SDE analysis of growth and energy intake for pigs

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KU Statistics Network meeting 2009
Jørlunde, January 22.

Outline

This is an application from my LIFE-time.

In short:

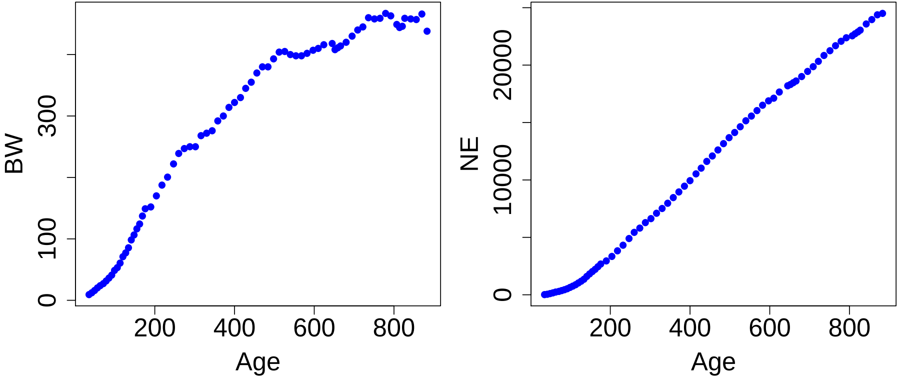
- What did we do already and what are the results?
- What is there to be skeptical about?

More detailed:

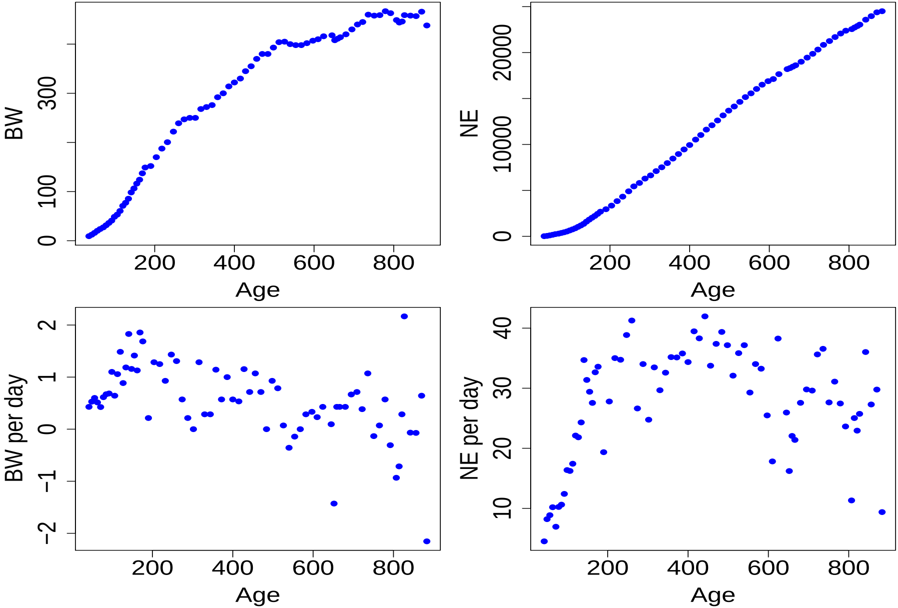
- The data and the questions
- The model: deterministic (ODE) and stochastic (SDE) version
- Estimation and results
- Investigation in a simpler model:
  - transformation
  - properties of the estimation procedure
  - random effects

Data from pig no. 6205: cumulated values

- Data from weaning to (near) maturity
- Bodyweight (*BW*) and net energy intake (*NE*) measured simultaneously weekly/every second week
- Data series to maturity for 13 pigs (shorter for another 175 pigs)



Data from pig no. 6205: increments per day



Questions of interest and concern

Nutrition

- Interplay between BW and NE — simultaneous model for (BW, NE)
- Estimation of maintenance requirement
- Prediction of body energy (BE) — only measurable at slaughter
- Estimation of population parameters and comparison of groups

Statistics

- SDE model as a way to incorporate 'dynamic' or 'intrinsic' noise?
- Variance homogeneity, transformation, auto-correlation
- Estimation methods and their properties, in particular their ability to distinguish between dynamic noise and measurement noise
- Random effects

Unusual data. SDE-models new to the animal science literature.

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The deterministic model

A two-dimensional ODE-model for (BW, NE).

Assumptions:

- NE rate quadratic as a function of metabolic weight ($BW^{0.75}$):

$$\frac{dNE}{dt} = \theta_1 \cdot BW^{0.75} + \theta_2 \cdot BW^{2 \cdot 0.75}$$

- Intake goes to maintenance and growth:

$$\frac{dBE}{dt} = \frac{dNE}{dt} - \theta_4 \cdot BW^{0.75}$$

- Relation between BW and BE (unobservable)

$$BW = \theta_5 \cdot BE^{\theta_6}$$

The deterministic model (cont'd)

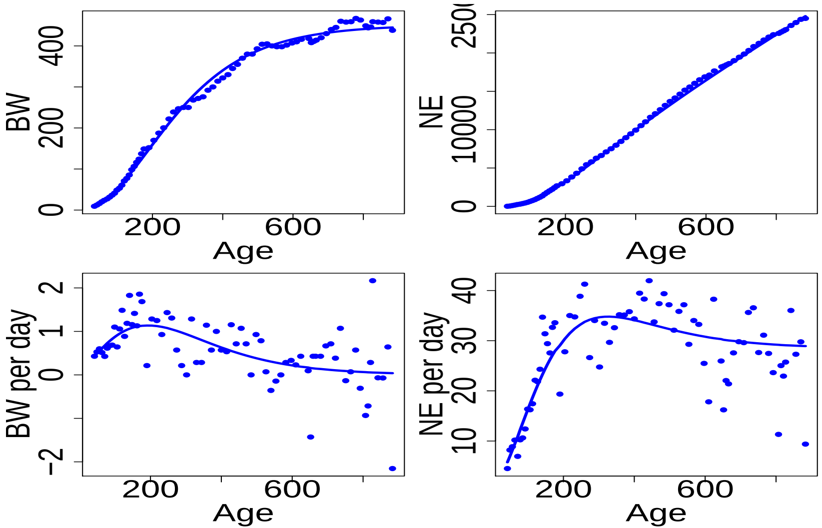
The assumptions lead to a 2-dimensional ODE for (BW, NE):

$$\frac{dBW}{dt} = f_{BW}(BW, NE, \theta_1, \theta_2, \theta_4, \theta_5, \theta_6)$$
$$\frac{dNE}{dt} = f_{NE}(BW, NE, \theta_1, \theta_2)$$

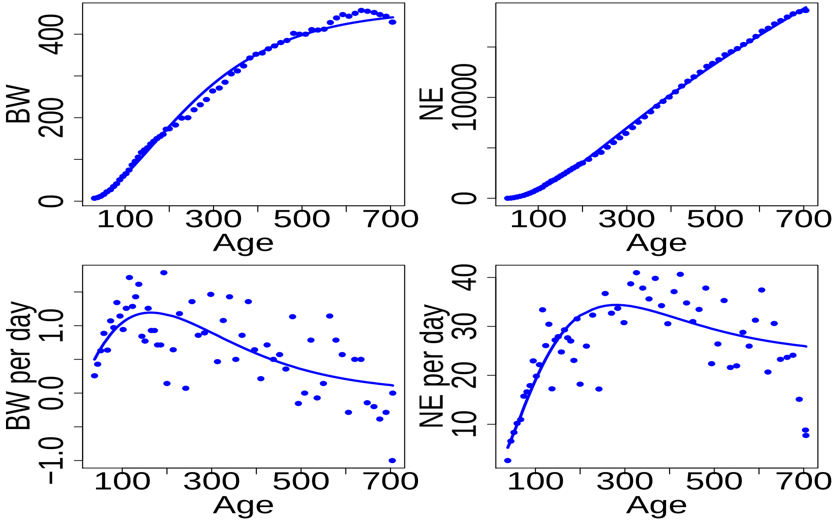
Is the model at all able to "catch" the gereral trends in the data?

- More or less, yes
- Auto-correlation (of course) in BW and NE
- The peak around 150–200 days for $\Delta BW/\Delta t$ perhaps not 'sharp' enough

Data from pig no. 6205



Data from pig no. 5365



Statistical models

Simple model for $y_i = (BW, NE)$:

$$y_i = \text{ODE solution} + e_i$$

with auto-correlated residuals.

Alternative: State space model with system equation defined by a SDE.

- SDE-model implicitly defines auto-correlation
- SDE-model defines models for increments over time-intervals of any length in a consistent way
- State space formulation: dynamic noise as well as measurement noise.
- Dynamic noise may originate from circumstances in the system that we cannot (or will not) include in the system model.
- The system equation is closely linked to scaled differences:

$$\frac{\Delta y}{\sqrt{\Delta t}} = \frac{\Delta(\text{ODE solution})}{\sqrt{\Delta t}}$$

SDE-based state space model

System (or state) equation: Two-dimensional SDE,

$$\begin{pmatrix} dBW \\ dNE \end{pmatrix} = \begin{pmatrix} f_{BW}(BW, NE, \theta) \\ f_{NE}(BW, NE, \theta) \end{pmatrix} dt + \begin{pmatrix} \sigma_1 & \sigma_{12} \\ \sigma_{12} & \sigma_2 \end{pmatrix} \begin{pmatrix} dw_1 \\ dw_2 \end{pmatrix}$$

where

- f_{BW} and f_{NE} come from the ODE model, depend on $\theta_1, \ldots, \theta_6$
- σ_1, σ_2 and σ_{12} are parameters
- w_1, w_2 are independent Wiener processes

Measurement equation: The k'th observation pair, at time t_k:

$$\begin{pmatrix} y_{1,k} \\ y_{2,k} \end{pmatrix} = \begin{pmatrix} BW_{t_k} \\ NE_{t_k} \end{pmatrix} + \begin{pmatrix} e_{1,k} \\ e_{2,k} \end{pmatrix}$$

where $(e_{1,k}, e_{2,k})'$ are independent, two-dimensional Gaussian.

Comments on the model

What does the system equation mean?

For Δt "small",

$$\begin{pmatrix} \Delta BW \\ \Delta NE \end{pmatrix} \approx \begin{pmatrix} f_{BW}(BW, NE, \theta) \\ f_{NE}(BW, NE, \theta) \end{pmatrix} \Delta t + \sqrt{\Delta t} \begin{pmatrix} \sigma_1 & \sigma_{12} \\ \sigma_{12} & \sigma_2 \end{pmatrix} \begin{pmatrix} u_1 \\ u_2 \end{pmatrix}$$

where u_1, u_2 are iid. standard normal.

Questions:

- What happens when Δt is not so small?
  True cond. distribution of $(\Delta BW_{t_k}, \Delta NE_{t_k})$ given $(BW_{t_{k-1}}, NE_{t_{k-1}})$?
- (BW, NE) observed with measurement noise (so observations are not Markov). Conditional distribution given the whole past?

Variance inhomogeneity and transformation

Not surprisingly, variance inhomogeneity is an issue.

One option: Diffusion coefficients and measurement noise variance defined as functions of states (BW, NE). Not handled by the software.

Another option: transformation.

Usually: 'SDE + transformation = Ito's formula'

Again, this is not handled by the software. And who says the original scale is the right one for constant variance?

Our approach: 'find scale where additive noise is reasonable'

- Transform-both-sides of the ODE-model so that parameter interpretations are maintained
- Diffusion term and measurement errors added as before

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Estimation

Parameters: the ODE-parameters (θ's), diffusion parameters (σ's), measurement noise variances (s's).

Estimation approach from Kristensen and Madsen, 2003 (DTU):

The conditional distribution of y_k given the past is approximated by the Gaussian distribution $\rightarrow$ likelihood function is a product of Gaussian densities.

The mean and variance are computed by the extended Kalman filter:

- prediction equations: predict state at time t_k from $y_1, \ldots, y_{k-1}$
- updating equations: 'predict' state at time t_k from $y_1, \ldots, y_{k-1}, y_k$

Implemented in the CTSM software (Kristensen and Madsen) and the R-package PSM (Mortensen and Klim).

Results from the analysis — and problems?

The square root transform turned out to work 'best'.

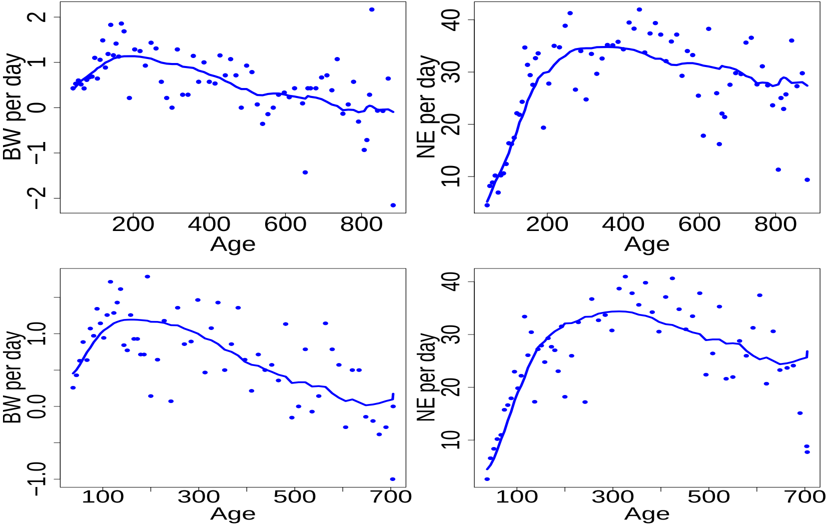
The good story:

- Reasonable fits and biologically meaningful parameter estimates
- Reasonable prediction of body energy — only measurable at slaugther.

The problems:

- Have used $\sigma_{12} = 0$ corr. to independent SDE noise for *BW* and *NE*. Not realistic — might affect SE's of the parameters of interest.
- Measurement noise variances estimated to zero for almost all animals. 'True' or is it too hard to distuinguish it from SDE noise?
- Properties of the estimation procedure: Bias? Coverage of confidence intervals? SDE noise versus measurement noise?
- The pigs analysed one by one. Would be natural to analyse all data simultaneously with random effects $\leftrightarrow$ population parameters.

Fitted drift for pig no. 6205 and 5365

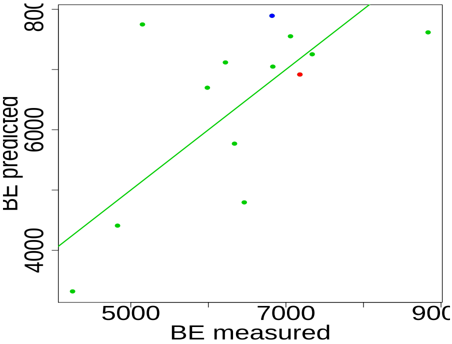


Prediction of body energy (BE)

The body energy (BE) was measured at slaughter.

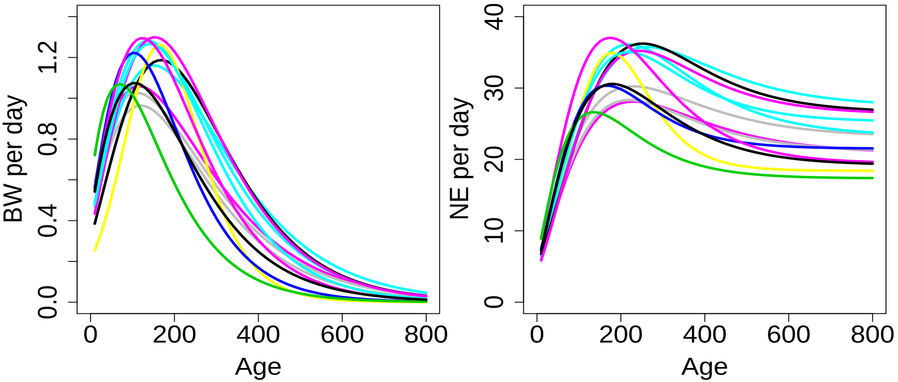
Predicted value,

$$\widehat{BE} = \left(\frac{BW}{\hat{\theta}_5}\right)^{1/\hat{\theta}_6}$$



Estimated ODE solutions for all pigs

Estimates correspond to the following increments of the ODE solutions:



- Natural to incorporate a random pig effect on some of the parameters
- Phase variation ↔ time-warping (functional data analysis)

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Properties of the estimation procedure

Investigations in a simpler set-up in order to speed up computations:

- Only weight observations (BW)
- Simpler ODE-model: Gompertz,

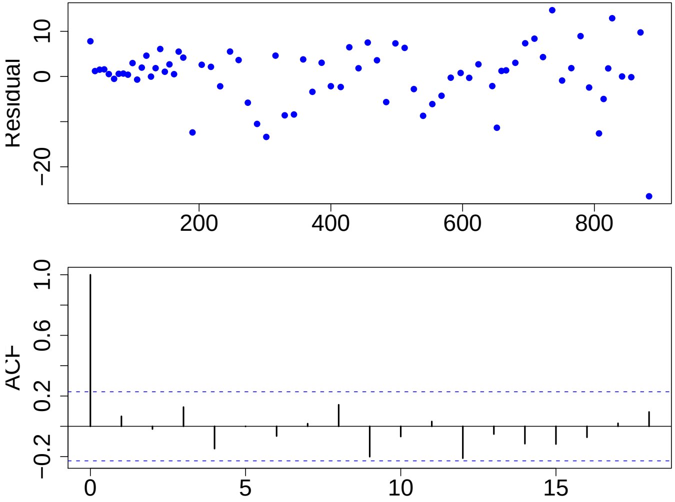
$$\frac{dBW}{dt} = \alpha \cdot BW \cdot \log(K/BW)$$

  where K is the 'asymptotic' and maximal weight, α determines the decrease in growth rate.

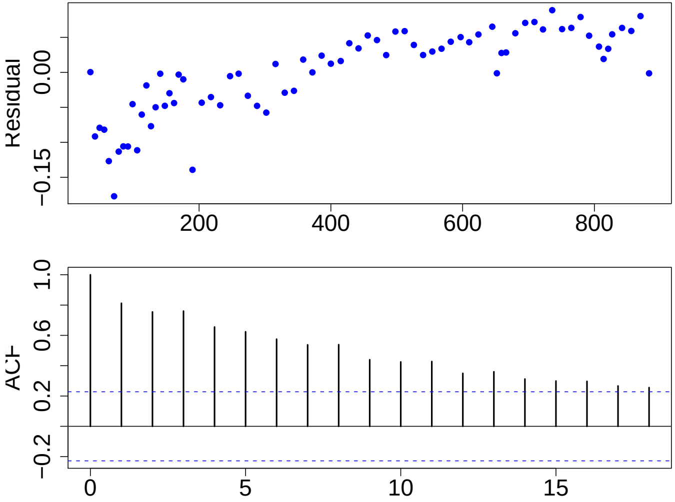
Statistical model: squareroot transformation of ODE, diffusion term, and measurement noise:

$$\begin{aligned} \frac{d\sqrt{BW}}{dt} &= \frac{1}{2}\alpha\sqrt{BW}\log\left(\frac{K}{\sqrt{BW}^2}\right)dt + \sigma\, dw_t \\ y_{1,k} &= BW_{t_k} + e_{1,k} \end{aligned}$$

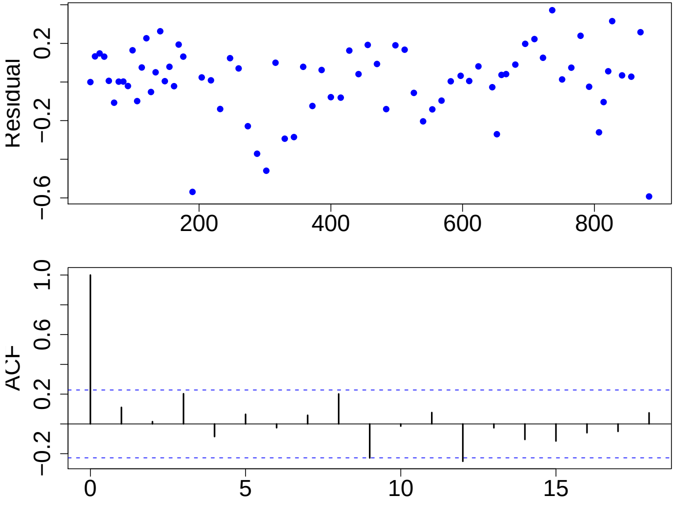
Original



Log



Squareroot



Simulations

Observation times equal to those of pig 6205.

Structural parameters b and K equal to values estimated for pig 6205:

$$K = 437, \qquad b = 0.00772$$

Three different regimes for σ (SDE noise) and s (measurement noise)

A: $\sigma \approx 1000 \cdot s$

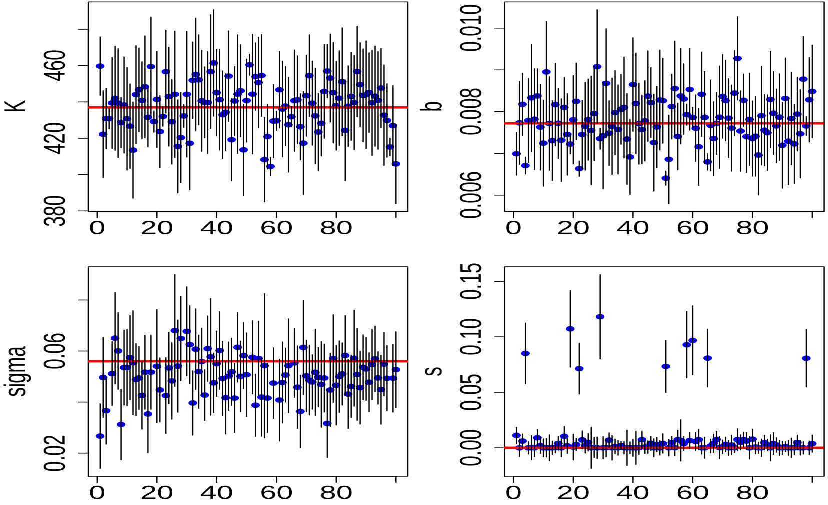
B: $s \approx 1000 \cdot \sigma$

C: $\sigma \approx s$

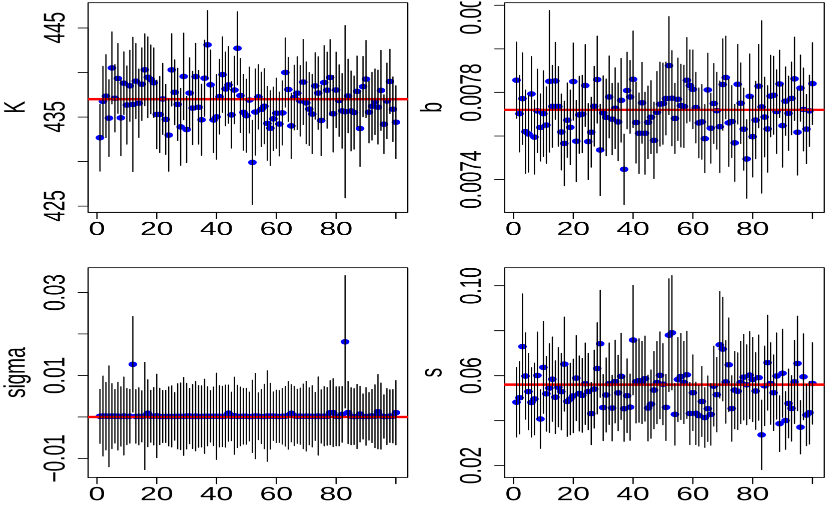
100 simulated paths.

For each path: computation of estimate and 95% confidence intervals (based on the estimated Fisher information).

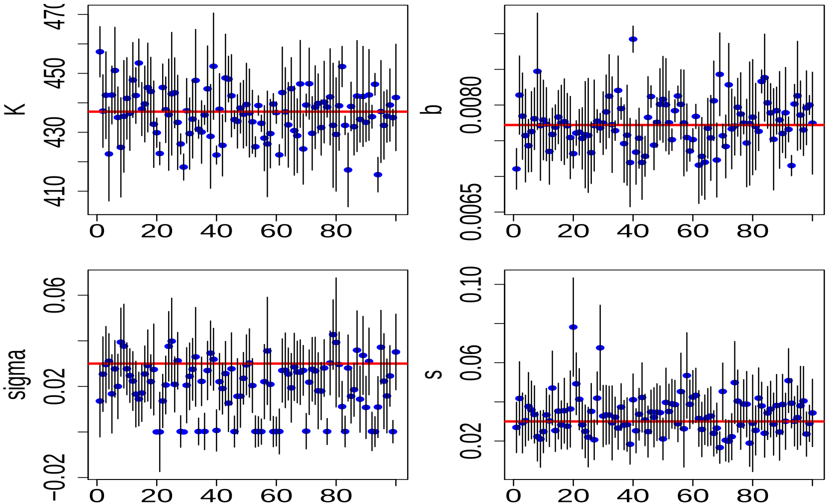
Case A: $\sigma = 0.0560$, $s = 0.00005$



Case B: $\sigma = 0.00005$, $s = 0.0560$



Case C: $\sigma = 0.03$, $s = 0.03$



Conclusions

Conclusions on simulations

- There *are* problems with the estimation of σ and s
- In particular the procedure sometimes finds the wrong regime (A: 9/100 and C: 18/100).
- ... but the K and b estimates are (almost) unaffected by this: no bias
- Coverage of K and b confidence intervals seems to be okay, except in case C where it is only about 0.8.

Comments on random effects

- Methods for SDE-models with random effects and measurement noise are implemented in the R-package PSM.
- ... at least in principle: I had serious problems with estimation of the between-animal variation of parameters
- Alternative approach: time-shifts/time-warping

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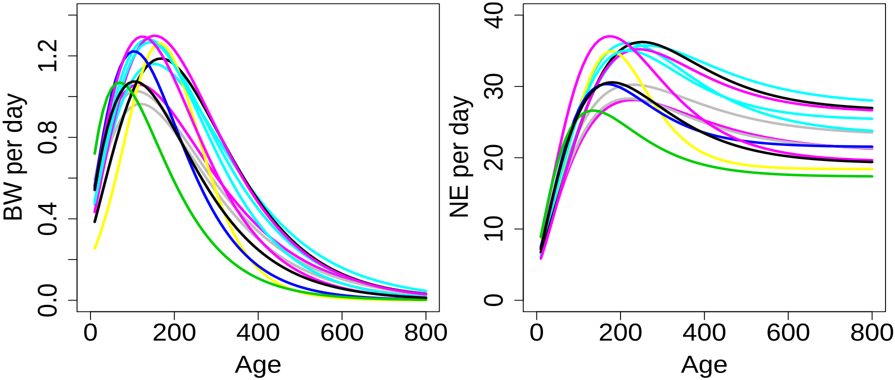

- Natural to incorporate random effects
- Phase variation $\leftrightarrow$ time-warping (functional data analysis)