Critical periods, intergenerational signaling and human health

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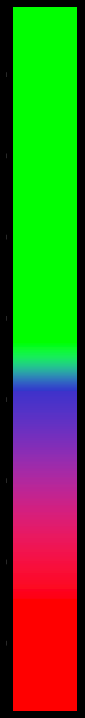
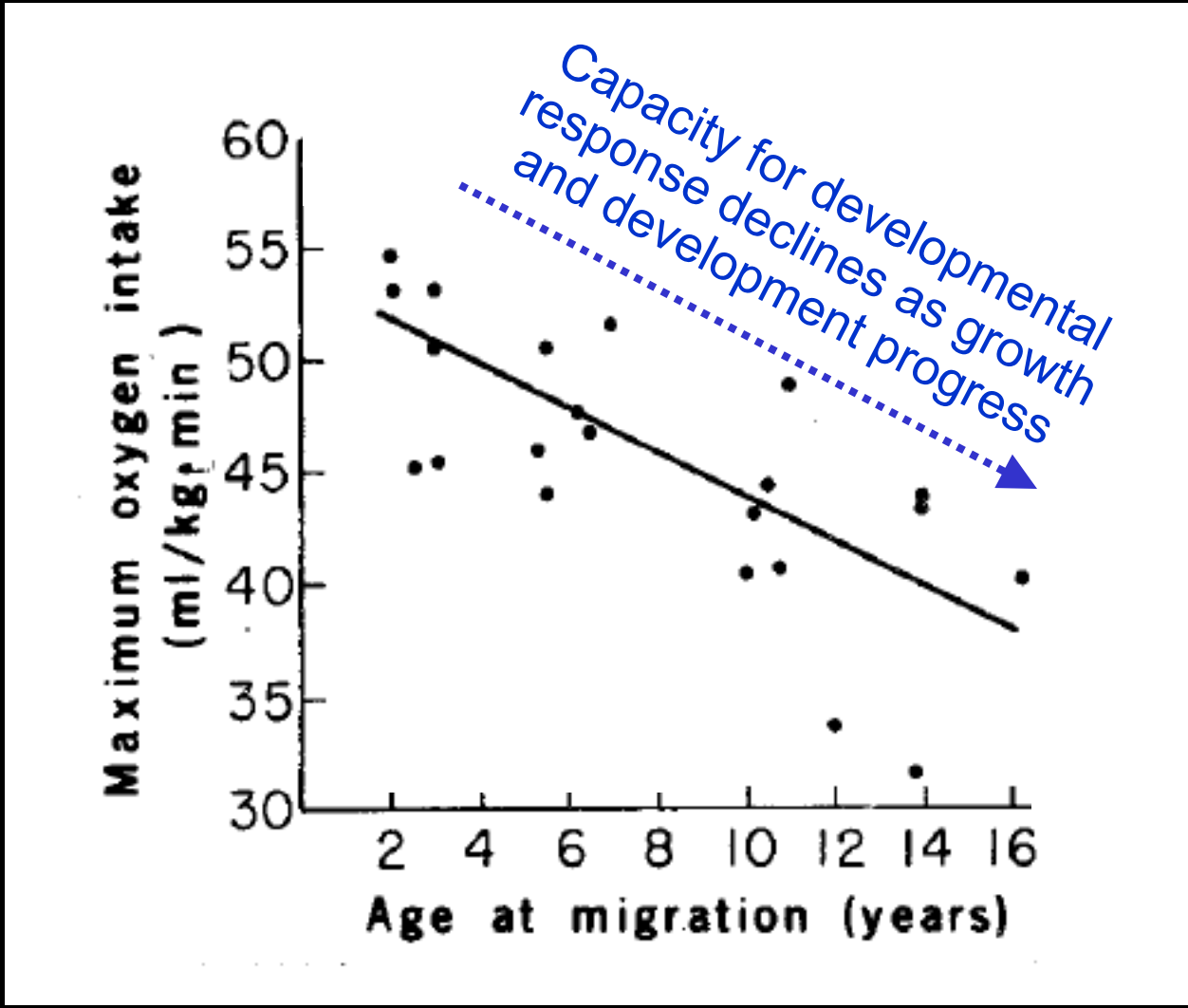
Modes of human adaptability

Cycle duration		Adaptation	
Years		Mode	Process
0.00000001	seconds		
0.0001	hours		
0.001	days	Physiologic	Homeostasis
0.1	months		
1	years		
10	decades	Developmental	Plasticity
100	centuries		
1000	millenia		
1000000	millions	Genetic	Natural selection



Kuzawa (2005), Amer J Hum Biol 17(1) 4-21.

Plasticity example:
Low oxygen at high altitude influences lung growth



Frisancho (1977), Int'l J Biometeor 21(2):135

Fetal and infancy nutrition predict many adaptively important traits:

- Energy partitioning and fat patterning
- Growth rate and caloric requirements
- Stature and lean mass
- Adult reproduction
- Metabolism
- Appetite

etc.

Developmental plasticity

Why commit to strategy <u>for life</u> so early in the life cycle?

Environment & experience

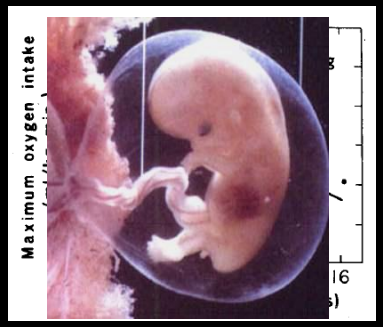
Brief critical period

Birth

Developmental response

Form comes to match function

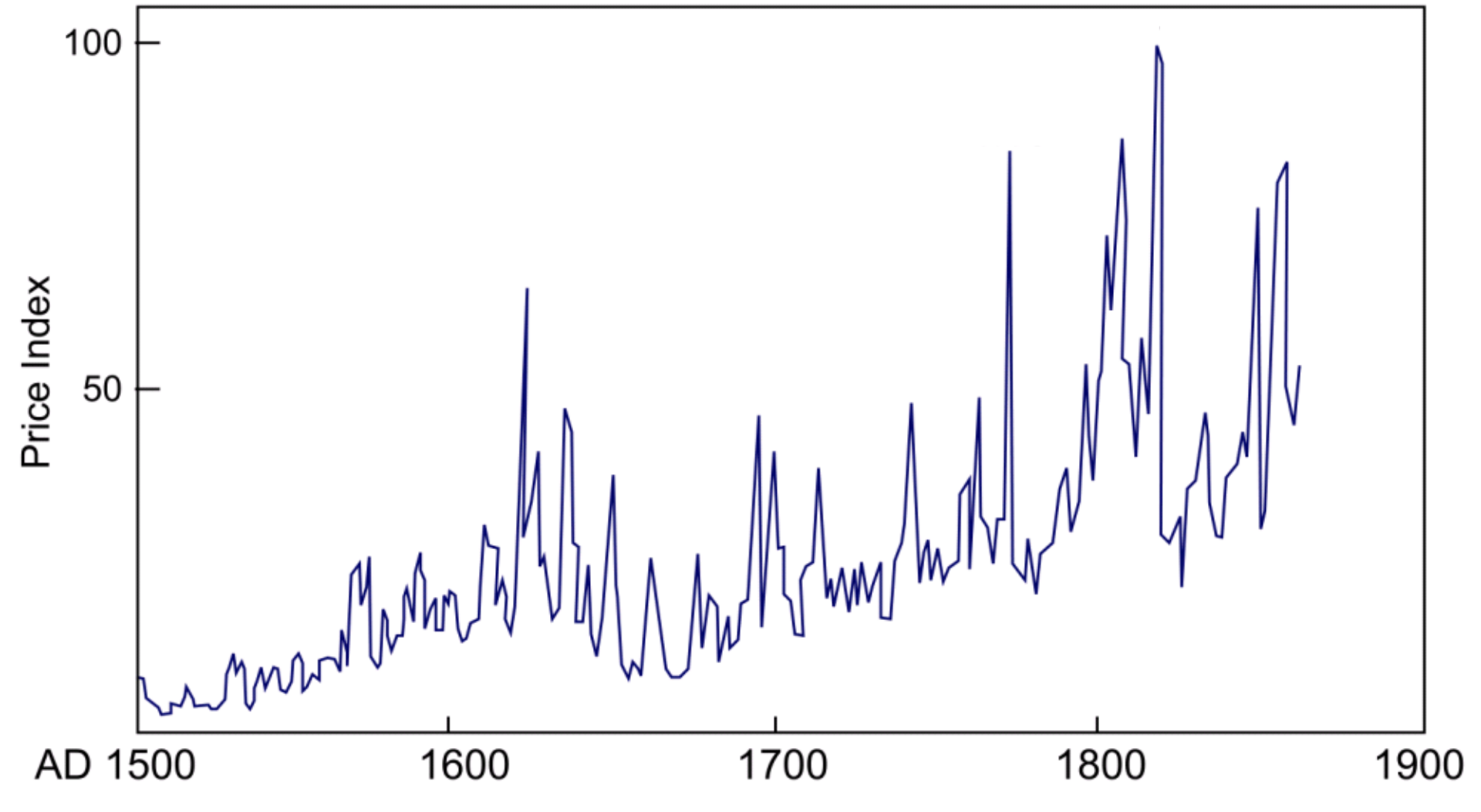
adaptive?



e.g. Gluckman & Hanson, Bateson, Kuzawa

Price of Rye in Germany

(Lamb 1995)



Evidence that fetal nutrition “ignores” transient ups and downs

What does fetal nutrition “track”?

Maternal influences

- Diet during pregnancy ← *Weak effect: e.g. pregnancy supplementations have low efficacy: 10,000 kcal → 28 g*
- Pregnancy weight gain
- Peri-conceptional nutrition
- Pre-pregnancy weight

} *Stronger predictors*

e.g. 1958 British Birth Cohort

Institute of Medicine (1990)

Today's talk

- Cebu study: fetal nutrition as an integrated cue of matrilineal nutritional experience.
- Hypothesis: intergenerational phenotypic inertia as a mode of adaptation.
- Summary: wrap-up and public health implications.

Study Setting:
Cebu City, Philippines

The Cebu Study

The Cebu Longitudinal Health & Nutrition Survey

Key collaborators:

U of N Carolina (Chapel Hill)

- Linda Adair

Office of Pop. Studies (USC - Cebu)

- Alan Feranil, Connie Gultiano, Judith Borja, Litlit Duazo and others

Northwestern University

- Thom McDade, Elizabeth Quinn

Cebu City, Philippines

Current research at Cebu

Developmental origins of inflammatory regulation, metabolic syndrome and CVD risk (NHLBI, NICHD, NIA)

The New York Times

In Study, Fatherhood Leads to Drop in Testosterone

By PAM BELLUCK
Published: September 12, 2011

This is probably not the news most fathers want to hear.

Enlarge This Image

Fe Lagardo

A father with his daughter in a rural area near Cebu City in the Philippines.

Testosterone, that most male of hormones, takes a dive after a man becomes a parent. And the more he gets involved in caring for his children — changing diapers, jiggling the kid on his knee, reading "Goodnight Moon" for the umpteenth time — the lower his testosterone drops.

So says the first large study measuring testosterone in men when they were single and childless and several years after they had

Multimedia

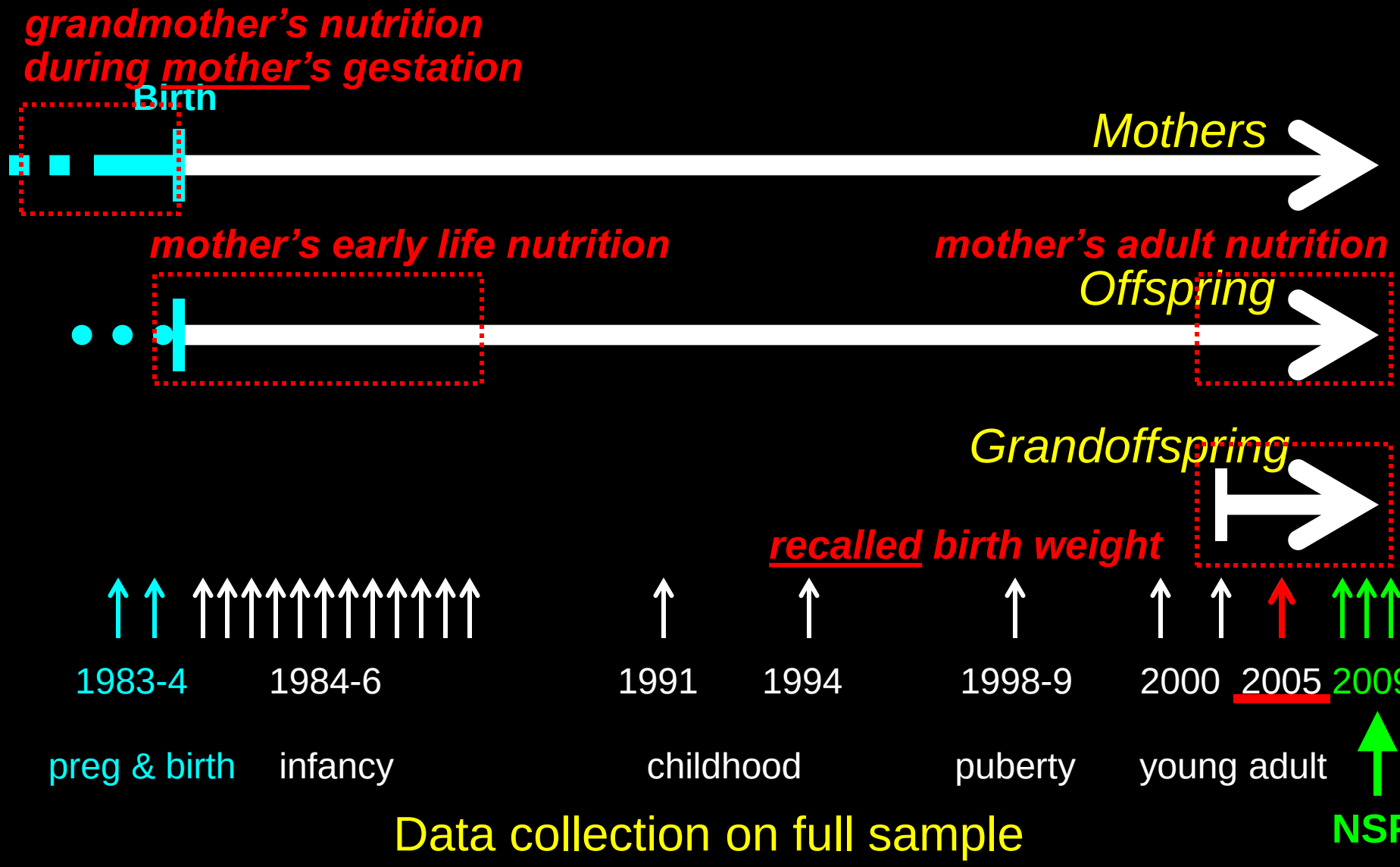
Current research at Cebu

Developmental origins of inflammatory regulation, metabolic syndrome and CVD risk (NHLBI, NICHD, NIA)

Male psychobiology and reproductive ecology (NSF, Wenner Gren)

(used with permission, photo EA Quinn)

The Cebu Study



Data collection on full sample

What does fetal nutrition "track"?

What information is (potentially) conveyed to the fetus?

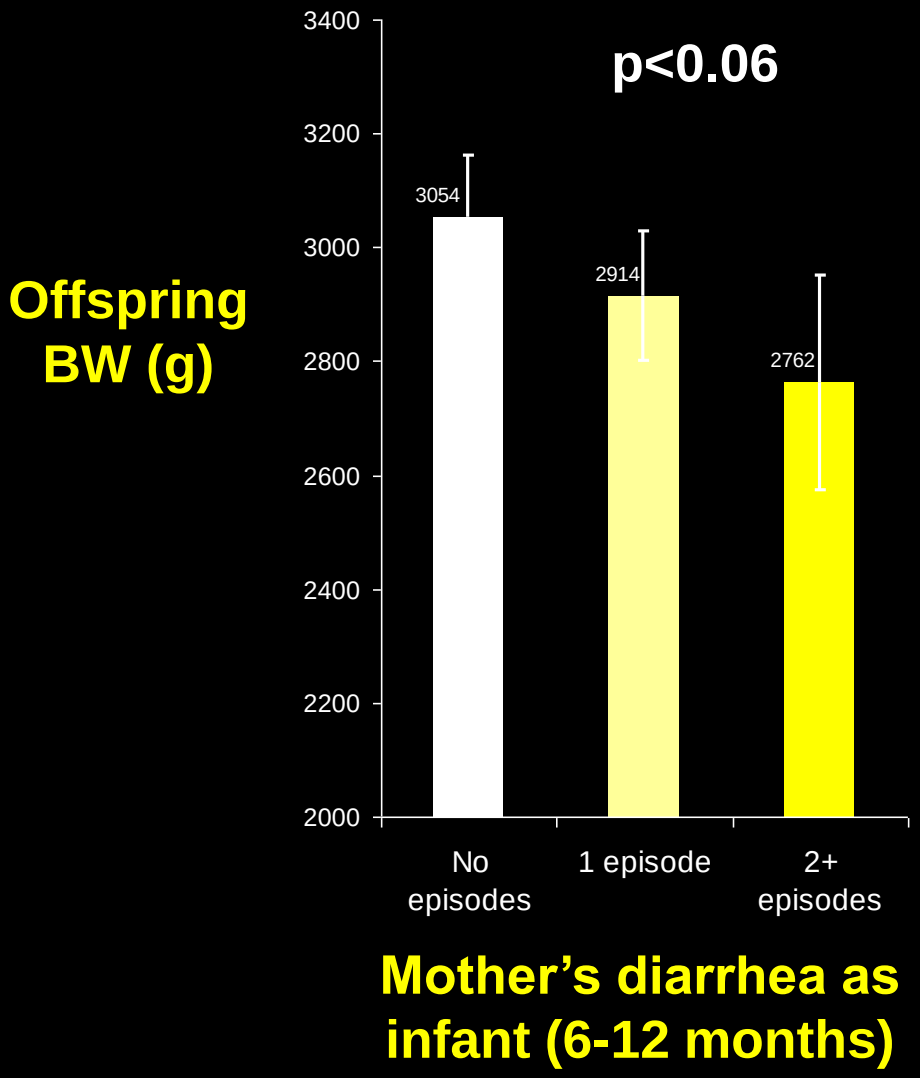
Question 1:

Does the mother's own infancy nutritional experience predict the birth weight of her future offspring?

Focus: post-weaning diarrhea & infancy breastfeeding

Mother's infancy nutrition → offspring BW

Mother's own infancy diarrhea

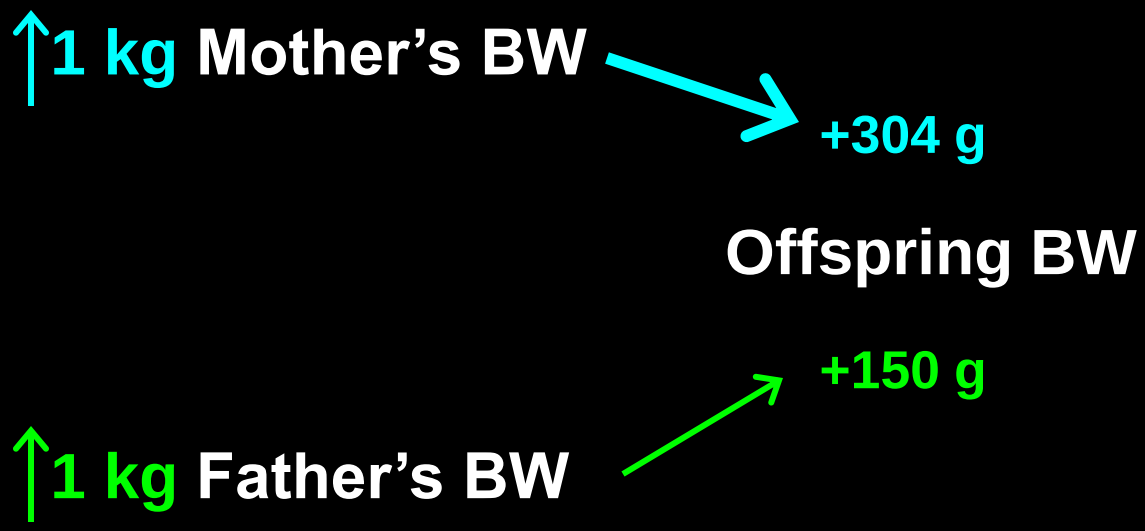


Question 2:

Does the mother's own fetal nutrition predict birth weight of her offspring?

The mother's own fetal growth rate is a proxy of her own fetal nutrition but <u>also</u> of genetic and other influences.

Mother's own birth weight is a stronger predictor of offspring birth weight than is father's own birth weight



Models adjust for: offspring sex, parity, gestational timing, mother's age and stature, antenatal care, work during pregnancy

Kuzawa et al (in prep)

At what ages does energy intake relate to offspring birth weight?

1983 1984 2005

Yes!

Grandmother's kcal in pregnancy

P<0.02

Yes!

Mother's own kcal in infancy

P<0.01

Mother's lifecycle

Predicting offspring BW

Mother's own kcal as adult

No!

Pilot analysis: predicting recalled BW

Final model:

- Sex of offspring
- Gestational duration
- Parity

Model $R^2 = 0.17$

Mother's early life nutrition & growth:

- Mother's fetal growth rate (BW for gestational age)
- Grandmother's kcal intake during pregnancy
- Post-weaning diarrheal morbidity
- Breastfeeding duration and exclusivity
- Nutritional intake in late infancy

→ *Many adult/current factors not significant:*
mother's adult height, macronutrient intake, income, education, urban status

What does fetal nutrition "track"?

What information is (potentially) conveyed to the fetus?

Fetal nutrition tracks mother's nutritional history

Maternal influence	Time depth
• Current diet intake	• Days
• Pregnancy weight gain	• Months
• Peri-conceptional nutrition	• Months
• Pre-pregnancy weight	• Years

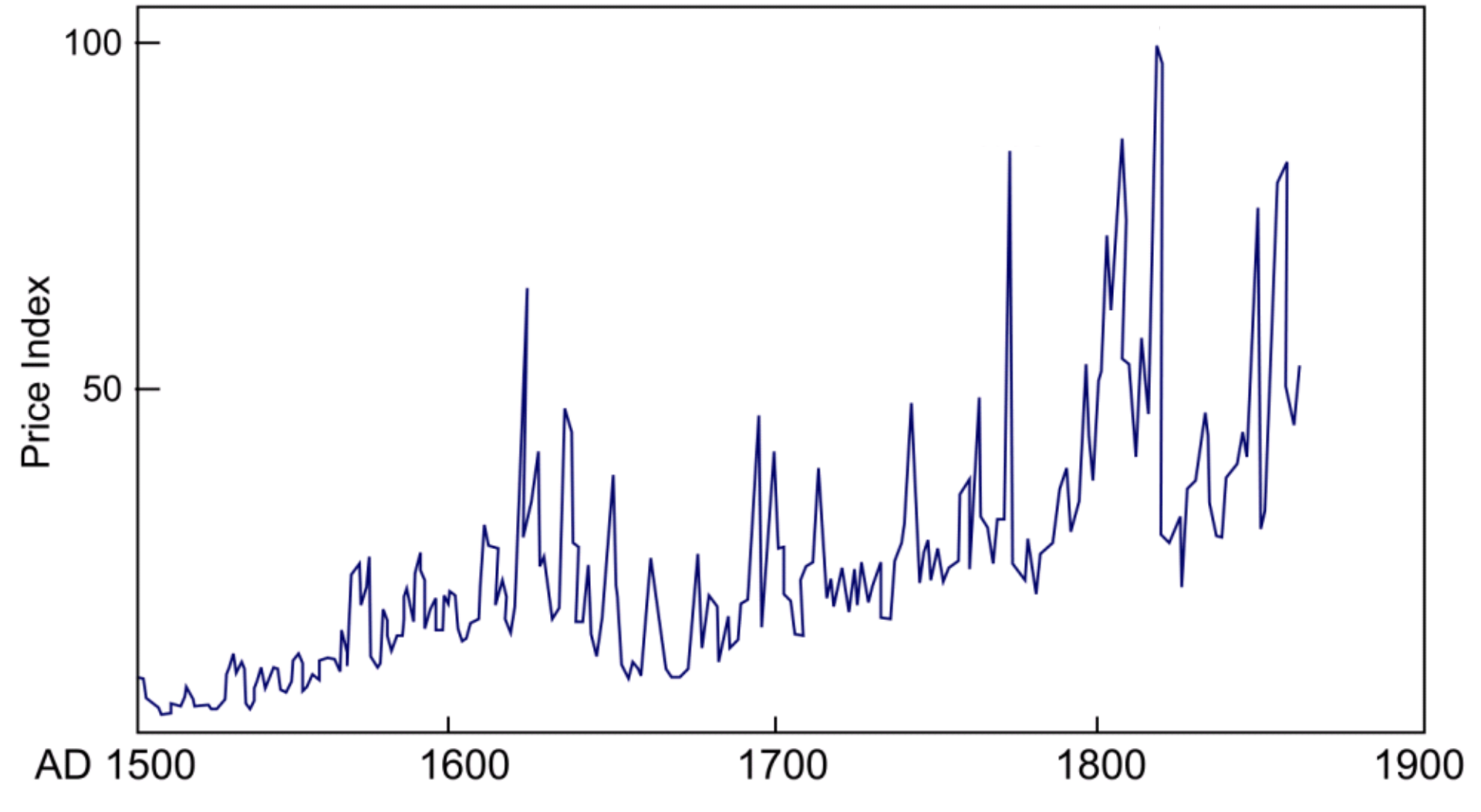
ilineal history

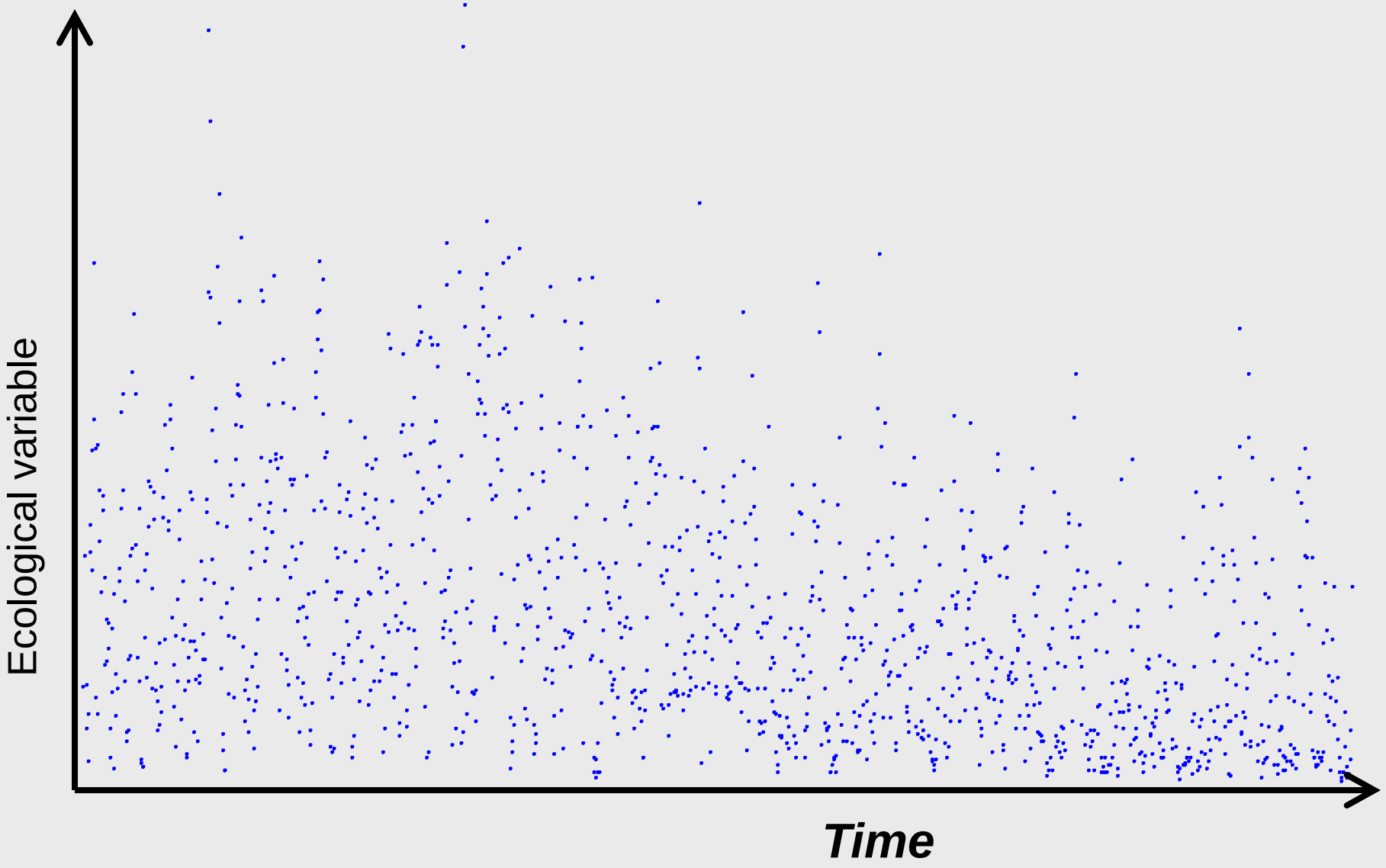
Hypothesis:

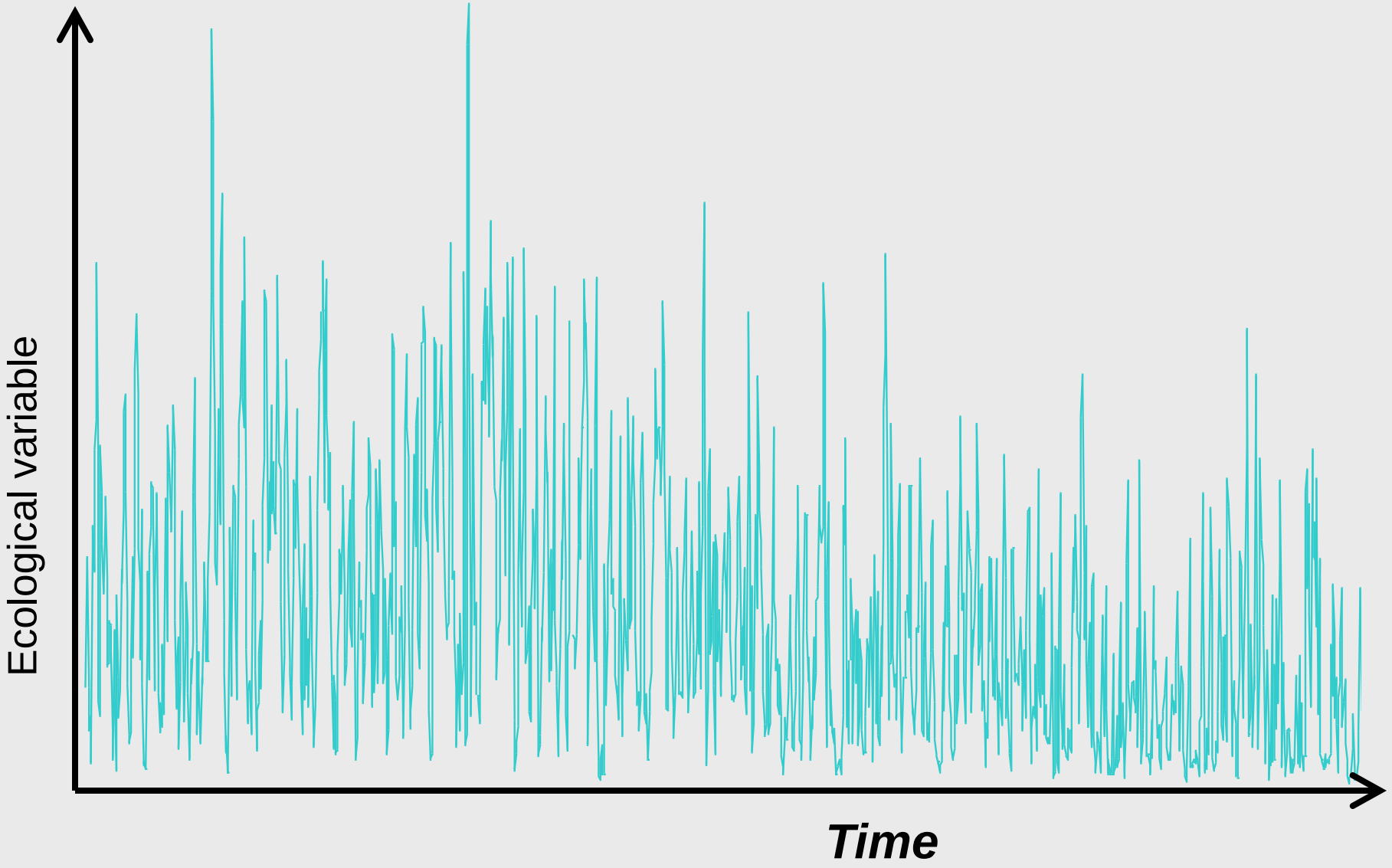
The benefit of setting fetal or infant nutrition to average recent matrilineal nutritional experience relates to the timescale of nutritional trends that are stable enough to warrant tracking rather than buffering.

Price of Rye in Germany

(Lamb 1995)




Ecological variable
Time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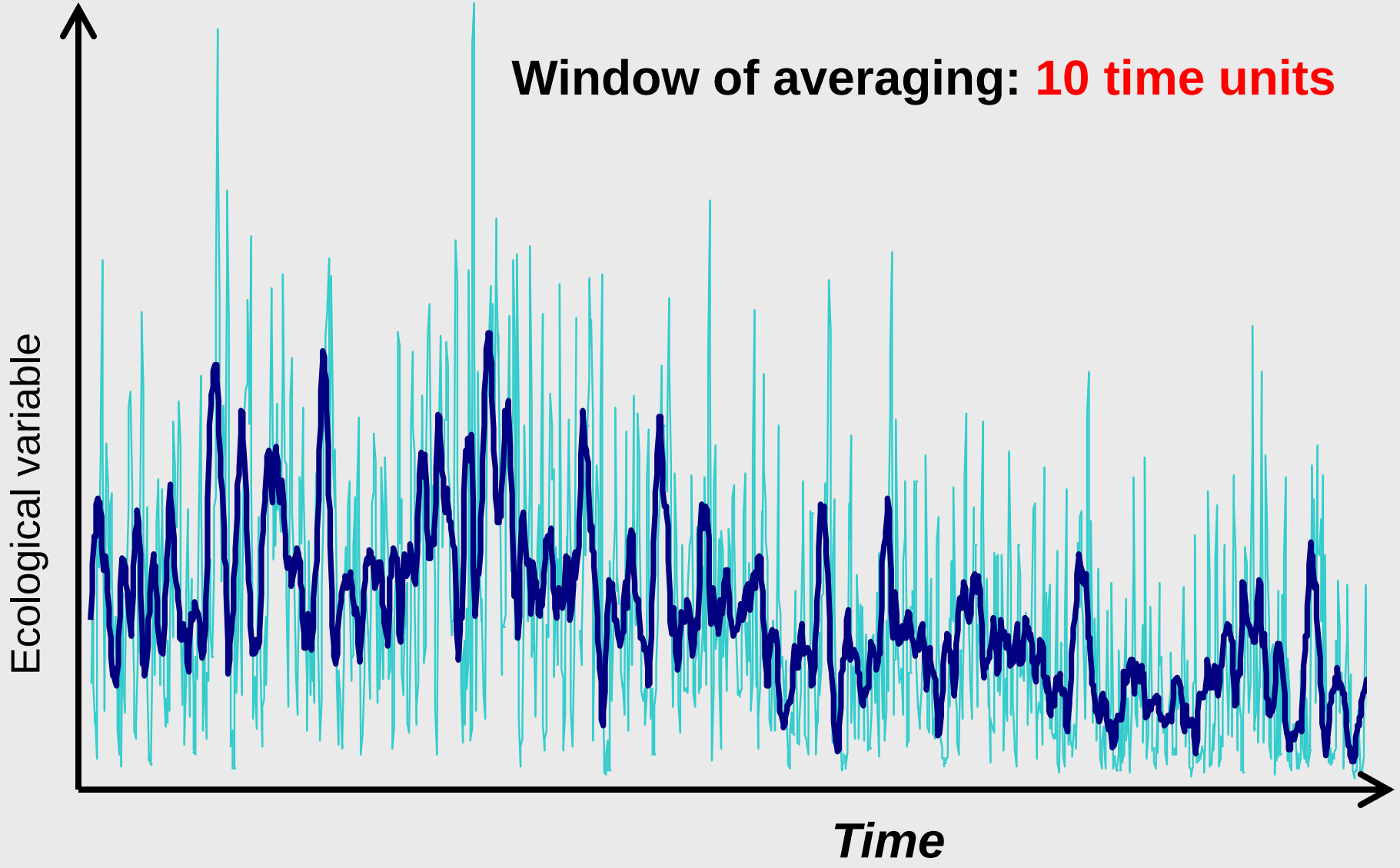
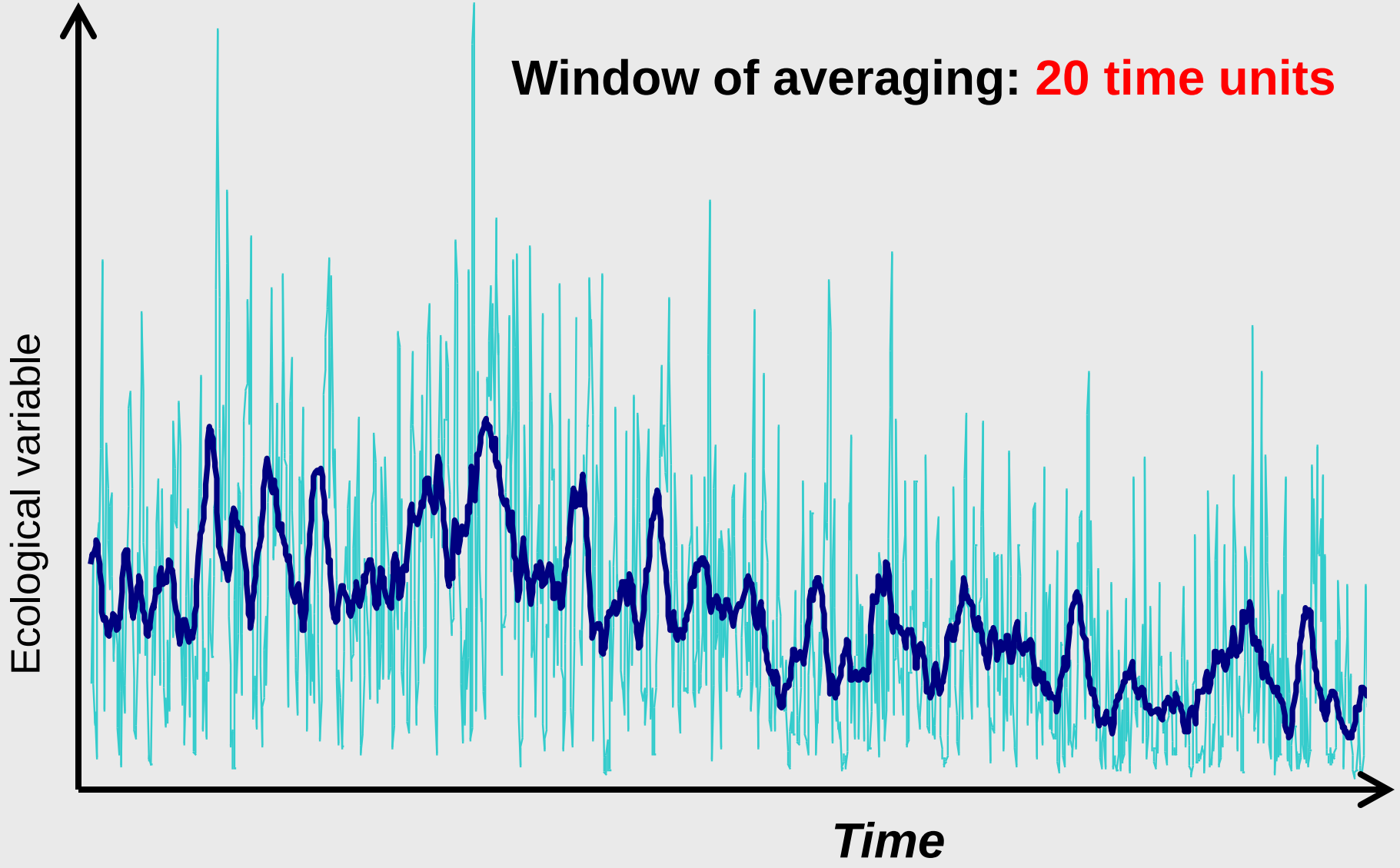
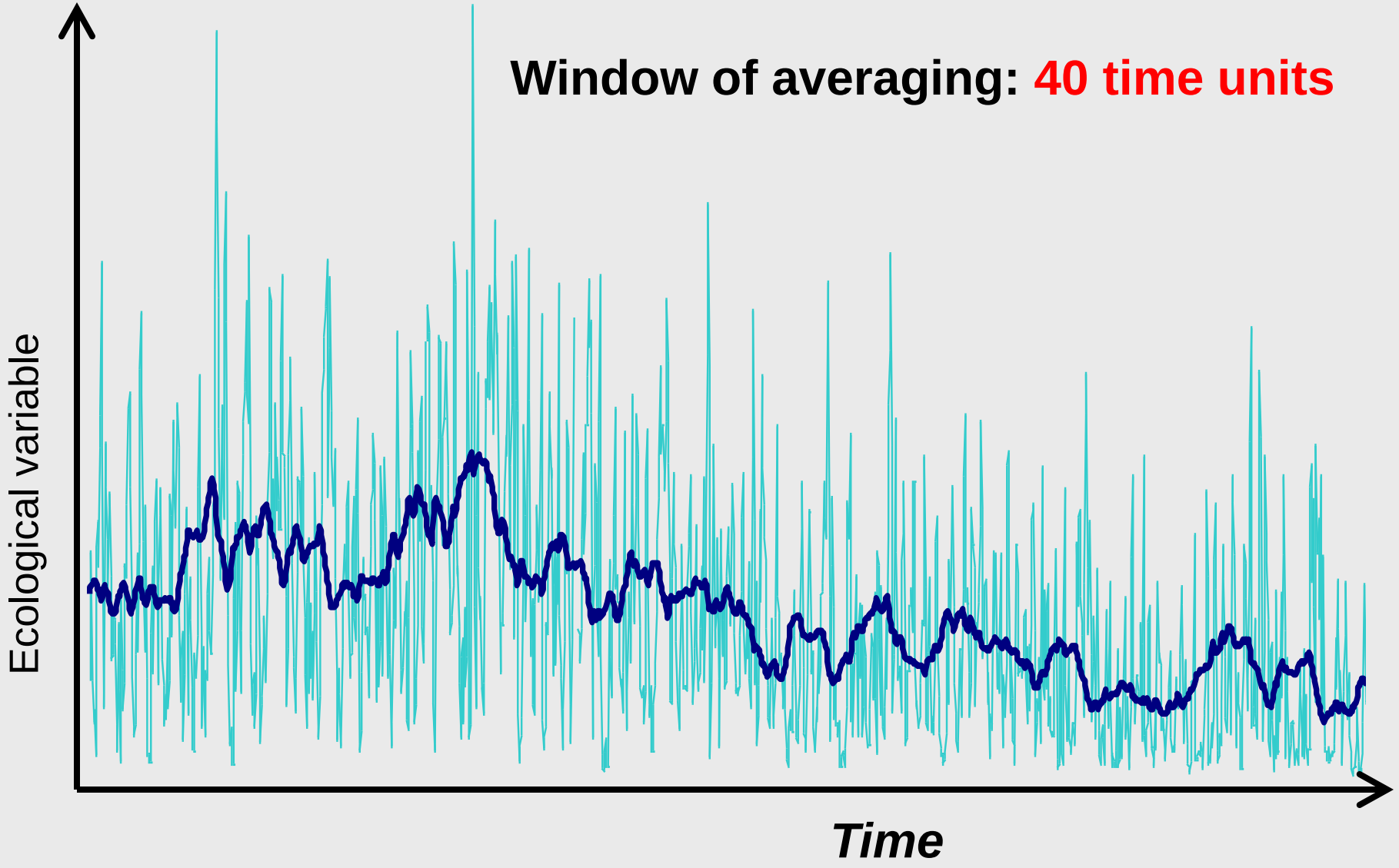
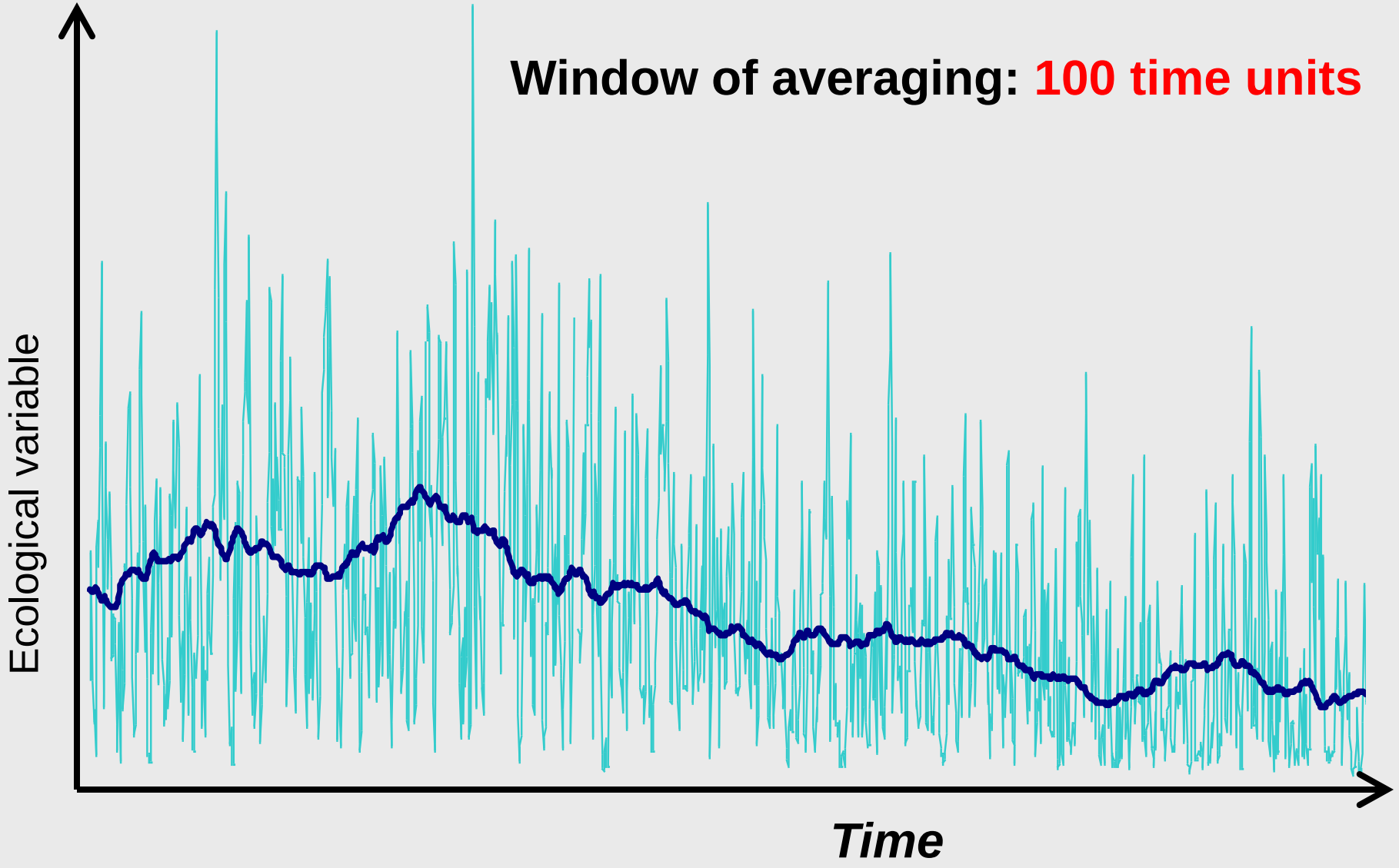

Window of averaging: 10 time units
Ecological variable
Time


Window of averaging: 20 time units
Ecological variable
Time


Window of averaging: 40 time units
Ecological variable
Time


Window of averaging: 100 time units
Ecological variable
Time

What does fetal nutrition signal?

- Fetal nutrition is buffered against transient, short-term ups/downs in mother's intake during gestation ("noise").
- Intergenerational averaging allows tracking of stable nutritional trends over longer timescales ("signal").
- Result: fetal nutrition calibrates to average recent nutrition, a more adaptively-relevant cue for adjusting long-term metabolic and biological strategy.

Adaptive mode: intergenerational phenotypic inertia

Kuzawa (2005), Amer J Hum Biol 17(1) 4-21.

Phenotypic inertia and adaptation

Cycle duration		Adaptation	
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1	years		
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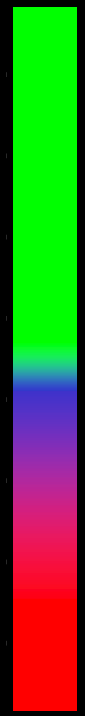
1000000	millions	Genetic	Natural selection



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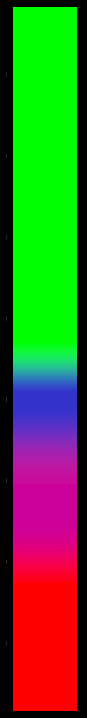
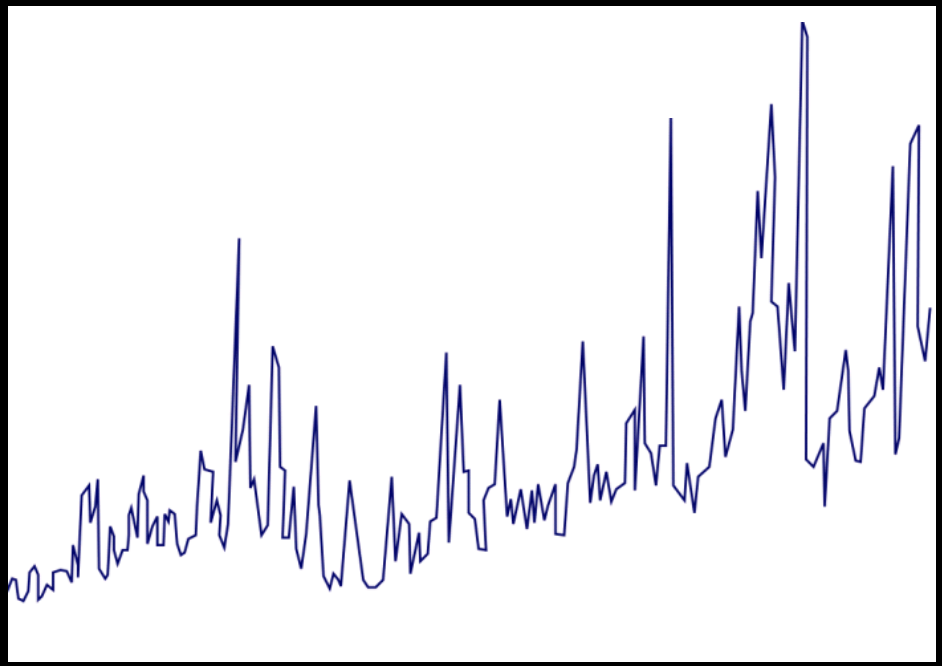


Kuzawa (2005), Amer J Hum Biol 17(1) 4-21.

Summary of argument

Why commit early?



Why setting strategy for life early might make sense

- The most reliable information is briefly available early: **maternal phenotype**, which embodies a record of experience in local social and physical environment.
- The early timing of critical periods may facilitate information flow between generations.

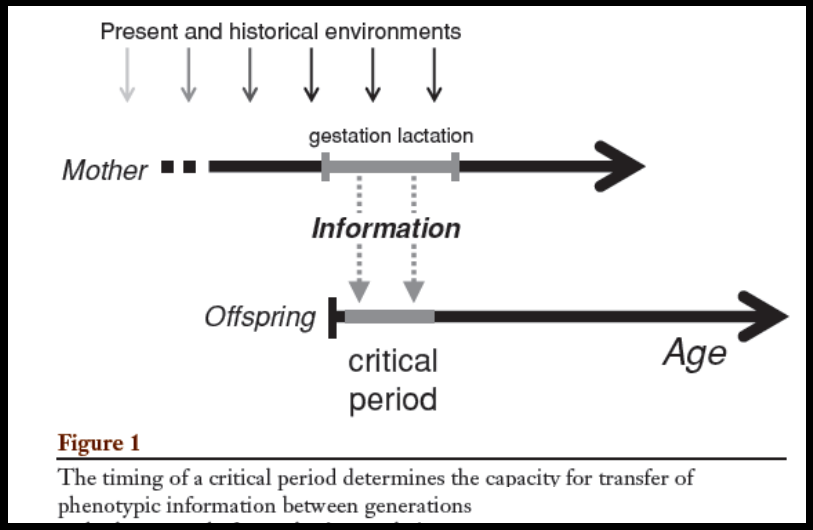


Figure 1

The timing of a critical period determines the capacity for transfer of phenotypic information between generations

Kuzawa & Quinn (2009) Ann Rev Anthropol

Designing more effective interventions

If developmental plasticity in a system is adaptive:

- We need to understand the timescale of environmental change that is being tracked.
- A subset of systems may be designed to ignore short-term deviations from normality.
- Failure to take timescale into account could help explain the limited success of some interventions.

  Example: poor performance of pregnancy supplementation (e.g. typical 10,000 kcal → 28 g)

Modes of human adaptability

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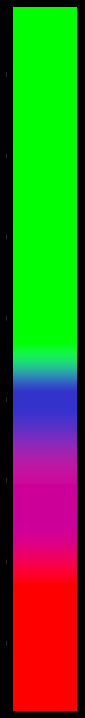

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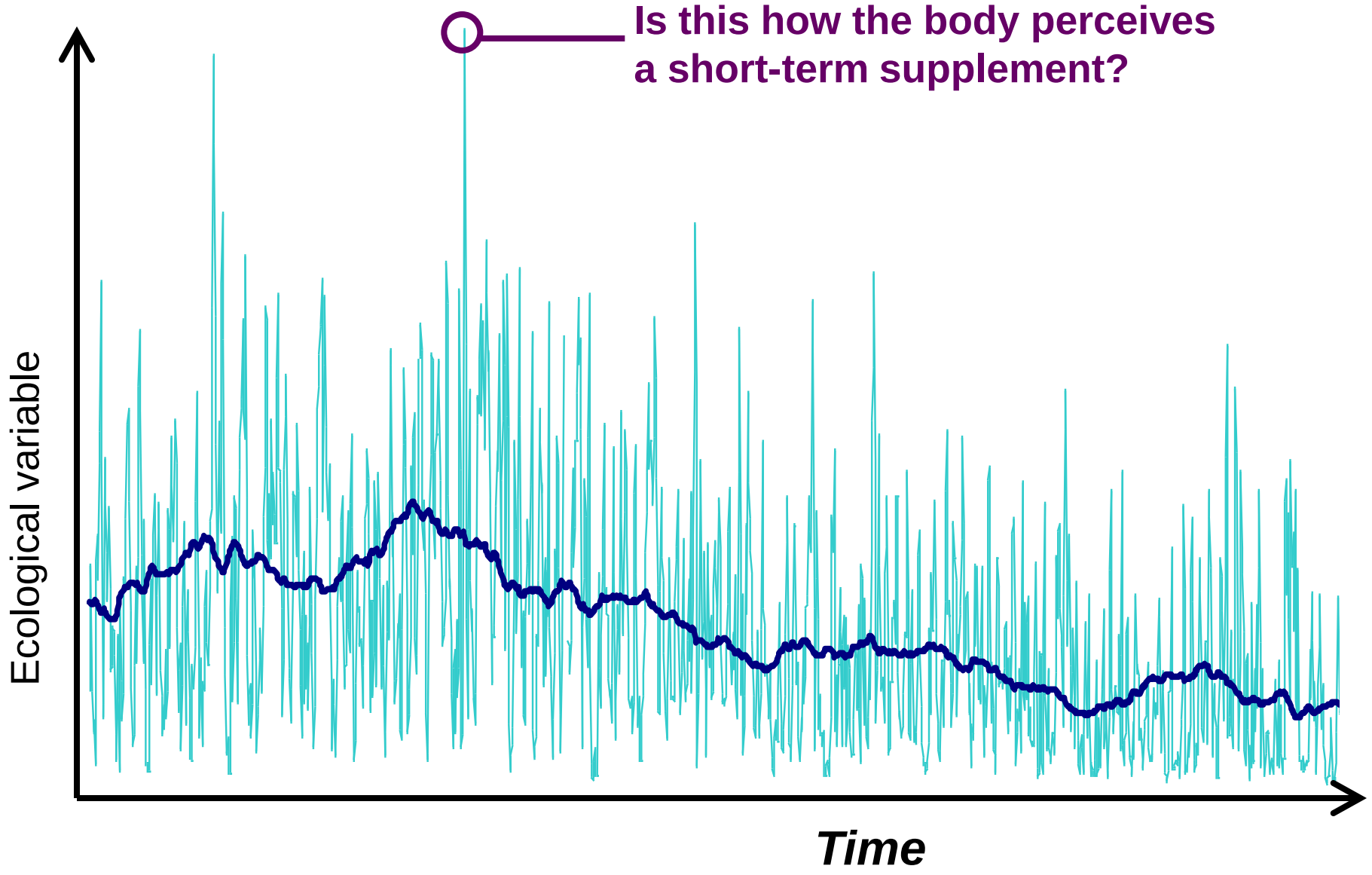
Is this how the body perceives
a short-term supplement?
Ecological variable
Time

Closing question:

How might we devise interventions that trick developmental biology and the epigenome into perceiving *sustained* social & ecological change?

See: Kuzawa & Thayer (2011), Epigenomics, 3(2) 221-34.

Acknowledgements

Collaborations, discussions, thanks

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