Towards a Systemic Use of Precision Livestock Measures and Precision Phenotyping in Dairy Herds

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Modélisation Systémique
Appliquée aux Ruminants

Where should we be heading?

- On-Farm monitoring
- Identifying events
  - e.g. clinical mastitis, oestrus, etc.
  - Usually using one measure/technology
- Anticipating events (e.g. André et al. 2011)
  - Probability of
  - Increasing need for multiple measures
- From monitoring to phenotyping

Why do we need precision phenotyping?

- Genomics
  - Massive increase in genotyping precision
  - Requires more precise phenotypes

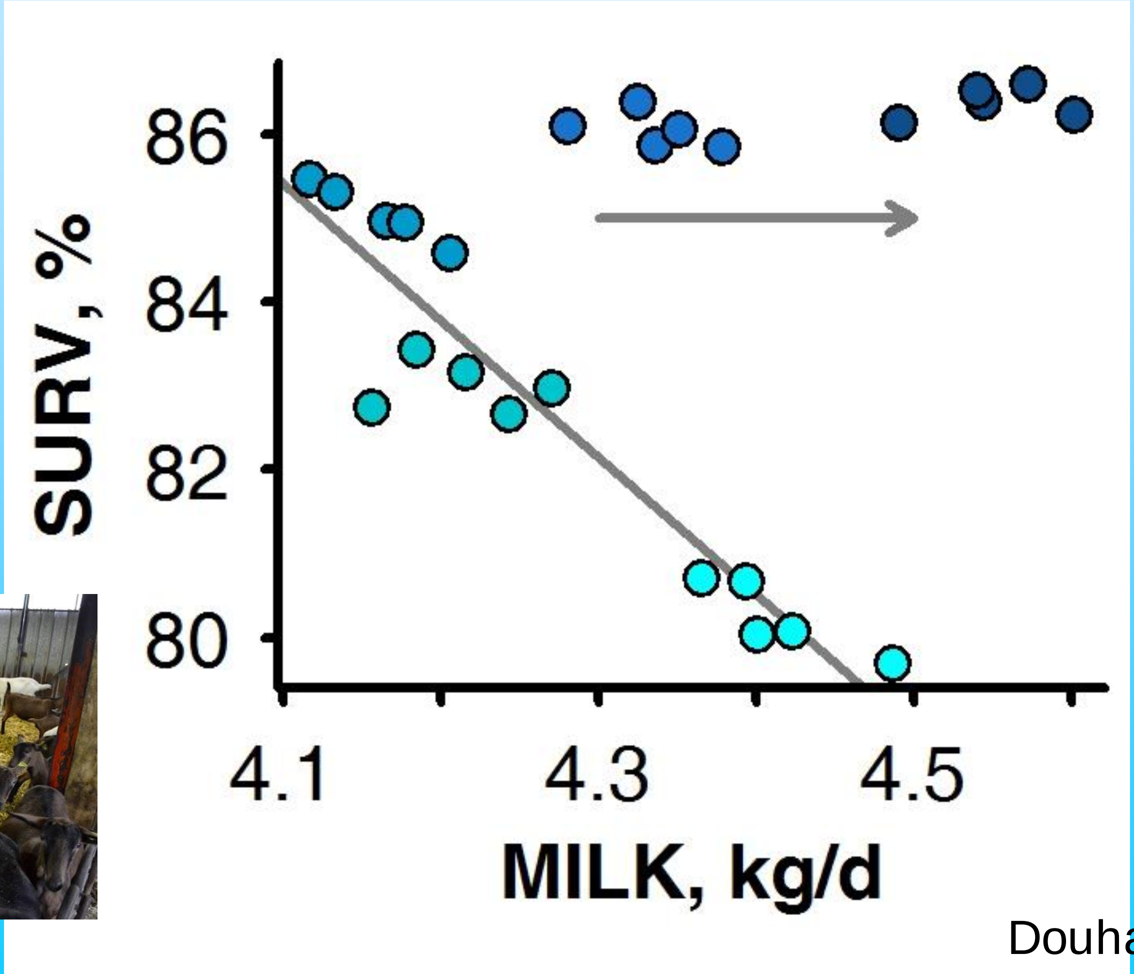
Example: Heritability (h^2) of reproductive traits

- Traditionally low $h^2 \sim 0.03$
- progesterone based $h^2 \sim 0.17$ (Royal et al)
- activity measures $h^2 \sim 0.17$ (Løvendahl and Chagunda)

Why do we need precision phenotyping?

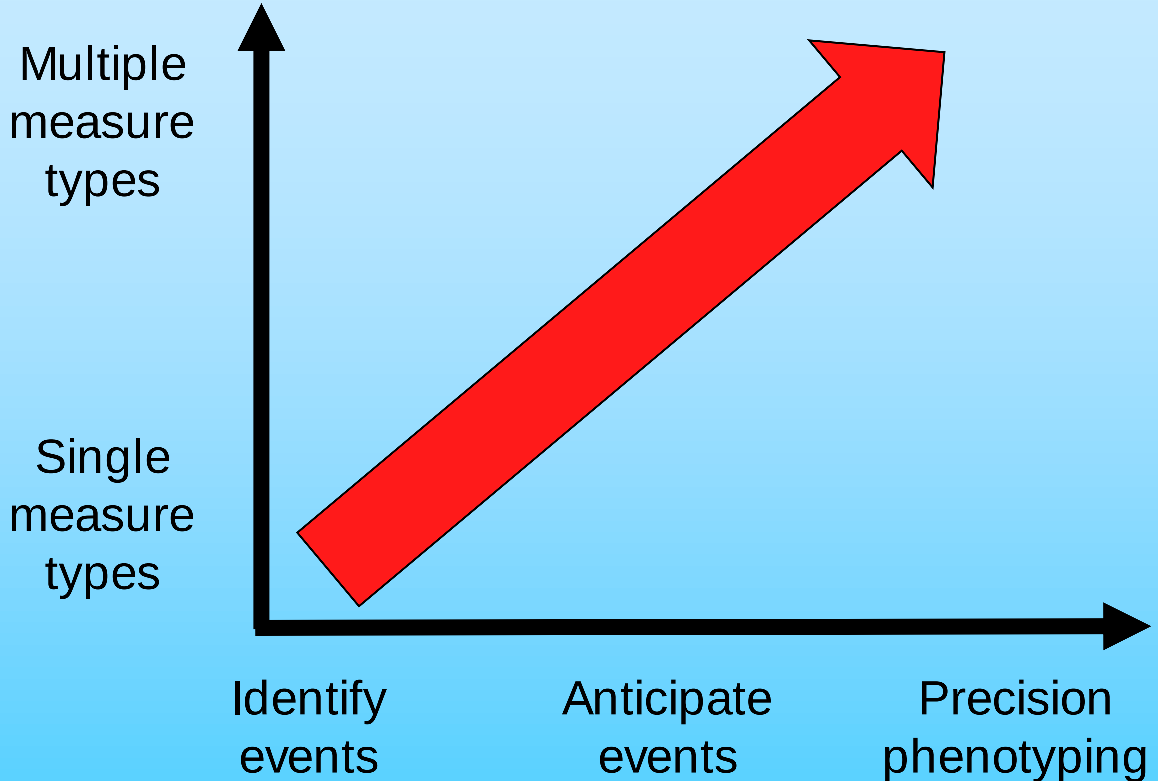
- Genomics
  - Massive increase in genotyping precision
  - Requires more precise phenotypes
- Opportunities to characterize more complex traits
  - Adaptive capacity, robustness, etc.
  - Realistic chance of selecting for these
  - These contribute to herd level resilience

Increased variability in age improves herd resilience



Douhard et al. 2014

From monitoring to phenotyping



- Multivariate time-series statistics…..
- But also a clear view of the biological system

Low-hanging fruit example: Energy Balance

- Traditionally EBal measured as
  - Difference between Eintake – Eoutput
  - Only research farms measure individual intake
- EBal = Body E change
  - Negative EBal = body reserve mobilization
  - Positive EBal = body reserve accretion
- EBal can be measured from body reserves

EBal from lipid and protein reserves

$$EBal = ec_l(dL/dt) + ec_p(dP/dt)$$

$$P = k(LFEB)$$

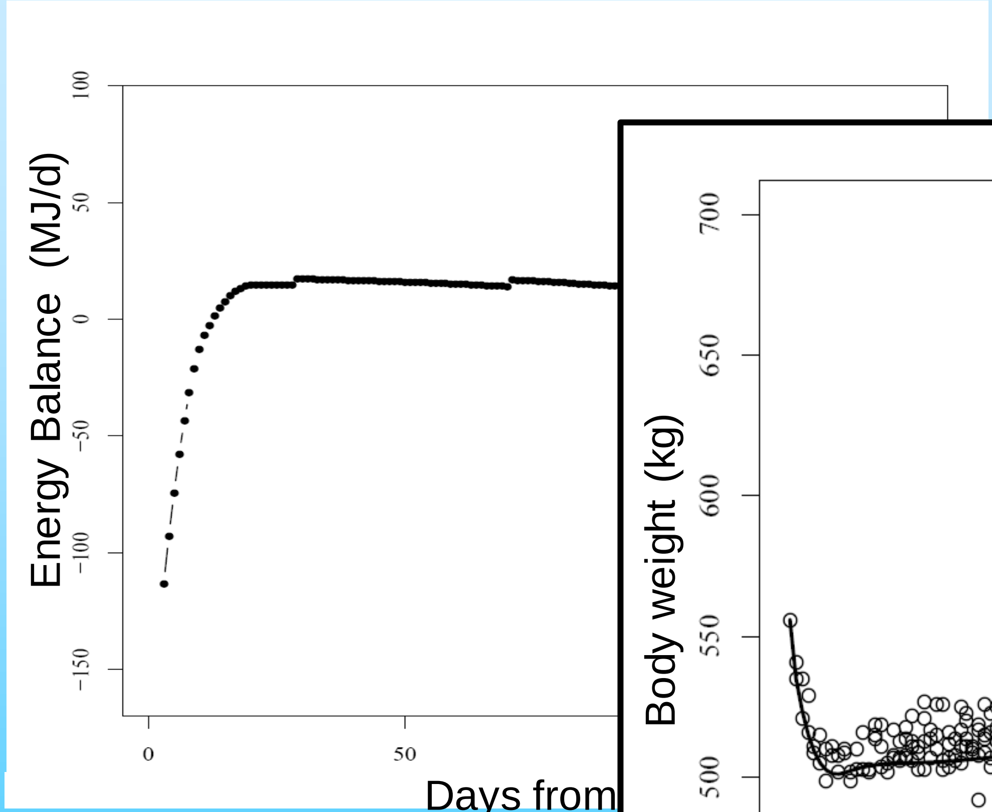
$$LFEB = EBW - L$$

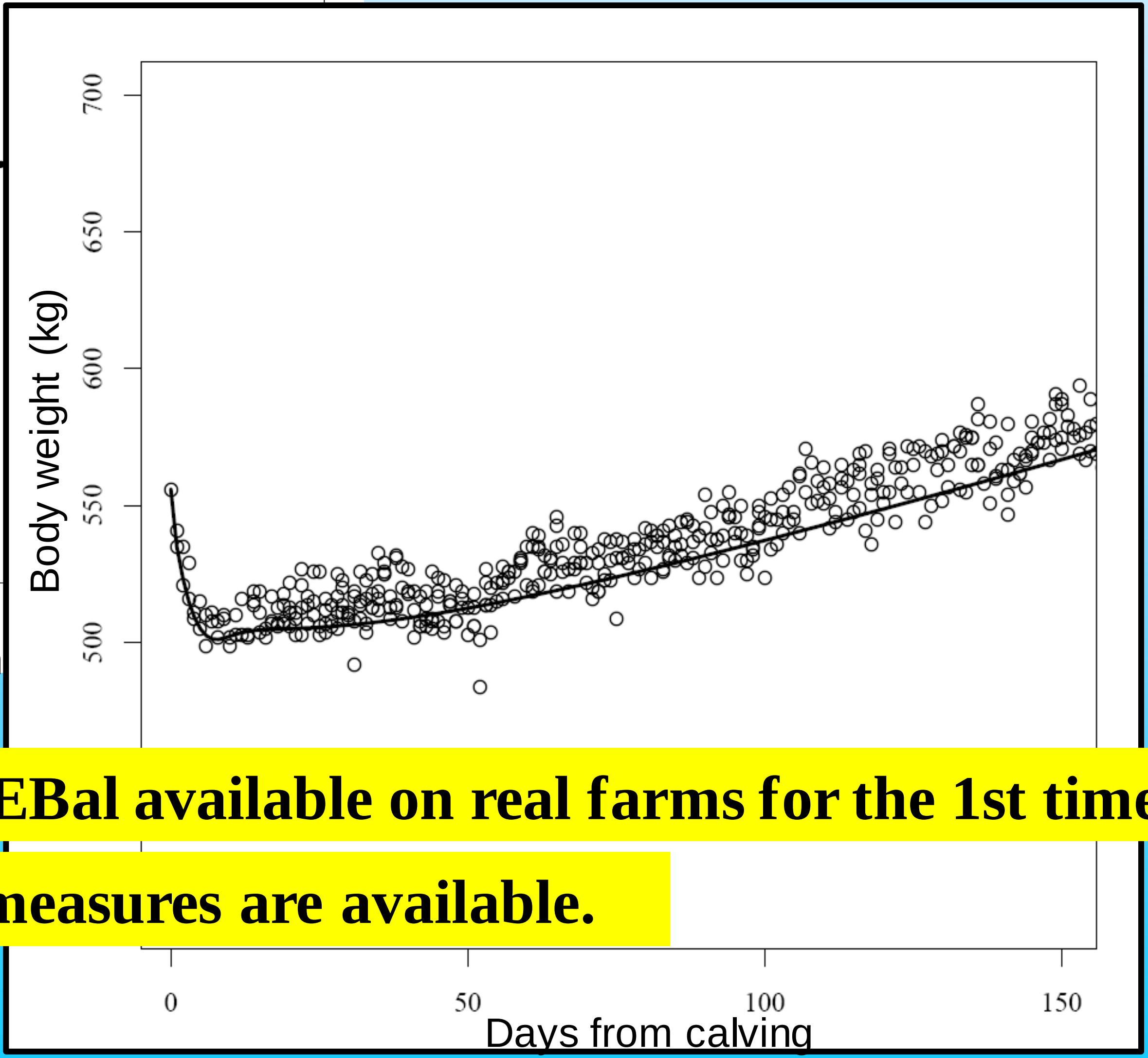
$$L = BFatContent \times EBW$$

$$= (a + b.CS).EBW$$

$$EBW = BW - Gutfill$$

Energy balance derived from BW and CS





No need for intake. EBal available on real farms for the 1st time

Provided frequent measures are available.

Thorup et al. 2012, J. Dairy Sci.
Thorup et al. 2013, J. Dairy Sci.

Biology vs Measures

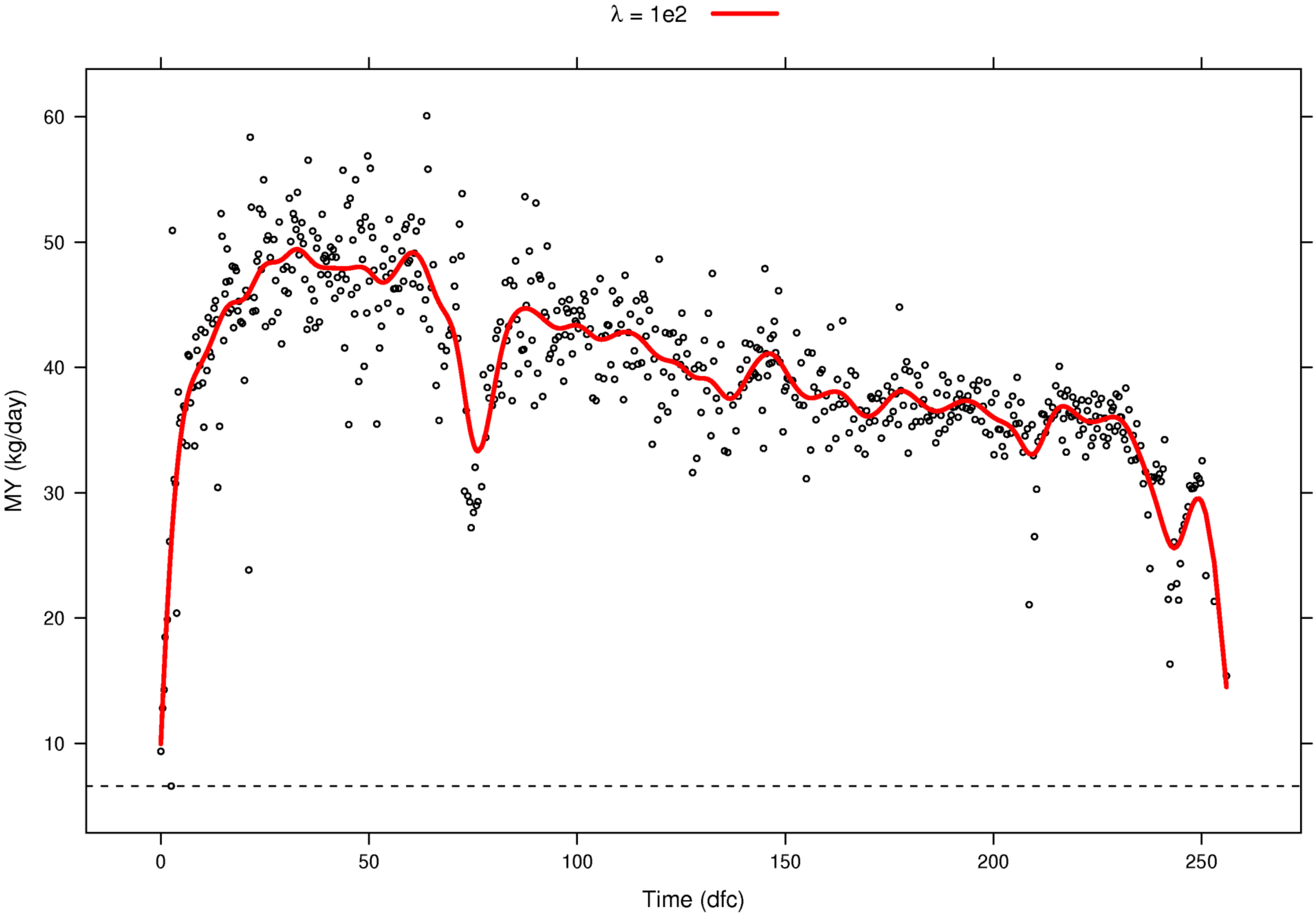
- Biological phenomenon
  - Unlikely that one measure captures the whole phenomenon
  - Distributed across a number of measures
  - Likely that one measure reflects several phenomena

- Biological feature extraction
- Combine features to describe latent process

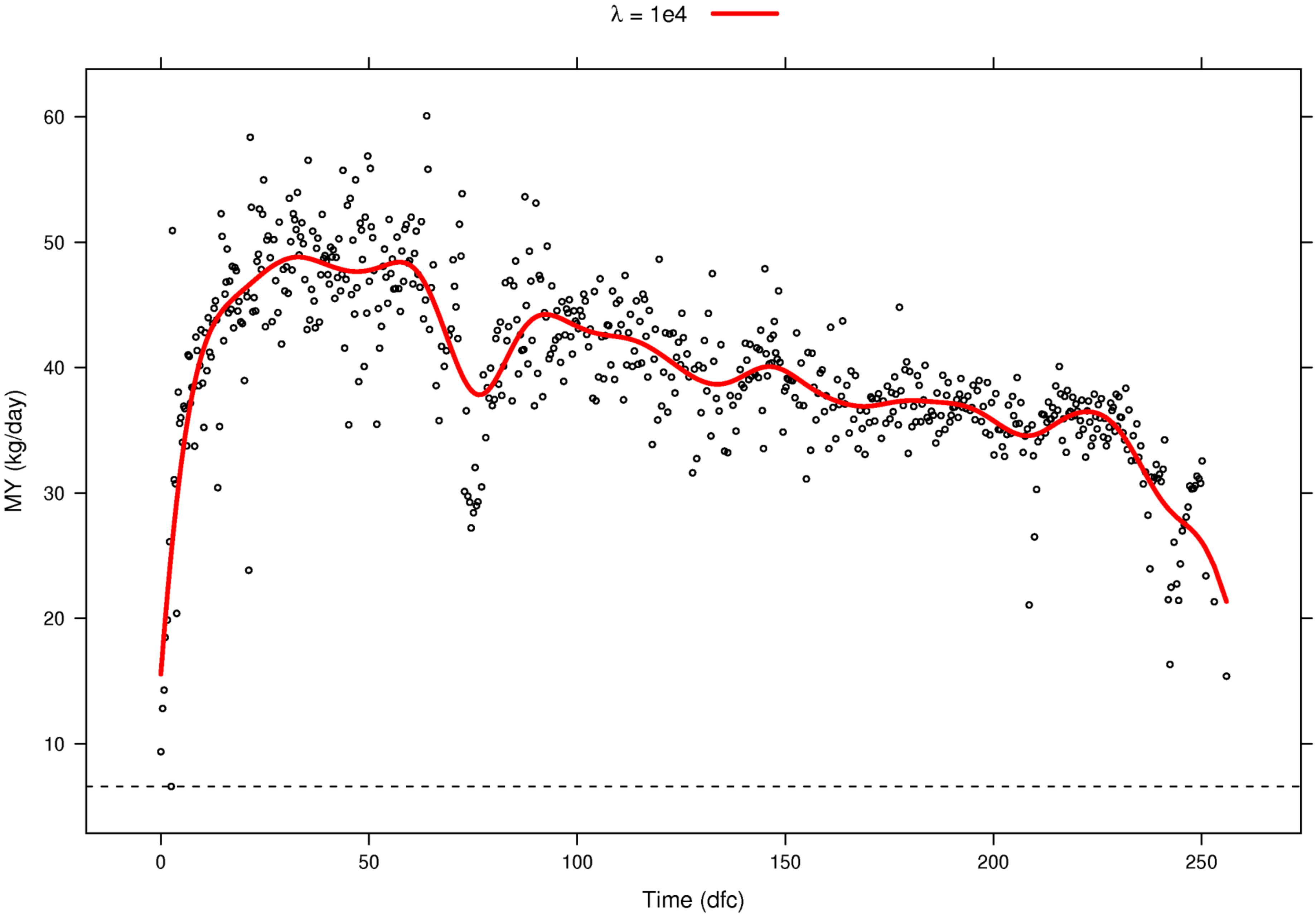
Two examples:

- Differential smoothing
  - Capture responses
  - Functional data analysis (Ramsay)

- Combining time-series measures
  - Latent process e.g. DOI
  - Real-time
  - State-space model



λ = 1e2
60
50
40
30
20
10
MY (kg/day)
0
50
100
150
200
250
Time (dfc)


λ = 1e4
MY (kg/day)
Time (dfc)
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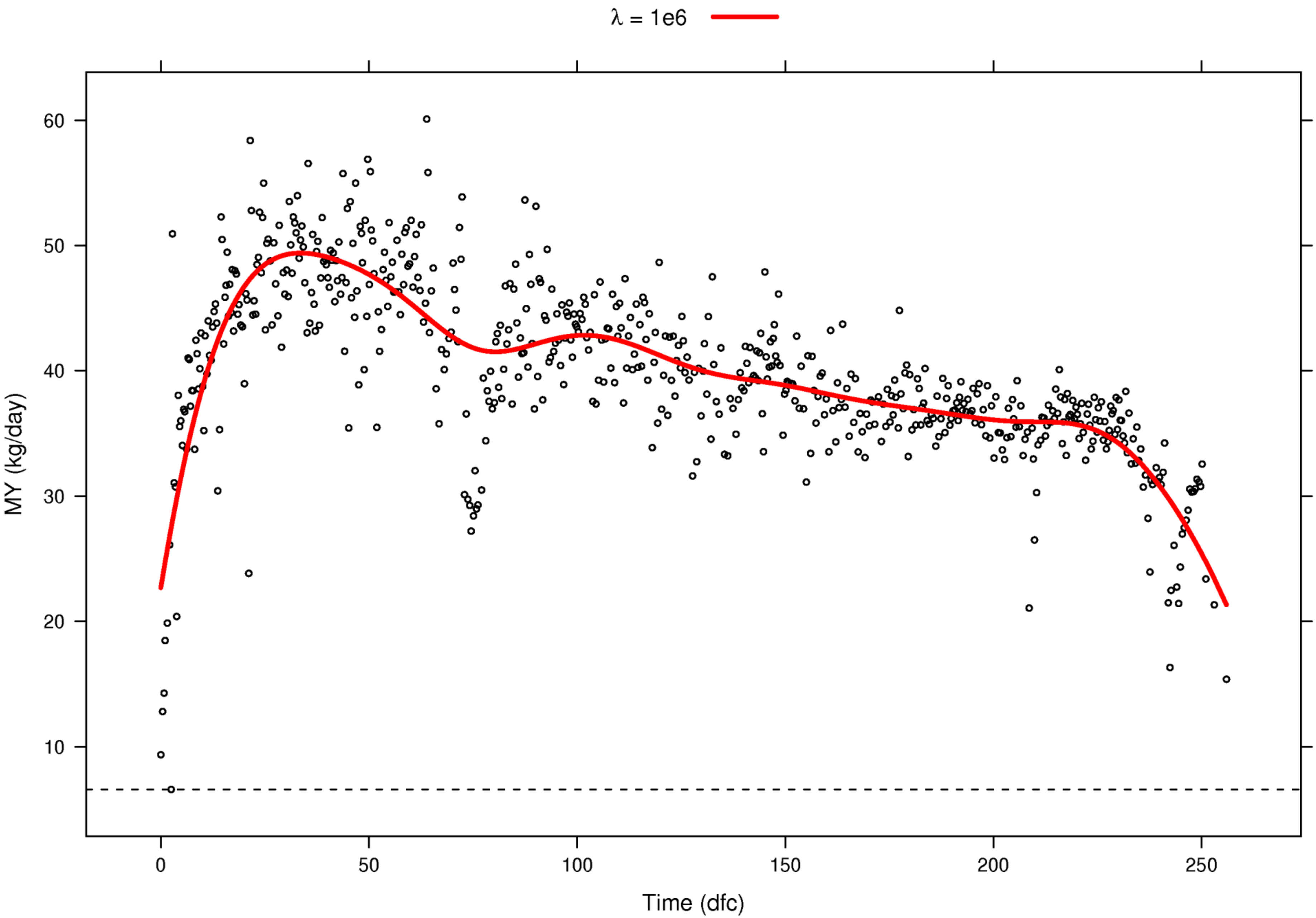
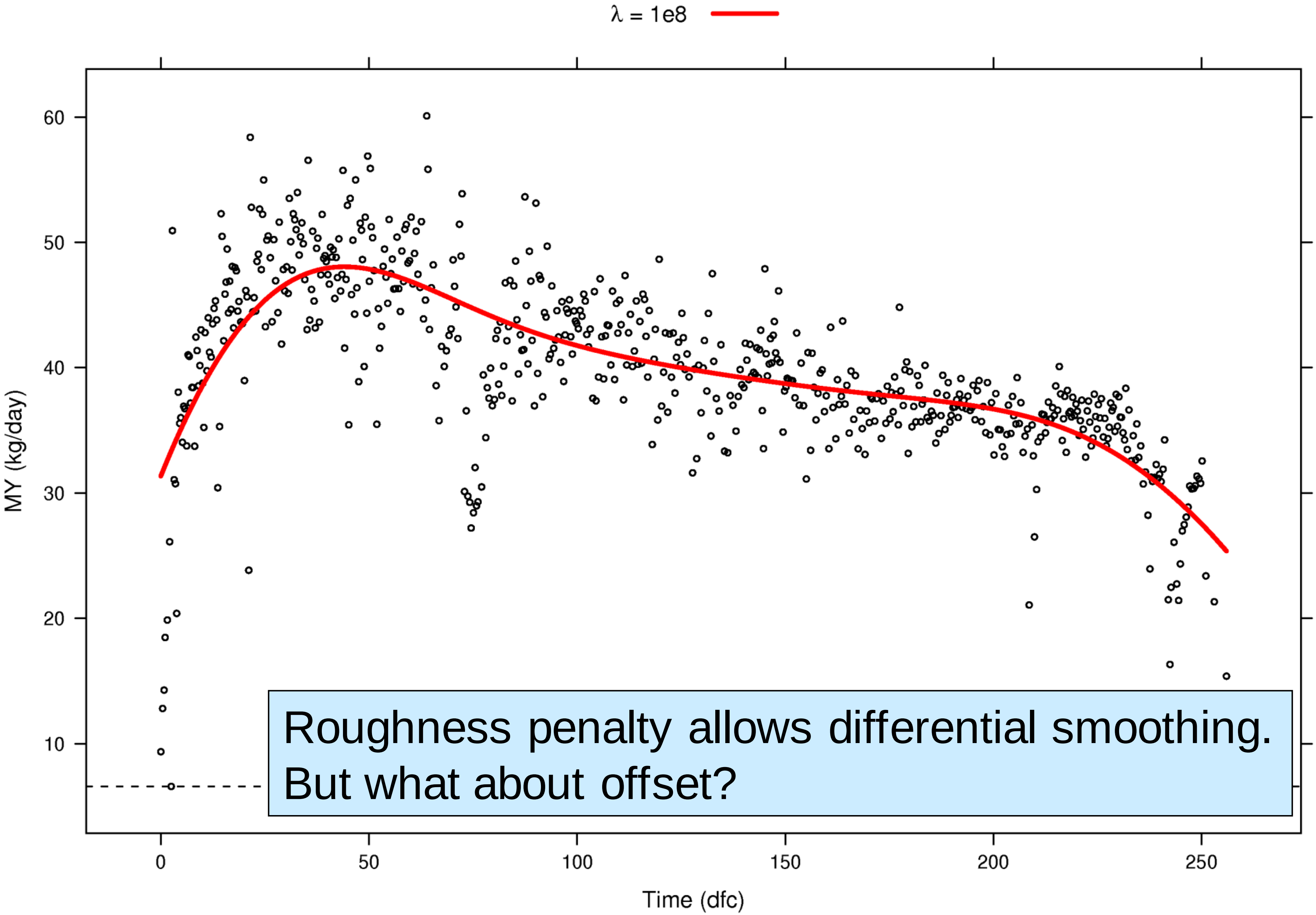
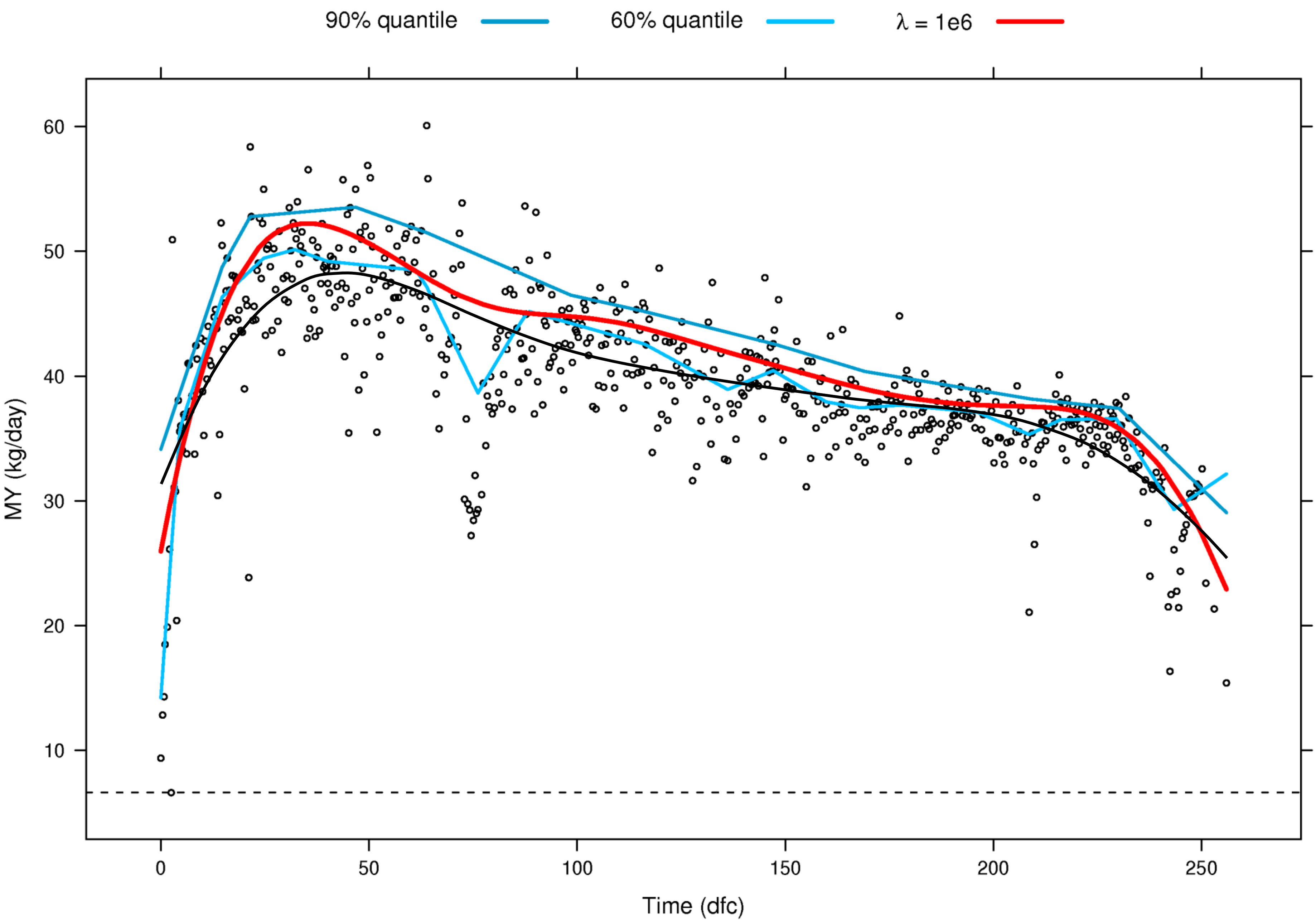
50
100
150
200
250
10
20
30
40
50
60



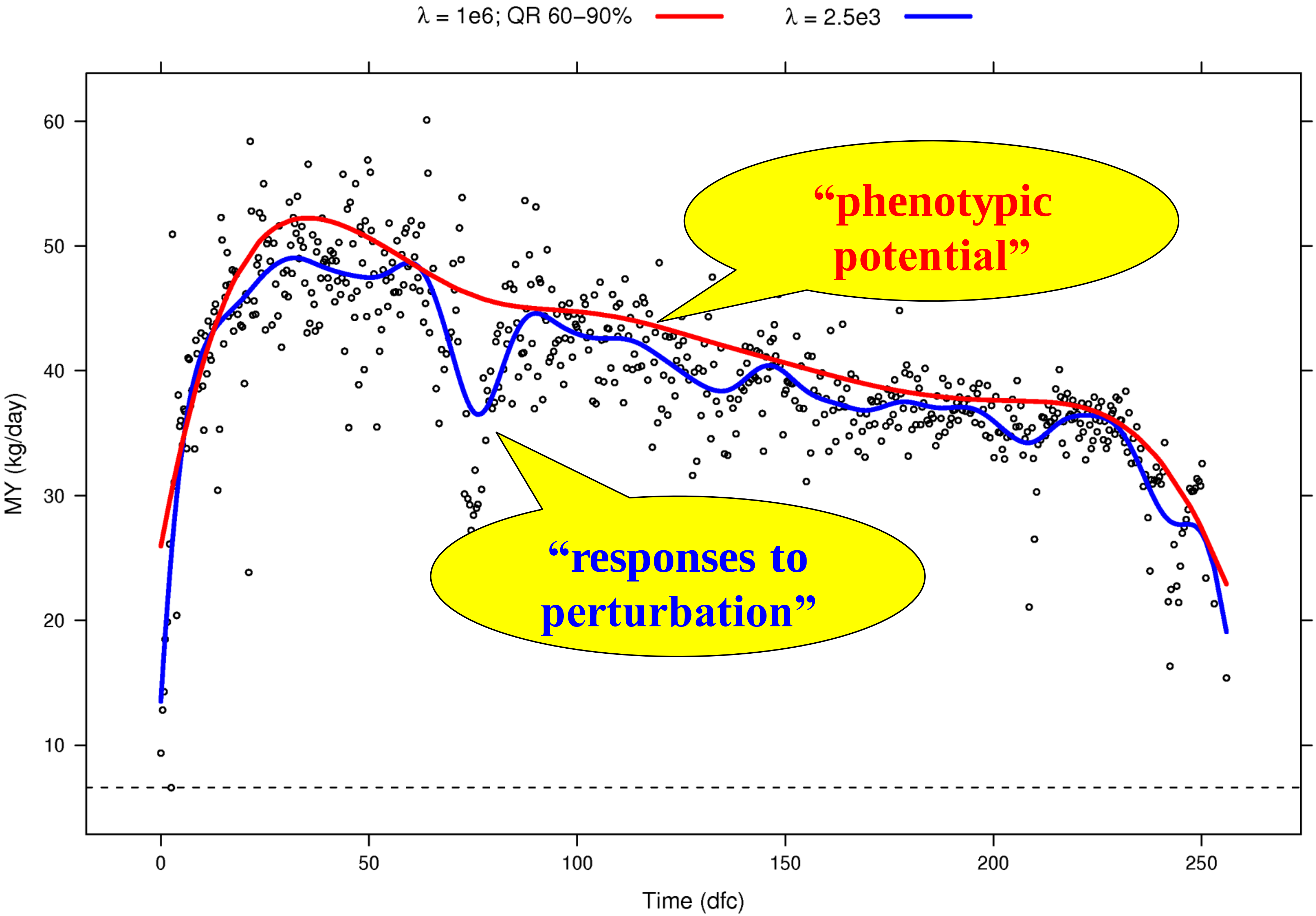
λ = 1e6
MY (kg/day)
60
50
40
30
20
10
0
50
100
150
200
250
Time (dfc)



Roughness penalty allows differential smoothing.
But what about offset?



90% quantile
60% quantile
λ = 1e6
MY (kg/day)
Time (dfc)
0
50
100
150
200
250
10
20
30
40
50
60



λ = 1e6; QR 60–90%
λ = 2.5e3
“phenotypic potential”
“responses to perturbation”
MY (kg/day)
60
50
40
30
20
10
0
50
100
150
200
250
Time (dfc)

Differential smoothing
(roughness penalty)

Offsetting
(quantile regression)

Capture response
(amplitude, rate of recovery, etc.)
Describe underlying baseline

Requires acceptance of parameters based on a biological rationale

Combining measures to describe a biological phenomenon: DOI

- Degree of Infection (DOI)
- Latent process reflected by mastitis indicators
  - Interquartile ratio electical conductivity
  - Log SCC
  - LDH

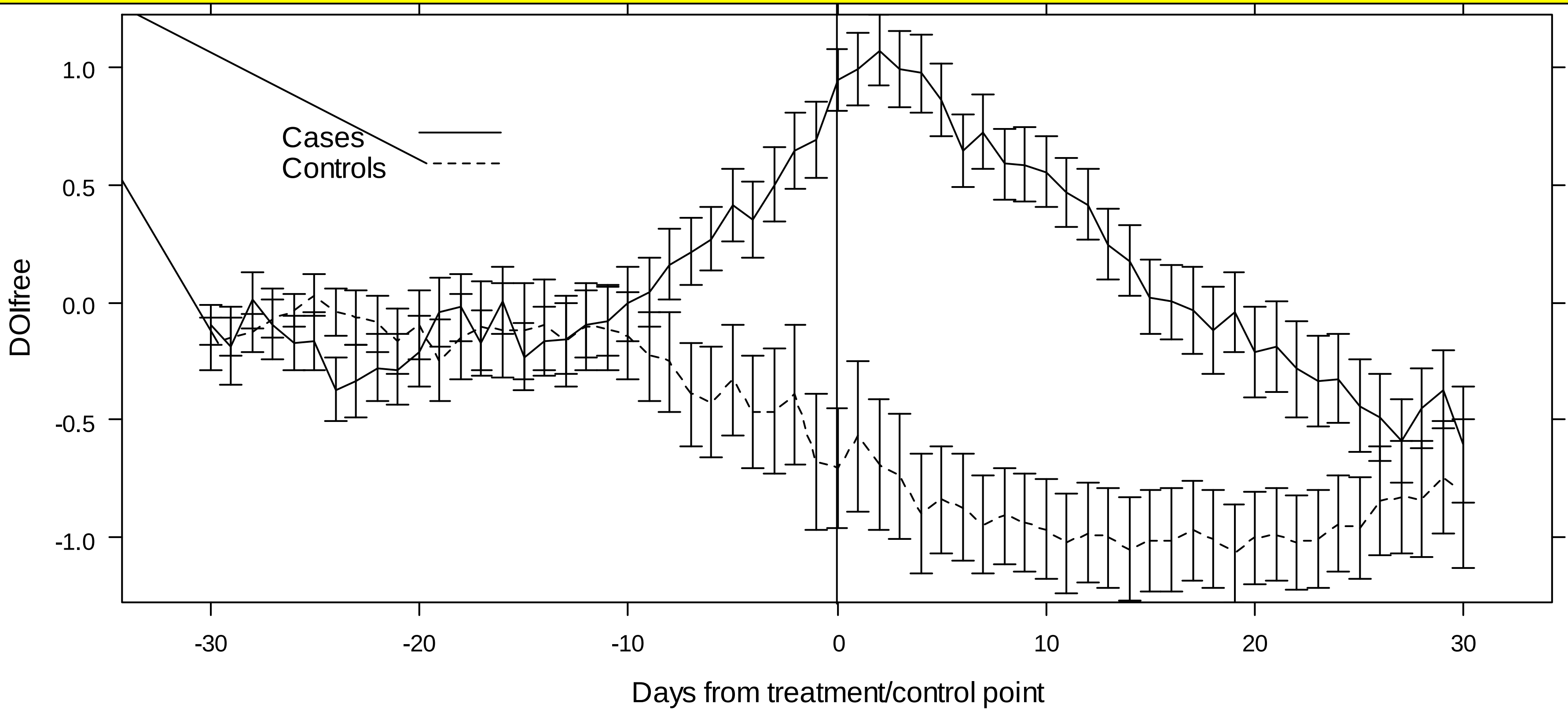
(Højsgaard and Friggens 2010)

$$y^k(t_j) = \beta^k(t_j) + \lambda^k DOI(t_j) + v^k(t_j)$$

- $\beta^k(t_j)$ Long-term trend
- $r^k(t_j)$ Short-term fluctuation
- $v^k(t_j)$ Error term
- λ^k Proportionality constant

DOI distinguishes mastitis cows 5 days prior to treatment

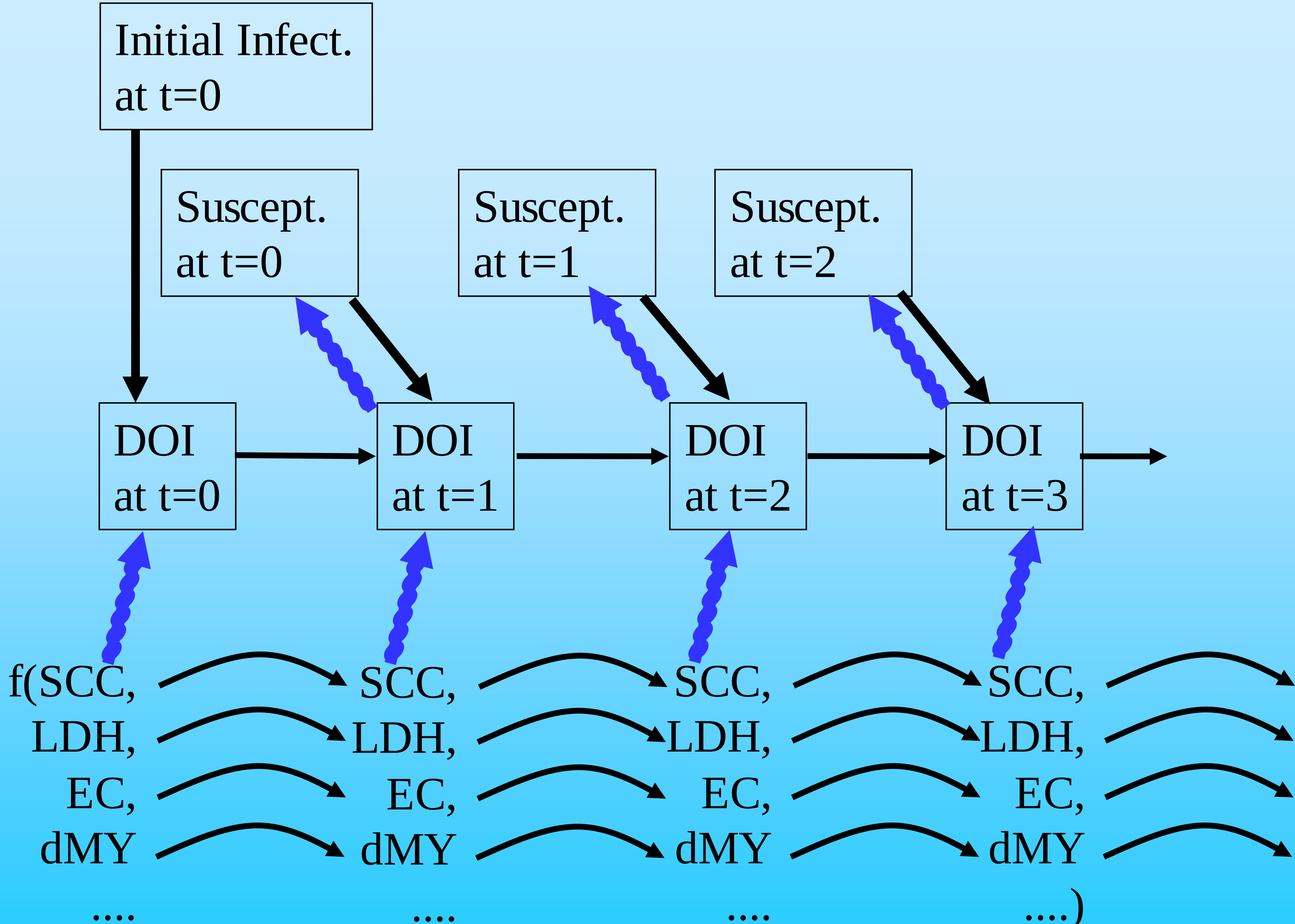
The notion of “degree of” is biologically sensible



58 cases, 71 controls. Matched for stage of lactation, parity, etc.

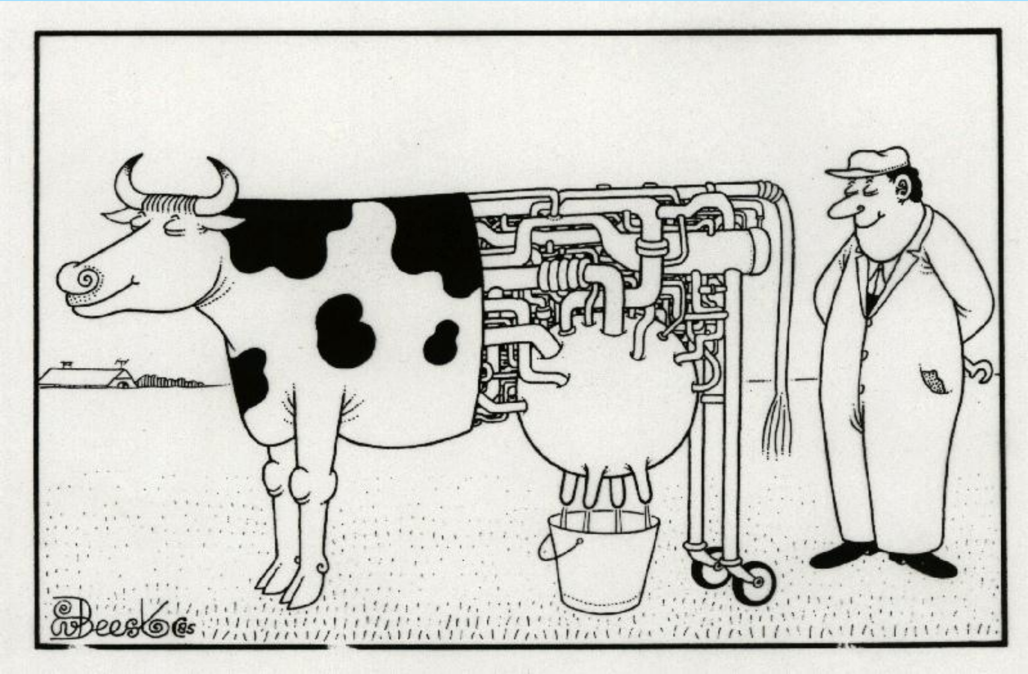
Degree of Infection

- Combining different measures
  - Strengthens the indicator
  - Captures multiple facets of infection
- The notion of “degree of”
  - Makes early anticipation easier
  - Gets away from the limitations of classifications (healthy vs sick)
  - Much better reflects the biology of the system


Initial Infect.
at t=0
Suscept.
at t=0
Suscept.
at t=1
Suscept.
at t=2
DOI
at t=0
DOI
at t=1
DOI
at t=2
DOI
at t=3
f(SCC,
LDH,
EC,
dMY
....
SCC,
LDH,
EC,
dMY
....
SCC,
LDH,
EC,
dMY
....
SCC,
LDH,
EC,
dMY
....)

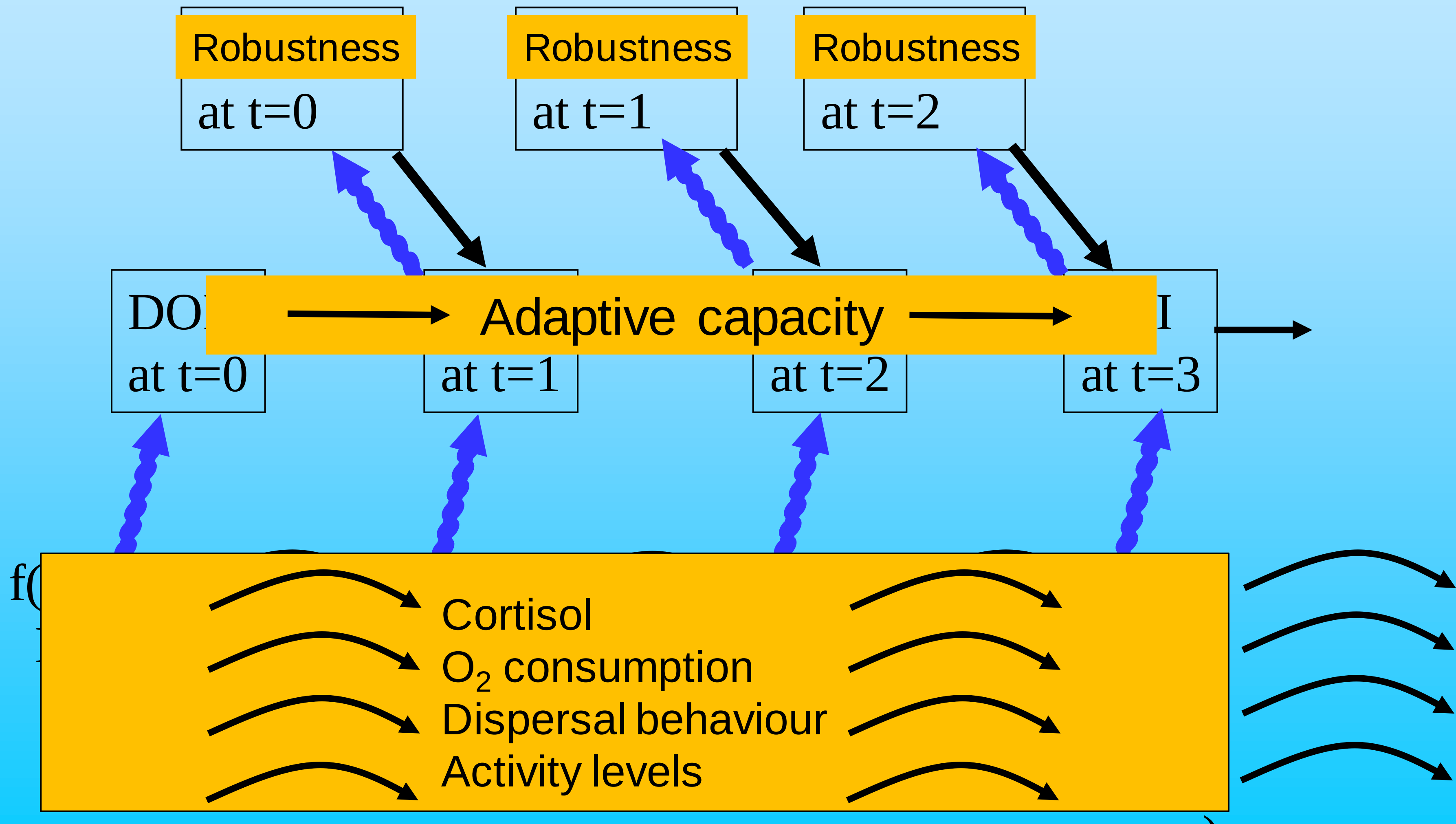
Towards Precision Phenotyping

- The above examples are generalisable representations of biological systems



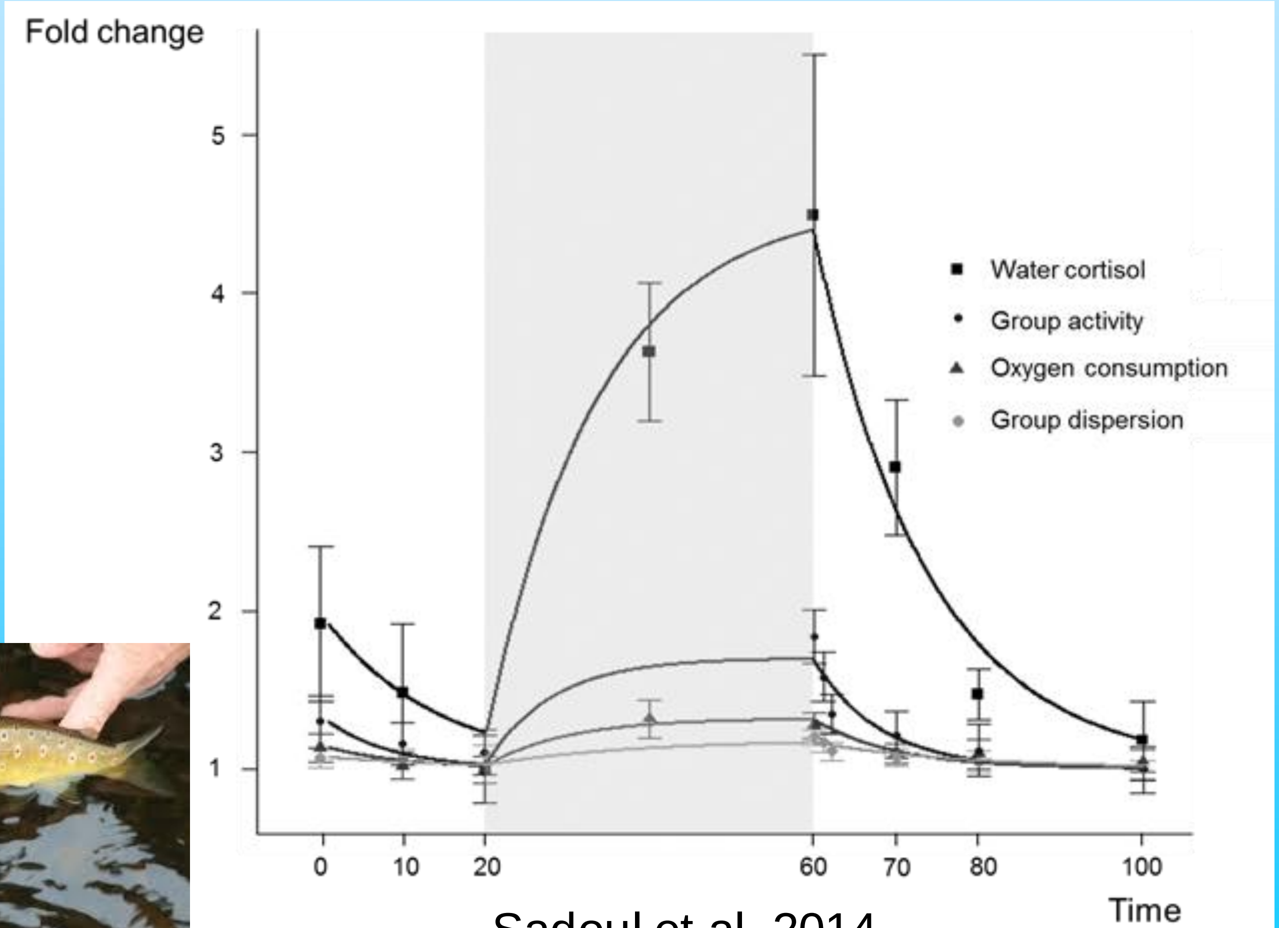
Towards Precision Phenotyping

- The above examples are generalisable representations of biological systems. e.g:



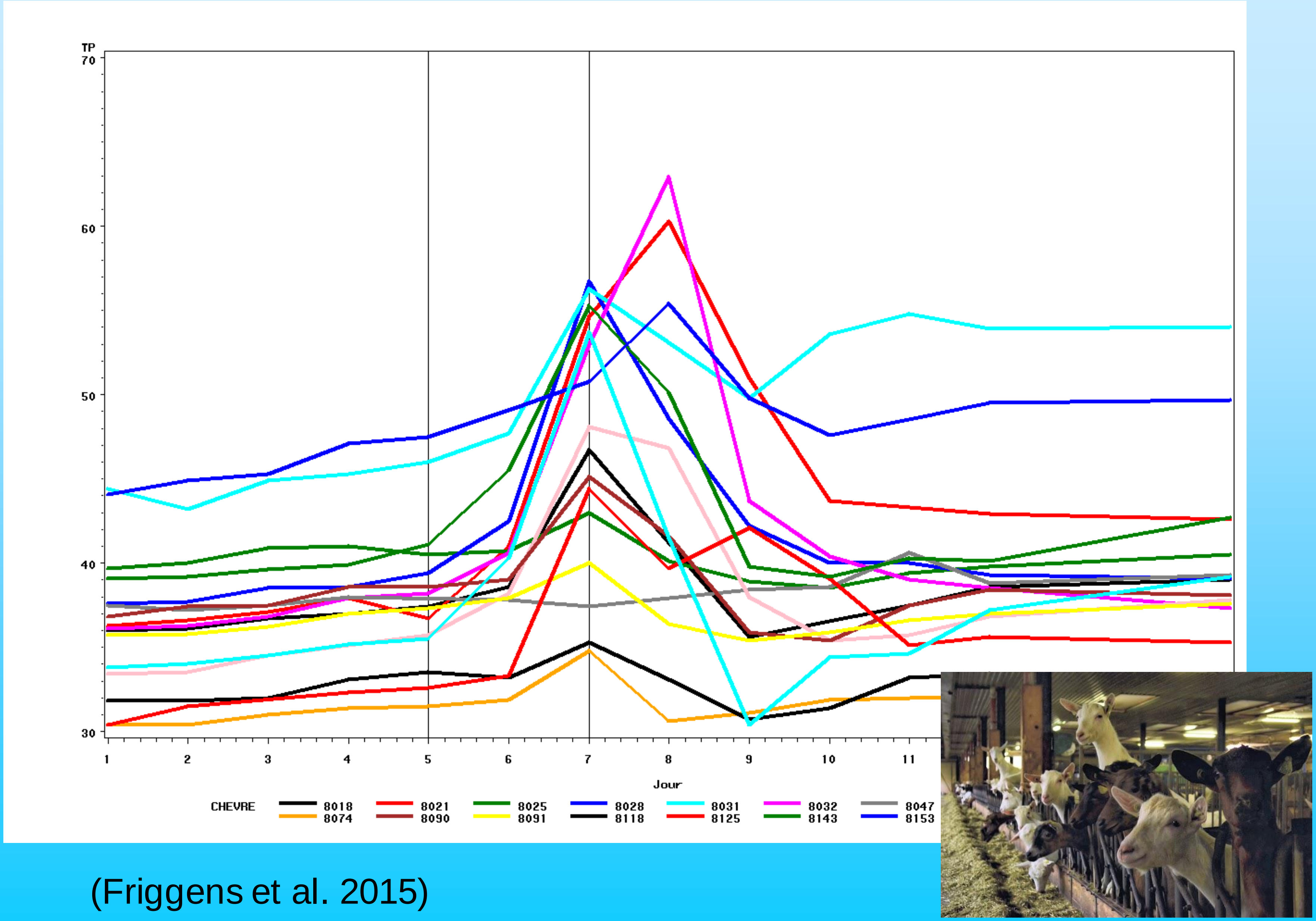
Towards Precision Phenotyping

- The above examples are generalisable representations of biological systems



Sadoul et al. 2014

Individual responses in milk protein content



(Friggens et al. 2015)

Towards Precision Phenotyping

- The above examples are generalisable representations of biological systems
  - Hierarchy of functions
  - Time-linked (state-space systems)

Hierarchy of functions

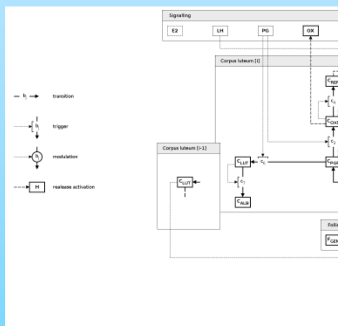
- Especially important when there is no direct (or useful) measure of the target trait
  - e.g. Robustness
  - Need operational definitions of robustness
  - If we cannot measure (some index of) robustness, we're not going to make much progress with phenotyping it!
- Which measures are biologically relevant for a given level
  - Combine to create an index of a higher function

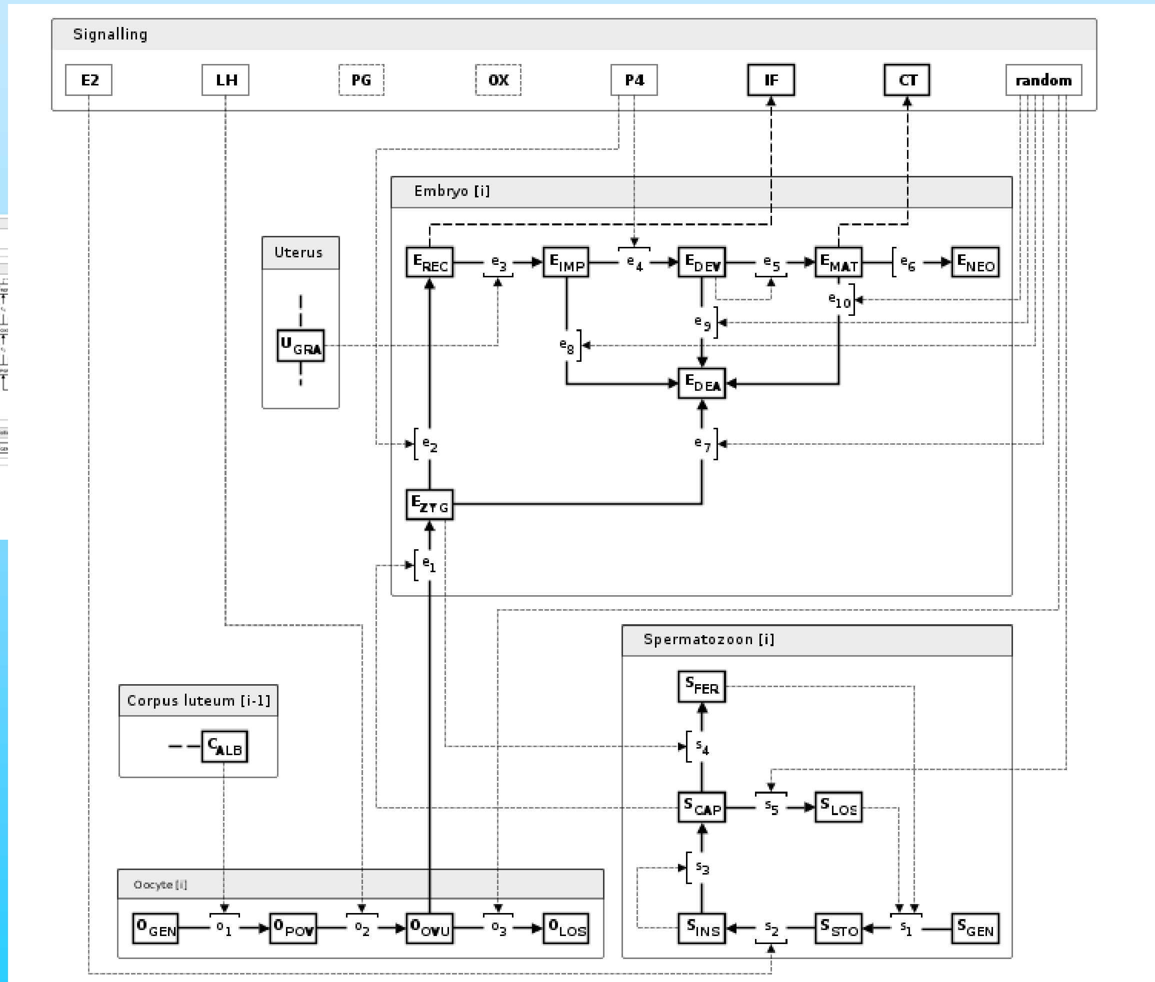
Which measures are biologically relevant?

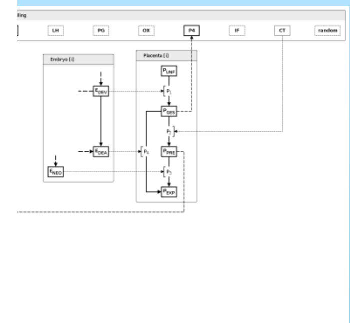
Towards new robustness phenotypes

- Define phenotypes from consideration of their biological properties and not just from available measures.
- Systemic view needed to do this
  - e.g. hierarchy of functions
  - But can go further
- Exploratory example: “reproductive robustness”

A systemic reproductive physiology model



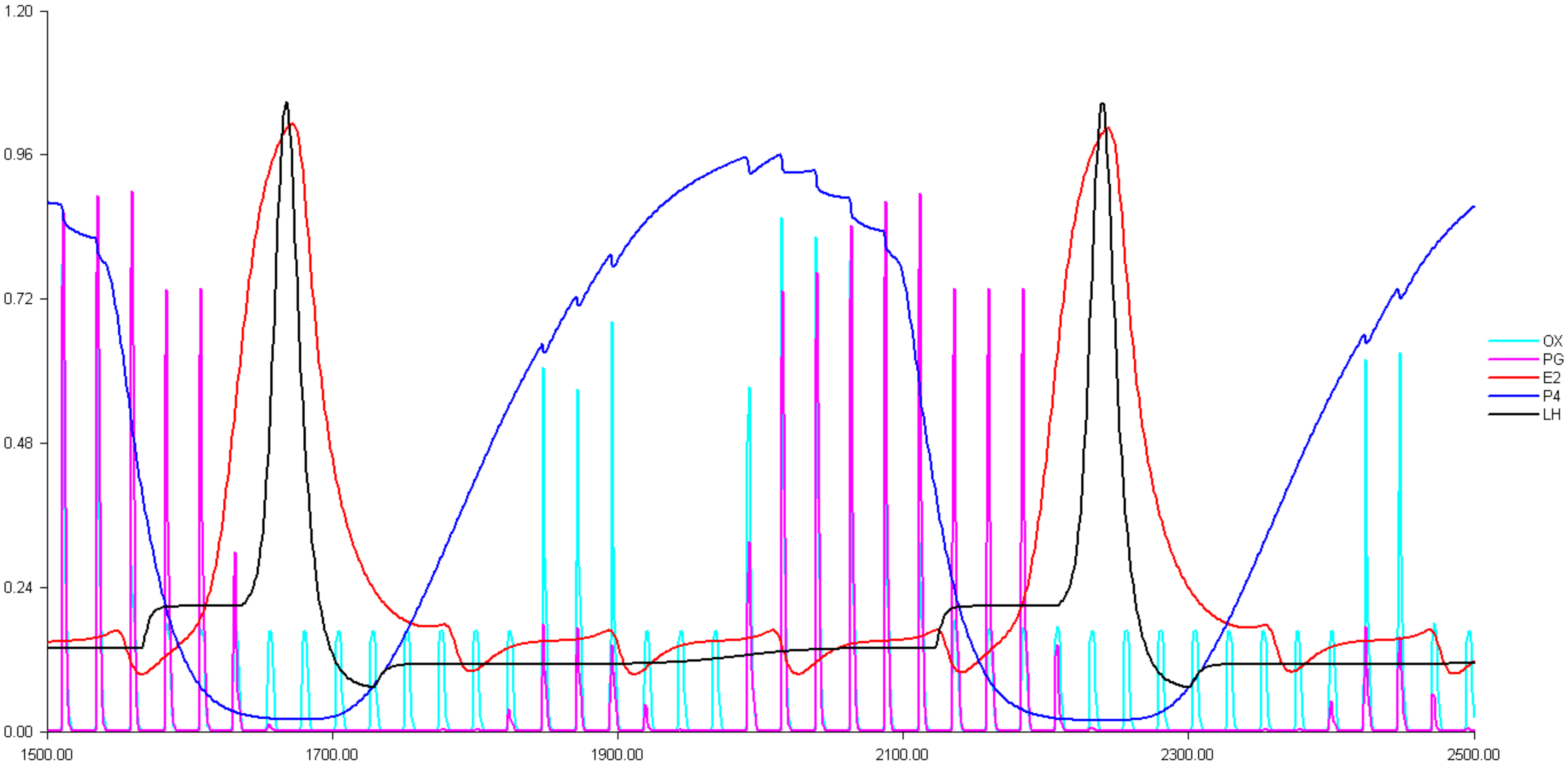




(Martin et al 2014)

Model simulations :

realistic hormonal profiles



Example: Reproductive Robustness

- Major factors that influence fertility are known (milk yield, energy balance, etc.)
- Far from clear which reproductive physiology mechanisms are impacted
- Systemic models of reproductive physiology can identify likely mechanisms that are implicated in abnormal profiles (Boer *et al.*, 2012)

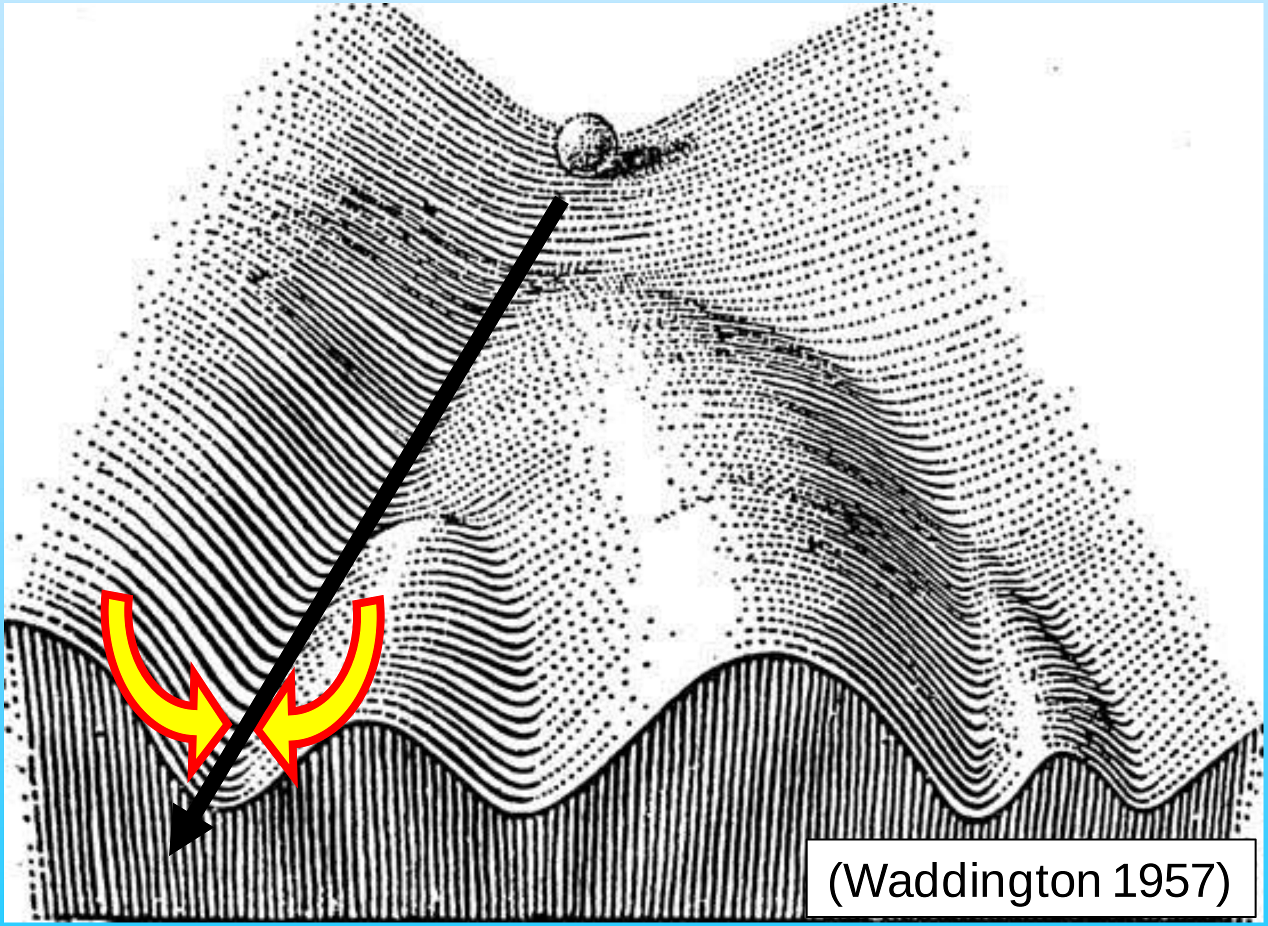
- Opens the door to target key robustness mechanisms, and relevant biomarkers

Towards Precision Phenotyping

- The above examples are generalisable representations of biological systems
  - Hierarchy of functions
  - Time-linked (state-space systems)

- Need to describe the underlying unperturbed, system
  - Not constant through time
  - Varying baseline for adaptive responses
  - Varying adaptive capacity

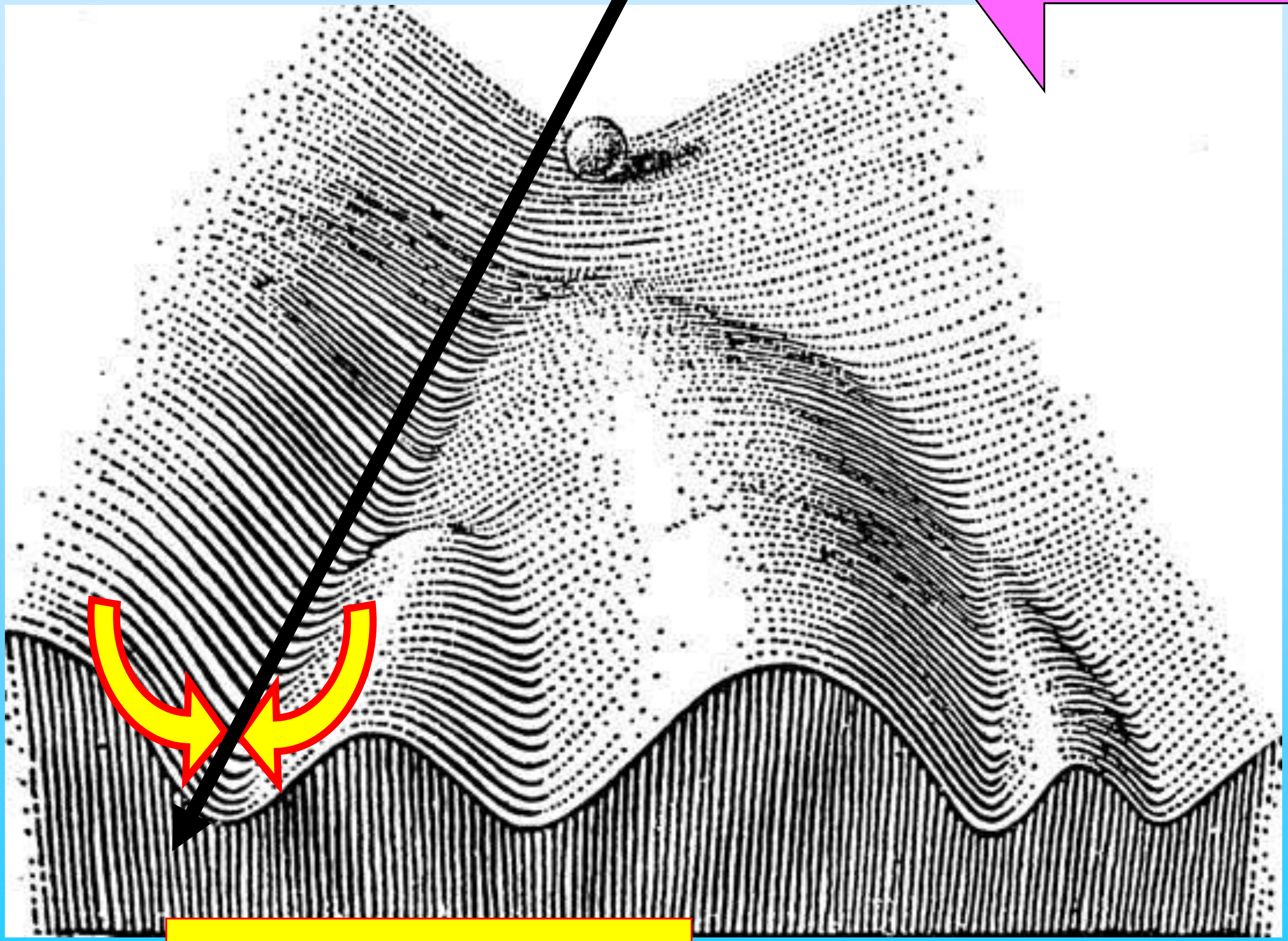
Influence of physiological state/age on adaptive capacity



Systemic considerations: the difference between homeorhesis and homeostasis

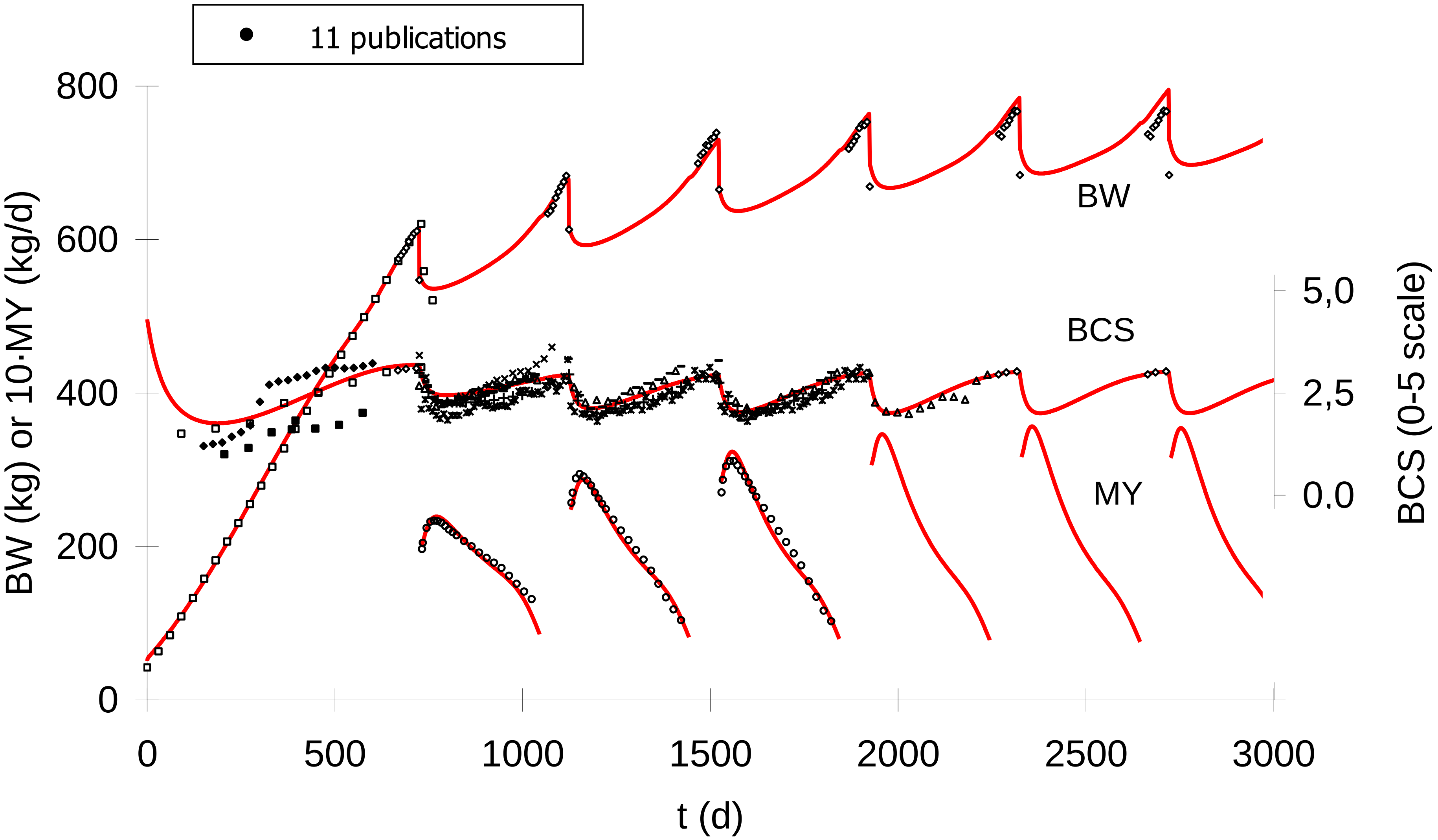
Normal, unperturbed trajectory

We can do this:
- **Genotypes**
- **Environments**

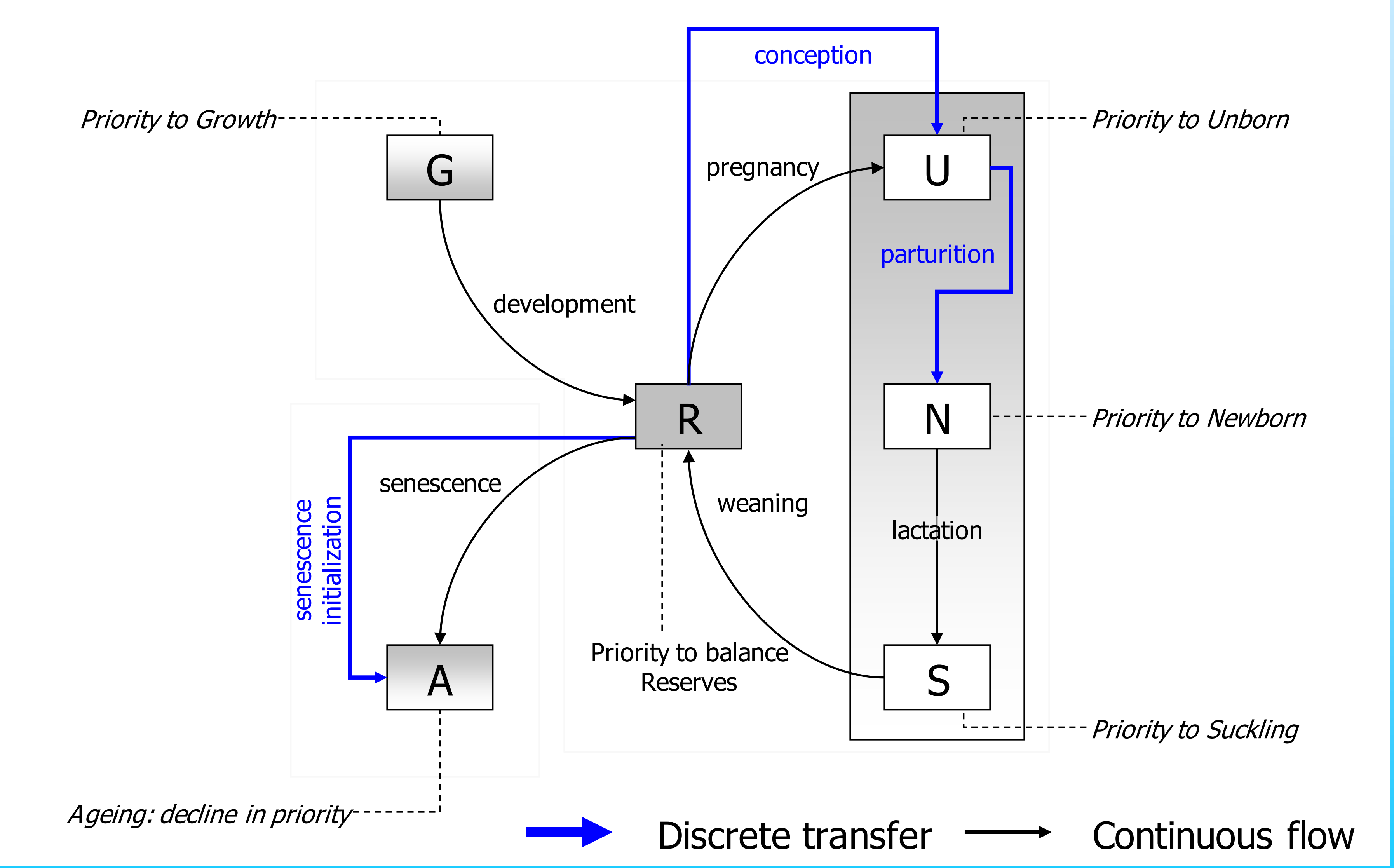


Adaptive capacity

Predicted vs observed trajectories

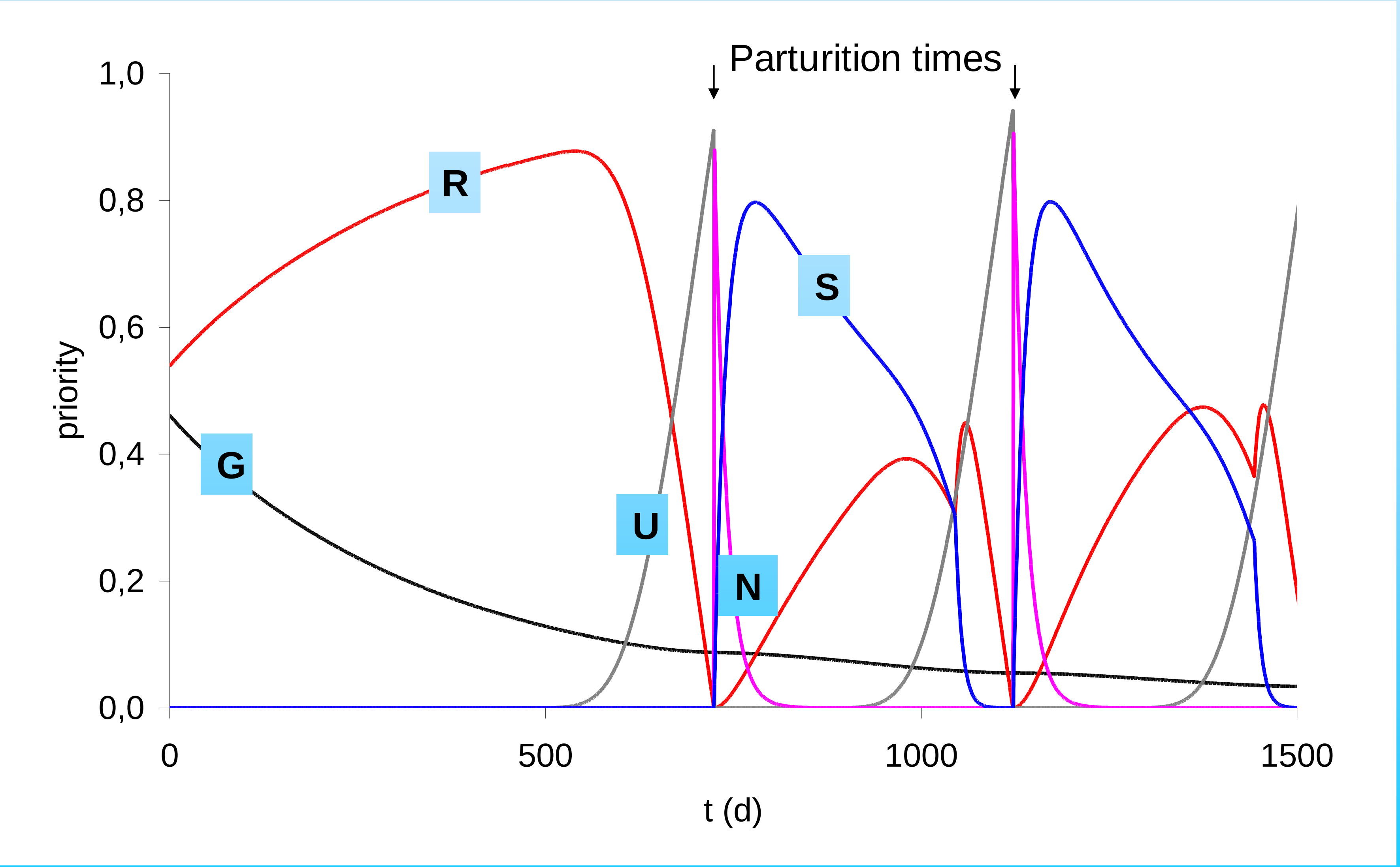


Teleonomic model of nutrient partitioning (Martin and Sauvant, 2010)

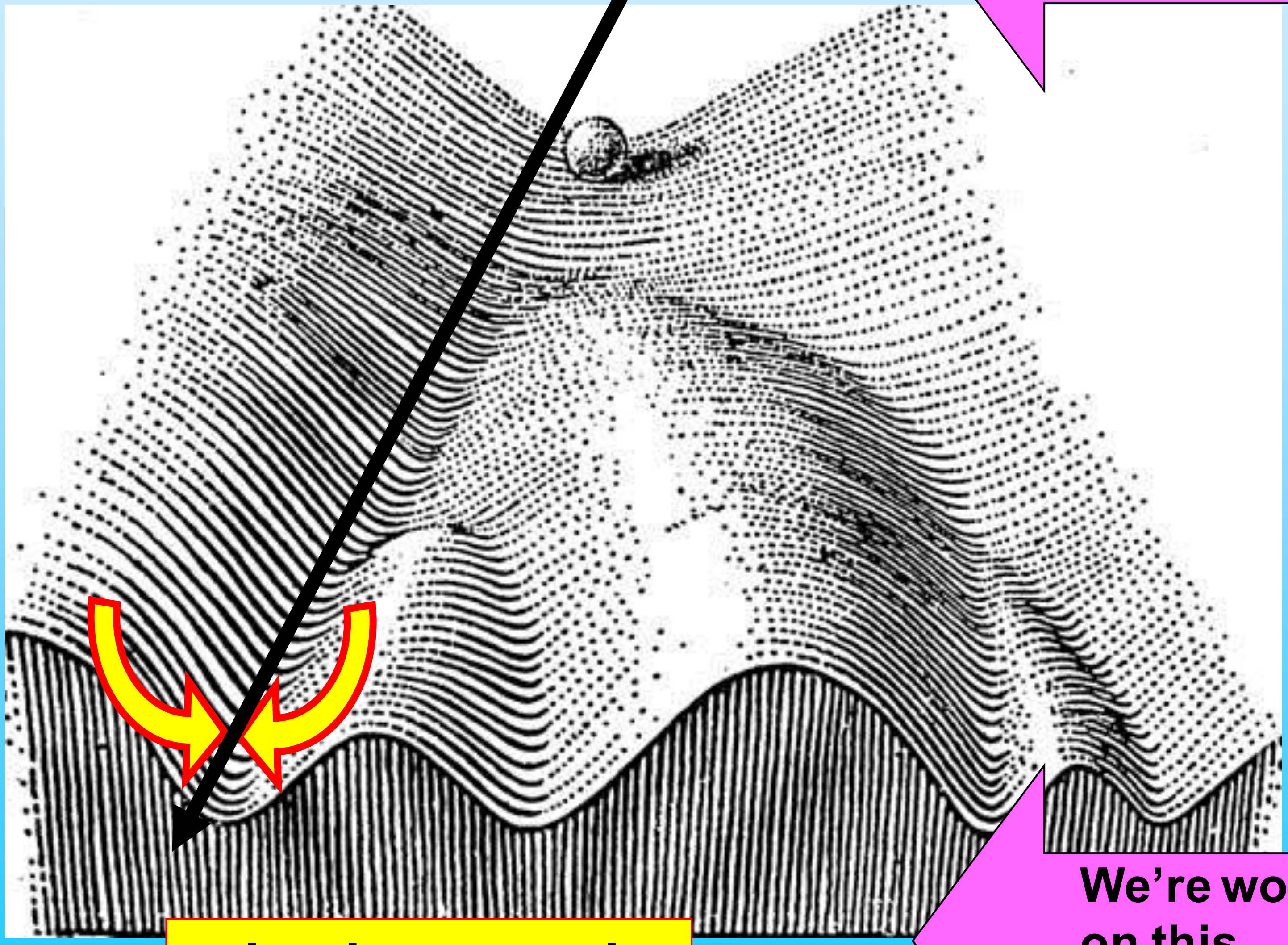


Relative priorities

(Martin and Sauvant, 2010)



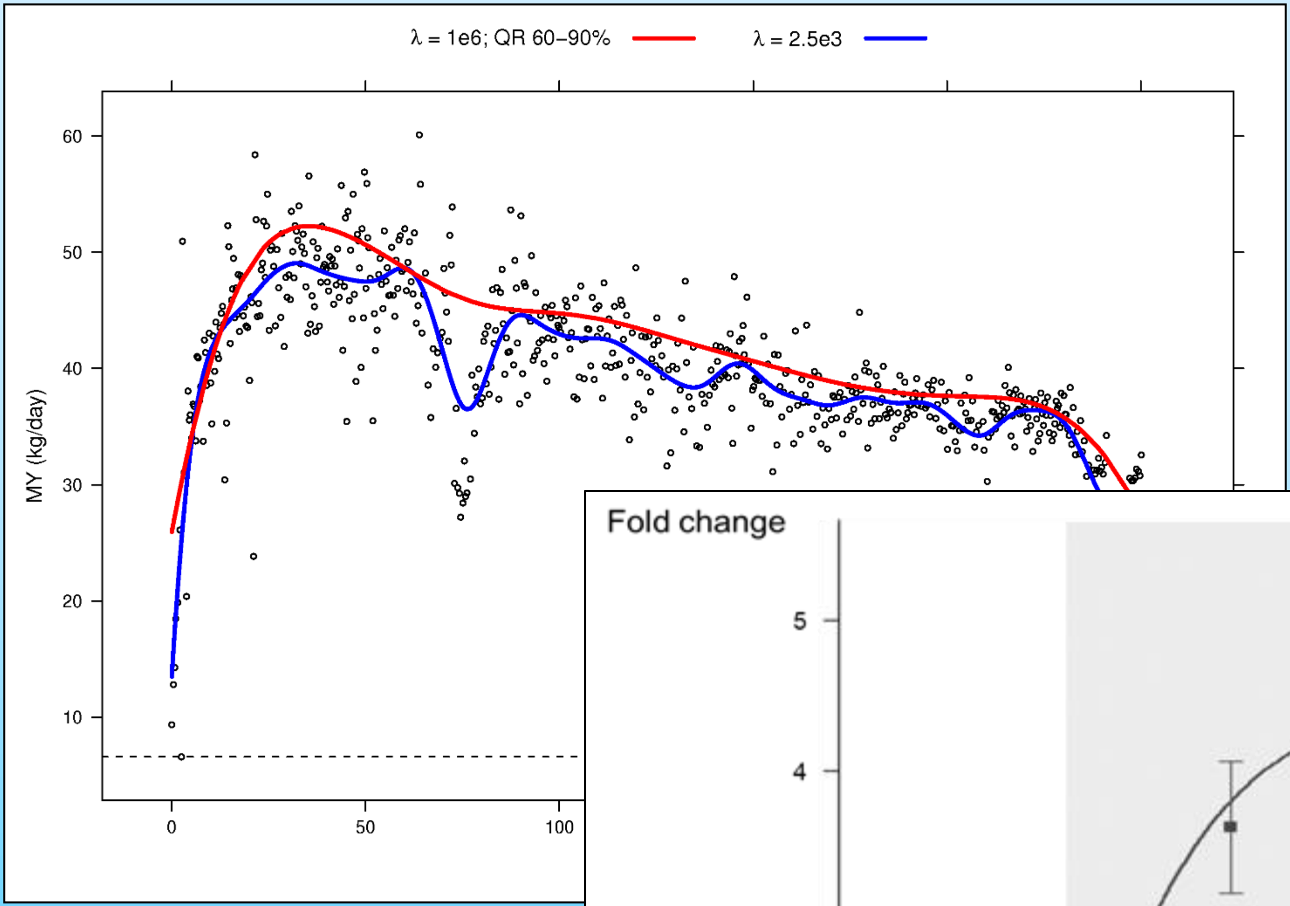
Normal, unperturbed trajectory



Adaptive capacity

We can do this:
- **Genotypes**
- **Environments**

We're working on this….
very little data


λ = 1e6; QR 60–90%
λ = 2.5e3
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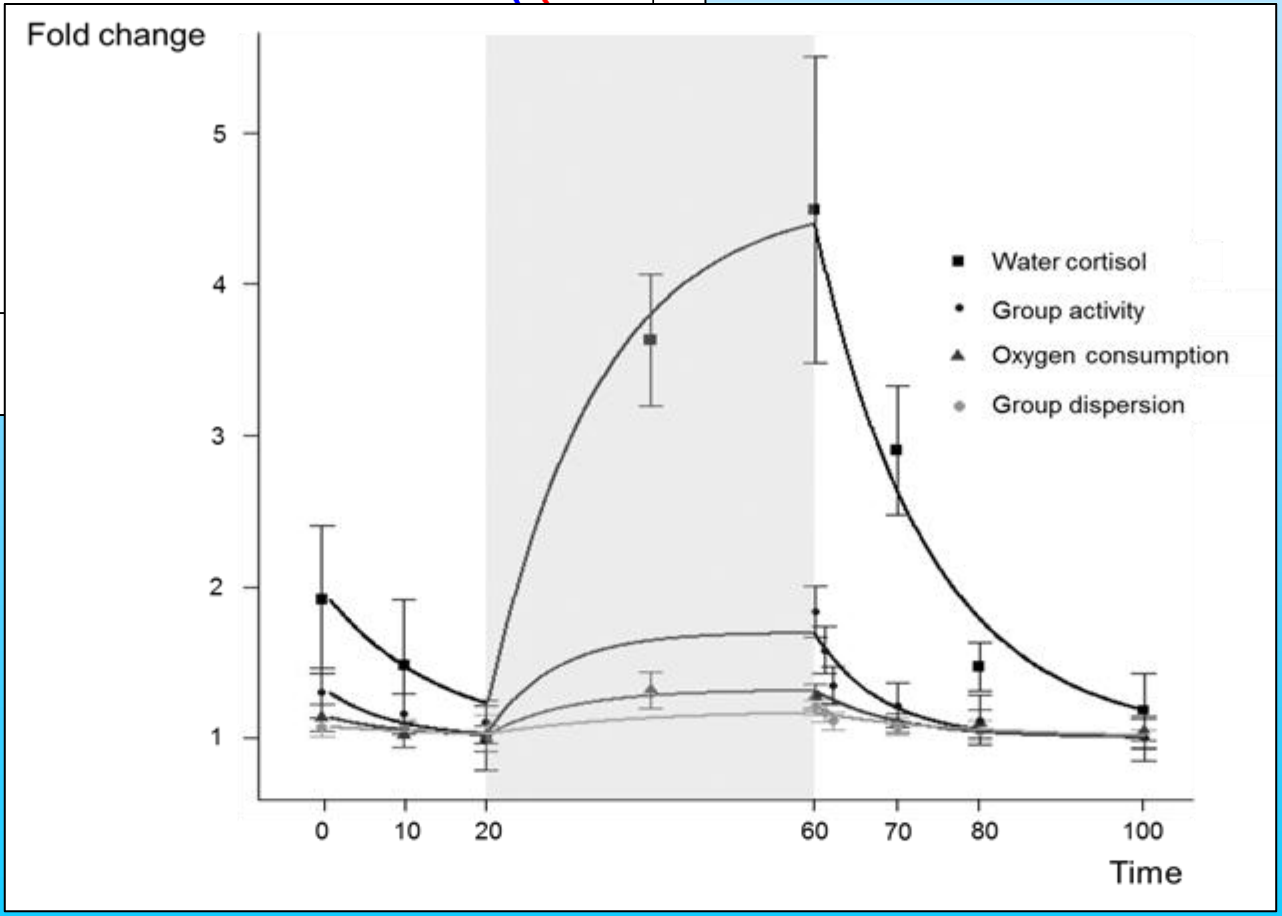
0
50
100


Fold change
Water cortisol
Group activity
Oxygen consumption
Group dispersion
5
4
3
2
1
0
10
20
60
70
80
100
Time

Towards understanding and exploiting the temporal aspects of robustness

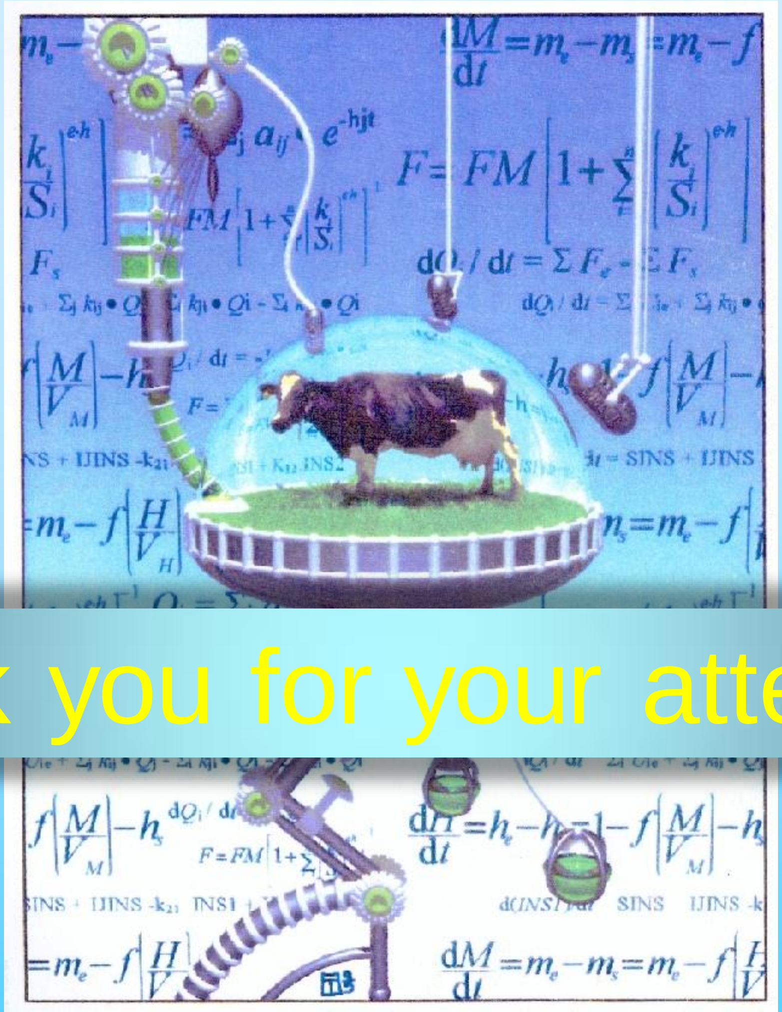
- Dynamic of response to an environmental challenge (amplitude, rate of recovery, etc)
  - reflects the size of the challenge and the animals adaptive capacity
- Influence of physiological state/age on adaptive capacity
- Dynamic of any acclimation processes

Relative contributions and the factors that affect them?

Conclusions: Systemic considerations

- Add value to time-series measures of biological indicators by feature extraction and combination across measures

- Provide means to improve description of animal states and thereby allow precision phenotyping of complex traits



Thank you for your attention

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In collaboration with:

Søren Højsgaard, Marius Codrea, Bastien Sadoul

The only good reason to avoid systemic modelling

Differential smoothing – milk yield
(Codrea et al 2011)

$$F(c) = \sum_j [y_j - x(t_j)]^2 + \lambda \int [D^4 x(t)]^2 \, dt$$

$$x(t) = c\phi(t)$$

c = coefficients
Φ = set of basis functions: **B-spline**

λ controls the **roughness penalty** (curvature in the 2nd derivative of *x*)

(Ramsay and Silverman 2005)

DOI example (Højsgaard and Friggens 2010): further details

- Time-dependency:

$$\beta^k(t_j) = \beta^k(t_{j-1}) + w\,(t_j), \qquad \text{where } w(t_j) \sim N(0,W)$$

- Same for trend in DOI
- Linear state-space model
- Estimate: λ^k, covariance matrix for v^k
- Factor analysis on healthy population
- 2 variance parameters W