# Practical ODE modelling

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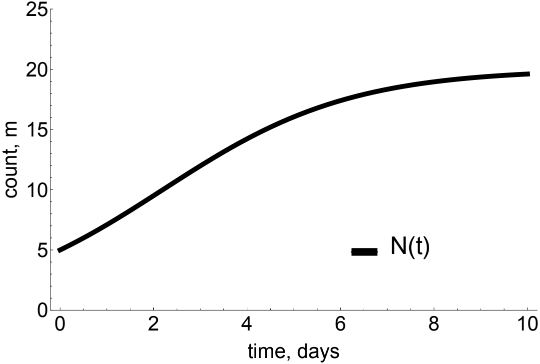
# Lecture outcomes

1. Explain difficulty with inference for ODEs;
2. Inference with PINTS and other libraries;
3. PINTS demo.

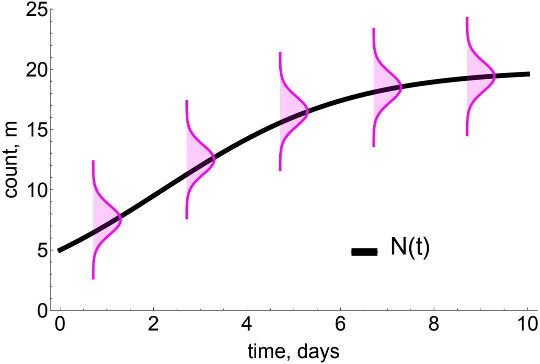
# Setting up the inference problem: forward model

$$\frac{dy(t)}{dt} = f(y, t; \theta). \qquad (1)$$



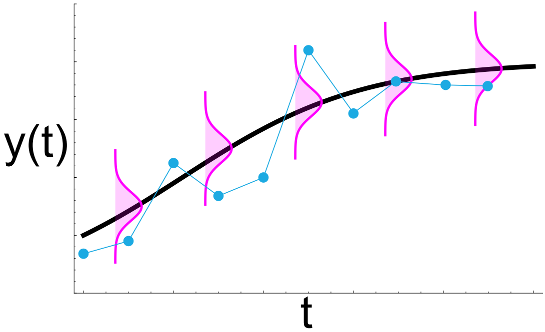
# Setting up the inference problem: noise model

$$y^*(t) \overset{i.i.d.}{\sim} \mathcal{N}(y(t;\theta), \sigma). \tag{2}$$



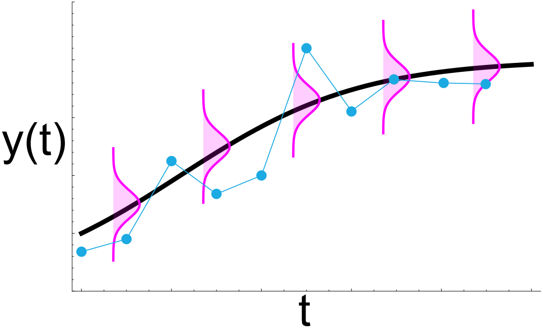
# Setting up the inference problem: data

$$\mathcal{L} = \prod_{i=1}^{S} \mathcal{N}(y^*(t_i)|y(t_i;\theta),\sigma). \tag{3}$$



# Setting up the inference problem: posterior

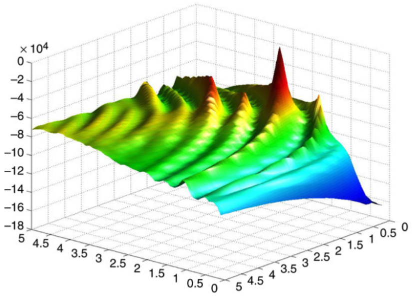
$$p(\theta|X) \propto p(\theta,\sigma)\prod_{i=1}^{S}\mathcal{N}(y^*(t_i)|y(t_i;\theta),\sigma). \tag{4}$$

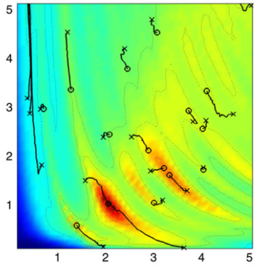


# Why is inference for ODEs hard?

- ODEs (typically) require numerical solutions $\implies$ expensive;
- Non-linearity $\implies$ posterior distributions can be complex / unidentified.

# Why is inference for ODEs hard?



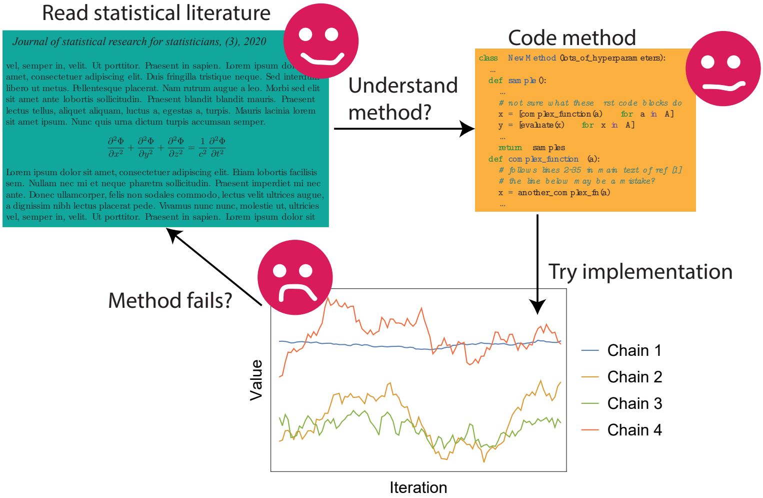

from "Bayesian inference for differential equations", Girolami (2008)

# How to make your life easier

Before you start inference:

- Fake data simulation followed by inference: make simulated data as similar to real data characteristics as possible;
- Profile likelihood method to assess identifiability;
- General mathematical analysis: assess sensitivity of outputs to parameters.

# How to fit model to data?



# Why does this cycle of misery persist?

- Statistical literature is written by methods experts for other experts;
- Statistics papers do not often contain high quality pseudocode;
- Software accompanying papers is typically not professionally developed;
- Software is typically idiosyncratic;
- Different problems require different solutions but solutions currently require reinventing the wheel;
- Not enough knowledge sharing between applied researchers about "Which method works best?".

# What is PINTS?

PINTS: **P**robabilistic **I**nference for **N**oisy **T**ime **S**eries, which covers two broad categories of inference methods:

- Optimisation: single set of parameters returned;
- Sampling: many sets returned.

It's an open-source Python library available on Github.

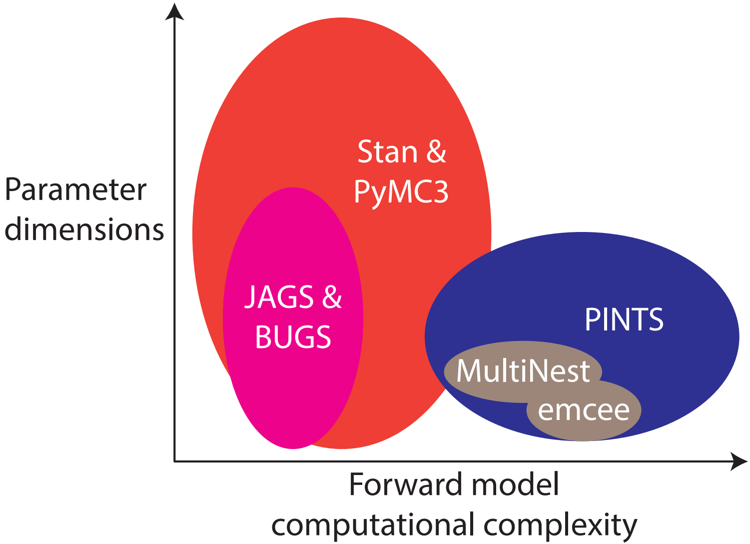
# What does existing literature do?

- Most other inference software pin their hope on a single sampler:
  - BUGS and JAGS: Gibbs sampler;
  - PyMC3 and Stan: No U-Turn Sampler (NUTS);
- Other libraries prepackage forward model solution methods with sampling method.

# How is PINTS different?

- PINTS not aligned to a single algorithm;
- PINTS is designed to interface with (other) probabilistic programming languages (for example, Stan);
- PINTS aimed at harder forward models: ODEs and PDEs;
- PINTS allows users freedom to use own forward model solution method.

# PINTS niche


Parameter dimensions
Stan & PyMC3
JAGS & BUGS
PINTS
MultiNest
emcee
Forward model computational complexity

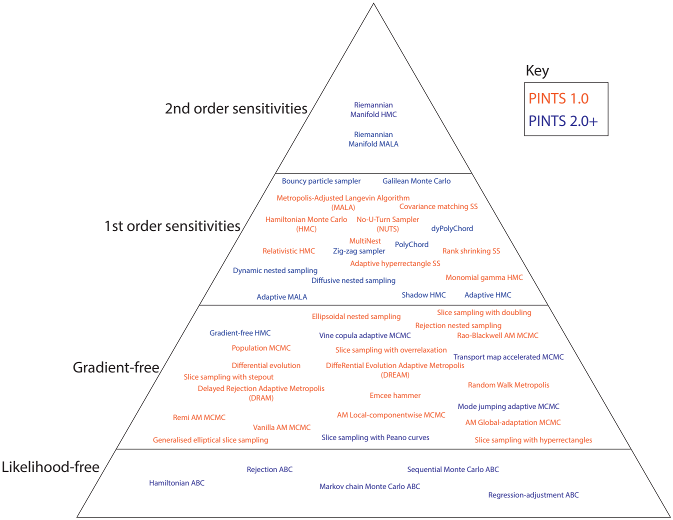
# Deciding on an approach

- For cheap forward model $\implies$ use Stan (you can always use PINTS' Stan interface if this doesn't work);
- For expensive forward models, potentially requiring bespoke solvers $\implies$ use PINTS.

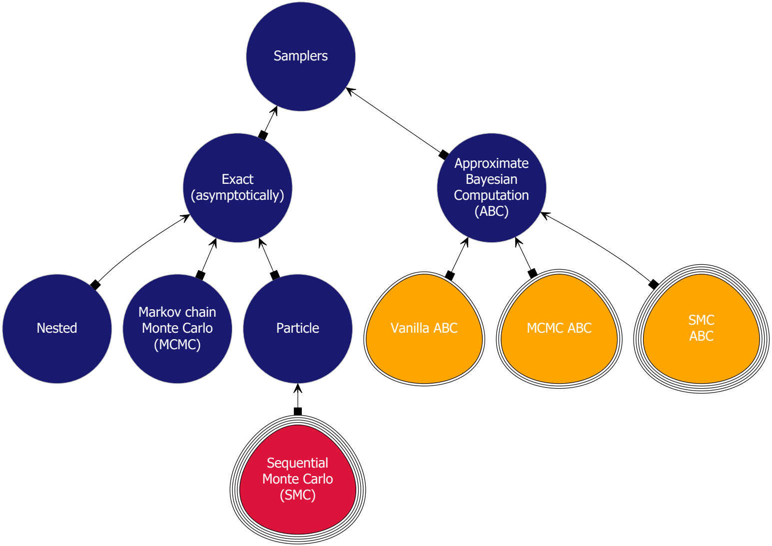
# PINTS in detail

- Literature emphasis on developing new algorithms;
- Literature dense with hard-to-decipher algorithm details;
- PINTS aims to make this research **useful**:
  - Common, easy-to-use, interface for lots of methods;
  - Rigorous software development practices;
  - Many levels of testing: unit, functional, and so on;
  - Collaboration with statisticians working on various methods;
  - Benchmark problems;
  - Pseudocode and tutorial papers which explain algorithms and their ecosystem.

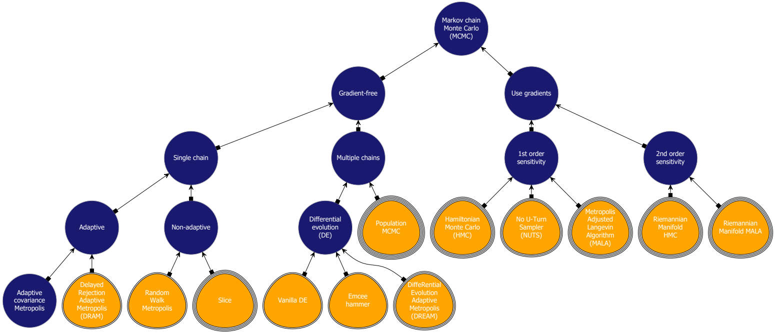
# PINTS roadmap: samplers



# Families of samplers: overall



# Families of samplers: within MCMC



# PINTS: optimisers

Optimisation more "solved" than sampling and have two families in PINTS:

- Gradient-free: CMAES, XNES, SNES, Nelder-mead, PSO, SHGO (planned);
- 1st order sensitivities: gradient descent, L-BFGS (planned).

# Conclusions

- Inference for ODE models is generally hard;
- Stan and PINTS are your current best bet for inference.