.
- Sunk costs accrue in foraging situations more than deliberation situations.
- Sunk costs depend on attention to the delay and only start to accrue after investment.
What does this imply for psychiatry?
An engineer’s view on psychiatry
This suggests a new view of psychiatry as neurophysiological computational dysfunctions in decision making.
In reliability engineering, a “failure mode” is a vulnerability inherent in the machinery.
Failure modes

In reliability engineering, a “failure mode” is a vulnerability inherent in the machinery.
In reliability engineering, a “failure mode” is a vulnerability inherent in the machinery.

If we know the failure modes, we can guide treatment.

**Computational Psychiatry** is about applying *reliability engineering* analyses to neural systems.
Psychiatric failure modes

All of these are computational failure modes.

OCD

an imbalance between planning and habit modes,
perhaps via problems with response inhibition,
or an inability to recognize completion of a target,
or an over-intensity of anxiety predictions?

Lock the door

Go back to check

What if I didn’t lock it?

That would be bad.

That worked.

Turn the key

You don’t need to do that ... again

What if I didn’t lock it?

That would be bad.

You don’t need to do that ... again
Coda: contingency management
Contingency management

If you don’t use drugs for a week (come in clean), then you receive a small reward.

**Current theory:**
- The reward is an *alternate reinforcer*.
- Losing it increases the *opportunity costs* of the drug.

*But the rewards are small.*

Increasing the cost of the drug on the street by that amount has little to no effect.
Coda: contingency management

Is it worth it?

Which one?
Contingency management

CM will depend on working memory.

We can train working memory.

CM will depend on prefrontal cortex and hippocampus.

We can test for prefrontal-hippocampal integrity.

How can we strengthen deliberation?

We can make the second option more concrete.

We can provide reminders.

Is it worth it?

Which one?
• Diagnosis should align to **failure modes** of information processing.

• Treatment should modify that information processing  
  – **Either** through changes in the patient itself  
  **OR** through changes in the environment

• Translation across species requires **computational validity**.
Computational models of information processing as a link across species allowing translation from fundamental discoveries to clinical practice

- Diagnosis should align to **failure modes** of information processing.

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- Translation across species requires **computational validity**.