CCN Lecture

Depression & Reinforcement Learning

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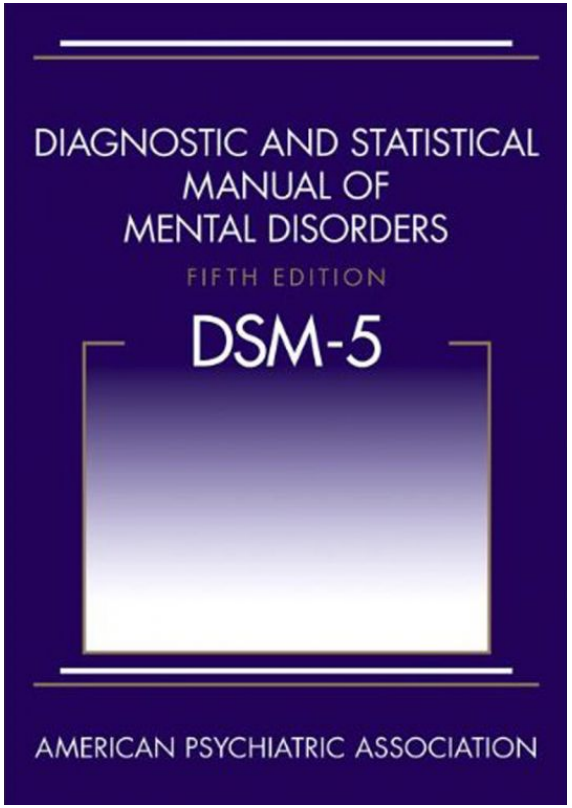
Sam Rupprechter

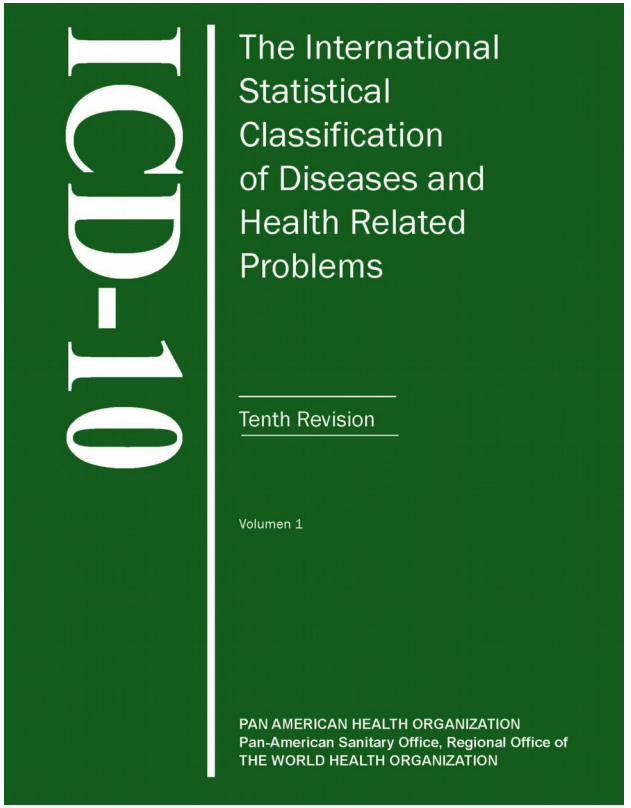
s1520312@sms.ed.ac.uk

Outline

- Depression
- Reinforcement Learning (RL)
- RL Impairments in Depression
- Modelling Theory

Major Depressive Disorder (MDD)





Major Depressive Disorder (MDD)

- Core symptoms:
  - **Depressed mood**
  - **Anhedonia** (inability to experience pleasure)
  - Loss of energy
  - Change in weight or appetite
  - Insomnia / Hypersomnia
  - Psychomotor agitation / retardation
  - Concentration difficulties
  - Suicidal thoughts / ideation

Major Depressive Disorder (MDD)

- Categorical view has little basis in biology?
  - Research moves towards dimensional view
- RDoC framework
  - Multiple levels of analysis
    - Neural circuitry, genes, behaviour
- Endophenotypes
  - Anhedonia
  - Neuroticism

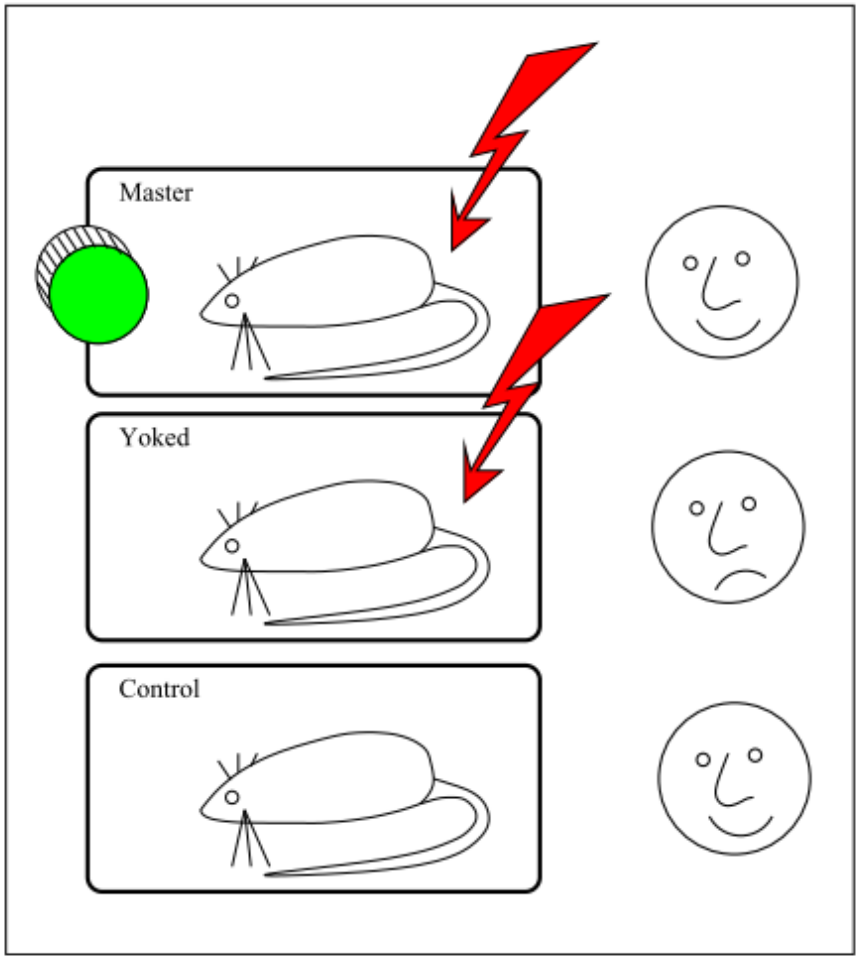
Treatment

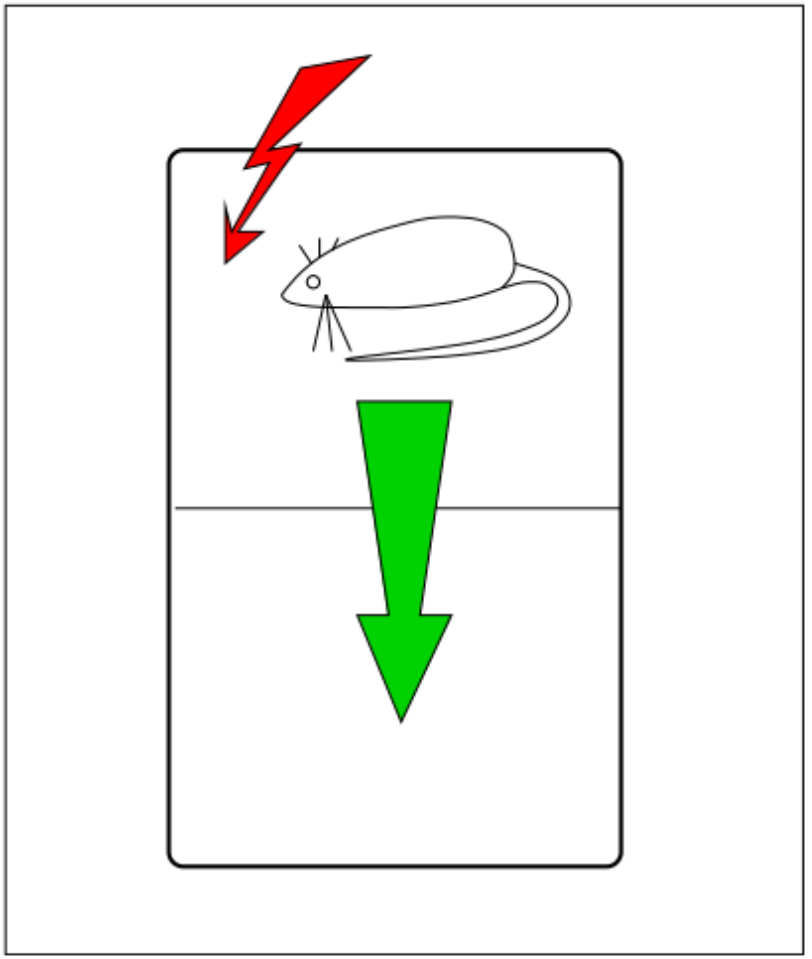
- Cognitive Behavioural Therapy (CBT)
- Antidepressant medication
  - Selective Serotonin Reuptake Inhibitors (SSRIs)
    - Primary first line treatment
  - Serotonin-Norepinephrine Reuptake Inhibitor (SNRIs)
  - Tricyclic Antidepressants (TCAs)
- Electroconvulsive therapy (ECT), Surgery
  - Very severe, treatment-resistant cases

MDD Theories

- Cognitive Theory (Beck, 2008)
  - Negative cognitive schemas (CBT targets those)
  - e.g. biased recalling of negative events
- Learned Helplessness (Seligman, 1972)

Learned Helplessness





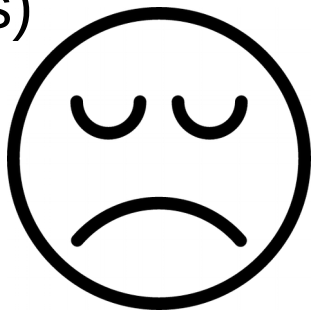
Huys et al., 2008; NIPS

MDD Theories

- Cognitive Theory (Beck, 2008)
  - Negative cognitive schemas (CBT targets those)
  - e.g. biased recalling of negative events
- Learned Helplessness (Seligman, 1972)
- Stress → deficits in reinforcement / reward processing (learning) → anhedonia (Pizzagalli, 2014)
  - 70-80% of Major Depressive Episodes preceded by major life event

Impact

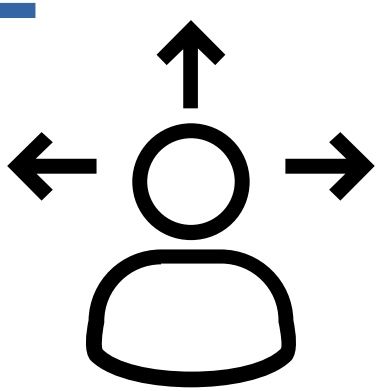
- High (lifetime) prevalence (esp. in developed countries)
  - USA: 16.2% (Kessler et al., 2003)
  - UK / Europe: 7-10% (Ayuso-Mateos et al., 2001)
  - Depression rates are rising (e.g. Mojtabai et al., 2016)



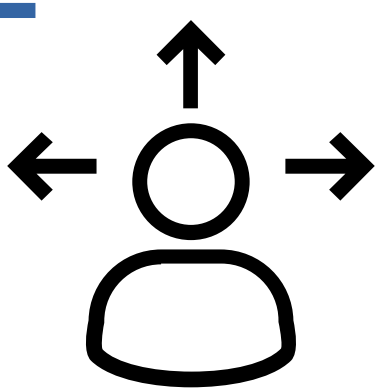
- High economic impact (Europe: €92 billion in 2010) (Olesen et al., 2012)
- People are suffering
  - Risk factor for suicide (Olfson et al., 2017)
    - And suicide rates are increasing
  - Cognitive Impairments (e.g. Snyder, 2013)
    - Attention, concentration, executive functioning, working memory, …
  - Impairments in Reinforcement Learning (Chen et al., 2015)

Reinforcement Learning (RL)

- Make a choice
  - Based on “internal values”
- Observe an outcome (reinforcer)
  - Often probabilistic
  - Generates prediction error
- Update internal values



Reinforcement Learning (RL)



- Update values

$$V(t+1) = m \times V(t) + \varepsilon \times (\rho \times r(t) - V(t))$$

- Decide between two options

$$p(a \mid V, \theta) = \frac{1}{1 + \exp(-\beta \times (V_a - V_b))}$$

- (Can be made more sophisticated; e.g. Q-learning)

RL Impairments in MDD

- Signal Detection Task
- fMRI studies
- Computational Modelling

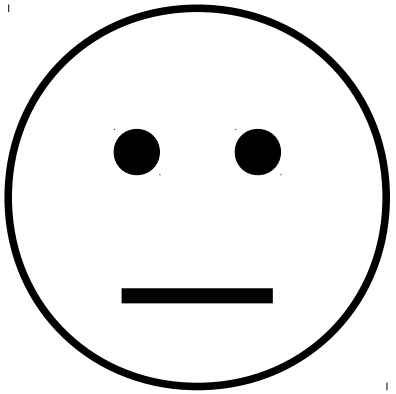
- Iowa Gambling Task (?)
- Reversal Learning (?)

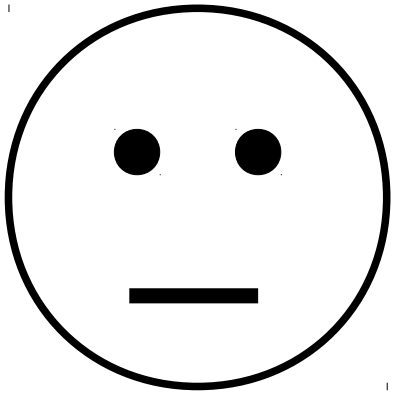
Signal Detection Task (e.g. Pizzagalli et al., 2005)

DEMO

(sort of)

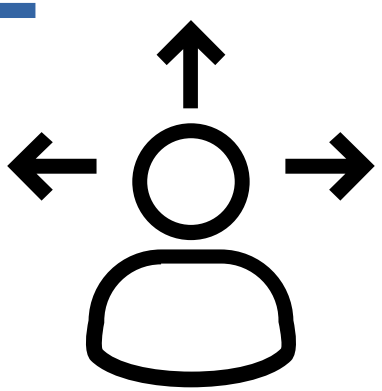
Signal Detection Task (e.g. Pizzagalli et al., 2005)





- One stimulus rewarded more often
  - (healthy) participants become biased towards it

Reminder: Reinforcement Learning (RL)



- Update values

$$V(t+1) = m \times V(t) + \varepsilon \times (\rho \times r(t) - V(t))$$

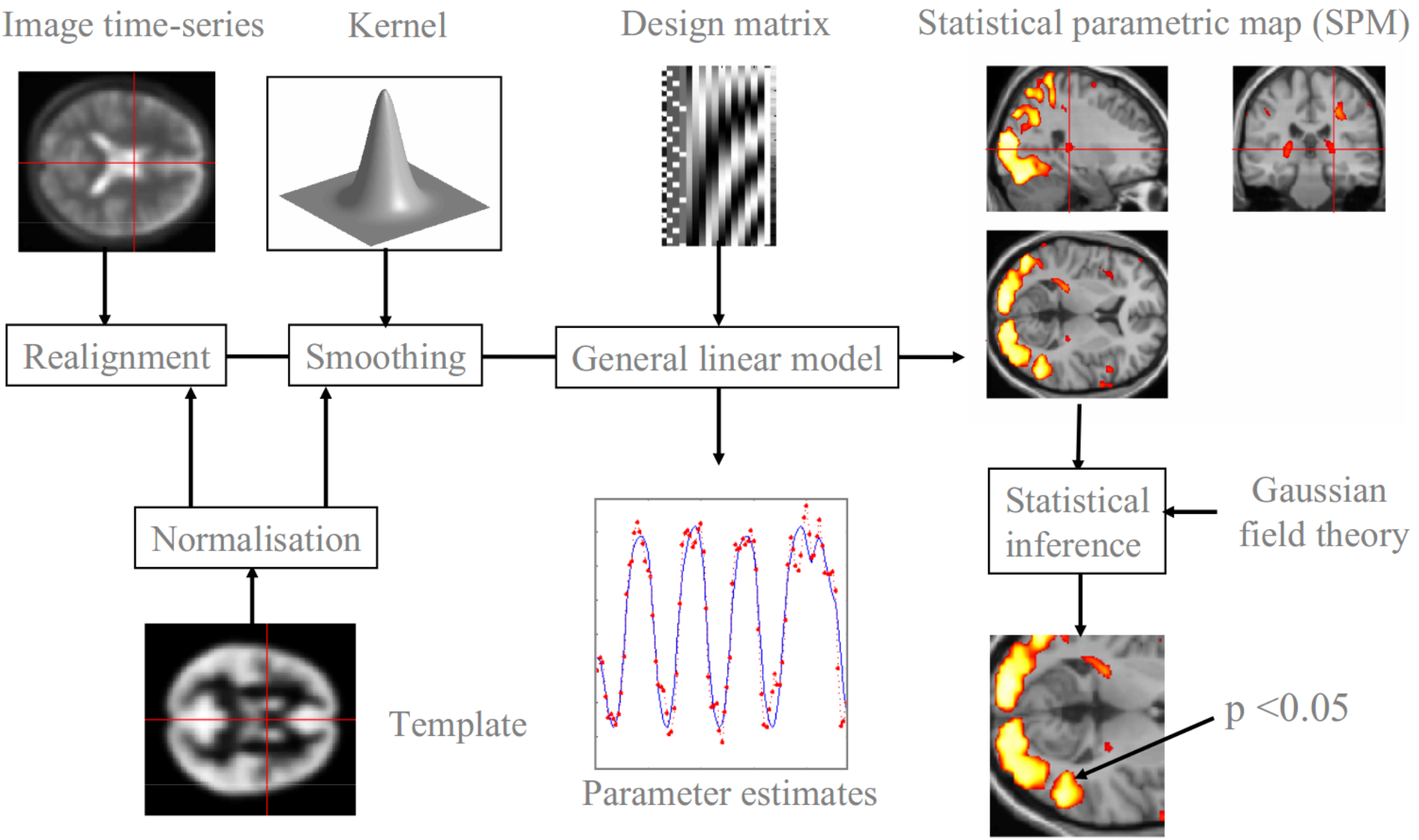
- Decide between two options

$$p(a \mid V, \theta) = \frac{1}{1 + \exp(-\beta \times (V_a - V_b))}$$

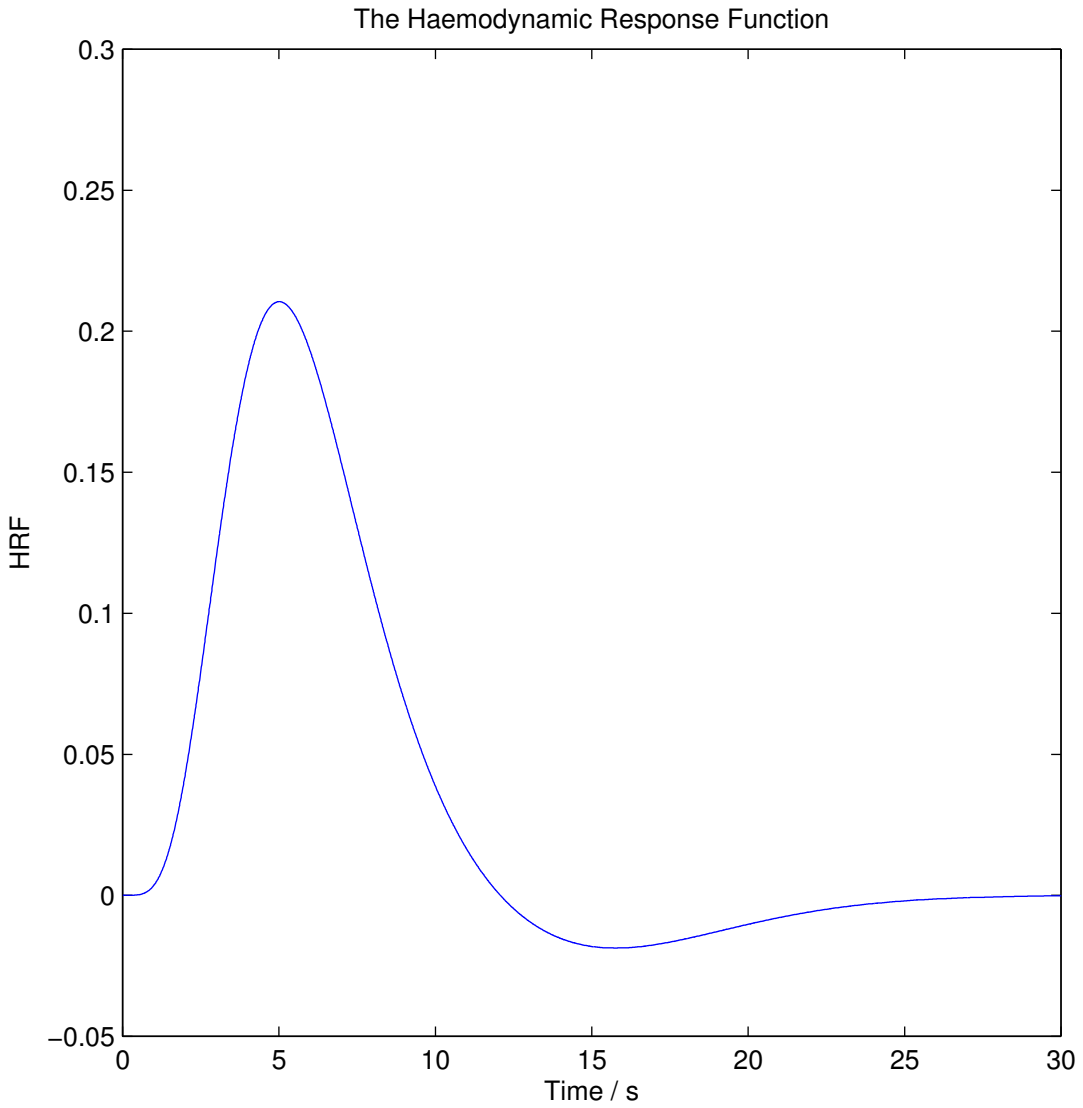
MDD Modelling Studies (behavioural)

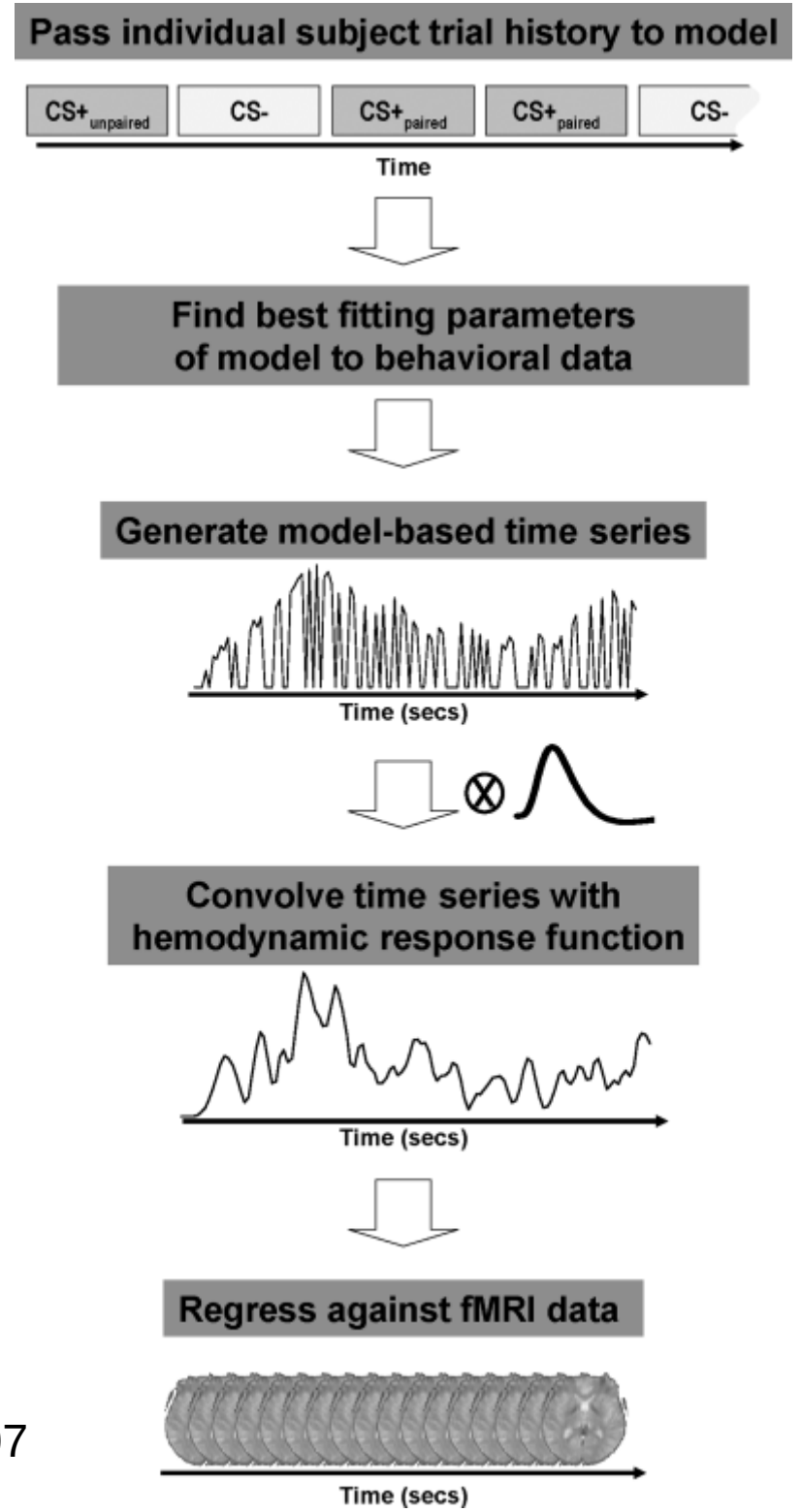
- Chase et al., 2010
  - Lower learning rates
- Kunisato et al., 2012
  - Lower temperature parameter
- Huys et al., 2013
  - Lower reward sensitivity
- Beevers et al., 2013
  - Higher temperature parameter
- Dombrovski et al., 2010
  - Lower memory [in suicide attempters]

Analysing fMRI Data (with SPM)



http://www.fil.ion.ucl.ac.uk/spm/doc/intro/intro.pdf





- “Model-based” fMRI →

O'Doherty et al., 2007

Back to MDD

- Model-based fMRI (e.g. Kumar et al., 2008; Gradin et al., 2011)
  - No real behavioural differences
  - Abnormal reward prediction errors
  - Abnormal expected reward values

(Behavioural) Modelling

- How do I actually “fit” a model to data?
  - Try to find “optimal” values for the parameters of the model that our data “most likely”

    (maximize the probability of observed choices)

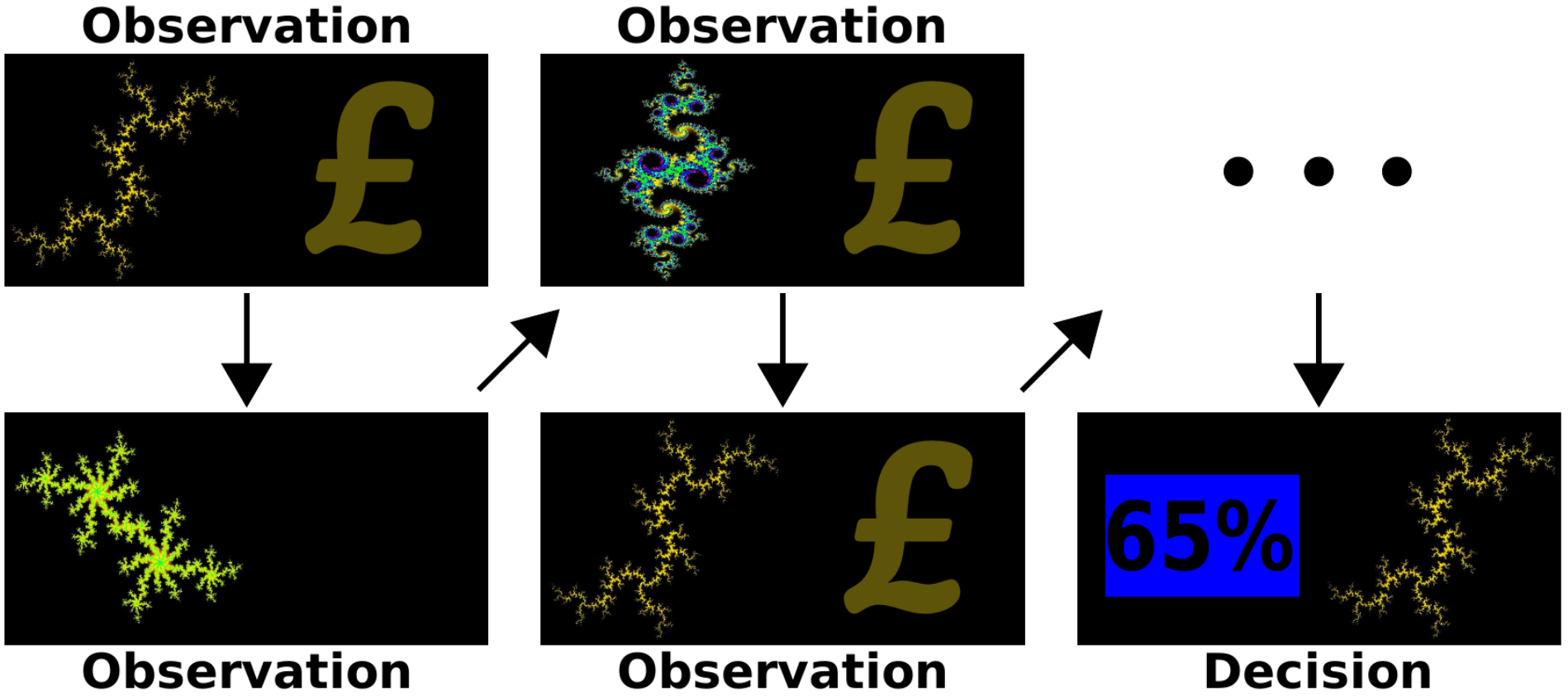
Maximize the Likelihood

$$L = p(A \mid V, \theta) = \prod_{a \in A} p(a \mid V, \theta)$$

- Multiplying lots of small numbers is a bad idea… take the log instead!
- Instead of maximizing log likelihood → we usually minimize negative log likelihood

$$NLL = -\sum_{a \in A} \log p(a \mid V, \theta)$$

Example Experiment



Stankevicius et al., 2014; Further work in progress

Our Model

- Value Update

$$V_i^{t+1} = A \times V_i^t + r_i^t$$

- Decision

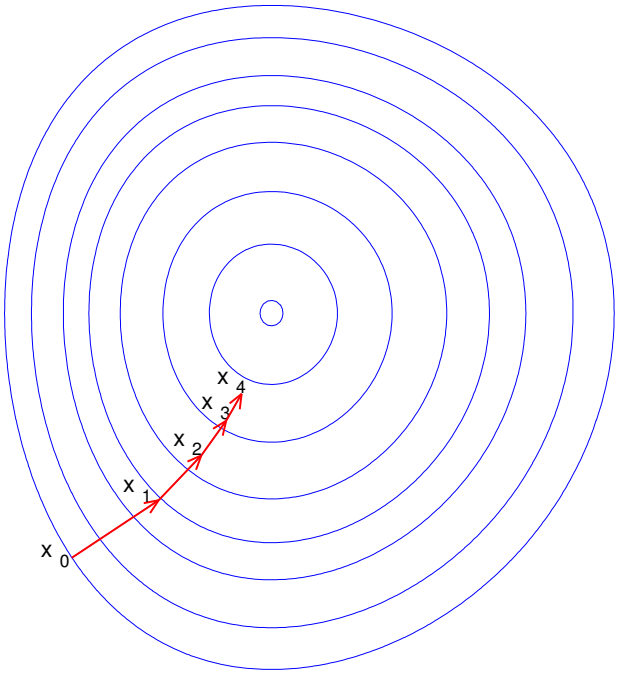
$$p(\text{choose fractal i}) = \frac{1}{1 + \exp(-\beta(f(V_i) - \phi_i))}$$

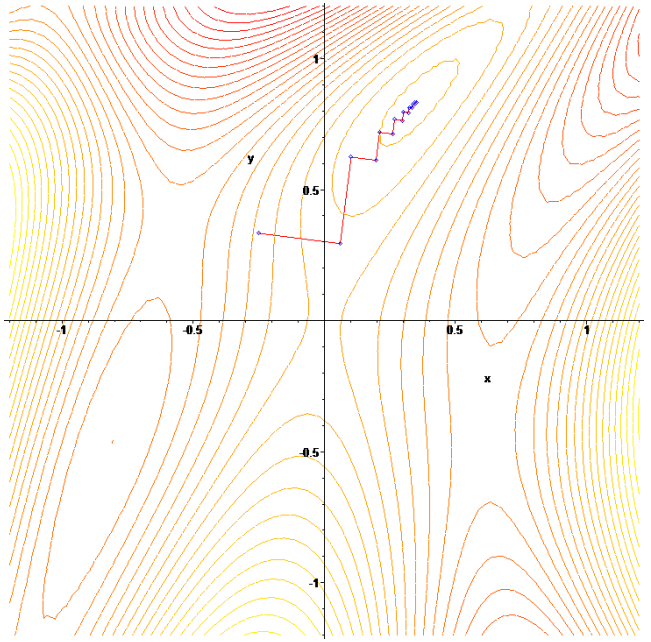
NLL in MATLAB

```
 1 function nll = neg_log_likelihood(data, theta)
 2     A = theta(1);
 3     beta = theta(2);
 4     X = data.decisions;
 5     T = data.num_trials;
 6     r = data.obs_rewards;
 7     p = data.phis;
 8     V = zeros(T, 1);
 9     for i = 1:size(r, 2)
10         V = A*V + r(:, i);
11     end
12     probs = logsig(X .* beta .* (V/4 - p));
13     nll = -sum(log(probs));
14 end
```

Estimate parameters

- Different options (e.g. gradient descent)
  - We will simply use one of the built-in functions





And in MATLAB

```
1 f = @(x)(neg_log_likelihood(data, x));
2 thetas = fminunc(f, [0;0]);
```

How good is our estimation?

- **Simulate data** from estimated parameters
  - **Does generated data look like the original data?**
  - Re-fit parameters to simulated data and compare parameters
- Look at the curvature (Hessian / 2nd order derivative) at the estimated point
  - Returned by `fminunc`
  - Take inverse to get covariance matrix

Correlated Parameters

- Might cause issues during inference
  - e.g. if two parameters are (highly) negatively correlated
    - Likelihood surface will have a “ridge”
    - We can arbitrarily change one of the parameters and then adjust the second parameter so as to keep the previous “maximum” likelihood (extreme example)
    - What does that mean if we are interested in the actual values of these parameters (e.g. for group comparisons)?

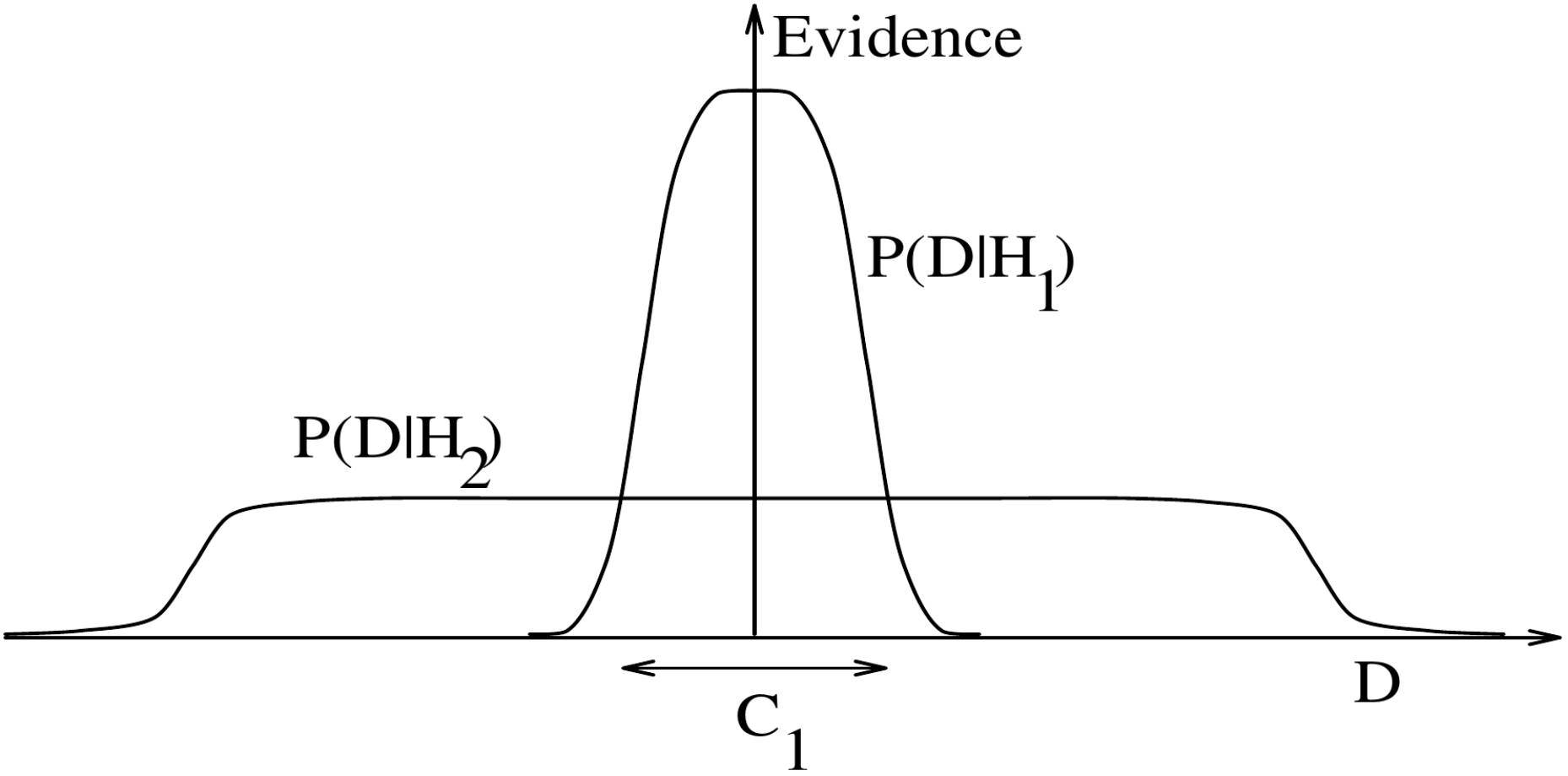
Correlated Parameters

- Parameters might actually be correlated
  - People who learn faster (higher learning rate) might be better at “remembering” what they learned (lower discounting)

Model Comparison

- How do we choose a model (hypothesis)?
- We want a Trade-off
  - Which model fits our data best? (accuracy)
    - Likelihood
  - Which model is the simplest? (complexity)
    - Number of parameters
- Turn to Bayesian model comparison…

Occam's razor



MacKay, 2003

Bayesian Model Comparison

- … or rather approximations

$$AIC = 2 \times NLL + 2 \times d$$

$$BIC = 2 \times NLL + d \times \log(n)$$

- Calculate for each model
- Choose model with **lowest** value
- Note that adding redundant parameters will affect the comparisons

Model Recovery Simulations

- **Do we have the data we need to answer the questions we are asking?**
- Confusion matrix
  - For each model m
    - Generate data from m
    - Fit all models to this data
    - Does model comparison choose m?
    - (repeat steps inside loop multiple times)

	H1	H2	H3
H1	20	0	0
H2	0	19	1
H3	0	1	19

References

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Images

- http://img.zanda.com/item/07091220000003/1024x768/Diagnostic_and_Statistical_Manual_of_Mental_Disorders.jpg
- http://new.paho.org/bulletins/images/stories/Bulletins/Epidemiological_Bulletin/Abril_2009/10_eng.jpg
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