

Models

Review

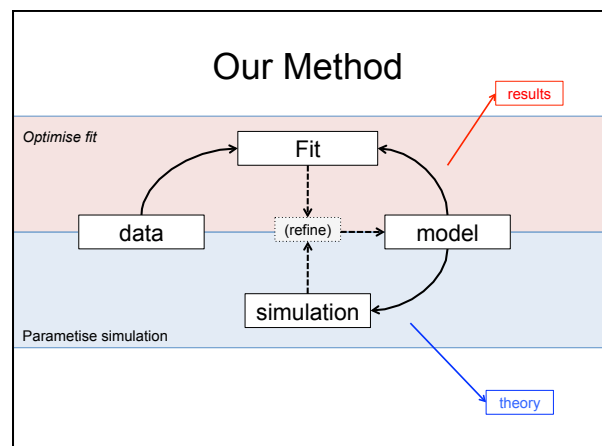
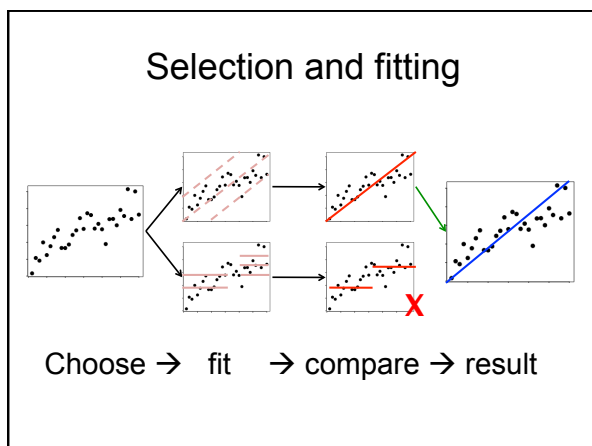
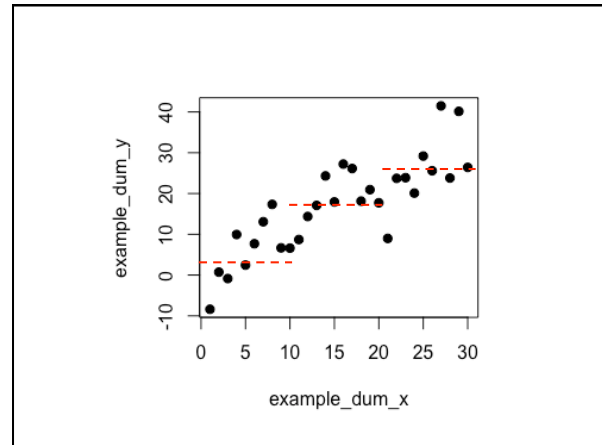
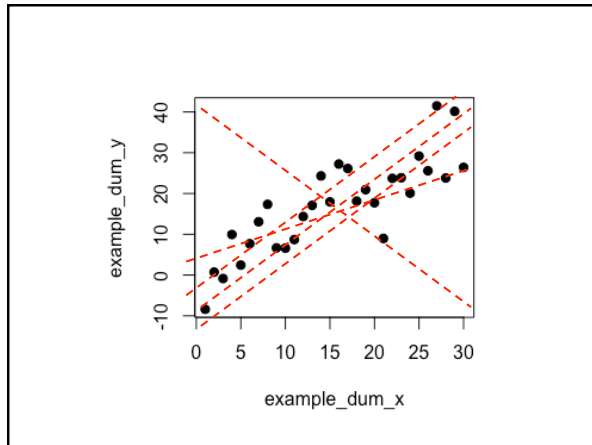
- Chi-squared
- Student's T
- ANOVA
- Regression
- General linear models

Review

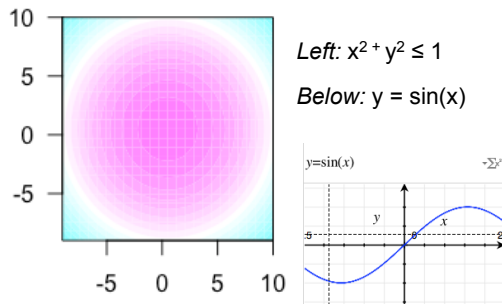
- Chi-squared → **evenly spread**
- Student's T → **one or two means**
- ANOVA → **multiple means**
- Regression → **straight line** ($y \sim a + bx$)
- General linear models → **combinations**

Review

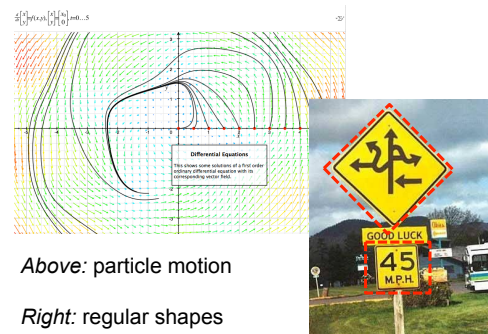
- These are all **models**
- They reflect our guesses about underlying phenomena, e.g.:
 - Chi-sq (smoking): *Cancer rates equal*
 - T-test (Mile End heights): *rich vs. poor lifestyles*
 - ANOVA (fertiliser): *Fertiliser A supplies Ca⁺, Fert. B doesn't*
 - Regression (height~rain): *more watering → more growth*
- Which to use?



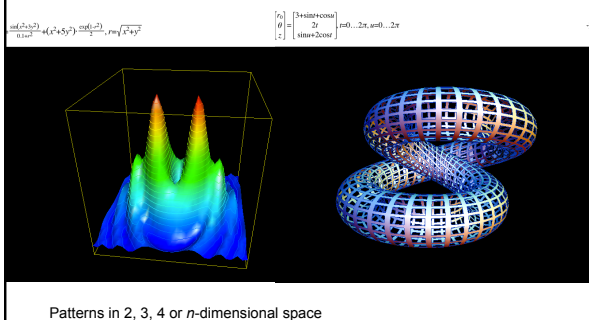
Other models are available



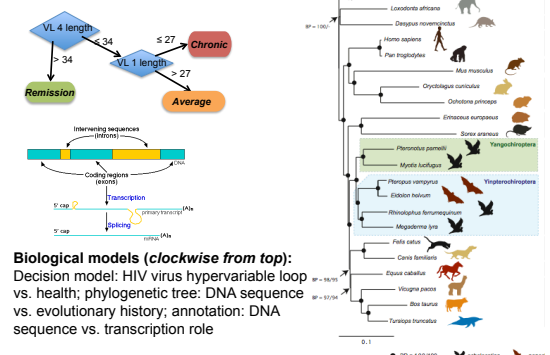
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Other models are available



Biological models



What is a model?

- A model is any statement that explains structure in the data
- Usually related to our guess about underlying phenomena
- Might describe:
 - Numerical observations, space, time
 - Genome structure, evolutionary relationships
 - Human language, anything else
- Usually expressed mathematically

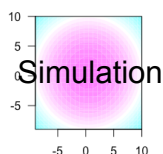
Errors and residuals

- The real world is noisy
- This is why spotting models is *hard*
- And why **fitting parameters** is *also hard*

Probability gives us a language to express our belief that a particular sequence of events (the **data**) have occurred due to some underlying process (the **model**), accounting for random disturbances (the **error**)

Simulation

- Simulation, modelling, error and inference are intimately linked
- “Does Model A describe x ?”
- “Does Model A-simulated data resemble x ?”



Parameters

- ‘A’ model really only makes general statements about the nature of the phenomenon
- To make specific, **predictive** statements, we need to **parametise the model**
- E.g. collect and interpret height data:
 - “Height is normally distributed”
 - $\text{Height}_{\text{MILE END}} = 1.78\text{m} \pm 15.2\text{cm}$
 - 95% of people chosen randomly between 1.63m and 1.93m
 - “Don’t stock XXS or XXL jeans”

Null hypotheses

- The '*null hypothesis*' is usually how we infer and test a model
- It is not special!
- Usually a minimal 'business as usual'-type description of the data
- But for complex data types (genomes; molecular interactions; evolution) even simple null models will still be *very* complicated

Model choice

- Sadly, relationships are rarely clear-cut
- Which model to use?
 - *Distribution: uniform? normal? exponential?*
 - *How many means? 1? 2? k?*
 - *Spatial shape: circle? polygon? irregular?*
 - *Substitution model: equal-rates? codon-bias?*
- Model selection doesn't just influence results; it **is** the results

Model comparison

- *We've met the basic principles*
 - **Efficiency** – we like models that are simple to understand
 - **Tractability** – we like models that are simple to fit/parametrise
 - **Significance** – we like models that explain variation
- **Model comparison:** statistically trading competing models off

Model comparison

- Number of d.f. / parameters
 - Total variation / variance
 - Mean variation
 - Test statistics (Chi-sq, T, F)
 - Information criteria, odds-ratios (AIC)
- (.... and: *Bayesian vs. frequentist traditions*....)

Algorithms

- Some models are straightforward to fit/parametrise, because mathematicians have derived solutions, e.g.:

$$\begin{aligned}\hat{\alpha} &= \bar{y} - \hat{\beta} \bar{x}, \\ \hat{\beta} &= \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sum_{i=1}^n (x_i - \bar{x})^2} \\ &= \frac{\text{Cov}(x, y)}{\text{Var}(x)}\end{aligned}$$

- Usually life is harder
- Especially in many dimensions

Algorithms

We use algorithms for two purposes, then:

1. **Model parametisation:** if we have a model to fit to complex data, we need a scheme to determine model coefficients
2. **Model selection:** even if parametrising a given model is trivial, there is an omnishambles of *possible models* to choose from

Search strategies

- Numerical answer (or approximation) easily derived
- Brute-force
- Stepwise / incremental search with gradient descent
- Random search (walk)
- Markov-chain Monte Carlo
- Combinations

Probability and confidence

- p – Probability of seeing data, *if* H_0 correct:
 $p = \Pr(D|H_0)$
- Not perfect but we're stuck with it
- For simple models p is straightforward to calculate; e.g. for coin-toss ($P_{\text{heads}}=0.5$) a sequence of k heads from n tosses $\{H, T, H, H\}$ k determined from the binomial distribution:
- $\Pr(k, n | P_{\text{heads}} = 0.5) = \binom{n}{k}$

Probability and confidence

- For other models (normally-distributed, and related) solutions to exact or approximate probabilities are available (T, F etc) allowing us to construct p -values and “accept or reject H_0 ”
- For more complex models (complicated distributions, high dimensions) calculating probability exactly becomes harder or impossible
- *Reminder: Variances, confidence intervals and p all depend on our ability to quantify belief*

Estimating confidence

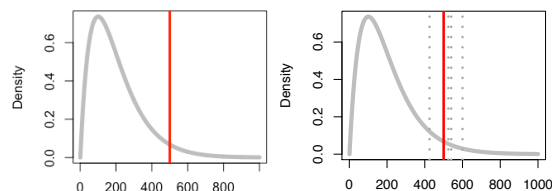
Where we can't calculate directly we may have to try our best:

- How sensitive is this estimate to the data? (bootstrap estimates)
- How sensitive is this estimate to the model? (vary parameters, empirically)
- How closely does this dataset resemble the null? (simulations)

Estimating confidence

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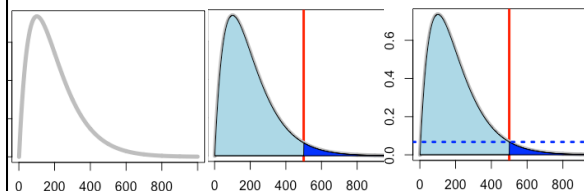
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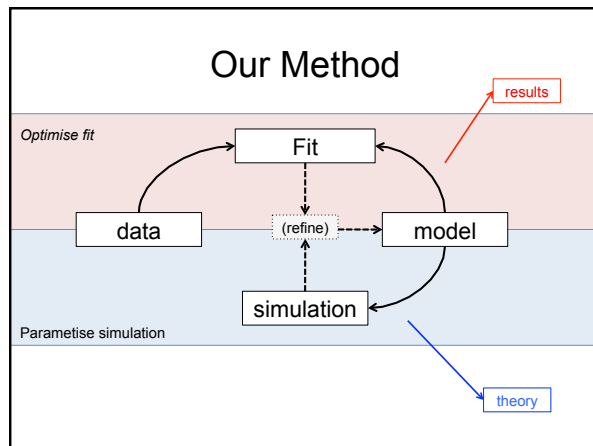


Estimating confidence

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Example: Phylogenetics

- An evolutionary tree is a hypothesis
- e.g., a *model*, of DNA sequence evolution
- Many trees are *possible*
- For neutral sites, approximate as a stochastic process on a *fixed* tree, then compare to successive *proposed* trees (Felsenstein, 1981)



Evolutionary Trees from DNA Sequences: A Maximum Likelihood Approach

Joseph Felsenstein

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Summary. The application of maximum likelihood techniques to the estimation of evolutionary trees from nucleic acid sequence data is discussed. A computer program is described for the calculation of the likelihood of a tree for a given set of data. The program is written in Fortran and runs on a variety of computers. The methods implicitly assume that change is improbable.

Example: Phylogenetics

- Consider two DNA sequences (A, B) with n orthologous sites, over time t . Assume mutations follow iid. Total will be a product:

$$\Pr(B | A, t) = \prod_{k=1}^n \Pr(B_k | A_k, t)$$

- At each site k , probability that a base i mutates j is given by:

$$P_{i \rightarrow j}(t) = e^{-\mu t} \delta_{i \rightarrow j} + (1 - e^{-\mu t}) \pi_j$$

where: μ denotes substitution rate ('speed'); δ the change function; π the equilibrium frequency

After Felsenstein (1981)

Example: Phylogenetics

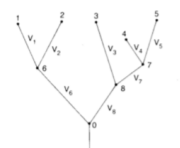


Fig. 1. The tree used in the discussion of computing the likelihood. The v_i 's are the lengths of the segments



Fig. 4. The maximum likelihood estimate of the phylogeny for 5S RNA sequences from five vertebrate species

- Simply divide the tree up into segments
- Sequences for unobserved (ancestral) taxa are unknown – so we compute for all possible states
- Sum of possible states: site likelihood
- Product of site likelihoods: tree likelihood (or sum, in LnL)
- Simple algorithm:
 1. For starting tree, parametise branches to optimise (maximise) likelihood
 2. Propose new trees and accept if they improve on the current one

Summary

- Statistics is the proposal and fitting of models to explain data
- Some models are simple, others complex. Some, we might invent ourselves
- Models must be parametrised, or fitted, to be useful
- Null hypotheses are just models, too
- With infinitely many possible models to choose from, they have to be compared to give the 'best' for our data
- Goodness-of-fit and likelihood cannot always be computed exactly – we may need to approximate, measure as ratios, or guess