



## Module 3

# Detecting Stress and evaluating ability to cope with stress

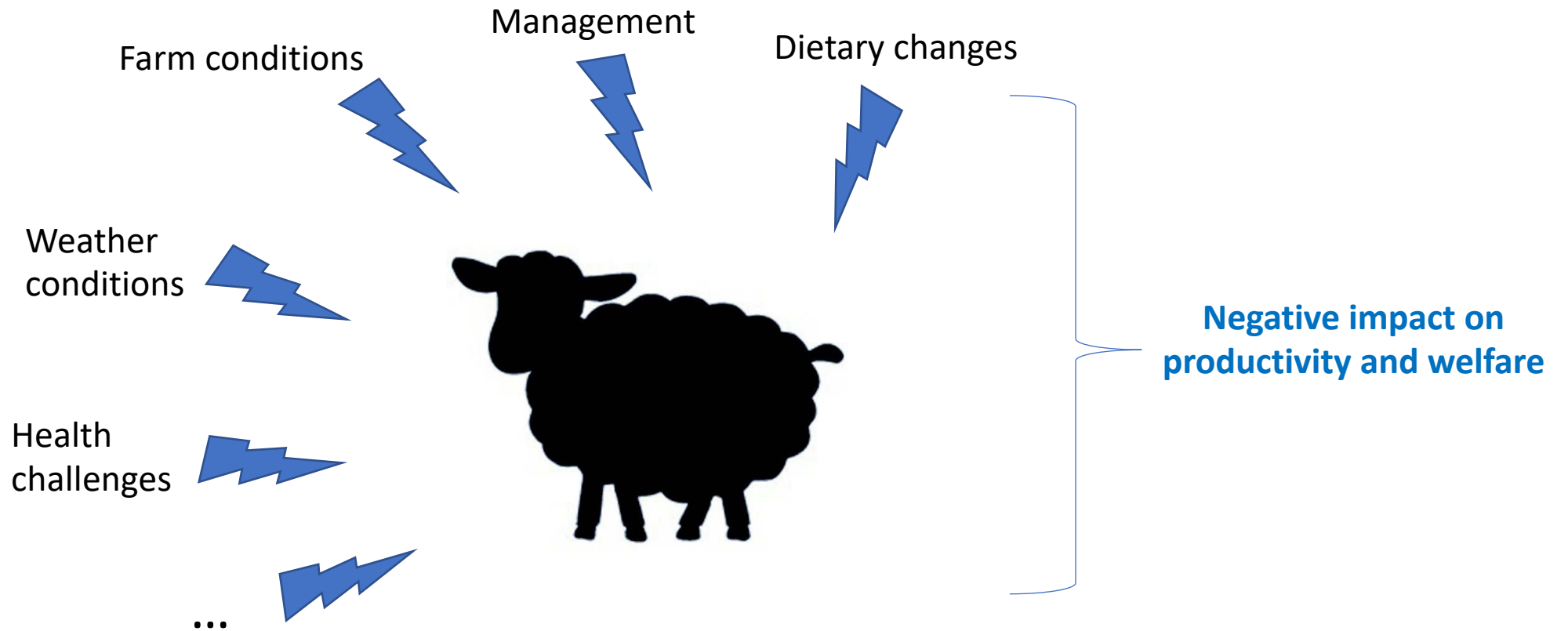
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## ➤ BACKGROUND



**Resilience** is the capacity of an animal to be minimally affected by disturbances or to rapidly return to the state pertained before exposure to a environmental challenge (Colditz and Hine, 2016; Berghof et al., 2019)

## ➤ BACKGROUND

- Small ruminants are commonly exposed to heterogeneous and changeful conditions
- In general, there is little control of environmental factors compared to other livestock species (production systems are more intensive)
- It is necessary to select animals capable of maintaining their production performance (or modifying it as less as possible) under this heterogeneous environment
- When an environmental challenge affects the whole population it is a good opportunity to select for resilience
- But environmental challenges may be recorded or not. Often, they are generally unrecorded and of unknown source

- How can we do a good work of selection under these conditions?



# Today

- Measures of stress
- Genotype x Environment interactions
- Norm reaction models to model effect of stresses
  
- Later today:
  - inferring unobserved stresses
  - selection for resilience



# Measures of stress

stress | stres |

noun

1 pressure or tension exerted on a material object: *the distribution of stress is uniform across the bar.*

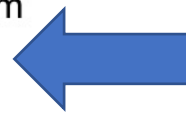
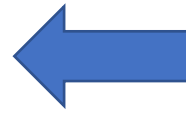
- the degree of pressure exerted on a material object measured in units of force per unit area.

2 a state of mental or emotional strain or tension resulting from adverse or very demanding circumstances: *he's obviously **under** a lot of **stress** | [in combination] : stress-related illnesses.*

- something that causes mental strain: *the stresses and strains of public life.*
- *Biology* physiological disturbance or damage caused to an organism by adverse circumstances: *in many areas irrigation is warranted to avoid plant stress.*

3 particular emphasis or importance: *we should **lay** greater **stress on** education.*

- emphasis given to a particular syllable or word in speech, typically through a combination of relatively greater loudness, higher pitch, and longer duration: *normally, the stress falls on the first syllable.*



- Can we *quantify* the stress?



# Measures of stress

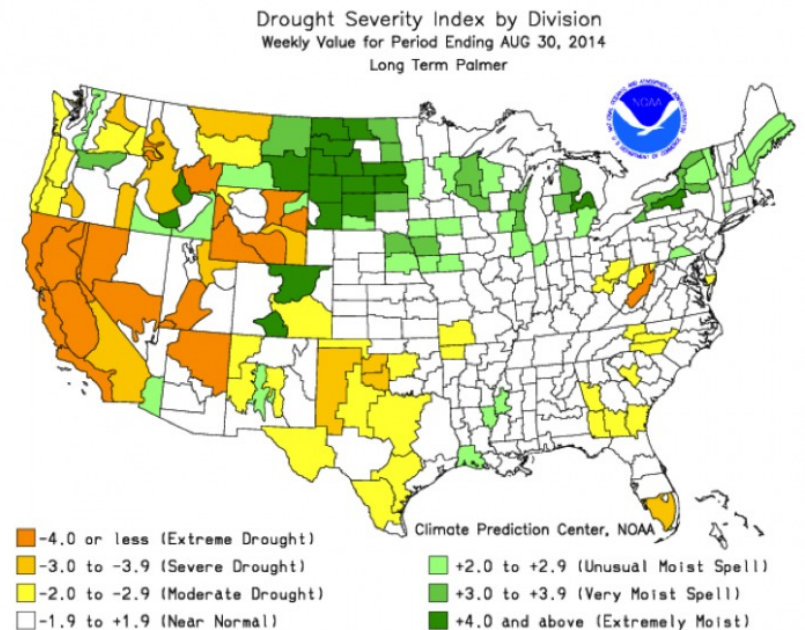
- Some examples in agriculture
  - Drought
  - Heat, humidity (THI index)
  - Bacterial & virus load
  - Ticks



# Drought

The most common index used to define and monitor drought is the Palmer Drought Severity Index (PDSI), which attempts to measure the duration and intensity of long-term, spatially extensive drought, based on precipitation, temperature, and available water content data.

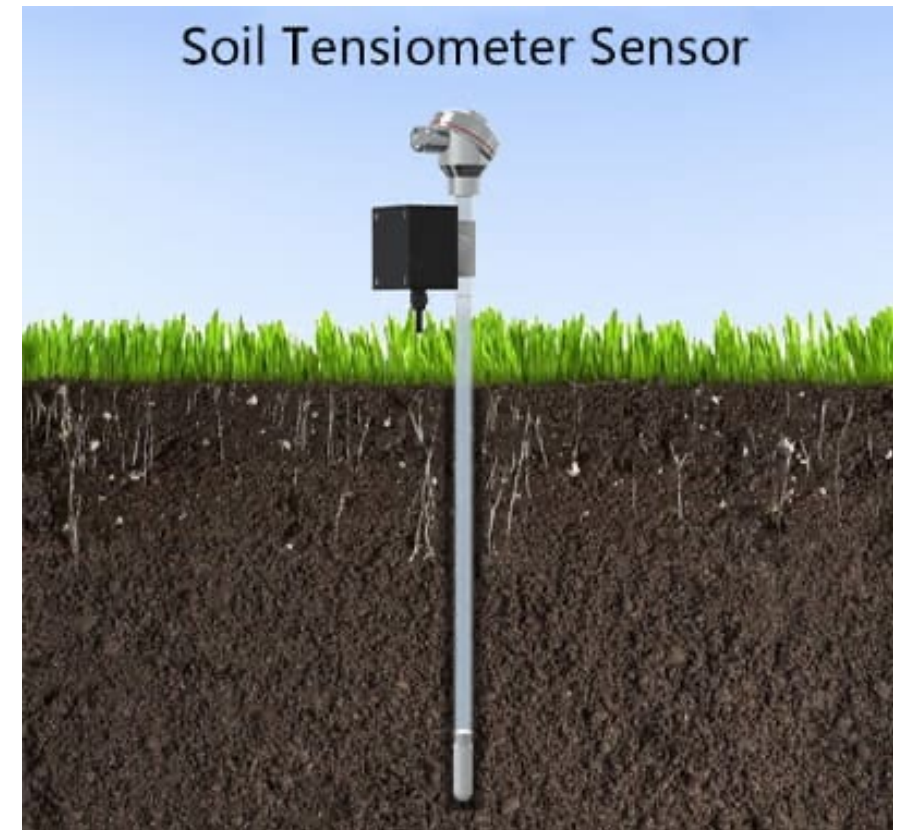
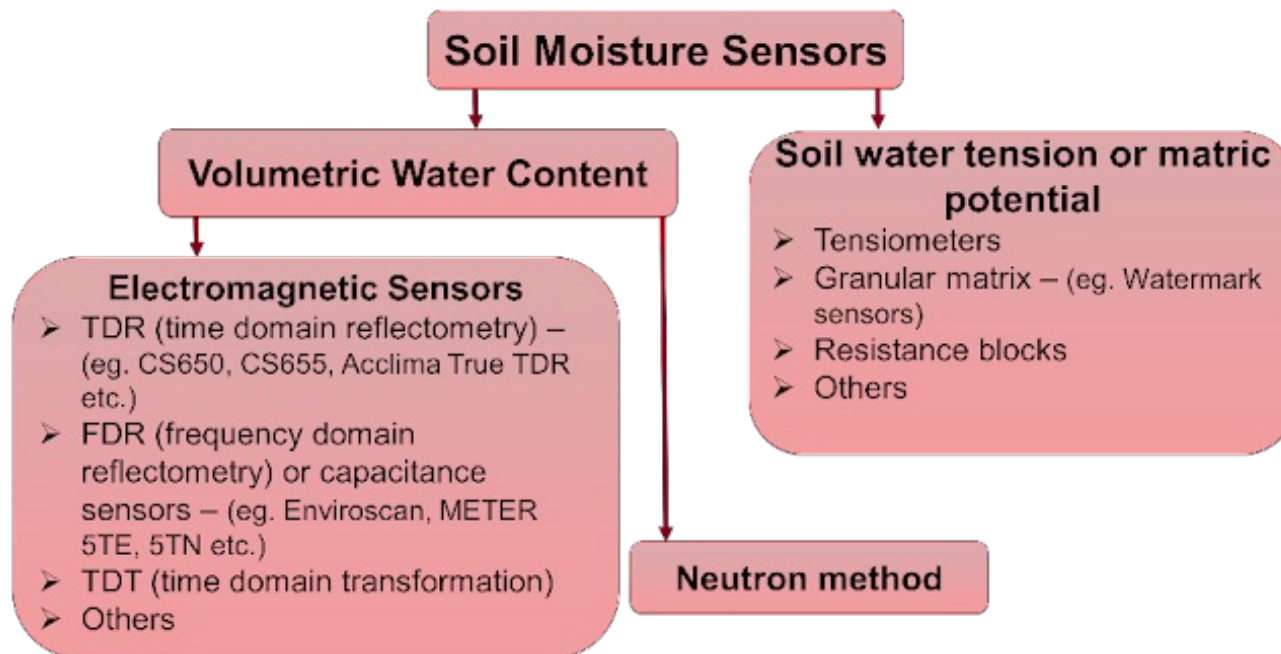
<https://www.e-education.psu.edu/earth111/node/900#:~:text=The%20most%20common%20index%20used,and%20available%20water%20content%20data.>





# Drought

<https://blog-crop-news.extension.umn.edu/2019/04/soil-moisture-sensors-for-irrigation.html>



# Heat, humidity

THI between 72 and 78



mild stress

THI between 79 and 88



moderate stress

THI between 89 and 98



severe stress

THI above 98



DEAD COWS!

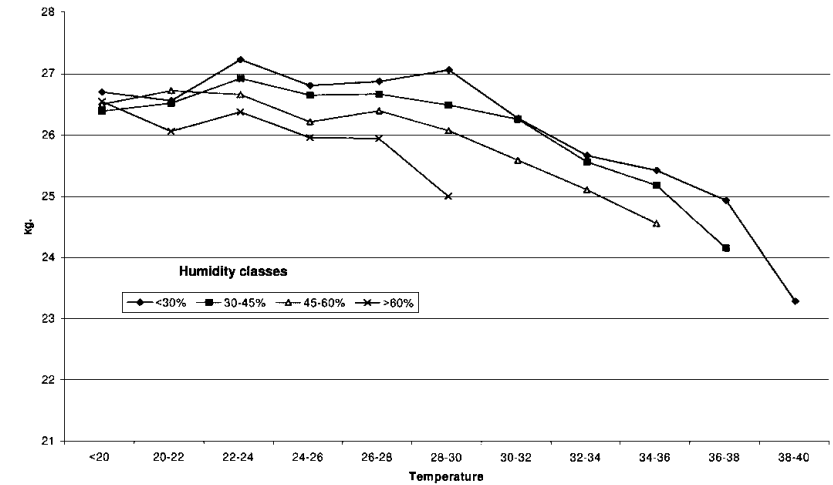
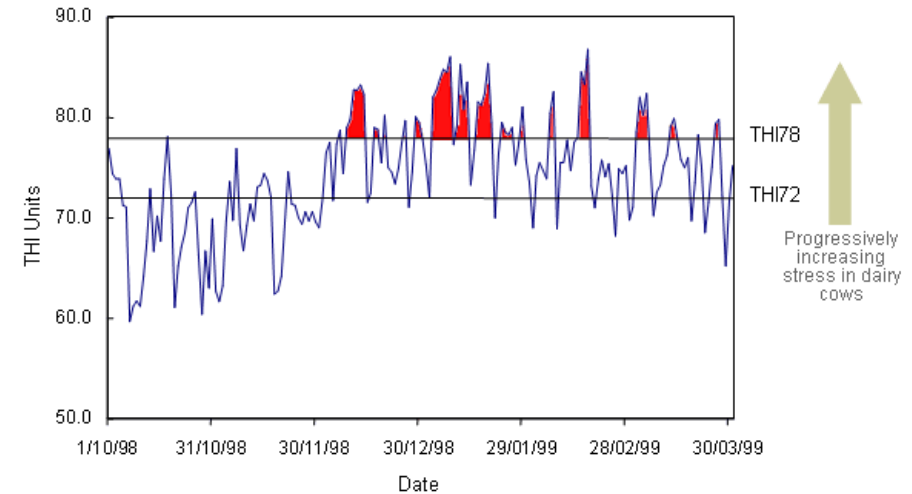


Figure 3. Effect of humidity and temperature on milk production.



<http://www.bom.gov.au/wat/about-weather-and-climate/risk/risk-example-temperature.shtml>



# Heat, humidity

- THI: Temperature-Humidity Index
  - Humidity increases the effect of heat
  - $\text{THI} = (9/5 \text{ temperature}^{\circ}\text{C} + 32) - (11/2 - 11/2 \times \text{humidity}) \times (9/5 \text{ temperature}^{\circ}\text{C} - 26)$
  - Ravagnolo and Misztal, 2000
  - where to get data?
    - closest weather station
    - Satellite-based: NASA Power data
    - (<https://power.larc.nasa.gov/data-access-viewer/> )



# **BREEDING AND GENETICS SYMPOSIUM: Breeding for resilience to heat stress effects in dairy ruminants. A comprehensive review**

[Get access >](#)

M. J. Carabaño , M. Ramón, C. Díaz, A. Molina, M. D. Pérez-Guzmán, J. M. Serradilla

*Journal of Animal Science*, Volume 95, Issue 4, April 2017, Pages 1813–1826,

<https://doi.org/10.2527/jas.2016.1114>



# Bacterial & virus load

- e.g. Foot and Mouth disease

(<https://www.woah.org/en/disease/foot-and-mouth-disease/> )

- The significance of FMD is related to the ease with which the virus can spread through any or all of the following:
- infected animals newly introduced into a herd (carrying virus in their saliva, milk, semen, etc.);
- contaminated pens/buildings or contaminated animal transport vehicles;
- ...



# Bacterial & virus load

- e.g. Methicillin resistant *Staphylococcus aureus* (MRSA)
  - Contaminated barn air may lead to transmission from animals to humans without direct contact or between animal carriers and non-carriers.
  - Air samples were collected using impingement and filtration methods in parallel. For impingement (n = 81) All-Glas-Impingers (AGI-30, Ace Glass Inc., Vineland, USA) filled with 30ml phosphate buffered saline (PBS) were used. ...
  - The second technique was air filtration using personal air sampler pumps
  - Five hundred microlitres of the original collection fluid of the impinger were streaked onto a chromogenic MRSA screen agar.
- OK this is way more difficult than THI !!

# Ticks

- “One of the main animal health problems in tropical and subtropical cattle production is the bovine tick, which causes decreased performance, hide devaluation, increased production costs with acaricide treatments and transmission of infectious diseases.”
- ...One to three subsequent tick counts on one side of each animal were obtained from...
- We can count ticks in animals but we can't count ticks on rangelands !

# Farm effect

- Some farms are better than others (cleaner, they give better food...)
- Some people tried to use the “average level of the farm” as an environmental covariate
- But of course, the farm average contains the “farm effect” and the sum of all animals’ effects
- This makes estimating the effect of “farm on animals” a bit complicated
  - See Su et al J. Anim. Sci. 2006. 84:1651–1657 for a long and technical solution





- So, we may have stresses that we can't count or we can't record
- (If we count stresses) how can we model stress for genetic selection?
  - we see this now
- (If we don't count stresses) can we “infer” that there was a stress?
  - we see this later



# Models for stress

- Genes may act differently depending on the environment
  - Alpha-Thalasemia gene gives you anemia but also resistance to Malaria
  - Malaria-infested regions; good for you
  - Non-malaria: bad for you



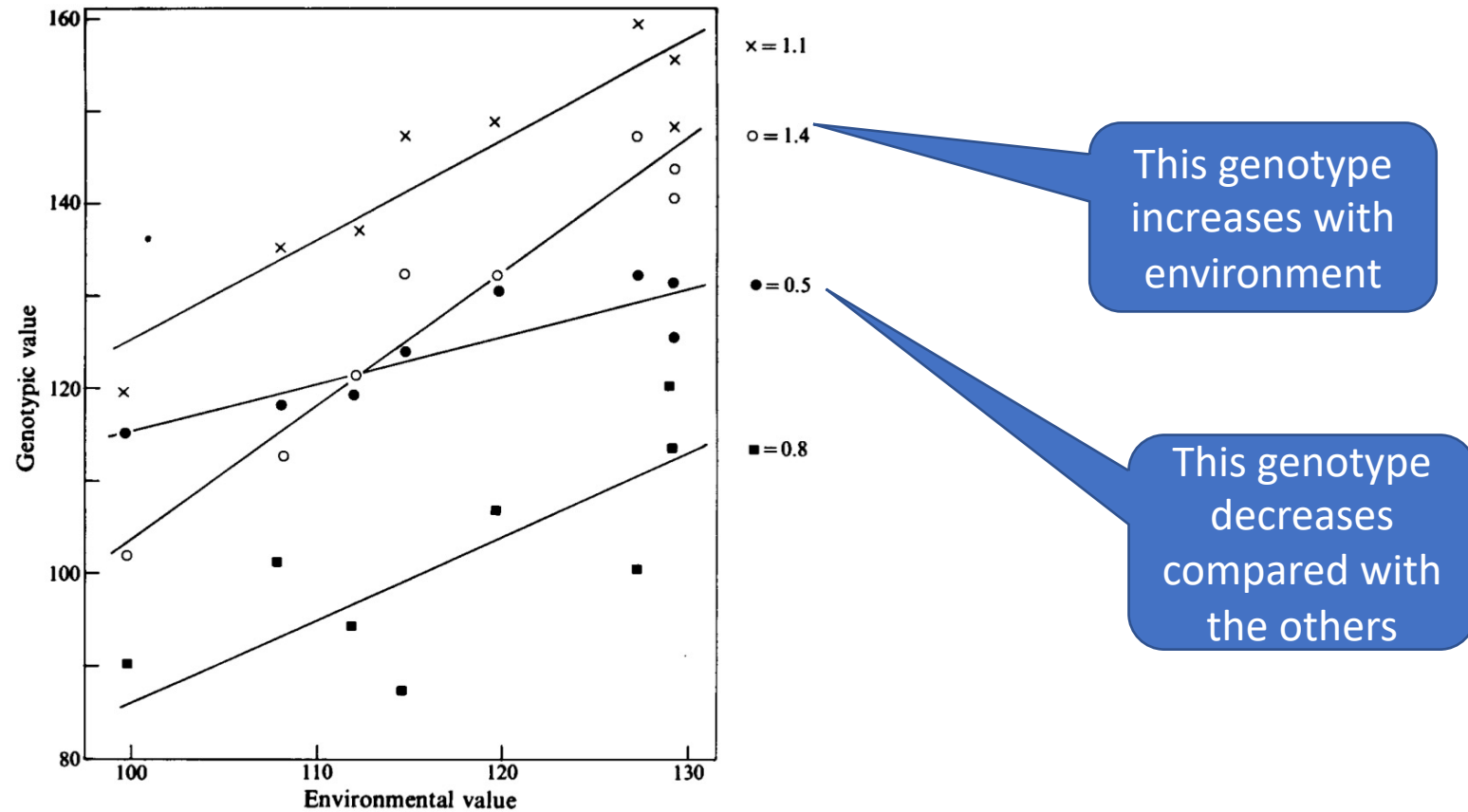
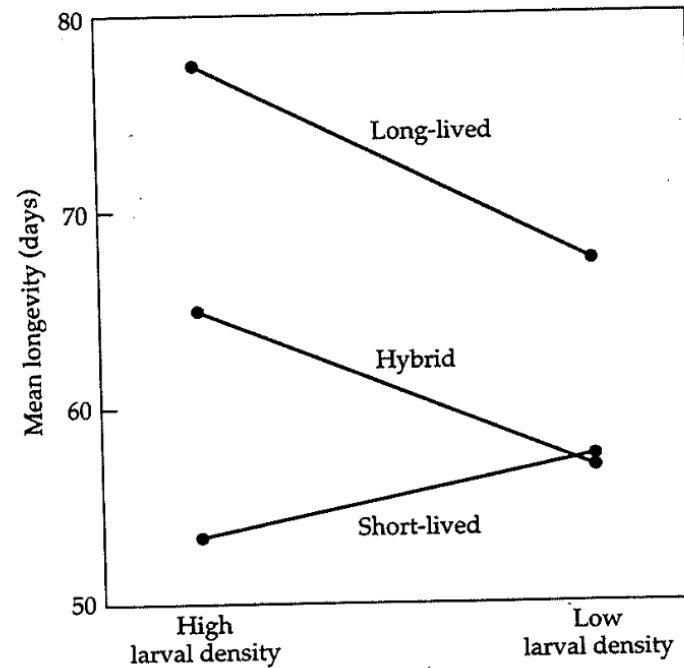


Fig. 8.2. Plant height (cm) of *Nicotiana rustica* genotypes grown in eight specific environments as explained in Example 8.3. (These are genotypes numbered 3, 6, 7, 10 in Tables 42 and 44 of Mather and Jinks, 1982.)

Falconer & MacKay, 4<sup>th</sup> edition



not for population means. (from via 1904.)



Two lines decrease and the other increases?

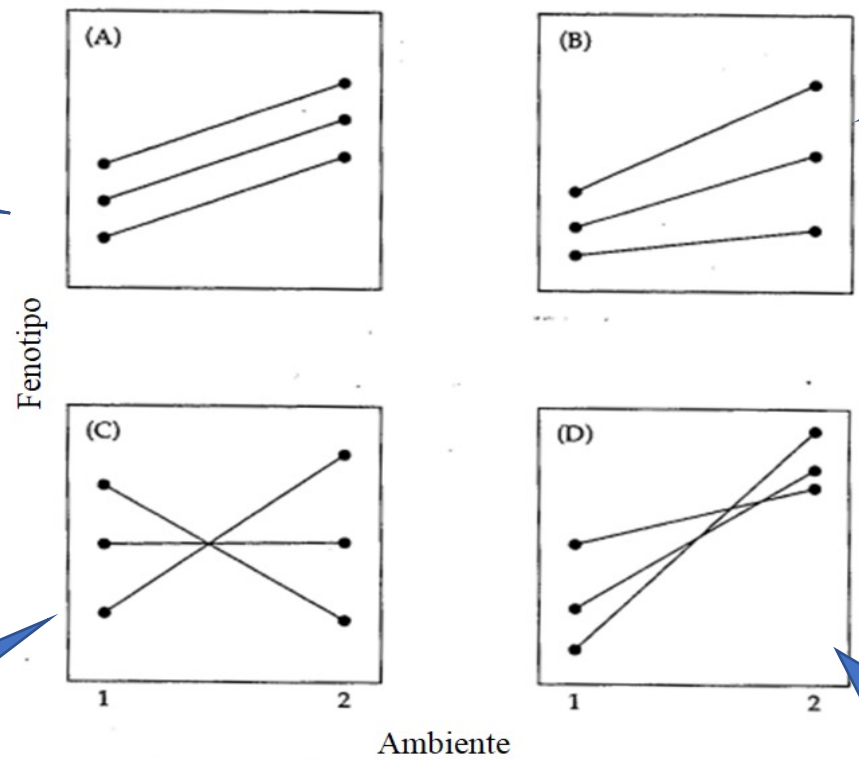
**Figure 6.7** The response of adult longevity to density treatment for lines of *Drosophila melanogaster* selected for short and long life spans and for their F<sub>1</sub> hybrids. Genotype × environment interaction is indicated by the nonparallel response of the short-lived line. (From Clare and Luckinbill 1985.)

Lynch and Walsh, 1998



The function that relates the average phenotypic response of a genotype to a change in the environment is called the **reaction norm**.

No GxE: change in environment changes all phenotypes equally

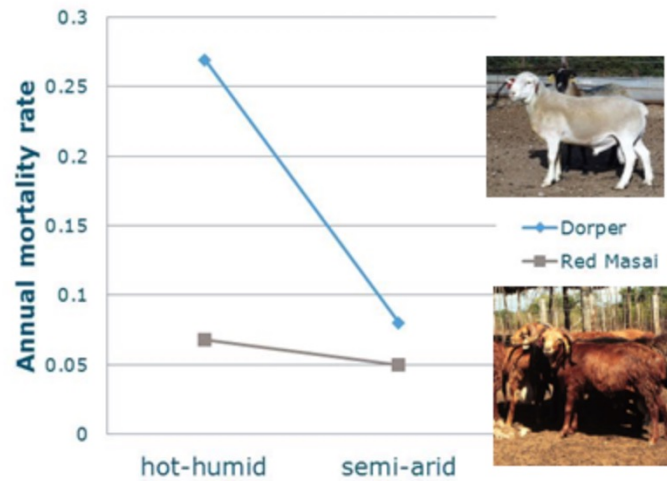


GxE  
change in scale but not in direction

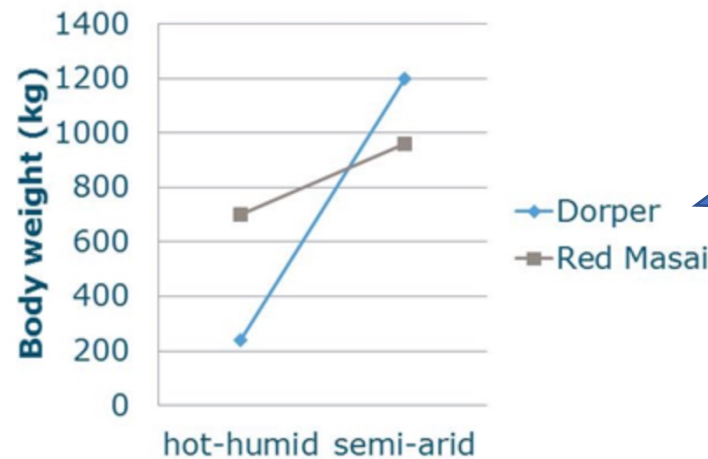
GxE  
Change of ranking

GxE  
shift, change of scale and of ranking

Lynch y Walsh (1998)



Dorper is always worse than Red Masai

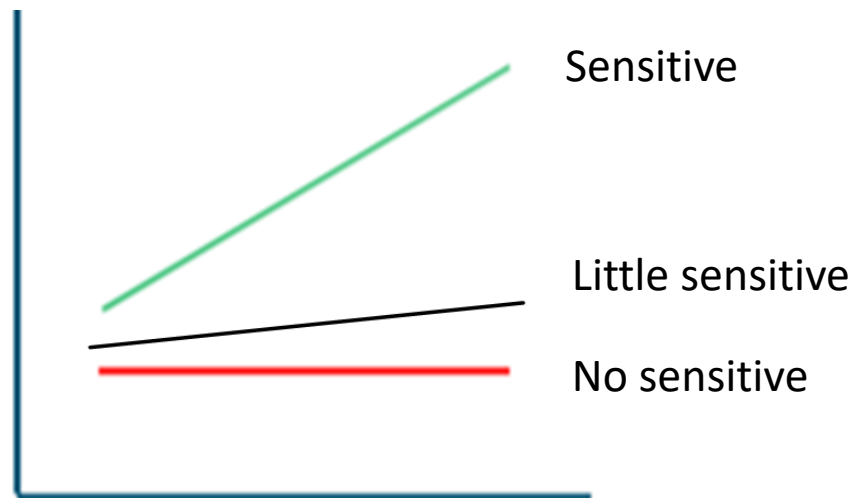


There's strong reranking

Textbook Animal Breeding and Genetics  
<https://wiki.groenkennisnet.nl/space/TAB/3735554/Textbook+Animal+Breeding+and+Genetics>

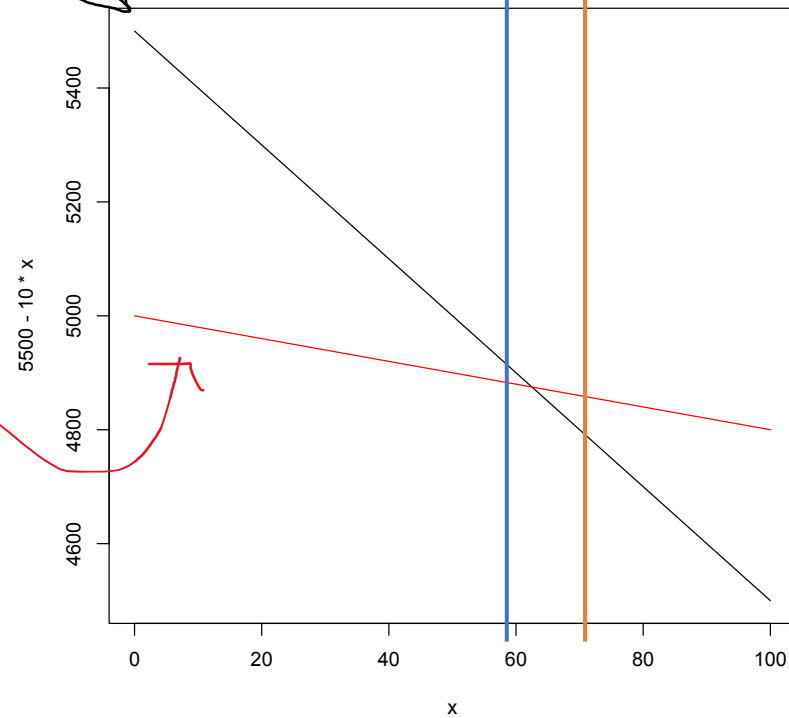
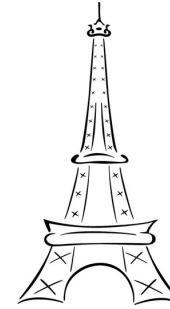


- Genotypes with a very steep slope (positive or negative) are sensitive to changes in environmental conditions.
- Those with slopes close to zero are very insensitive (or not sensitive at all if the slope is zero).



# Example

- Imagine that milk yield of sheep 1 and 2 is:
  - $y_1 = 5500 - 10THI$
  - $y_2 = 5000 - 2THI$





# Example

- Imagine that milk yield of sheep 1 and 2 is:
  - $y_1 = 5500 - 10THI$
  - $y_2 = 5000 - 2THI$
- You have a farm in Paris and another one in Cordoba – which one do you put at each farm?
  - Paris: that day 14C, 72% humidity: THI 58
    - $y_1 = 5500 - 10THI = 5500 - 10 * 58 = 4920$
    - $y_2 = 5000 - 2THI = 5000 - 2 * 58 = 4884$
  - Cordoba: that day 30C, 90% humidity: THI 71
    - $y_1 = 5500 - 10THI = 5500 - 10 * 71 = 4790$
    - $y_2 = 5000 - 2THI = 5000 - 2 * 71 = 4858$



# The same holds at the genetic level

- The BV depends on the environment “ $t$ ”
- $u_{total} = u_{baseline} + u_{slope}t = u_0 + u_1t$
- There is a baseline BV and a “slope” BV that scales the environment
- As a result, BV for the same animals will differ for different  $t$ ...
- The amount of “reranking” moving from one “ $t$ ” to another “ $t$ ” will depend on the magnitude (variances) of  $u_{baseline}$ ,  $u_{norm}$  and their correlation  $r_{g(b,s)}$

$$\bullet \text{Var} \begin{pmatrix} u_0 \\ u_1 \end{pmatrix} = \mathbf{G}_0 = \begin{pmatrix} \sigma_{u(0)}^2 & r_{g(0,1)}\sigma_{u(0)}\sigma_{u(1)} \\ r_{g(0,1)}\sigma_{u(0)}\sigma_{u(1)} & \sigma_{u(1)}^2 \end{pmatrix}$$

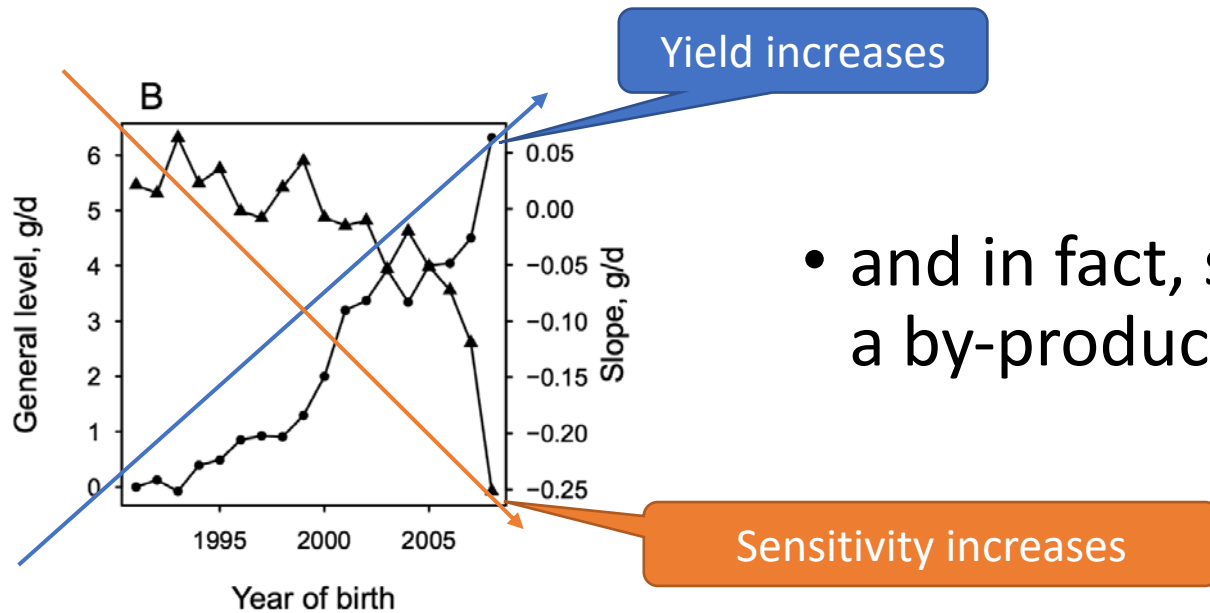
- Also the correlation indicates the trade-off between “baseline” ability and “answer to the environment” ability
- An animal makes a choice between spending reserves for production (growth, milk yield) or keeping them “just in case”
- We expect animals that have high baseline to be sensitive to stress in the environment
- This is shown by a negative correlation  $r_{g(0,1)}$

**Table 2.** Review of estimated genetic correlations between intercept (general level of production) and slope of decay after the heat tolerance threshold from Broken Line reaction norms in different studies

Breed	Milk yield			Protein yield			Fat yield		
	Parity 1	Parity 2	Parity 3	Parity 1	Parity 2	Parity 3	Parity 1	Parity 2	Parity 3
US Holstein <sup>1</sup>	-0.46	-0.38	-0.47	-0.43	-0.36	-0.48	-0.39	-0.29	-0.30
Italian Holstein <sup>2</sup>	-0.51	-0.33	-0.36	-0.49	-0.53	-0.48	-0.31	-0.52	-0.56
Spanish Holstein <sup>3</sup>	-0.34	–	–	-0.31	–	–	-0.31	–	–
Manchega sheep <sup>4</sup>		-0.45			-0.77			-0.77	
Valle de Belice sheep <sup>5</sup>		-0.81				-0.83			
Payoya goats <sup>6</sup>		-0.36				-0.37			

Carabaño et al., 2017





- and in fact, selection for high yielding animals, as a by-product, may select more sensitive animals

**Figure 2.** Genetic trends for the level of production (line with circles) and slope of decay under HT (line with triangles) for milk yield in Holstein cattle (Panel A), fat plus protein yield in Manchega sheep (Panel B) and fat

Carabaño et al., 2017

# Genetic evaluation using Norm Reaction model

- Assume 1 trait (e.g. growth) and 1 environmental covariate  $t$
- We have one phenotype but two breeding values per animals
  - the intercept:  $u_0$  and the regressor:  $u_1$
- For a single individual:
  - $y_i = X_i\beta + bt + u_{0(i)} + u_{1(i)}t + e_i$

fixed  
regression on  
the covariate

regression on  
the covariate

We will see how to fit this  
model during the exercise

- $Var \begin{pmatrix} \mathbf{u}_0 \\ \mathbf{u}_1 \end{pmatrix} = \mathbf{H} \otimes \mathbf{G}_0, Var(\mathbf{e}) = \mathbf{I}\sigma_e^2$

# Genetic evaluation using Norm Reaction model

regression on  
the covariate

- This the “norm reaction”:
  - $y_i = X_i\beta + bt + u_{0(i)} + u_{1(i)}t + e_i$
- In the Animal Breeding literature, models where we put a regression on a covariate and we assume the regressor ( $u_{1(i)}$  in this case) to be heritable and different for each animal, with a normal distribution ( $Var \begin{pmatrix} \mathbf{u}_0 \\ \mathbf{u}_1 \end{pmatrix} = \mathbf{H} \otimes \mathbf{G}_0$ ) are called “random regression models” (i.e. the regression coefficients are random effects)
- Two free set of notes in the topic:
- RANDOM REGRESSION IN ANIMAL BREEDING Course Notes Julius van der Werf: <https://jvanderw.une.edu.au/CFcoursenotes.pdf>
- Animal Models L. R. Schaeffer : <https://animalbiosciences.uoguelph.ca/~lrs/BOOKS/AMTAP.pdf>



# Genetic evaluation using Norm Reaction model

- Digression on notation
- people fitting RR models can be very complicated e.g.
  - $y_i = X_i\beta + bt + u_{0(i)} + u_{1(i)}t + u_{2(i)}t^2 + p_{0(i)} + p_{1(i)}t + p_{2(i)}t^2 + e_i$
  - 0 : regression on  $t^0$  (intercept)
  - 1: regression on  $t^1$  (linear)
  - 2: regression on  $t^2$  (quadratic)
  - there are also regressions on things like  $\exp(t)$ ,  $t^{3/2}$  ...
  - $p_0$  etc: regressors that depend on the permanent environment
  - also they like using “Legendre polynomials” which are basically centered and scaled  $t$
  - they may fit different  $Var(e)$  depending on levels of  $t$ ...
- it all sounds very mystical but after seeing a few examples it’s simpler than it looks (although preparing the data set & parameter file can be quite painful)



# How do we use results from this model

- First, to understand what's going on
- If selection for trait (say yield) is based mostly on the intercept [because most animals had  $t=0$ ], it will generate a correlated selection response on the “trait” “slope to environmental covariate”:
  - $\Delta G_{intercept} = \Delta G_0$  (say liters)
  - $\Delta G_{slope} = \Delta G_1 = \Delta G_0 r_{g(0,1)} \frac{\sigma_{g(0)}}{\sigma_{g(1)}}$  (say liters/Celsius degree)
- If we change to a more unfavorable environment (climate change, introduction to another country) the actual phenotypic gain will be less than expected





# How do we use results from this model

- For instance (the numbers are invented)
  - assume that we increase milk yield by  $\Delta G = 100$  liters in 20 years
  - correlated response in “slopes” is
- $\Delta G_{slope} = \Delta G r_{g(0,1)} \frac{\sigma_{g(0)}}{\sigma_{g(1)}} = 100 * (-0.5) \frac{2}{20} = -2$
- now we move to a country with +10 C
- $\Delta$  in yield:  $\Delta G_0 + \Delta G_1 * 10 = 100 + (-2) * 10 = 80$
- we have lost 4 years of genetic improvement ☹️ and our animals are more sensitive

# How do we use results from this model

- Another point of view is to think in genetic correlation across environments
- For instance we improve in a “good” environment (G) with no bacteria or virus ( $t=0$ ) and we move those animals to a “bad” environment (B) ( $t=1$ )
- This could be state or company farms vs. commercial farms
- The genetic progress in “B” is  $\Delta G_B = \Delta G_G r_g \frac{\sigma_G}{\sigma_B}$
- low  $r_g$  : low genetic progress



# How do we use results from this model

- For this simple case, remember

BV is function of t

$$u = u_0 + u_1 t;$$

BV in "good": t=0

$$u_G = u_0 + u_1 * 0;$$

BV in "bad": t=1

$$u_B = u_0 + u_1 * 1$$

$$r_{g(G,B)} = \frac{Cov(u_G, u_B)}{\sqrt{Var(u_G)Var(u_B)}} = \frac{\sigma_{u(0)}^2 + r_g \sigma_{u(0)} \sigma_{u(1)}}{\sqrt{\sigma_{u(0)}^2 (\sigma_{u(0)}^2 + 2r_g \sigma_{u(0)} \sigma_{u(1)} + \sigma_{u(1)}^2)}}$$

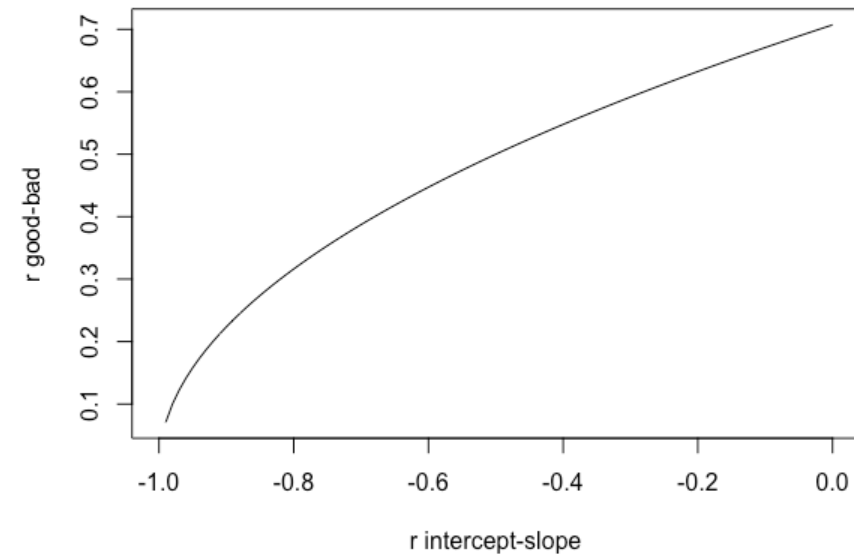
variance of the intercept

correlation of both

variance of the slope

# How do we use results from this model

- For a silly simulated example ( $\sigma_{u(0)}^2 = \sigma_{u(1)}^2 = 300$ )
- the negative correlation of “intercept” with “sensitivity” to stress leads to inefficient selection



# How do we use results from this model

- it would be more efficient either
  - to select on “bad” environment
  - or to select for resilience
- can we directly select for resilience using these models?
- Yes if:
  - we can measure stress
  - there’s no much loss on general ability (intercept) as to loose money!
- How can we do that



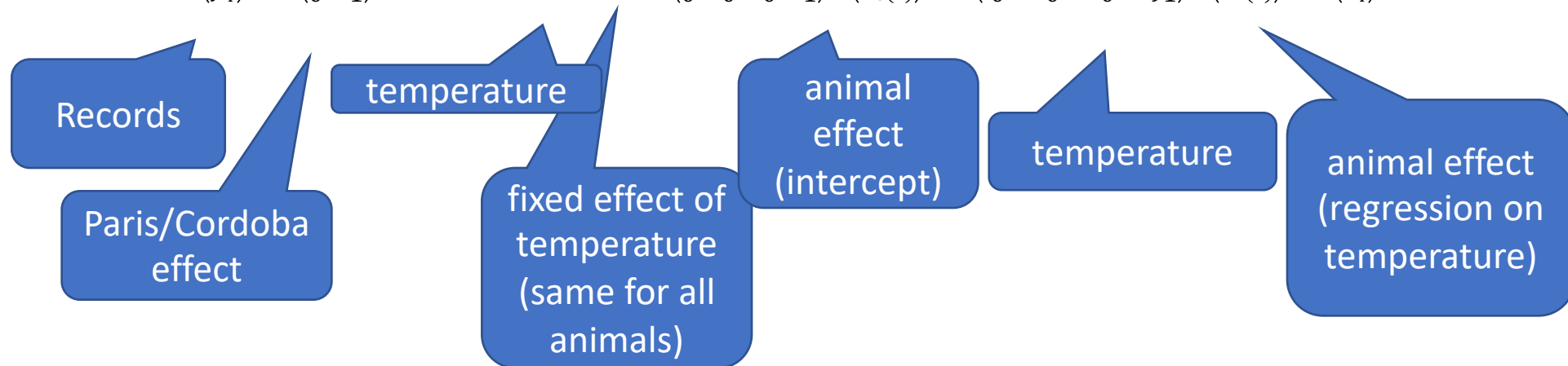
# Example

- Numbers here are completely invented !!
- We have two pairs mother-offspring in Paris (3 records) and in Cordoba (1 record)

$$y = Xb + Zu + e$$

- Assume that we fit a “fixed” effect for Paris and another for Cordoba. Matrices  $Z$  now include a value of 1 for the animal intercept  $u_0$  and a covariate for the temperature

$$\begin{pmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \end{pmatrix} = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \end{pmatrix} \begin{pmatrix} b_{Paris} \\ b_{Cordoba} \end{pmatrix} + \begin{pmatrix} 58 \\ 60 \\ 71 \\ 91 \end{pmatrix} b_t + \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} u_{0(1)} \\ u_{0(2)} \\ u_{0(3)} \\ u_{0(4)} \end{pmatrix} + \begin{pmatrix} 58 & 0 & 0 & 0 \\ 0 & 60 & 0 & 0 \\ 0 & 0 & 71 & 0 \\ 0 & 0 & 0 & 91 \end{pmatrix} \begin{pmatrix} u_{1(1)} \\ u_{1(2)} \\ u_{1(3)} \\ u_{1(4)} \end{pmatrix} + \begin{pmatrix} e_1 \\ e_2 \\ e_3 \\ e_4 \end{pmatrix}$$



# Example

- We want to estimate 11 effects out of 4 records, but we have relationships and genetic variances and covariances:

$$\text{Var} \begin{pmatrix} \mathbf{u}_0 \\ \mathbf{u}_1 \end{pmatrix} = \mathbf{A} \otimes \mathbf{G}_0 = \begin{pmatrix} 1 & 0 & 0.5 & 0 \\ 0 & 1 & 0 & 0.5 \\ 0.5 & 0 & 1 & 0 \\ 0 & 0.5 & 0 & 1 \end{pmatrix} \otimes \begin{pmatrix} 30 & -1 \\ -1 & 3 \end{pmatrix}$$

relationships

trait  
covariances

- animals 1,3: family A; animals 2, 4: family B
- $\text{Var}(e) = 2$
- $\mathbf{y} = [3000; 2500; 1500; 2000]$

# Example

- Final MME are:

1.5	0.0	94.5	0.5	0.5	0.5	0.0	29.0	30.0	35.5	0.0
0.0	0.5	45.5	0.0	0.0	0.0	0.5	0.0	0.0	0.0	45.5
94.5	45.5	10143.0	29.0	30.0	35.5	45.5	1682.0	1800.0	2520.5	4140.5
0.5	0.0	29.0	0.544944	0.0	-0.0224719	0.0	29.015	0.0	-0.00749064	0.0
0.5	0.0	30.0	0.0	0.544944	0.0	-0.0224719	0.0	30.015	0.0	-0.00749064
0.5	0.0	35.5	-0.0224719	0.0	0.544944	0.0	-0.00749064	0.0	35.515	0.0
0.0	0.5	45.5	0.0	-0.0224719	0.0	0.544944	0.0	-0.00749064	0.0	45.515
29.0	0.0	1682.0	29.015	0.0	-0.00749064	0.0	1682.45	0.0	-0.224719	0.0
30.0	0.0	1800.0	0.0	30.015	0.0	-0.00749064	0.0	1800.45	0.0	-0.224719
35.5	0.0	2520.5	-0.00749064	0.0	35.515	0.0	-0.224719	0.0	2520.95	0.0
0.0	45.5	4140.5	0.0	-0.00749064	0.0	45.515	0.0	-0.224719	0.0	4140.95

$$\begin{pmatrix} \hat{b}_{Paris} \\ \hat{b}_{Cordoba} \\ \hat{b}_t \\ \hat{u}_0(1) \\ \hat{u}_0(2) \\ \hat{u}_0(3) \\ \hat{u}_0(4) \\ \hat{u}_1(1) \\ \hat{u}_1(2) \\ \hat{u}_1(3) \\ \hat{u}_1(4) \end{pmatrix} = \begin{matrix} 3500.0 \\ 1000.0 \\ 306250.0 \\ 1500.0 \\ 1250.0 \\ 750.0 \\ 1000.0 \\ 87000.0 \\ 75000.0 \\ 53250.0 \\ 91000.0 \end{matrix}$$



# Example

- with solutions:

9448.42   12428.2   -113.38   -0.36   0.41   -0.25   0.2   2.21   -2.43   1.44   -1.22

The two first solutions are “Paris” and “Cordoba” means, had the temperature be 0;

the 3<sup>rd</sup> solution is the effect of temperature in yield, for all animals

the 4 to 7 solutions are the breeding values of the animals, at 0 temperature

the 8 to 11 are the breeding values of “regression on temperature”



# Example

- with solutions:

9448.42   12428.2   -113.38   -0.36   0.41   -0.25   0.2   2.21   -2.43   1.44   -1.22

the 4 to 7 solutions are the breeding values of the animals, at 0 temperature

the 8 to 11 are the breeding values of "regression on temperature"

- What two animals would you choose for selection for climate change?
- How much are they going to yield?



# Output of Norm Reaction models

- we have a collection of breeding values for intercept (overall yield level) and slope (e.g. times stress  $t$ ) e.g.  $\widehat{u}_0$  ,  $\widehat{u}_1$
- assign weights  $\mathbf{c}$  to  $\widehat{u}_0$  ,  $\widehat{u}_1$  to create an Index  $I = c_0\widehat{u}_0 + c_1\widehat{u}_1$
- select animals according to  $I$
- which weights to assign? this is a good question 😊
- if you select in “good” conditions for performance in “bad” conditions, then assign weights to perform optimally in “bad” conditions
- in mixed cases, I don’t have a clear answer