The Neurobiology of the Language of Thought

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Pre-linguistic Thought

- We share with non-linguistic animals a rich representation of the experienced world
  - Even insects have a cognitive map
  - Even insects learn times of day (circadian phase) at which events happen and the durations of intervals between events
  - Mice learn rates and probabilities
  - They compute ratios and differences of durations

Relation to Language

- Pre-linguistic thought is translated into language when we speak
- When we understand speech or writing, we translate what is said into our pre-linguistic thought

Fodor’s Language of Thought

- Any representation requires symbols
- These symbols often refer to aspects of the experienced world (e.g., objects, actions, durations, distances, stochastic parameters)
- They enter into the computations that mediate thought (as when the be computes the current solar bearing of the food source)

Linguistics and Neuroscience

- Linguists drive neuroscientists crazy and vice versa
- Profound mutual incomprehension
- Because neuroscientists have no idea what a symbol might look like in the brain
- They have never really bought into the computational theory of mind—despite what they may say

Symbols Live in Memory

- The function of a symbol is to carry information forward in time in a manner that makes it accessible to computation
- Serves the same function in time as action potential serves in space
- The neuroscientific story about memory is profoundly incoherent; they believe:
  - Information is stored in the brain by changes in synaptic conductances (the philosophers' 'associations')
  - But there is no way to store a number in a change in synaptic conductance(s)

Revolutionary Results

- Recent experimental results imply memory is inside neurons
- If so, then so is the computational machinery, *because* computation and memory are intimately linked

Argument

- Many of the brain's computations are done by molecular-level structures inside neurons, rather than by circuit-level structures, ***because***
  - *S*ynaptic theory of memory is a conceptual and empirical failure
  - The known biological structures specialized for information storage are molecules
  - Molecular Information storage and computation is orders of magnitude more compact and energy efficient
  - More than fast enough

The Recent Results

- Hesslow lab, Lund (Johansson, et al. “Memory traces and timing mechanism localized to cerebellar Purkinje cells”, PNAS, 2014, 111, 14930–14934)

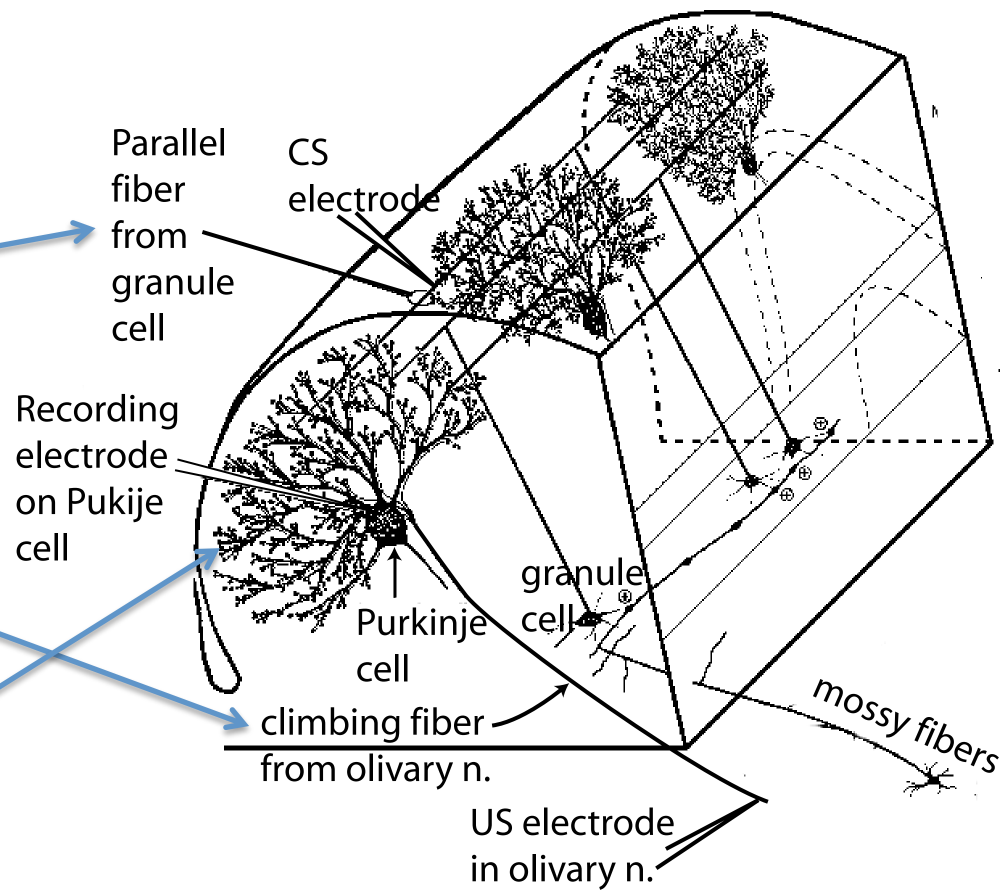
- McGann lab, Rutgers (Kas, et al. 2013, “Fear learning enhances neural responses to threat-predictive sensory stimuli.” *Science*, 342, 1389-1392 --*will skip this but check it out*

Durations Are Stored

- Latency of conditioned responses proportional to the CS-US interval (in e.g., Pavlov's experiment)
- So duration of CS-US interval stored in memory
- Where and how ?
- Usual answer to 'where': "in the synapses"
- Usual answer to 'how': **?**
  - there is no specification of a <u>synaptic code</u> (for duration or anything else)
- Results from Hesslow lab imply that duration of the CS-US interval in eye blink conditioning stored <u>inside</u> the Purkinje cell

Direct Conditioning of Purkinje Cells

- Conditioned eye blink mediated by cerebellar circuit
  - Parallel fibers from the granular cells convey CS signal to dendrites of Purkinje cells
  - Climbing fiber conveys US signal
  - Purkinje cell is the cerebellar output; it controls the *timed* blink



Purkinje Cell Pause

- CS-US "conditioning" produces a *timed* pause in the spontaneous firing of the Purkinje cell
- Duration of firing pause equal to CS-US interval (Wetmore, et al, 2014)
- Duration of firing pause determines the latency of the blink (Heiney, et al, 2014)

Johansson et al experiment

- Record from Purkinje cell
- Generate *artificial* CS signal by stimulating parallel fibers <u>at 100 pps for 800 ms</u>
- Generate *artificial* US signal in climbing fiber by single pulse to olivary nucleus
- Vary interval from CS onset to US pulse between preparations: <u>150 ms, or 200 ms, or 300 </u>ms

(NB: during conditioning CS signal always continues beyond US pulse for at least 500 ms)

Results

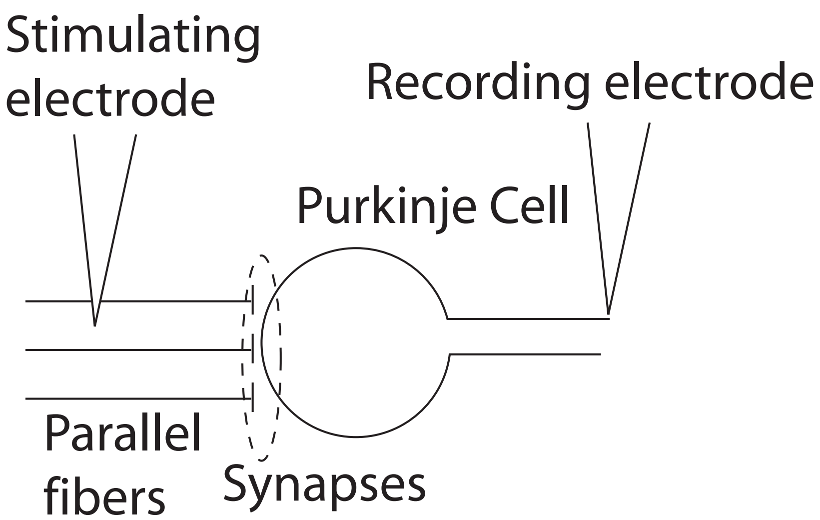
- *Unconditioned* Purkinje cell responds to artificial CS with an <u>increase</u> in firing rate <u>*lasting as long as the CS signal (800 ms)*</u>
- Not surprising: parallel fiber–>Purkinje cell synapse excitatory (glutaminergic)
- BUT, conditioning induces profound pause in Purkinje cell firing, beginning a few ms after onset of CS stimulation and <u>*lasting only as long as the CS-US interval*</u> (150, 200 or 300 ms)

Key Result

- Learned pause independent of CS stimulation parameters
- CS stimulation at 500 pps lasting only 17.5 ms produces same pause as original CS stimulation at 100 pps lasting 800 ms
- *The acquired information about the CS-US interval, which determines the duration of the neuron's firing pause, appears to reside inside the neuron itself, and to be independent of the <u>patterning</u> of synaptic input*

Interpretive Logic

- Memory for interval duration resides somewhere between point of stimulation & point of recording
- In this simple prep, it must reside <u>either</u> in synapses <u>or</u> inside Purkinje cell



In Traditional Conception of Synapse:

- Post-synaptic effect of presynaptic signal <u>joint function</u> of that signal and synaptic conductance
- Synapse only amplifies (or deamplifies) input signal
- Therefore, it cannot perform the observed transformation, which is independent of the parameters of the input signal
- Must be done by a memory inside neuron itself

Time to Move Beyond Hebb

- Synaptic theory of memory is a **conceptual failure**, because it doesn't explain how altered synaptic conductances:
  - carry acquired information
  - make it accessible to computation
- See Gallistel & King (2010) *Memory and the computational brain*

Time to Move Beyond Hebb

Synaptic theory of memory is an **empirical failure**, because no measurable property of LTP & LTD corresponds to any behaviorally measured property of associative learning

– LTP & LTD have critical intervals measured in 10s of ms

But there is no critical interval in associative learning and behavioral time scale is 2-3 orders of magnitude longer

– For LTP & LTD, the longer the interval between "pairings", the weaker their cumulative effect

But opposite is true at the behavioral level; the more widely separated the trials, the fewer are required for learning

Time to Move Beyond Hebb

Empirical failure continued:

- Conditioned behavior persists to some extent indefinitely (the memory never dies)

  But LTP & LTD decay rapidly (hours or days)

- "Forgotten" or extinguished conditioned behavior reacquires rapidly and persists at high strength longer

  But decayed LTP & LTD does not reacquire more rapidly nor persist longer

- Conditioning depends on learning the durations of the protocol intervals

  But no evidence that LTP & LTD encode interval durations

See Gallistel & Matzel (2013) Neuroscience of learning: Beyond the Hebbian synapse. *Annual Review of Psychology*

Time to Move Beyond Sherrington

- The cell, hence the neuron, is a MUCH more complicated entity than Sherrington and his contemporaries imagined
- It contains elaborate information processing machinery, implemented at the molecular level
- **But** <u>in most cognitive neuroscience modeling</u>, neuron is simply a leaky integrator with a threshold (a capacitor and a diode in parallel)

Do Molecules Carry Information?

- Of course
- Most conspicuous are DNA and RNA
- We know how to store numbers in DNA or RNA
- *If you can store a number, you can store any kind of information!*
- We do not know how to store numbers in altered synaptic conductances!

Other Possibilities

- Isomerization of molecules like the opsins, which are thermodynamically stable in both forms and enzymatic in one form (readable switches)
- Methylation
- Phosphorylation
- Cell fate switches
- *Any thermodynamically stable, biochemically active molecular switch can store information*

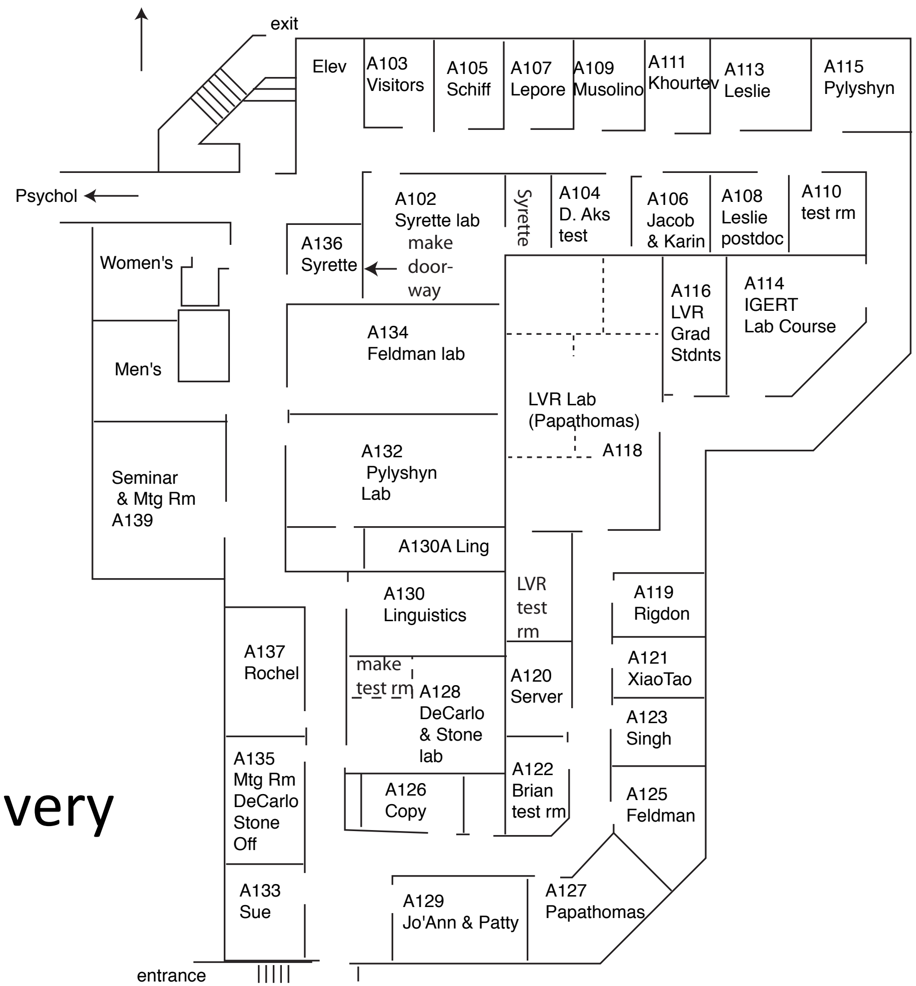
How Much Information?

- 3 billion (3×10^9) nucleotides in human DNA
- 98% are non-coding
- 2-bits/nucleotide
- Non-coding DNA in a single neuron could carry roughly 750 megabytes of information
- Many thousands of micro RNAs routinely synthesized inside most cells; most have no known function

Much More Than Needed

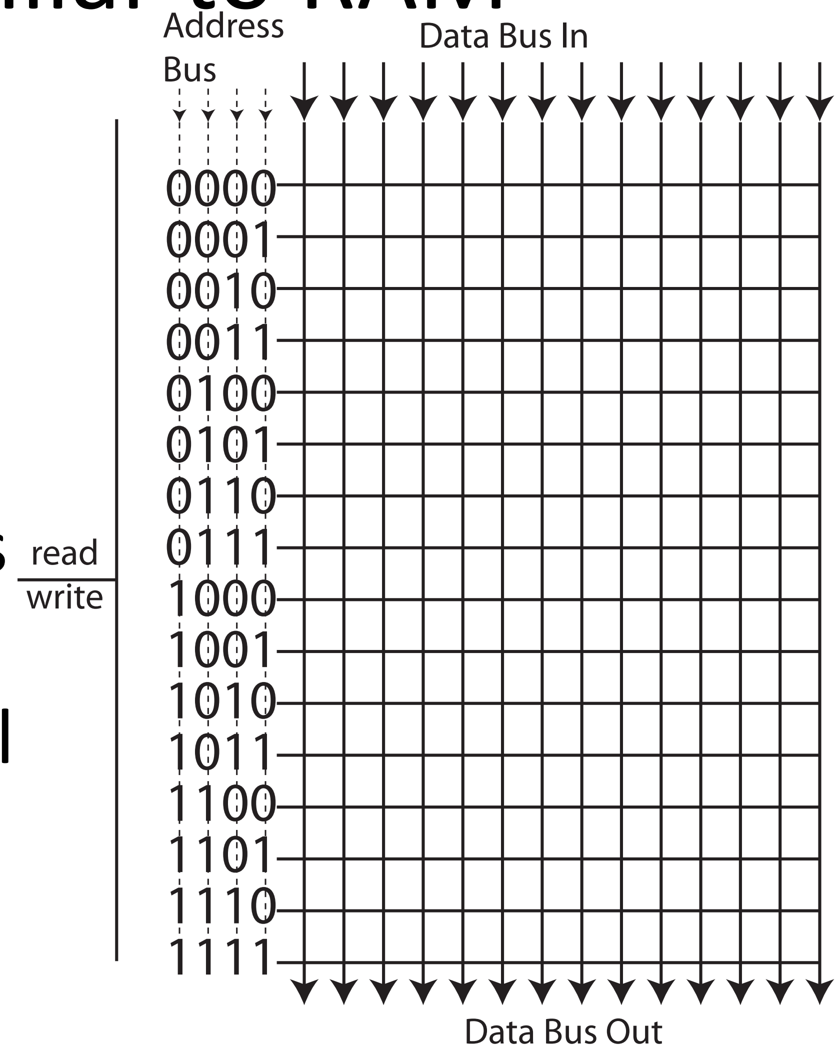
File size: 160 kilobytes, < 0.03% of the capacity of the non-coding DNA in one neuron

Geometry of the rat's experienced environment <u>could</u> be encoded inside every hippocampal neuron



Architecture of Genetic Information Storage Similar to RAM

- A <u>coding</u> portion (<u>data</u>)
- And an Operon (promoter/repressor) portion (an address)
- This architecture makes possible variable binding and hierarchical data structures, in RAM <u>and</u> in DNA



Do Molecules Compute?

- Logic gates are implemented in the transcription of genes:
  - AND: dimer of 2 transcription factors (tfs) binds to promoter but neither constituent does
  - NAND: dimer of 2 tfs binds to repressor but neither constituent does
  - OR: either of 2 tfs binds to promoter
  - XOR: either tf binds to promoter but dimer doesn't
  - NOT: tf binds to repressor

Vastly More Efficient

- Adleman (1994) used DNA to find Hamiltonian path through directed graph
  - 10^{14} operations/s using picomole quantities
  - Each operation hydrolyzed 1 ATP. This is 2×10^{19} operations/joule – within order of magnitude of theoretical limit
- It costs only 1-2 ATPs to add nucleotide during RNA symthesis (2 bits stored per ATP hydrolyzed)
- One turn of DNA contains 11 nucleotides (so can store <u>22 bits</u>) in a volume of 1.1×10^{-26} meters (11 cubic <u>**nanometers**</u>)

By Contrast

- $7x10^8$ ATPs hydrolized per each action potential
- Assuming 1 operation/spike, it would require on the order of 10^{14} spikes/s to achieve rates achievable at molecular level = 3500 joules/s = 1/3 total human energy expenditure per day
- One neuron has a volume on the order of $2x10^{-14}$ meters (20,000 **cubic microns**) and it takes at least two neurons to make a neural circuit—a 12 to 15 orders of magnitude difference in the required volumes

And Fast Enough

- Could information stored in molecules within neurons be accessed fast enough to be behaviorally useable?
- Vision depends on an externally triggered change in an intracellular molecule (the isomerization of a photopsin)
- 6 intracellular biochemical processes connect this change to the hyperpolarization of the receptor membrane
- Yet (some) people can hit Djokovic's serves and Tanaka's fast balls (some of the time)

In Conclusion

- There is now evidence that acquired information is stored inside neurons
- Presumably in molecules
- If the information on which computation depends is stored in molecules, then the computational machinery is likely also realized at the molecular level
- Known molecular machinery has the capacity to store and process information
- So this outlandish proposal may be worth further consideration....
- Because contemporary neuroscience has no coherent story about memory and...
- *memory is as central to computation as DNA is to life*

Thank You

- And to the NIMH, which has funded my research
- And to those of you who I hope will ponder whether this suggestion is worth thinking further about

Class 2

The Computational Foundations of Modularity in Learning

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Learning processes are those by which we acquire knowledge of the world

They are computational processes, because...

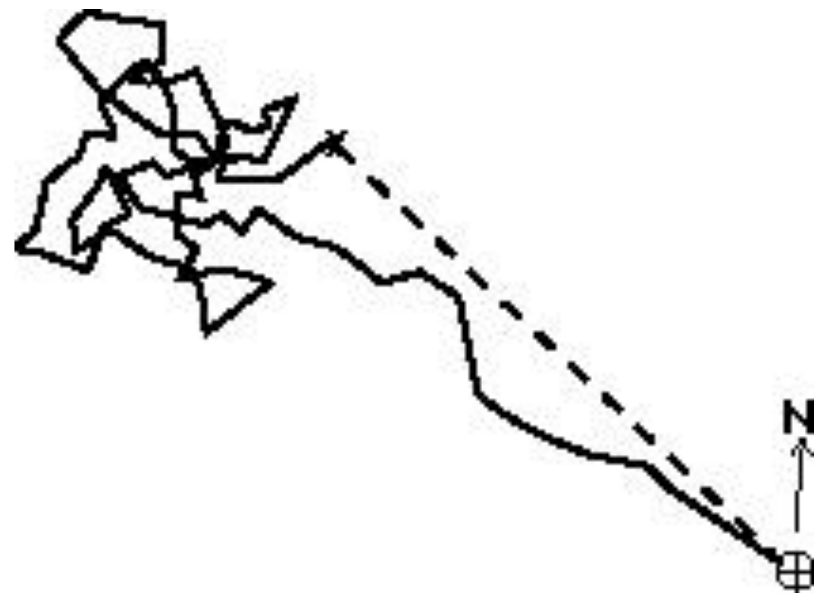
- What we need to know is not directly given by sensory experience
- It must be computed from what is directly given

Different kinds of knowledge require different kinds of computations

- Dead reckoning requires integrating velocity with respect to time
- Learning the solar ephemeris requires fitting an innately specified function to the data
- Learning language requires determining parameter values in a universal grammar
- Pavlovian conditioning requires multi-variate, non-stationary time series analysis

Dead Reckoning

The foraging ant knows where it is



--Harkness & Maroudas, 1985

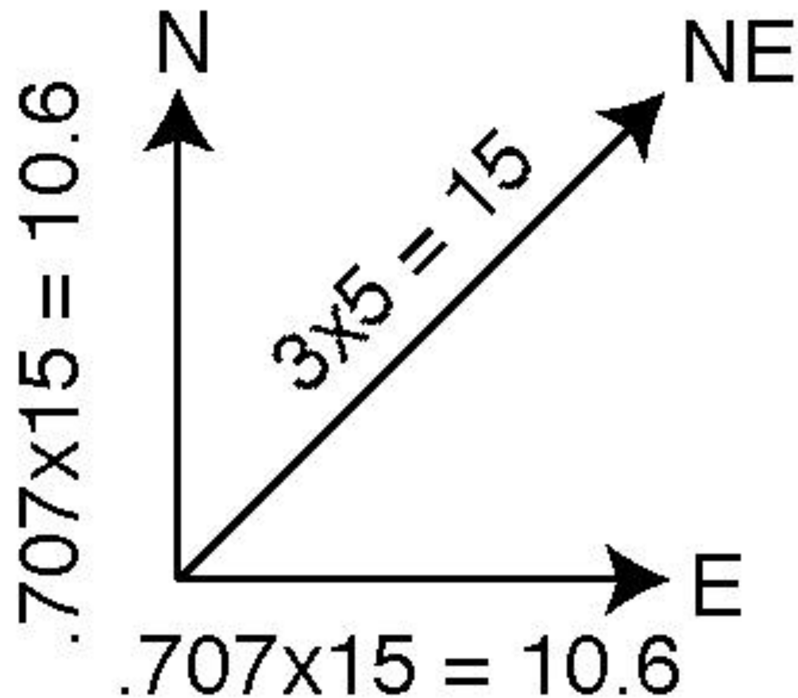
Dead Reckoning

- It does so by integrating velocity with respect to time
- Structure of the computation reflects analytic structure of the world

$$P(t) = \int v(t)dt$$

Dead Reckoning

Sailing northeast for
3 hours at 5 knots
puts you 15 nautical
miles northeast of
where you were
or 10.6 miles north
and 10.6 miles east.



Dead reckoning is a problem-specific knowledge-acquisition mechanism

- **Environmental fact:** Position is the integral of velocity with respect to time
- **Biological fact:** animals integrate their velocity with respect to time to estimate their position
- **This computation solves only this problem**

The sun is the preferred directional referent in dead reckoning

- **But the sun moves**
- **To estimate your compass direction from your solar orientation, you need...**
  - A clock (to provide knowledge of the time of day)
  - Knowledge of the solar ephemeris

Solar ephemeris must be learned

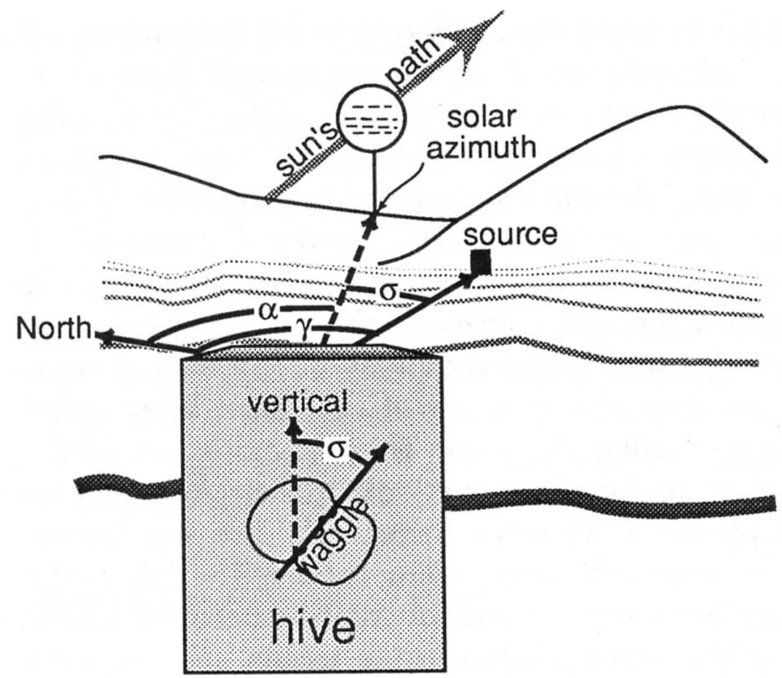
- **because it varies as a function of**
  - Latitude
  - Season

Bees learn the solar ephemeris by curve fitting

- **A built-in function is fit to the data**
- **Ergo, what they learn transcends what they experience (cf Chomsky's poverty of the stimulus argument)**
  - Bees in northern hemisphere believe the sun is due north at midnight (Lindauer, 1957)
  - Bees who have only seen the sun in the late afternoon believe it is in the east in the morning (Dyer & Dickinson)

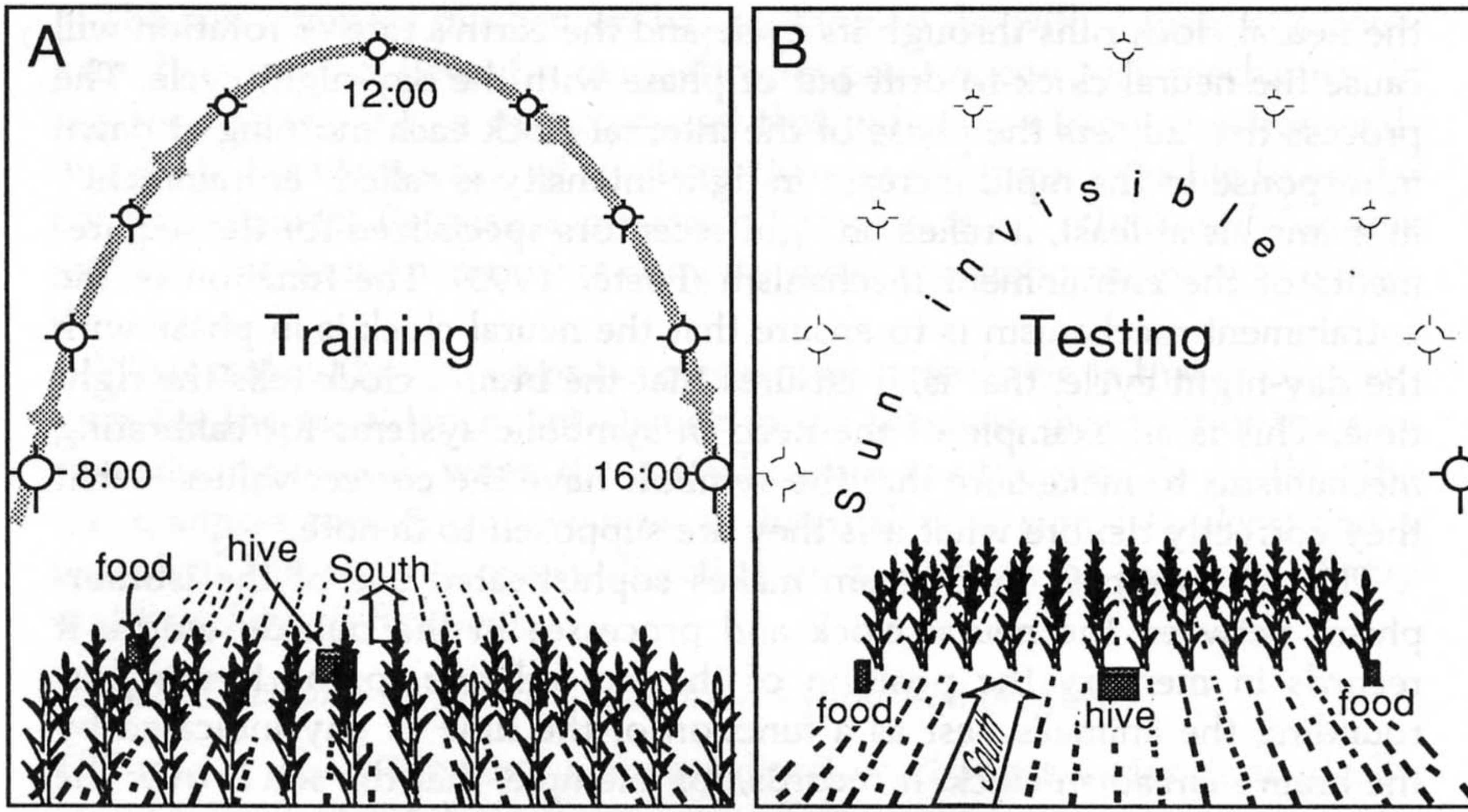
Learning from the Dance

- Returning forager does a dance to tell other foragers the location (range & bearing) of source
- Compass bearing, γ, specified by specifying current solar bearing, σ
- Range specified by number of waggles

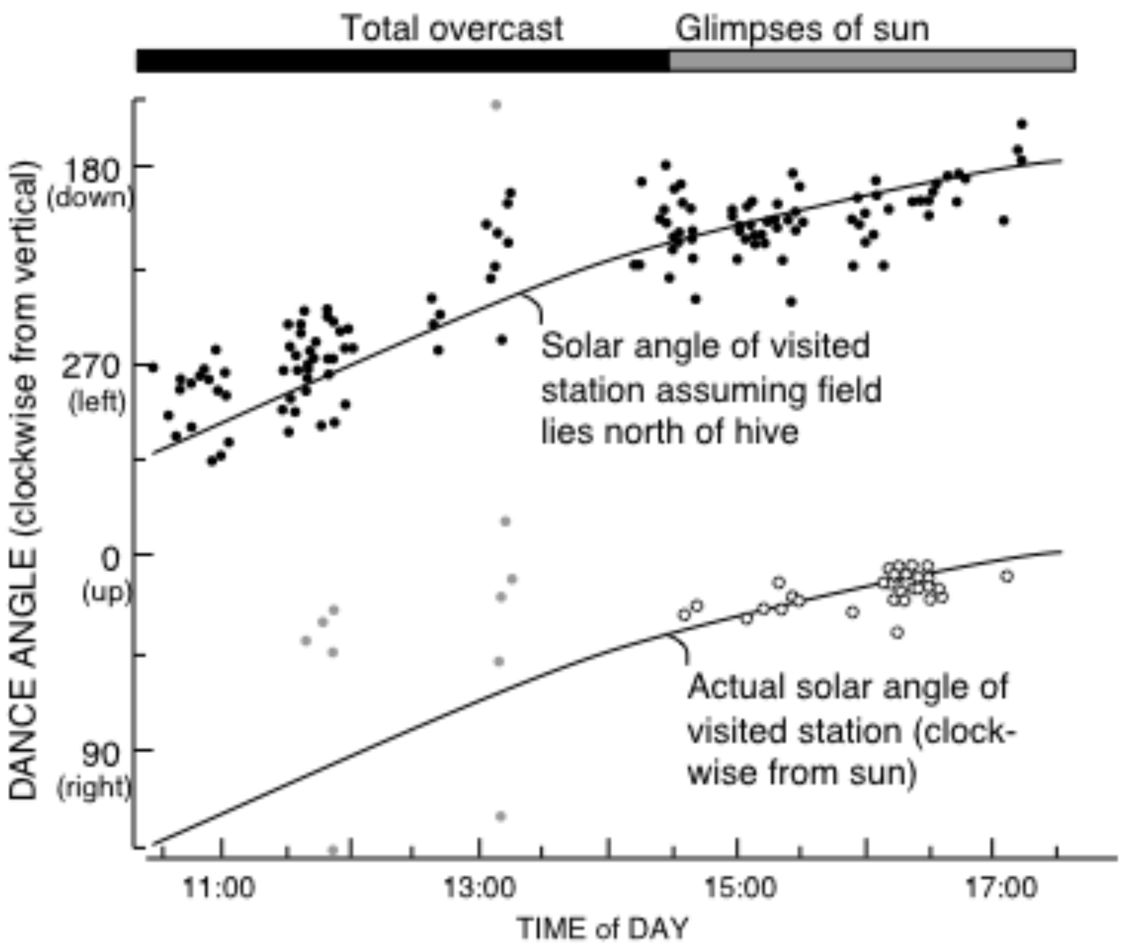


α = compass bearing of sun
γ = compass bearing of source
σ =solar bearing of source

Ephemeris Framework



Deceived Dancing

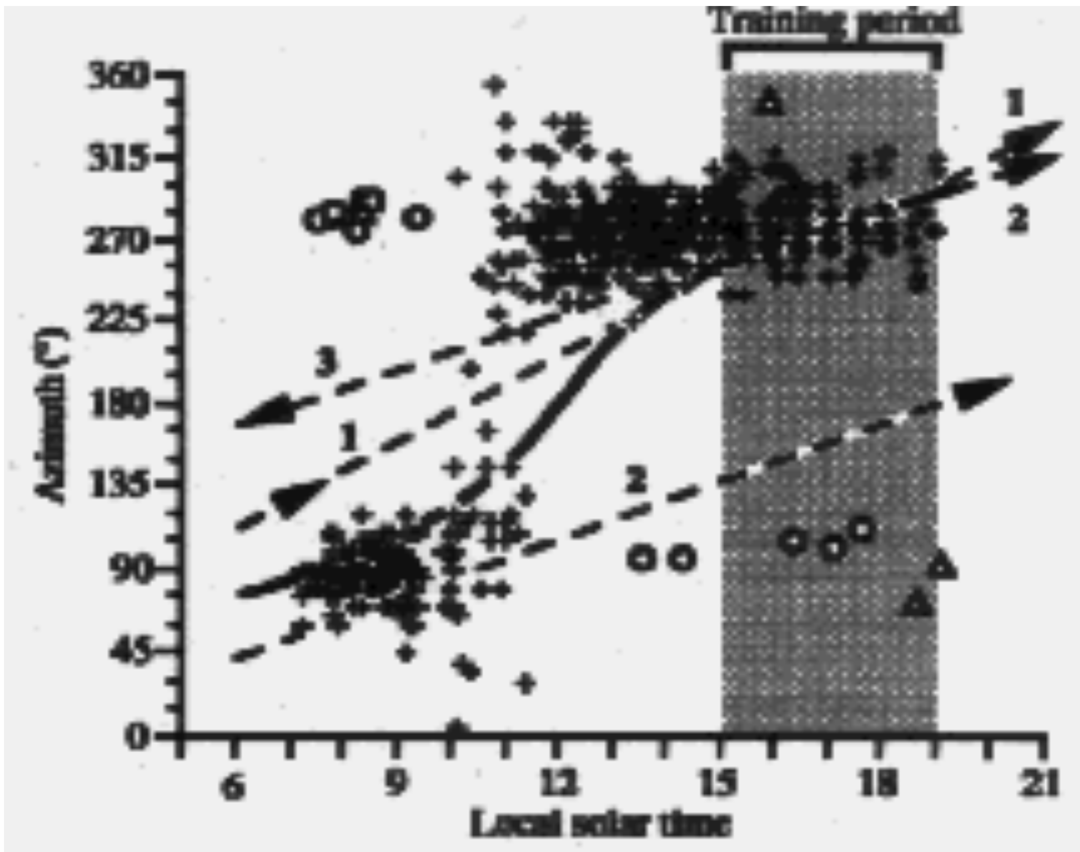


Dyer, 1987

Poverty of Stimulus

- Dyer & Dickinson, 1994
- Incubator raised bees allowed to forage to station due west of hive but only in late afternoon when sun declining in west
- On heavy overcast day, allowed to forage for the first time in the morning, when sun is in the east
- Experimenter observes dance of returning foragers to estimate where they <u>believe</u> the sun to be

Bees Believe Earth is Round



Implications

- Form of solar ephemeris equation is built into the nervous system
- Only its parameters are estimated from observation
- Solves poverty of the stimulus problem: the information about <u>universal</u> properties of the ephemeris in the priors
- Neural net without this prior information could not generalize as bees do

Humans learn a language by parameter estimation

- A universal grammar is built into the learning mechanism
- Learning a particular language involves learning the right parameter values (e.g., head-first vs head-final)

Is all learning mediated by problem-specific modules?

- **What about "associative" learning--the learning that occurs in Pavlovian conditioning?**
- ***What is the problem for which the mechanism that mediates this learning is specifically structured?***

Conditioning paradigms are...

- **Problems in time series analysis**
  - **US occurrence depends in a statistical sense on CS occurrence**
- **<u>Multivariate</u> problems**
  - **More than one CS may affect likelihood of US occurrence**
- **Nonstationary problems**
  - **Dependence changes with time (at, for example, onset of extinction)**

A Problem-specific model of Pavlovian conditioning

(Gallistel & Gibbon, 2000)

- **Conditioned responses appear when**
  - **ratio between expected intereward intervals exceeds a decision threshold**

$$\frac{I\hat{R}I_{\mathrm{b}}}{I\hat{R}I_{\mathrm{cs}}} > \beta$$

Rate Estimation Process

- Assumes rates are additive
  - This leads to systems of simultaneous linear equations
  - Solved by matrix inversion and multiplication
- Minimizes the number of predictors
  - Redundant CSs not credited with predictive power (in, for example, blocking)

Change-Detecting Process

- Compares interval since last reward to the expected interval between rewards
- Responding ceases when this ratio exceeds a decision threshold

$$\frac{\hat{I}_{\mathrm{csNoR}}}{\hat{IRI}_{\mathrm{cs}}} > \beta_{\mathrm{e}}$$

Problem-Specificity

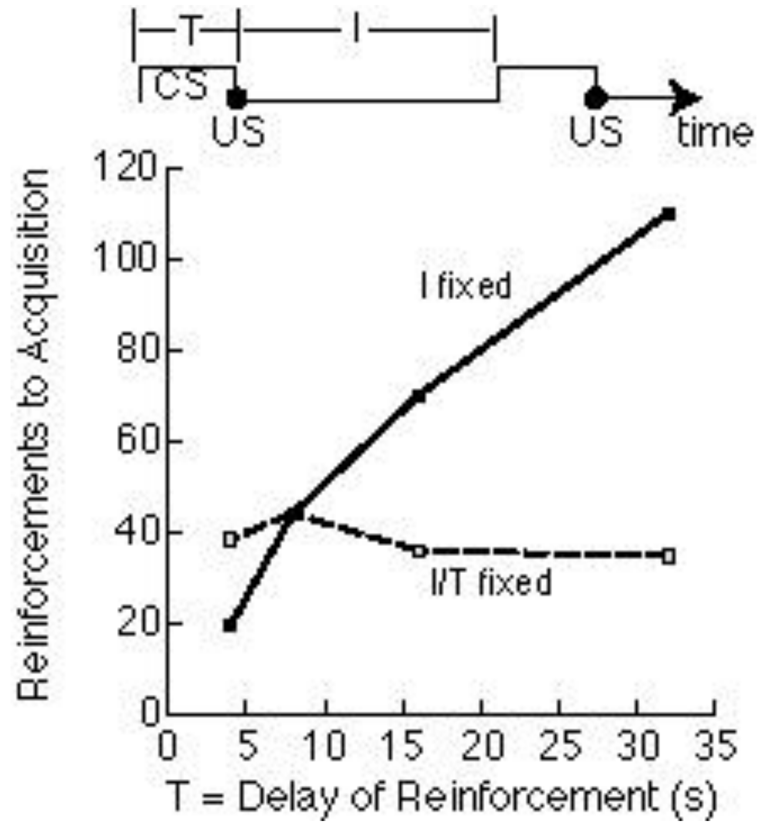
- These computations specific to mutivariate, nonstationary time series with additive rates
- Computational structure of the learning mechanism reflects inherent structure of the problem
- Not a general purpose learning mechanism

Why Prefer Problem-Specific Model?

- Explains time-scale invariance
- Changing the time-scale of a conditioning protocol has no effect on the results

Example of Time Scale Invariance

- Increasing delay of reward has no effect on rate of conditioning <u>provided </u>intertrial interval is increased by same factor

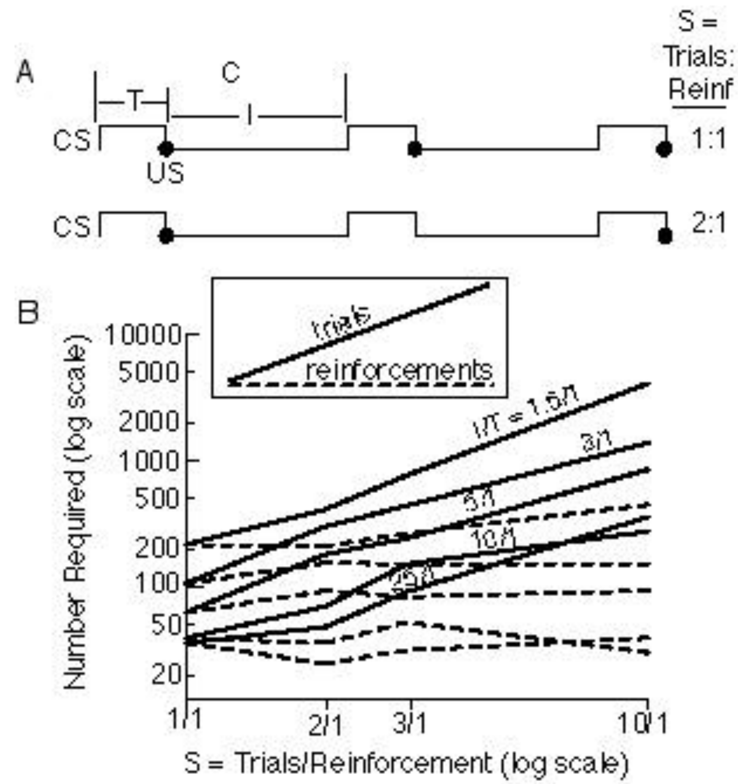


Replot of data
from Gibbon, et al., 1978

Second Example of TSI

- Partial reinforcement does not affect rate of acquisition

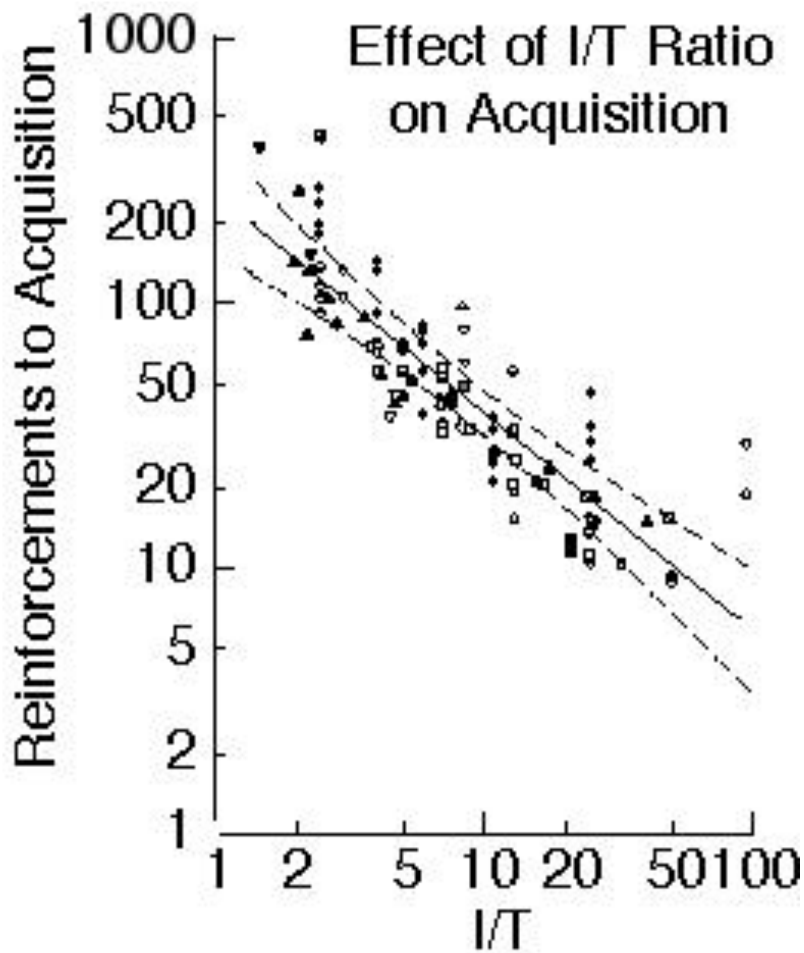
Replot of data from Gibbon, et al., 1980



Altering temporal proportions does affect conditioning

- Increasing the intertrial interval changes the proportion between intervals when CS is present and intervals when it is not present

(From Gibbon & Balsam, 1981)



Is Memory Itself Specialized?

Not in the Associative Framework

- No clear distinction between learning and memory
- System conceived of as something that maps inputs to outputs, not something that stores information about the world
- Learning alters the mapping: it rewires the system to make it behave more adaptively

The associative strengths <u>are</u> the "memory"

- Because they are the only enduring changes
- Do not encode information about world
- Cannot because mapping from facts of experience to assoc. strength many->one
- Thus, there is no clear notion of retrieval from memory (nothing to retrieve)

Information Processing Framework

- Learning computes facts about world; it extracts information from experience
- <u>Memory carries the extracted information forward in time</u>
- Retrieval processes read the information out for use in the decision processes that determine behavior

Information is Information

- In computer science
- In genetics
- In neurobiology

Universality Hypothesis

- The mechanism that carries information forward in time in the nervous system is the same regardless of the content of that information
- Only problem that has determined the evolution of this mechanism is the problem of preserving large amounts of information over long periods of time with minimal expenditure of energy

Retrieval Processes Not Universal

Different “memories” recognized by psychologists arise from the problem-specific nature of the processes that determine how and when information in memory is read out to inform current behavior