Robust Efficiency in Healthy Heart Rate Control and Variability

- Robustness/Efficiency Tradeoffs
- Healthy
  - Heart Rate Control
  - Heart Rate Variability (HRV)
- Universal
  - laws
  - architectures

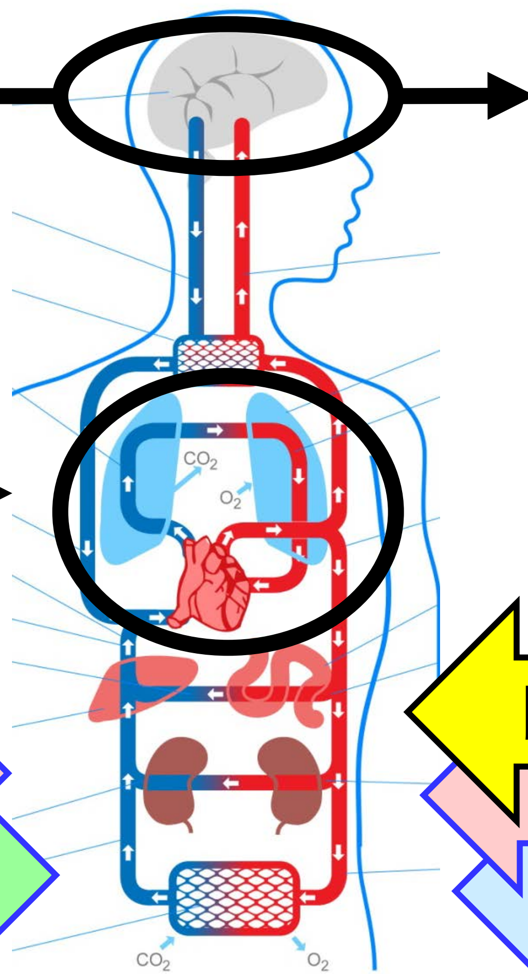
Homeostasis

controls

- **heart rate**
- **ventilation**
- vasodilation
- coagulation
- inflammation
- digestion
- storage
- …

errors

- **O2**
- **BP**
- pH
- Glucose
- Energy store
- Blood volume
- …



energy

trauma

infection

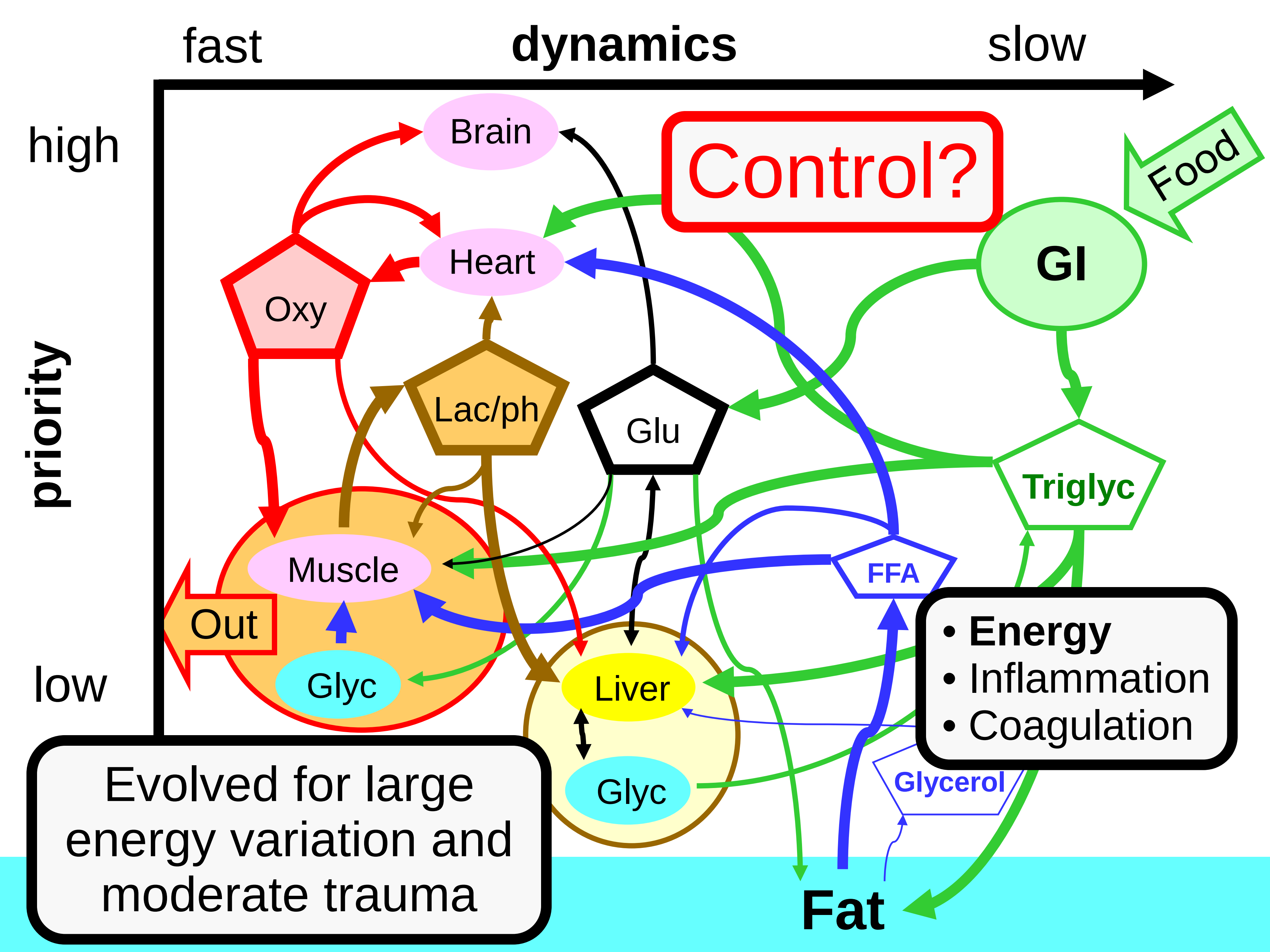
external disturbances

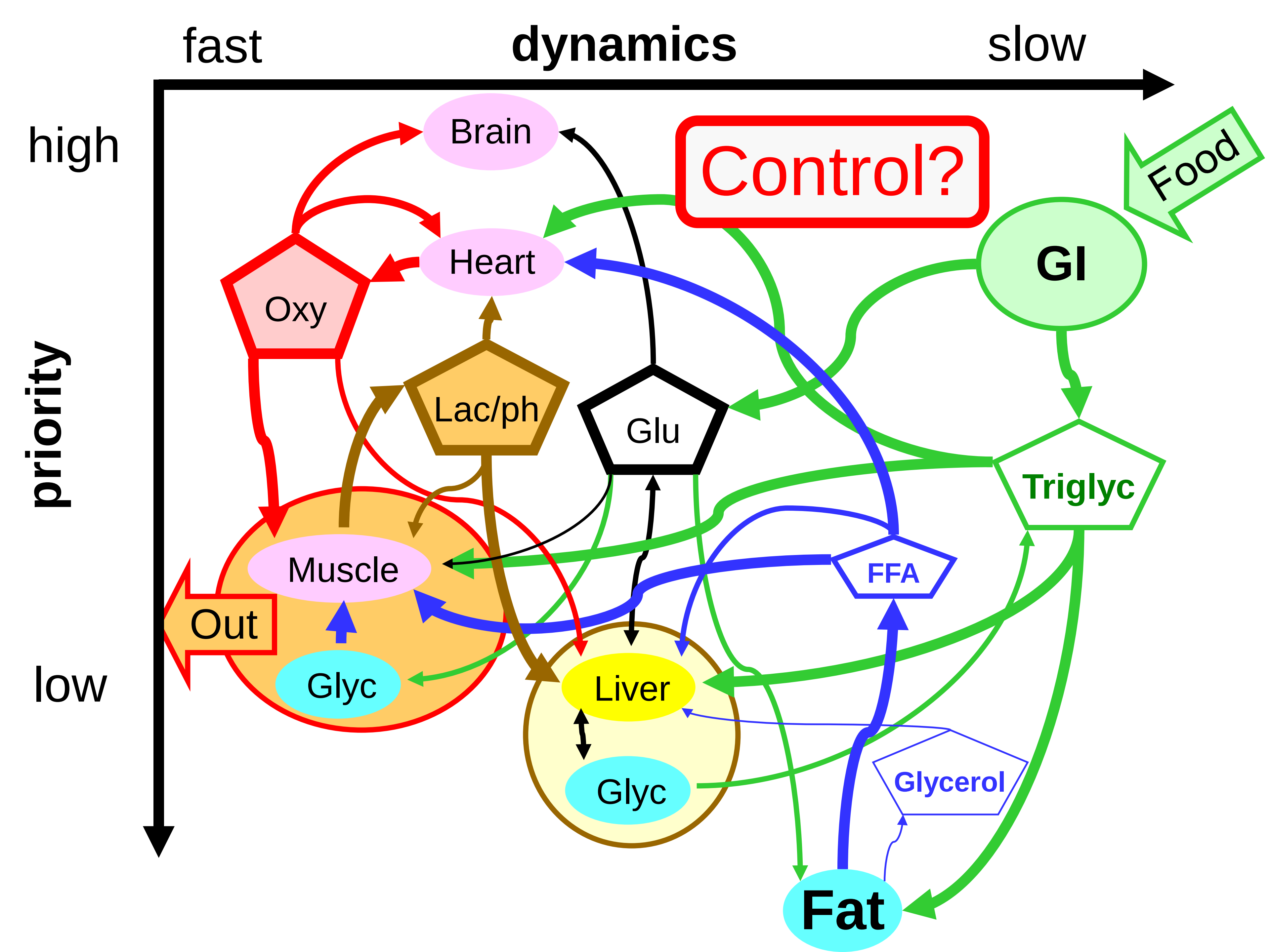
breath

heart beat

sensor

internal noise


fast
dynamics
slow
high
priority
low
Brain
Heart
Oxy
Lac/ph
Glu
Control?
Food
GI
Triglyc
Muscle
FFA
Out
Glyc
Liver
Glyc
Glycerol
• Energy
• Inflammation
• Coagulation
Evolved for large energy variation and moderate trauma
Fat



fast
dynamics
slow
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priority
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Brain
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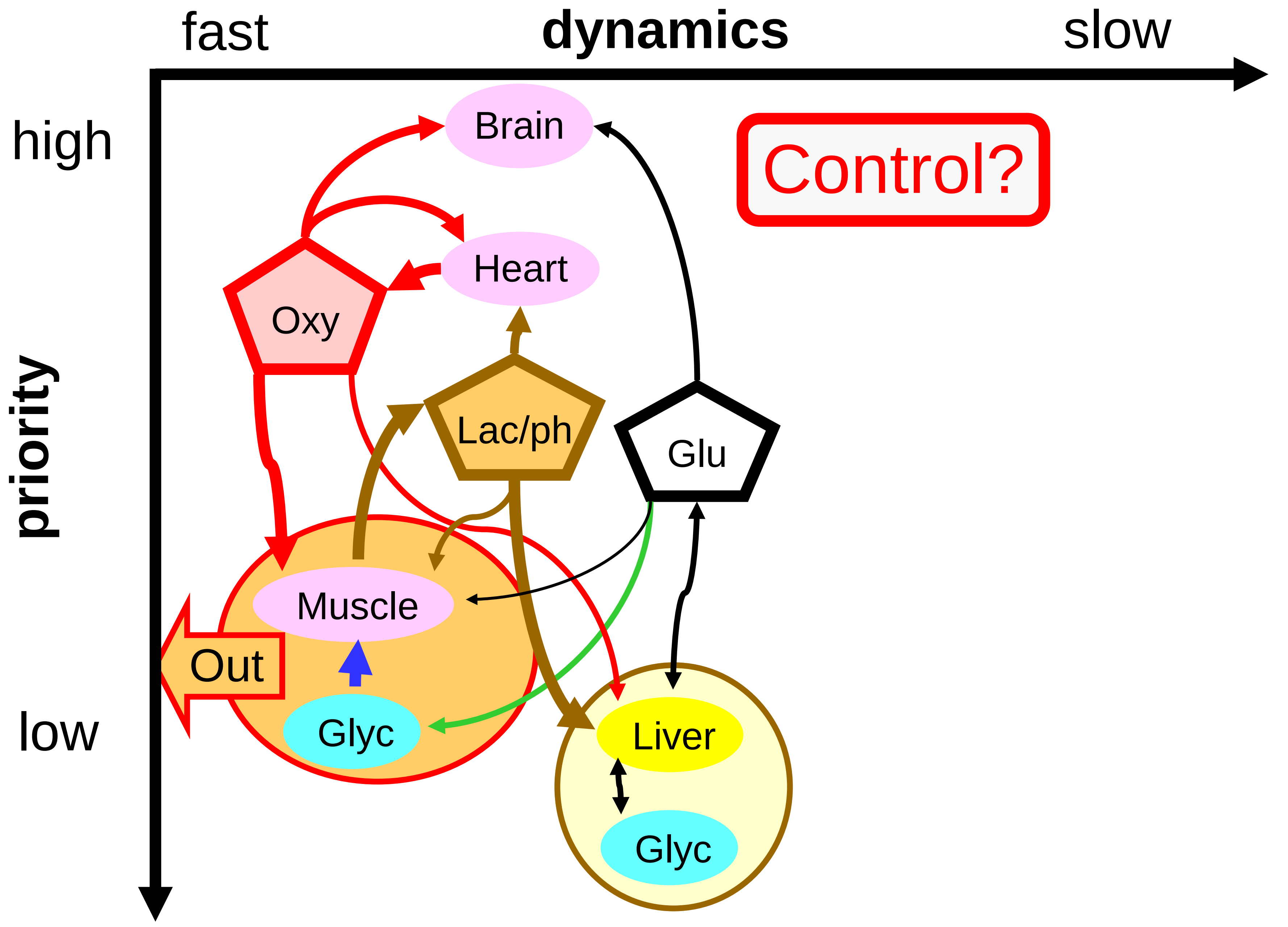
Muscle
FFA
Out
Glyc
Liver
Glycerol
Glyc
Fat


fast
dynamics
slow
high
priority
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Heart
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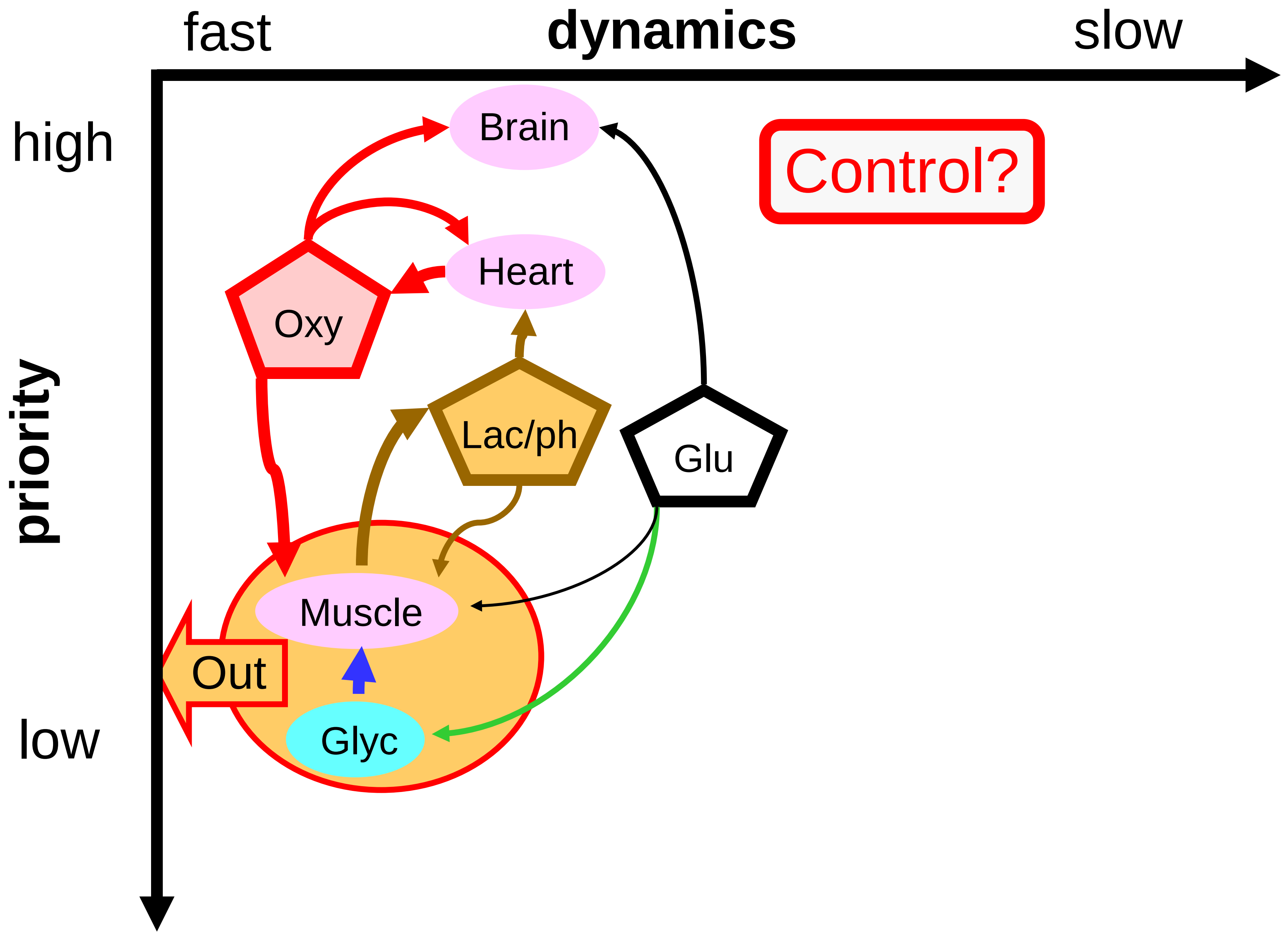
Glu
Muscle
Out
Glyc
Liver
Glyc


fast
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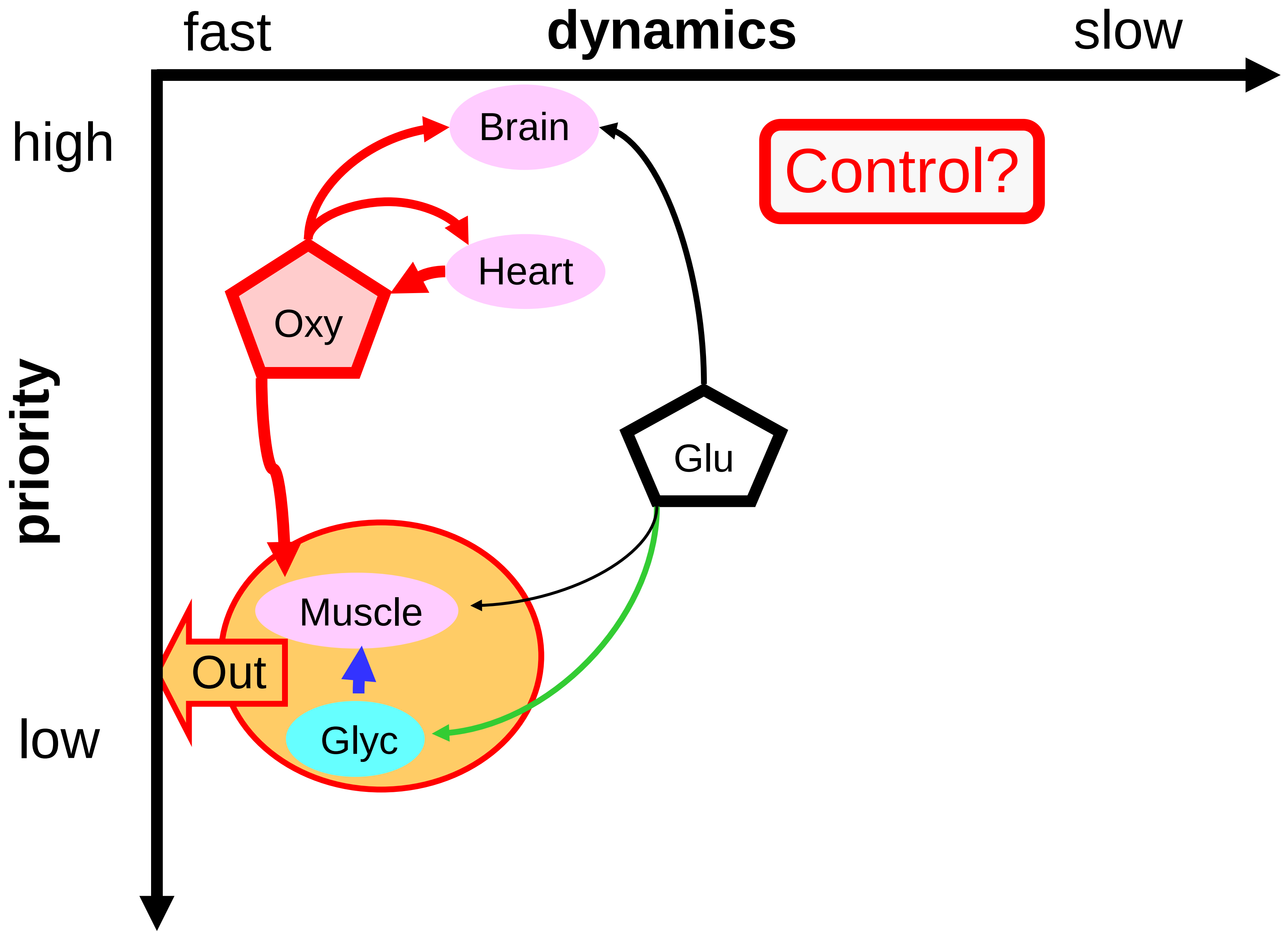
Muscle
Out
Glyc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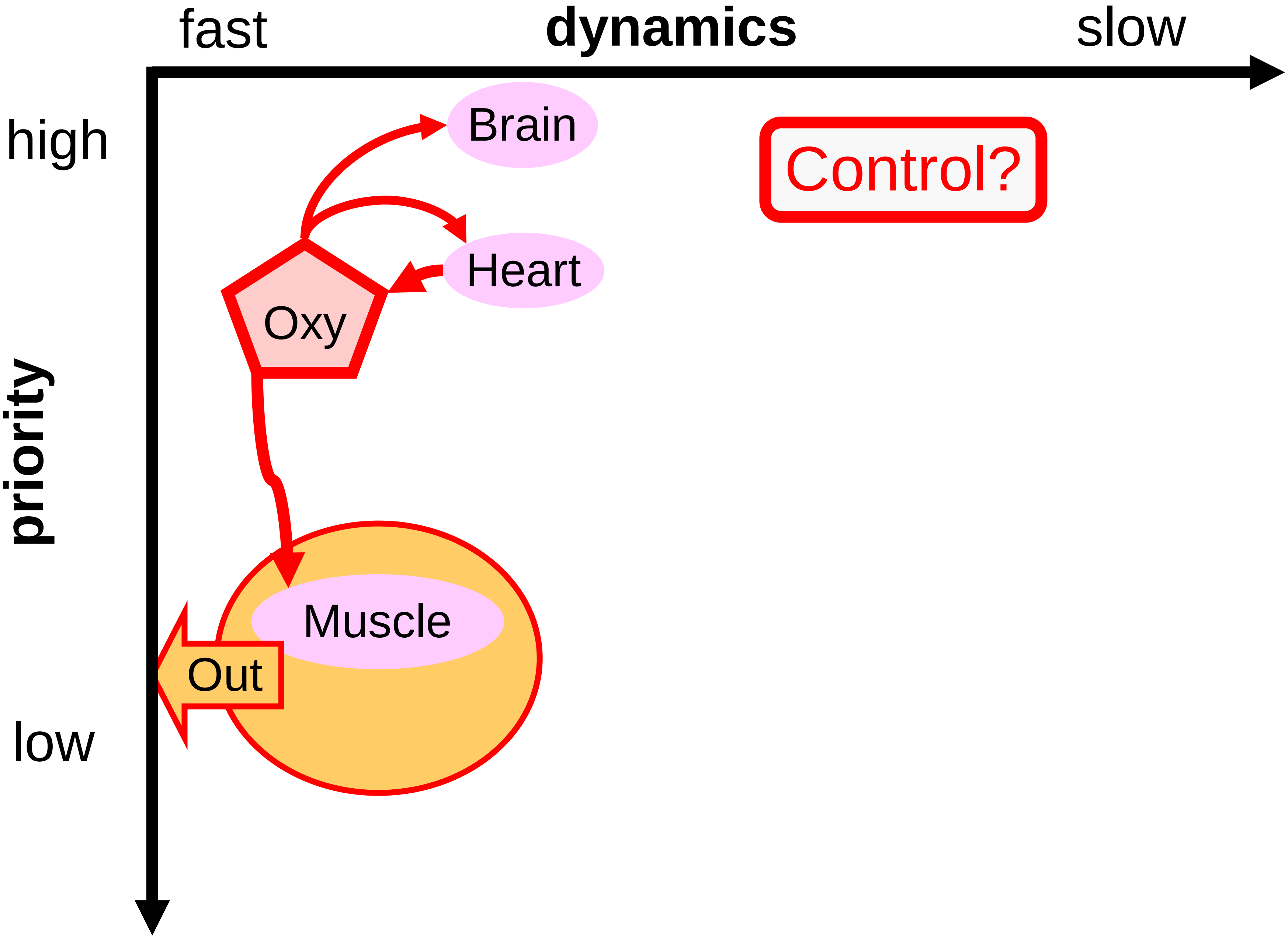
fast
dynamics
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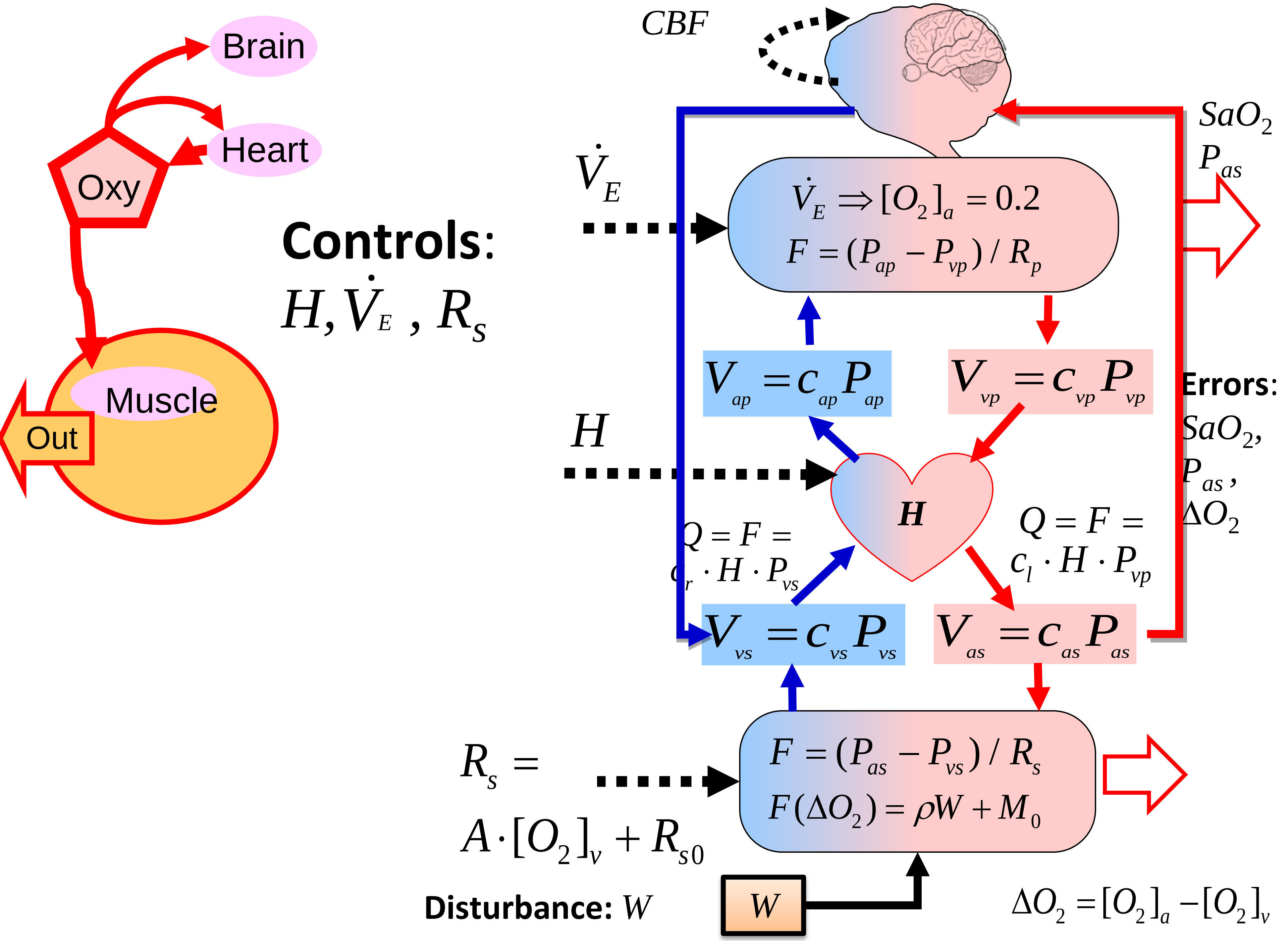
Heart
Oxy
Muscle
Out



Brain
Heart
Oxy
Muscle
Out
Controls:
$H, \dot{V}_E, R_s$
CBF
$\dot{V}_E$
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
SaO_2
P_{as}
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
H
Errors:
SaO_2,
P_{as},
ΔO_2
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
Disturbance: W
W
$\Delta O_2 = [O_2]_a - [O_2]_v$

~~Physiology?~~

is old fashioned

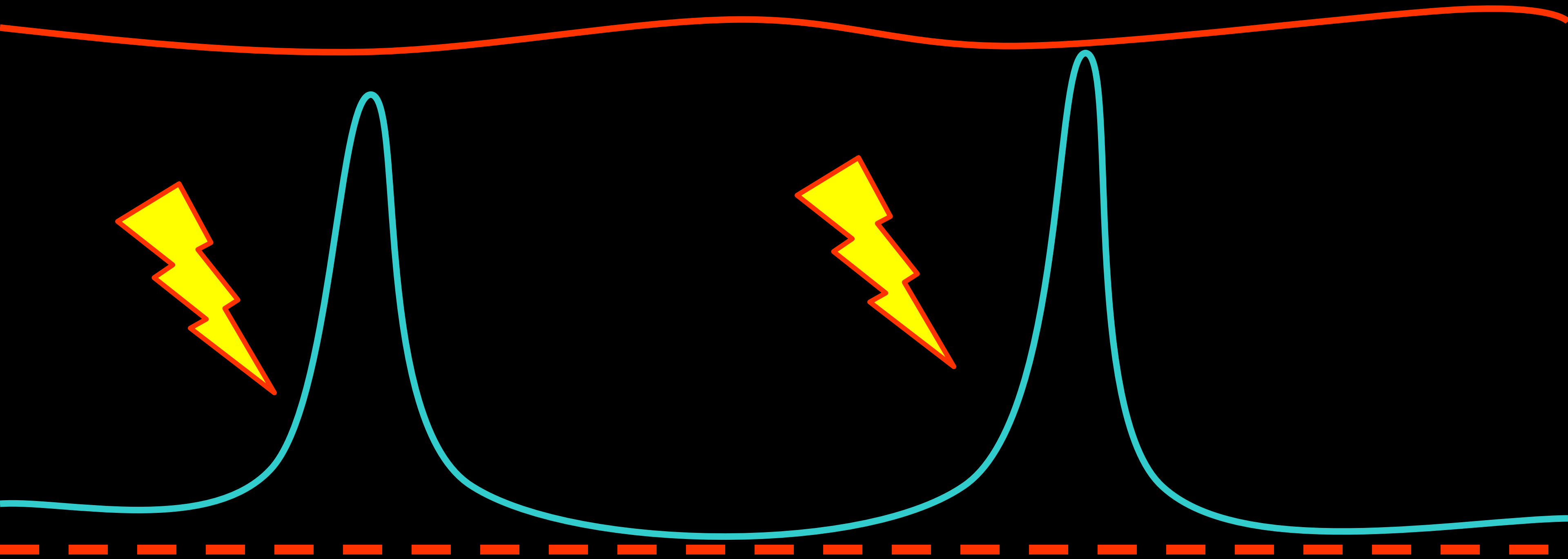
Robust	Fragile
☺ Metabolism	☹ Obesity, diabetes
☺ Regeneration & repair	☹ Cancer
☺ Healing wound /infect	☹ AutoImmune/Inflame

Mainstream "scientific" view

- ***no boring*** old fashioned physiology, tradeoffs, homeostasis, allostasis, constraints, architecture…

- health = "good" genes
- health = emergent, edge of chaos, order for free…

- change is hopefully coming



Death

☹ Fat accumulation
☹ Insulin resistance
☹ Proliferation
☹ Inflammation

Controlled
Dynamic

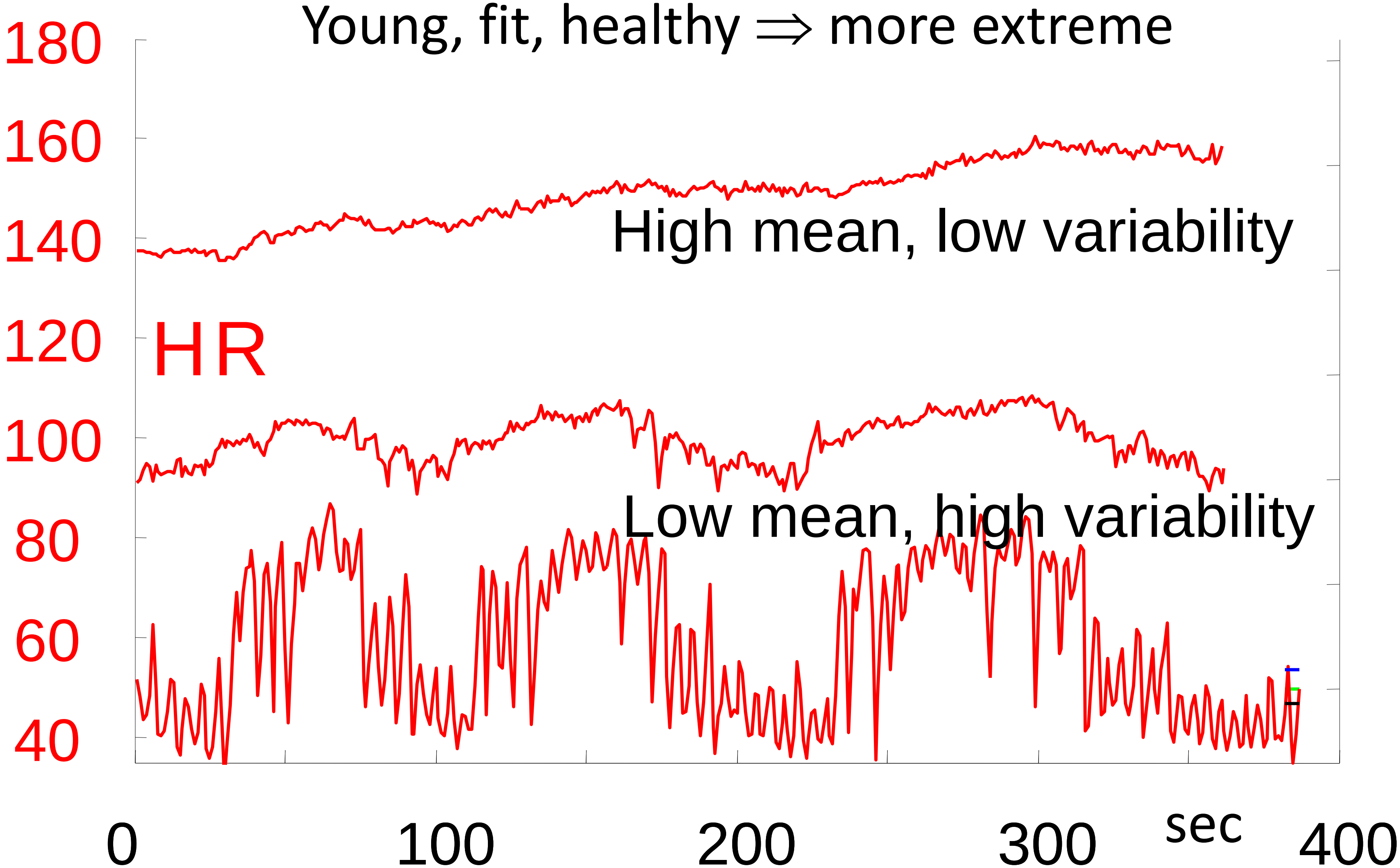
Low mean
High variability

Uncontrolled
Chronic

High mean
Low variability

The persistent mystery

Young, fit, healthy ⇒ more extreme



Seeking mechanistic explanations

Many diseases associated w/decrease HRV

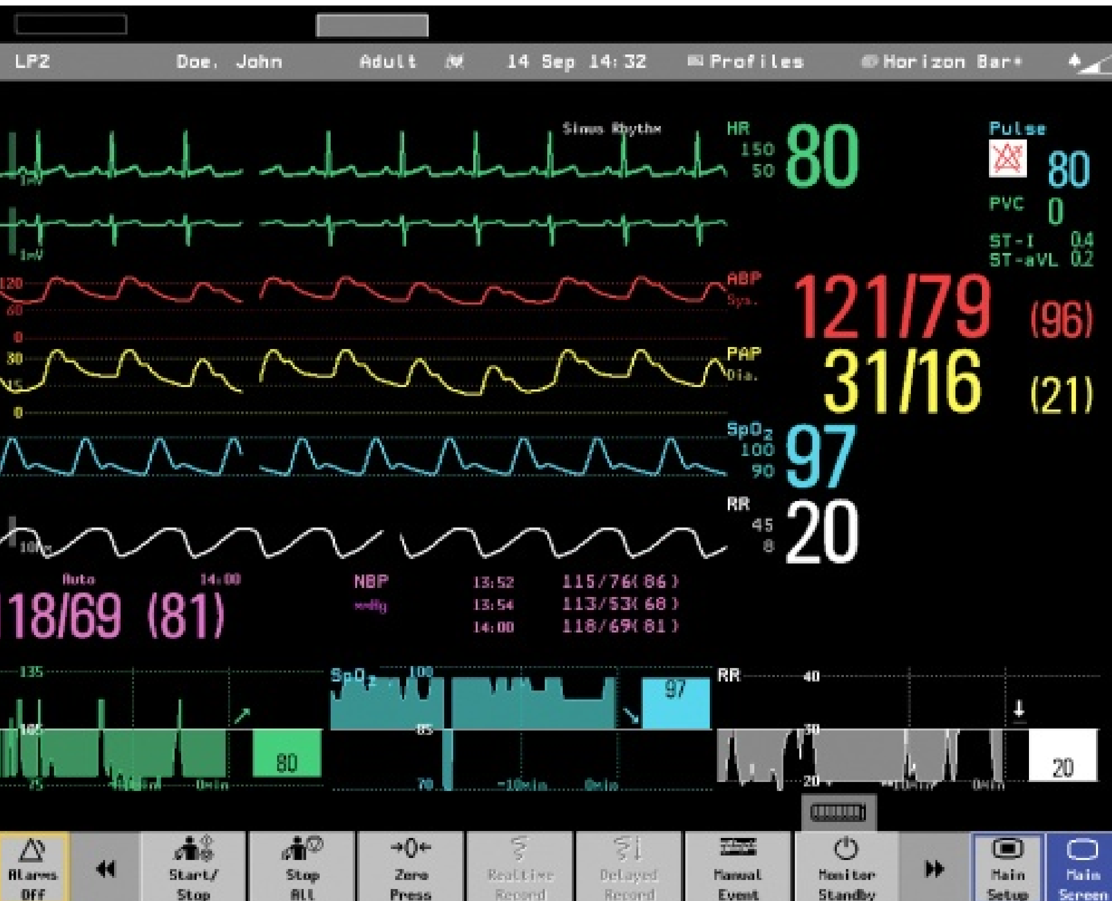
- *Poon et al*, **Decrease of cardiac chaos in congestive heart failure**, Nature, 1997.
- *Carney et al*, **Depression, heart rate variability, and acute myocardial infarction**, Circulation, 2001.
- *Malpas et al*, **Heart-rate variability and cardiac autonomic function in diabetes**, Diabetes, 1990.
- *Pontet et al*, **Heart rate variability as early marker of multiple organ dysfunction syndrome in septic patients**, Journal of critical care, 2003.
- *Tateishi et al*, **Depressed heart rate variability is associated with high IL-6 blood level and decline in the blood pressure in septic patients**, Shock, 2007.
- *Roche et al*, **Depressed heart rate variability is associated with high IL-6 blood level and decline in the blood pressure in septic patients**, Circulation, 1999.
- Kleiger et al, **Decreased heart rate variability and its association with increased mortality after acute myocardial infarction**, Am Journal of Cardiology, 1987.
- Liao et al, **Age, race, and sex differences in autonomic cardiac function measured by spectral analysis of heart rate variability**, Am Journal of Cardiology, 1995.

Google scholar search

Search ***exact*** phrase “heart rate variability” for 2011 returns

- 695 papers with phrase in the title,
- 9330 papers appearing anywhere…
- …of which 891 have at least one of the following words: chaos, chaotic, or fractal

Future patient monitor with HRV alert will be???



Warning: Reduced HRV
Patient is at Risk of

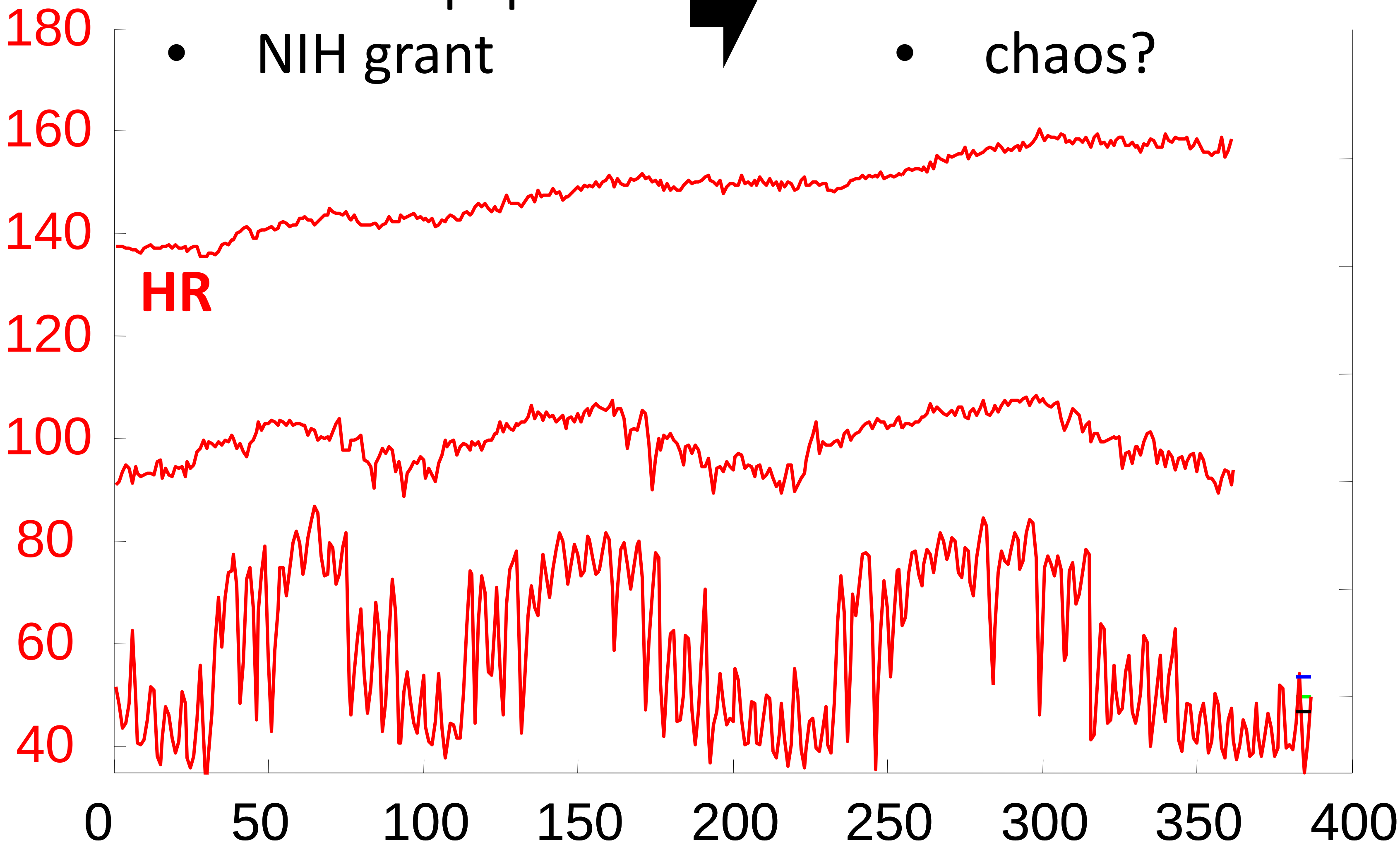
Autonomic system dysfunction
Sepsis
Respiratory Failure
Kidney Failure
Multi-organ dysfunction
Myocardial ischemia
Coronary artery occlusion
Heart failure
Diabetes
Sleep Apnea
Getting Old....

Want a

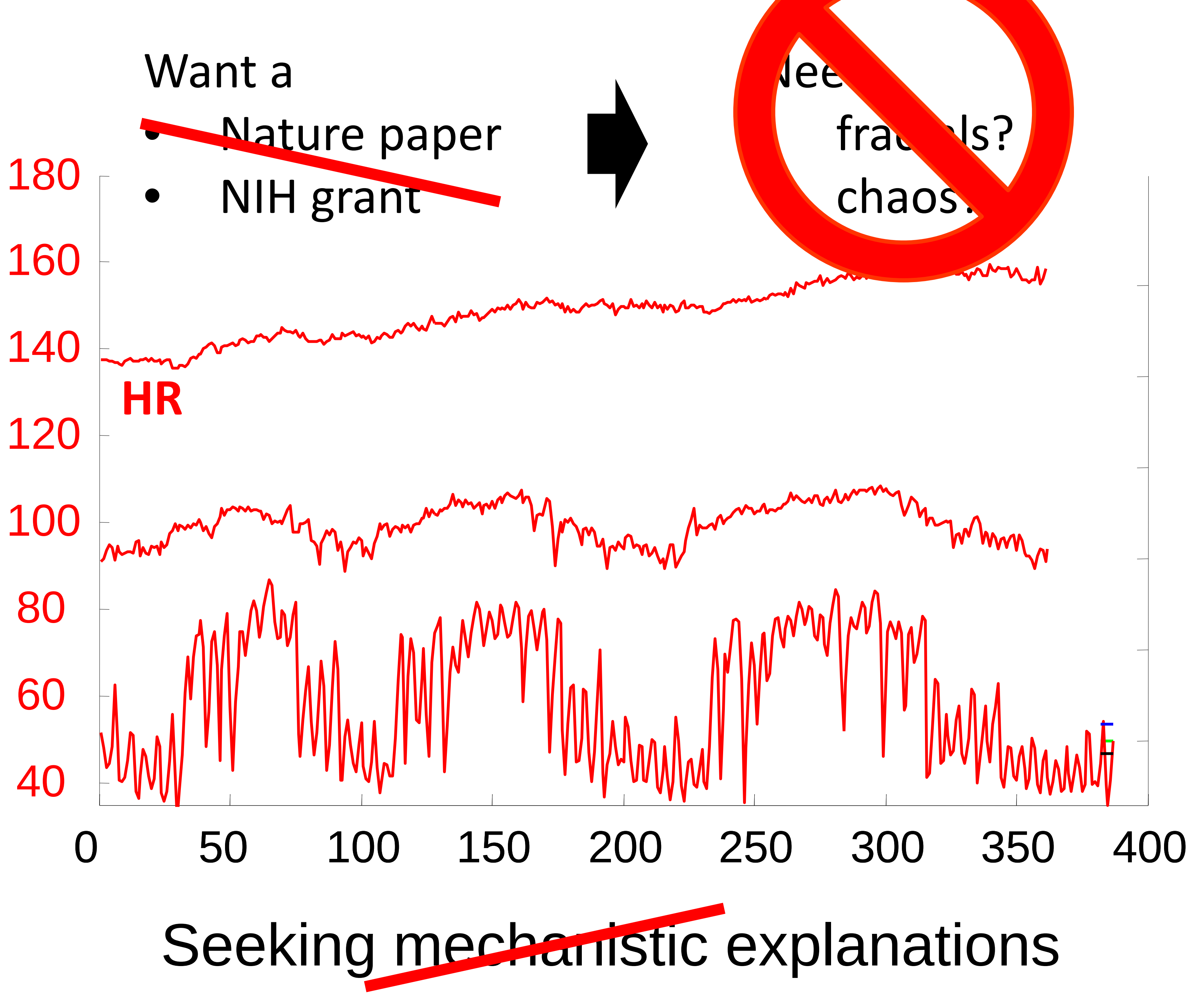
- Nature paper
- NIH grant

Need

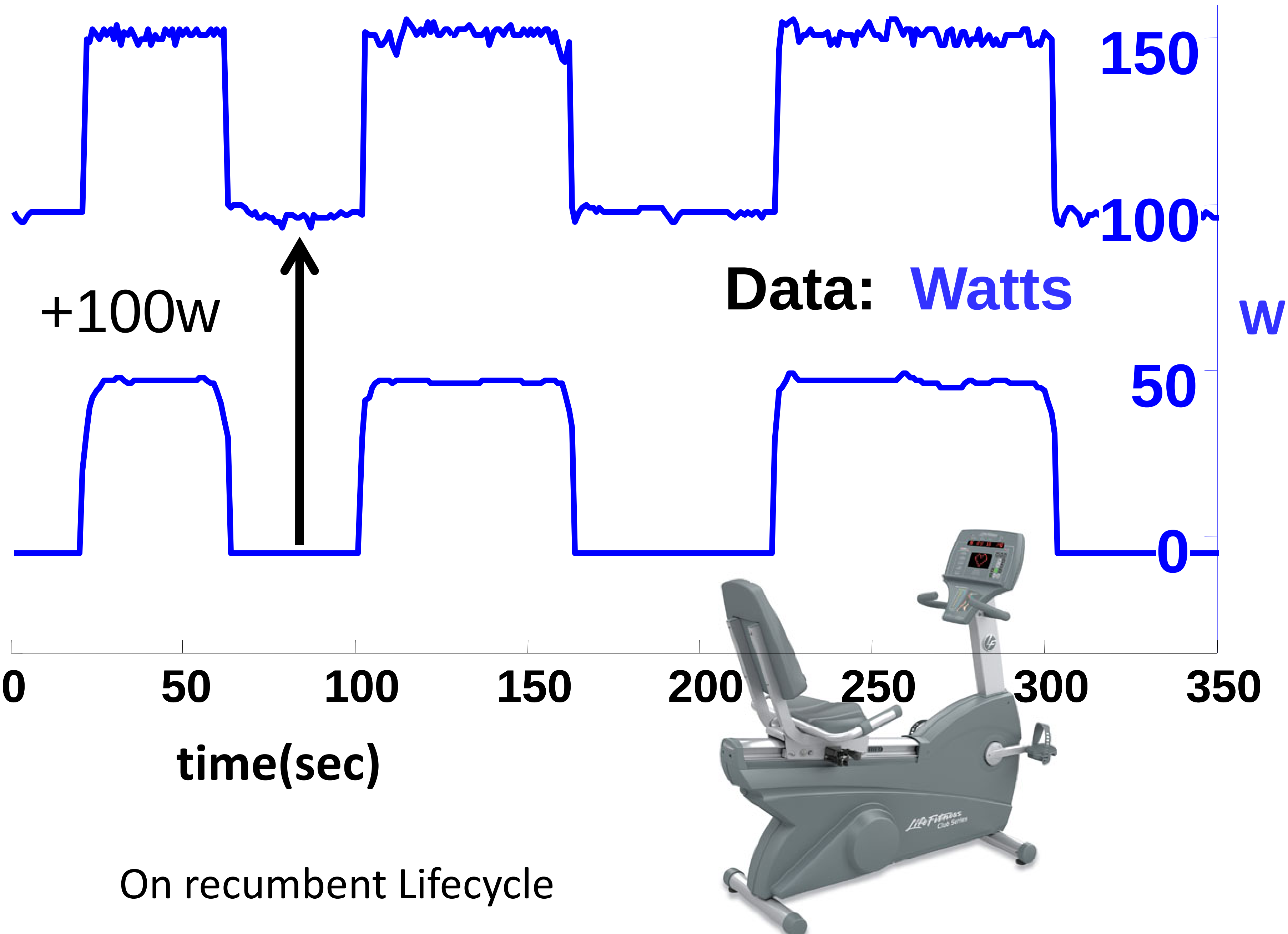
- fractals?
- chaos?



Seeking ~~mechanistic~~ explanations

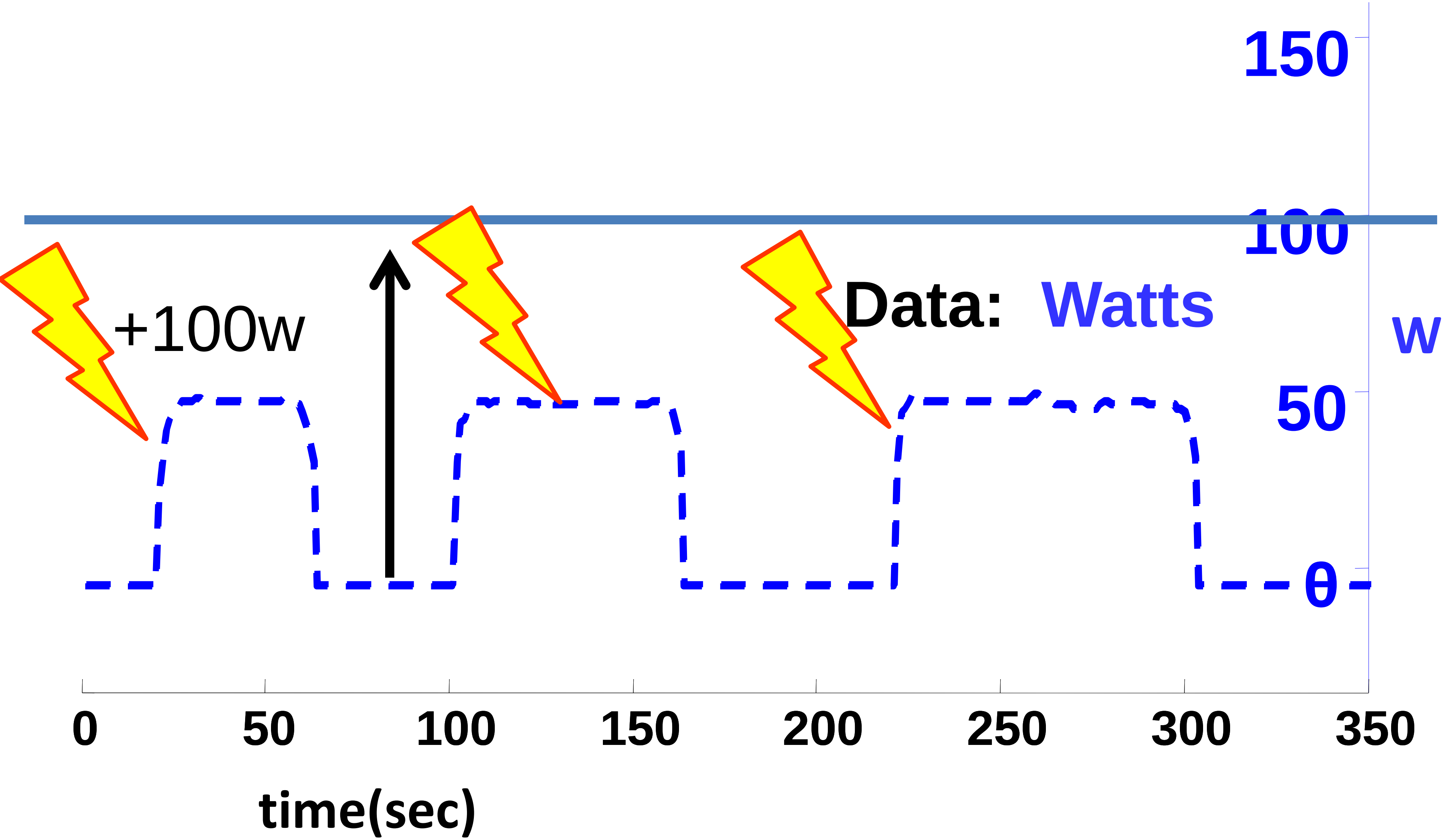

Want a
• Nature paper
• NIH grant
Nee
fra ls?
chaos
HR
180
160
140
120
100
80
60
40
0
50
100
150
200
250
300
350
400
Seeking mechanistic explanations

Two experiments

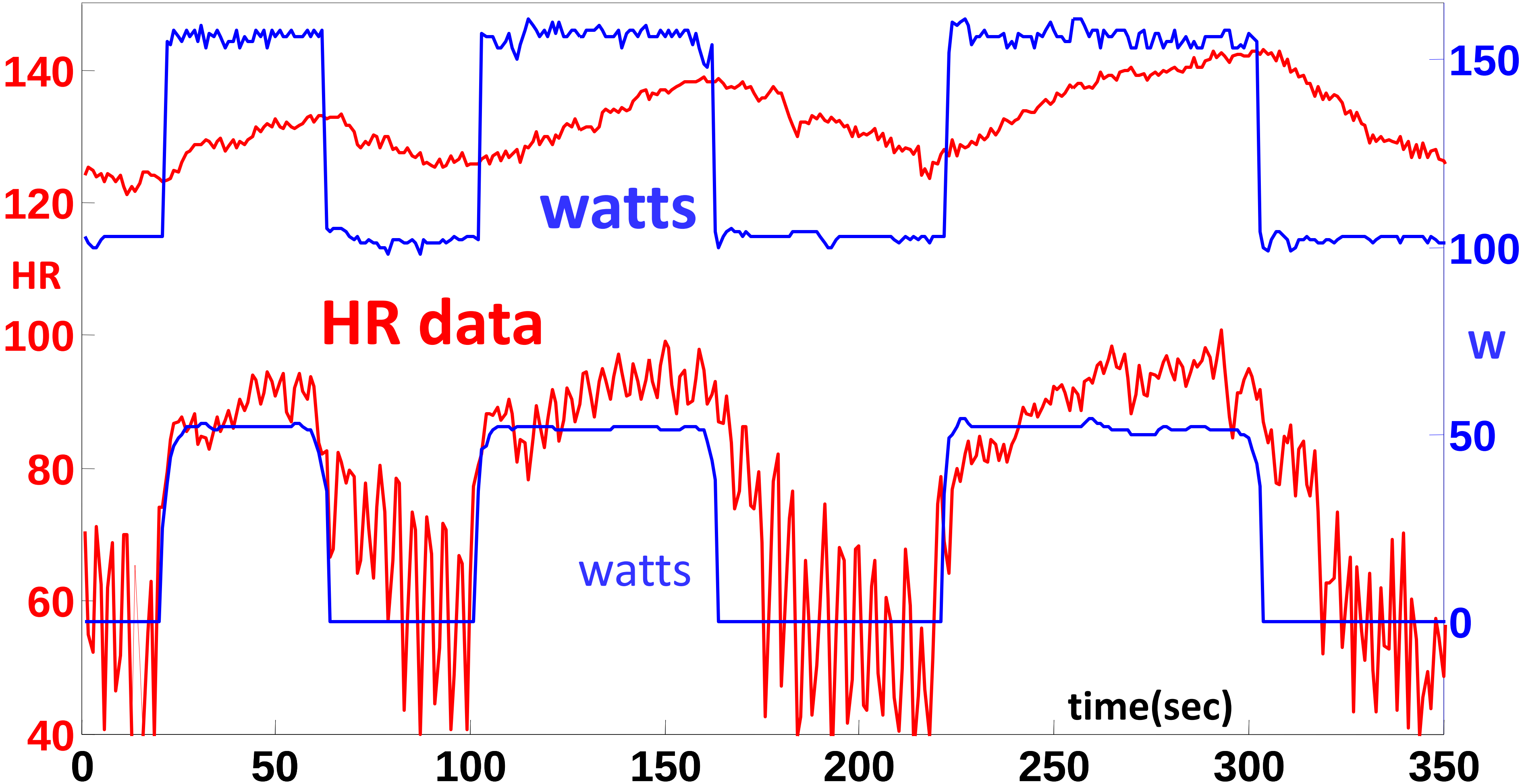


On recumbent Lifecycle

Stress= “perturbation + background”

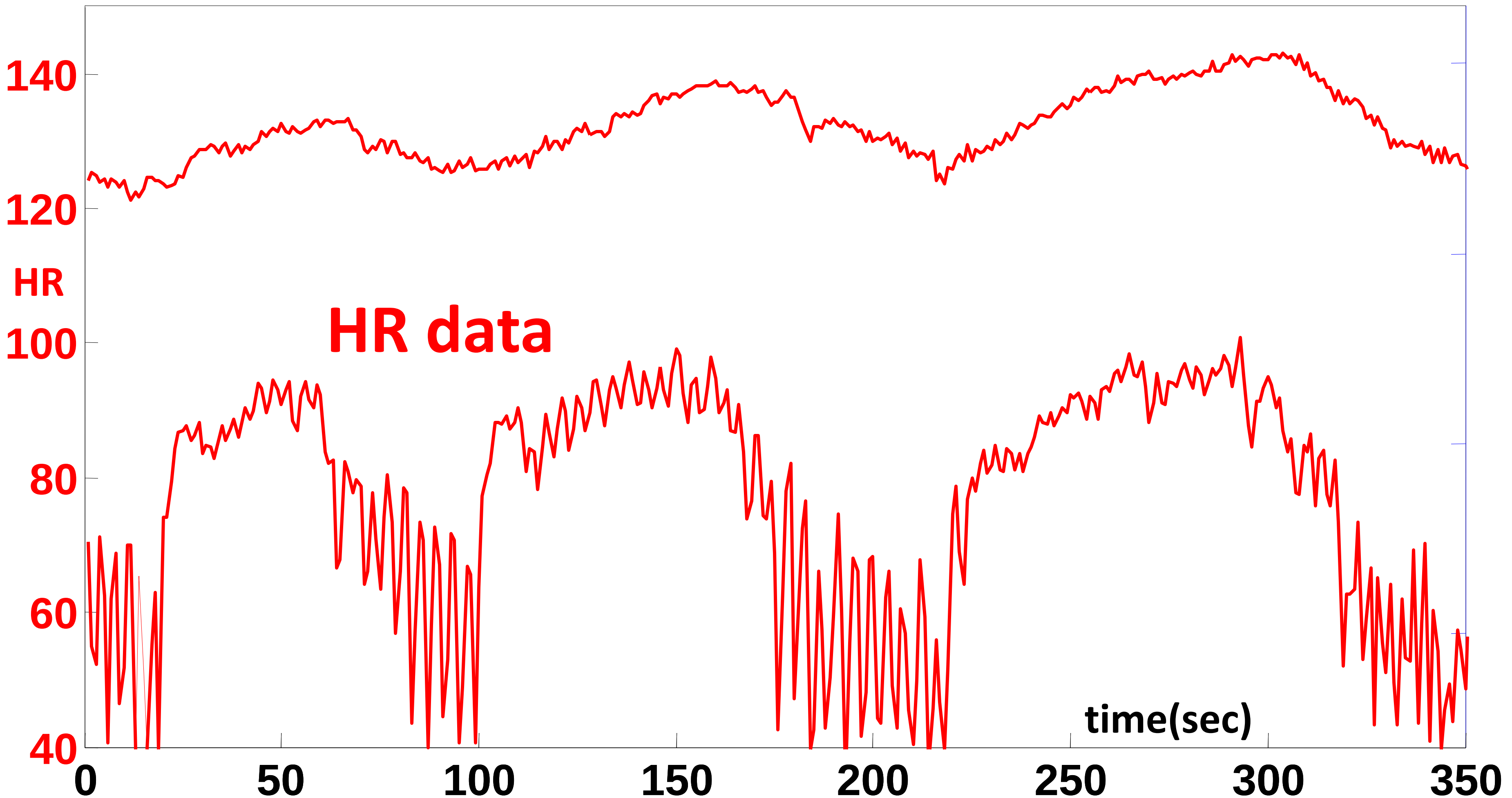


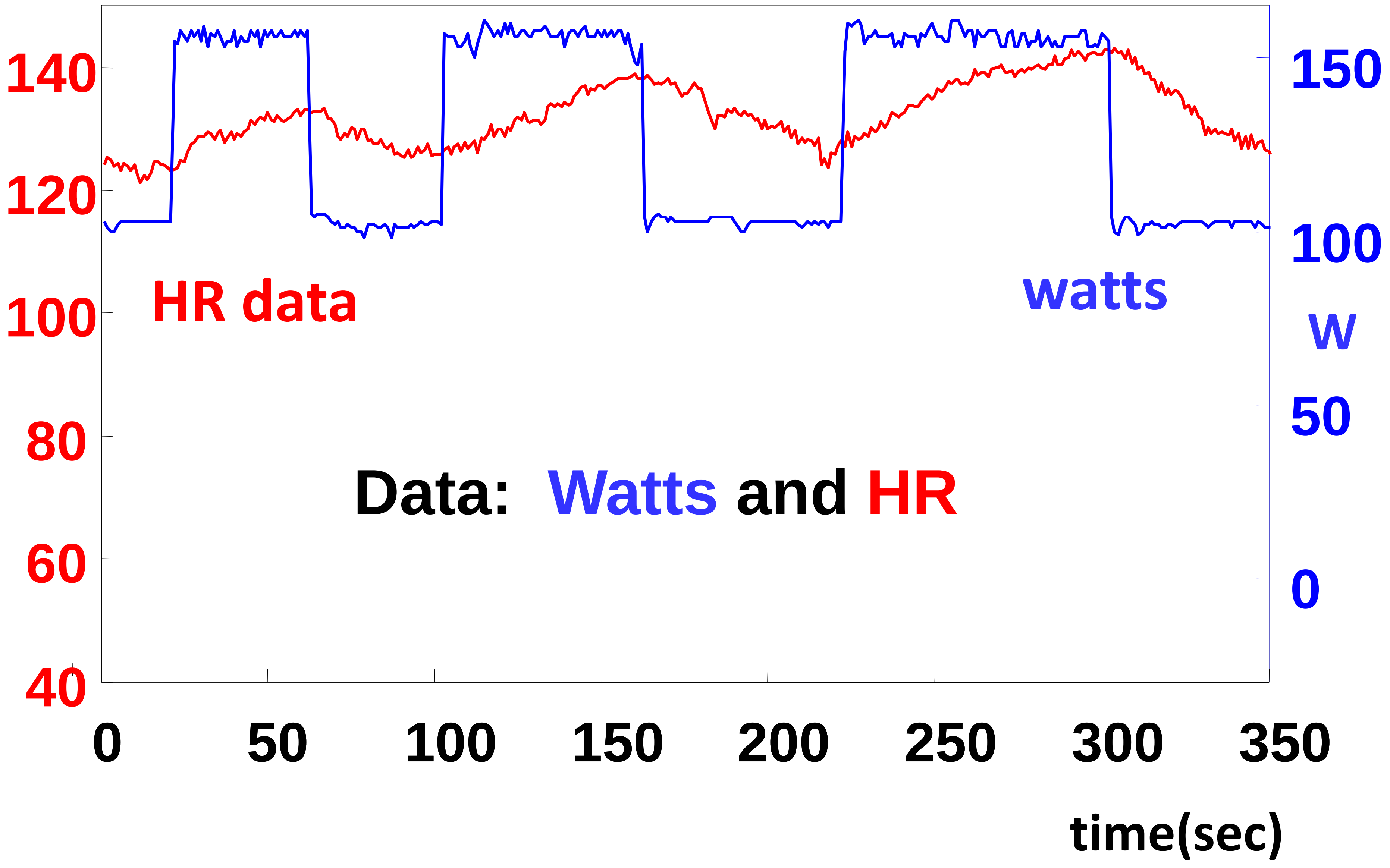
Two experiments with same subject #1



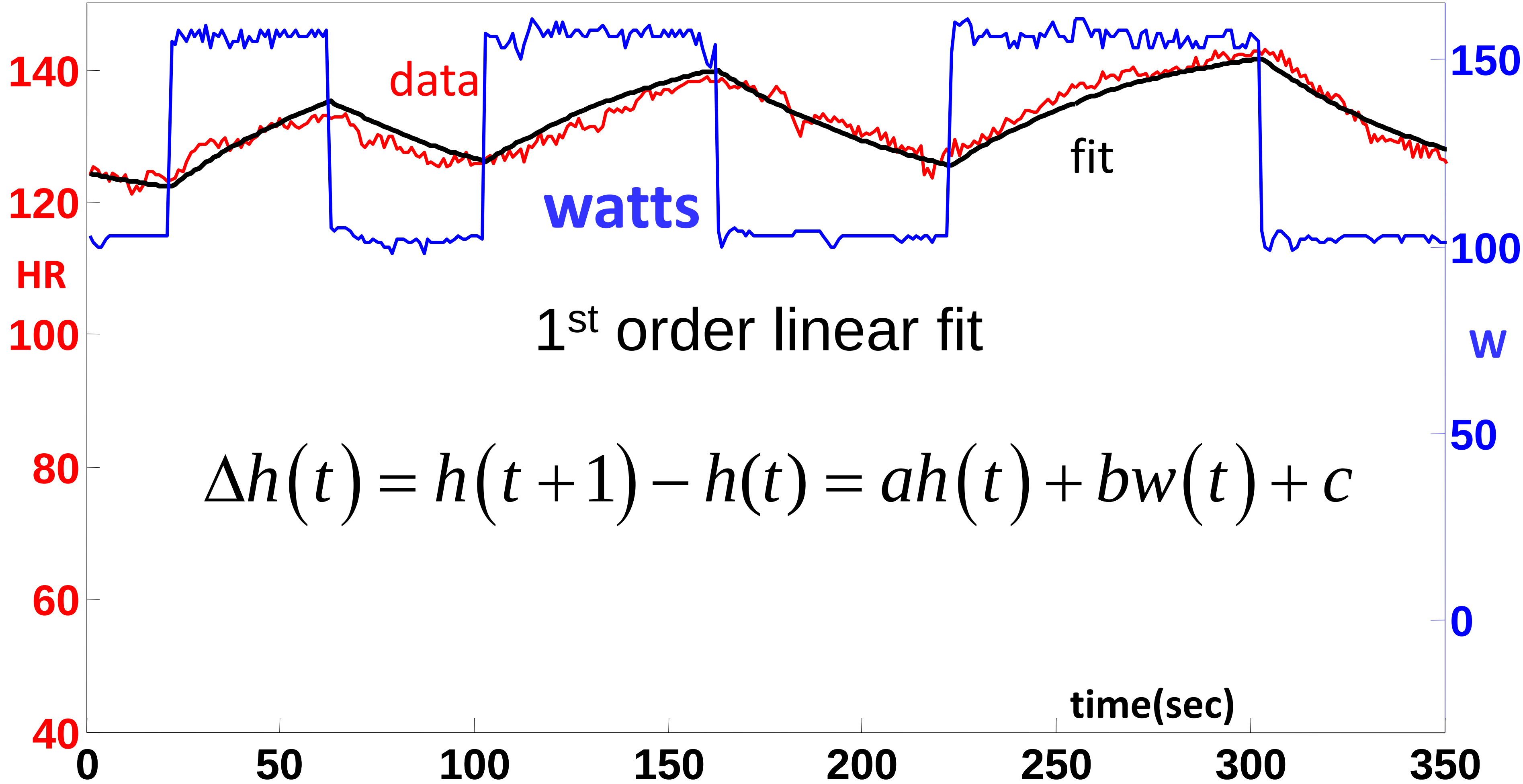
Data: Watts and HR

Two experiments with same subject #1





140
120
100
80
60
40
HR data
watts
W
150
100
50
0
Data: Watts and HR
0
50
100
150
200
250
300
350
time(sec)



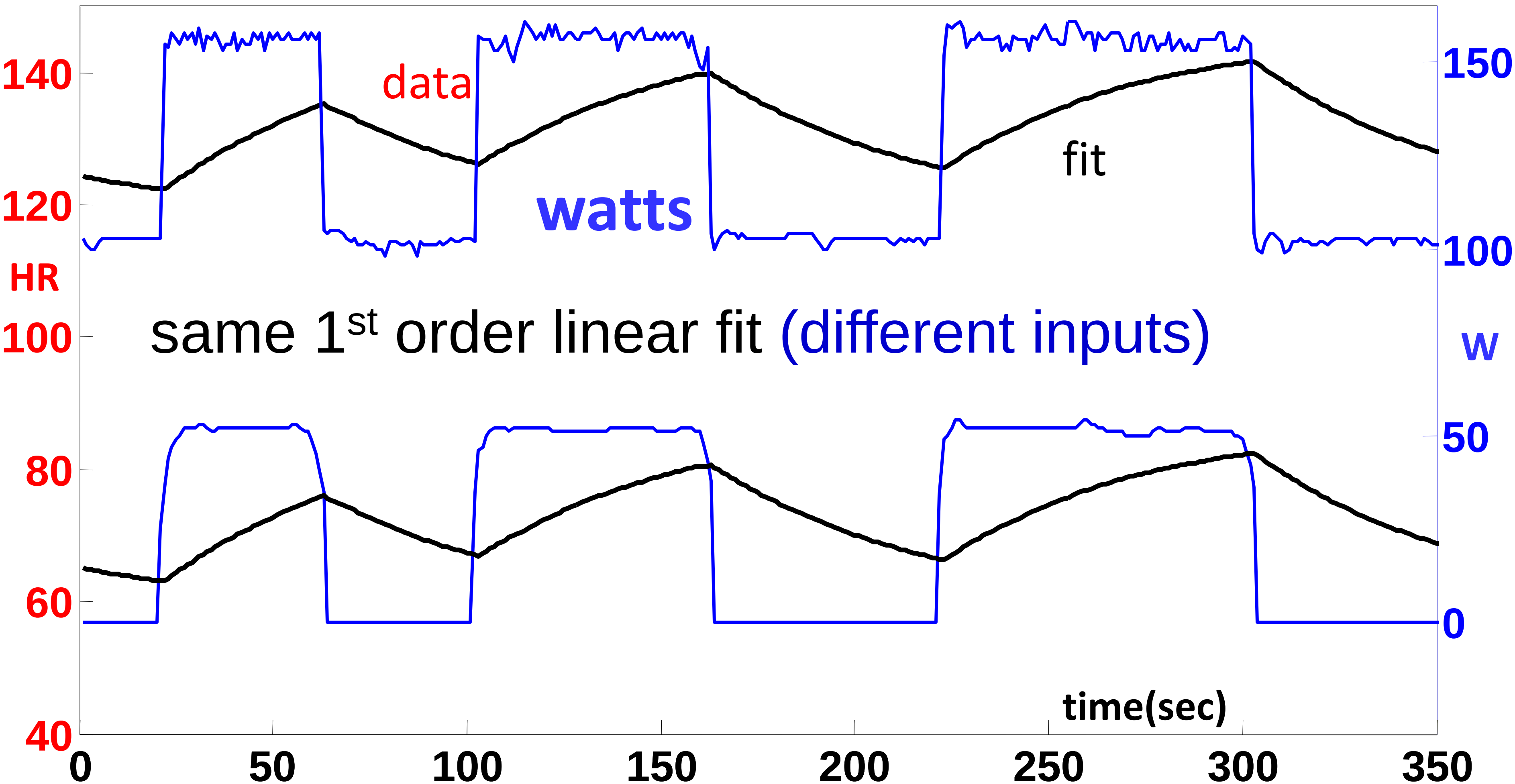
1st order linear fit

$$\Delta h(t) = h(t+1) - h(t) = ah(t) + bw(t) + c$$

3 parameters (*a*, *b*, *c*)

$$\approx (-0.018, 0.01, 1.1)$$

$$@100w$$



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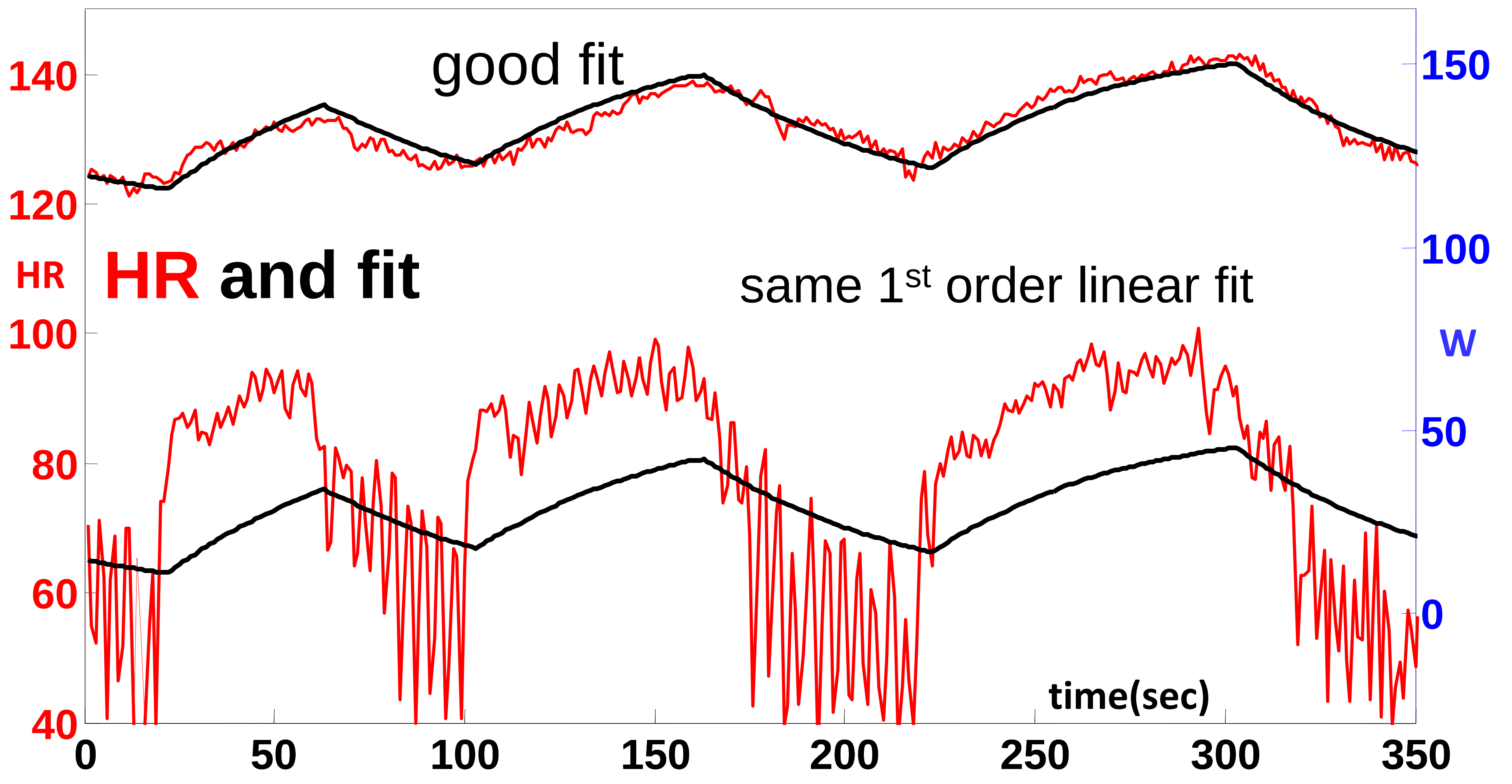
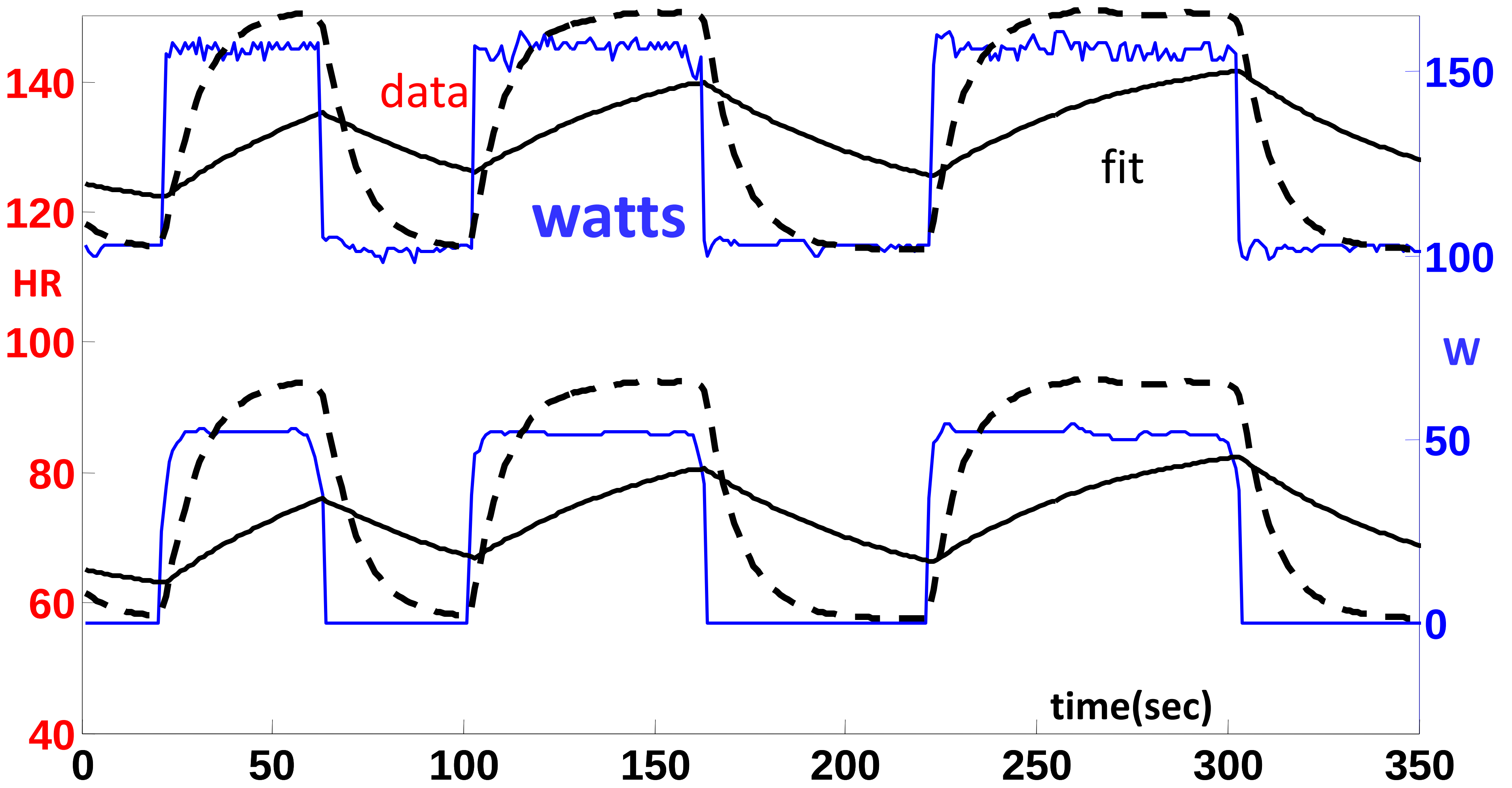
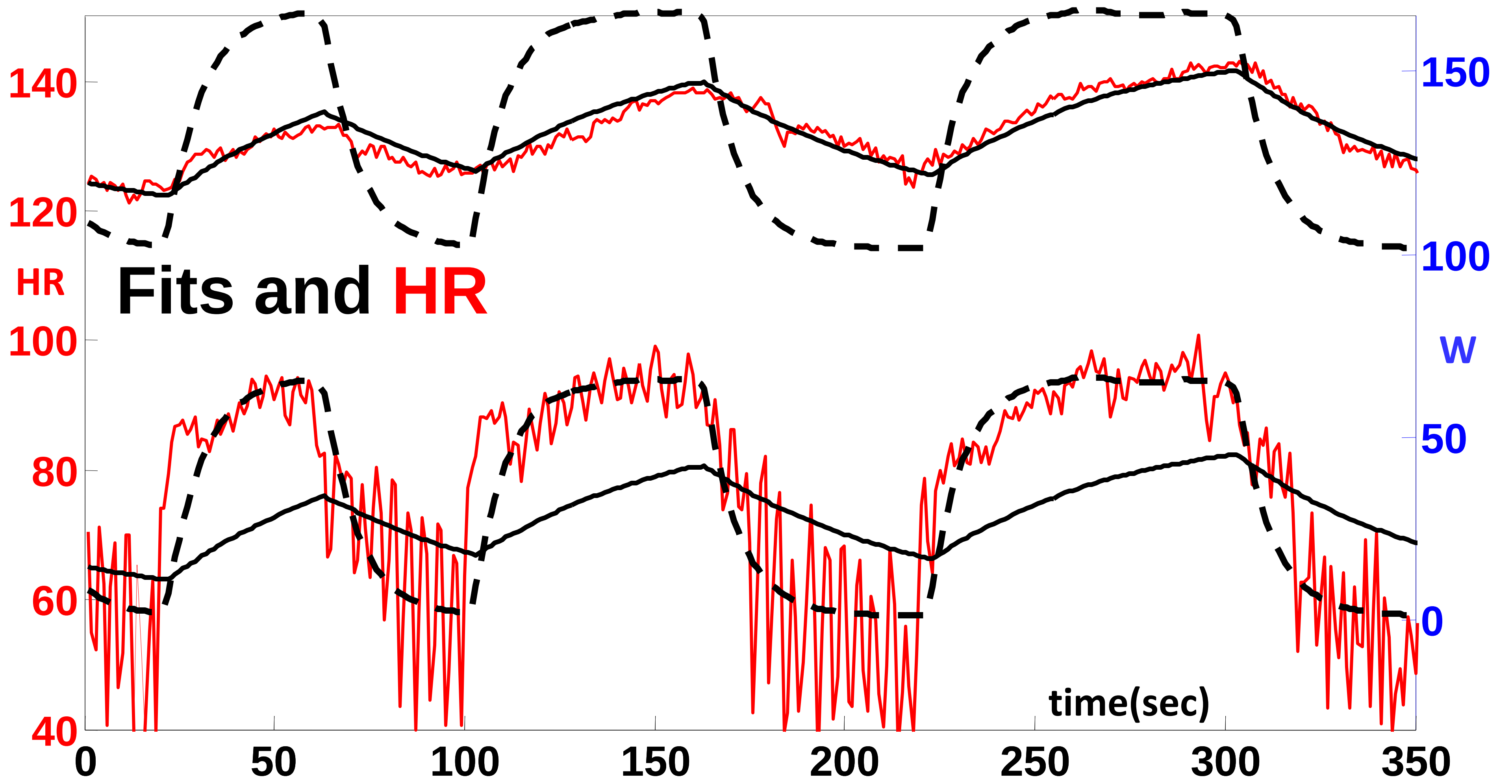


poor fit @ low watts

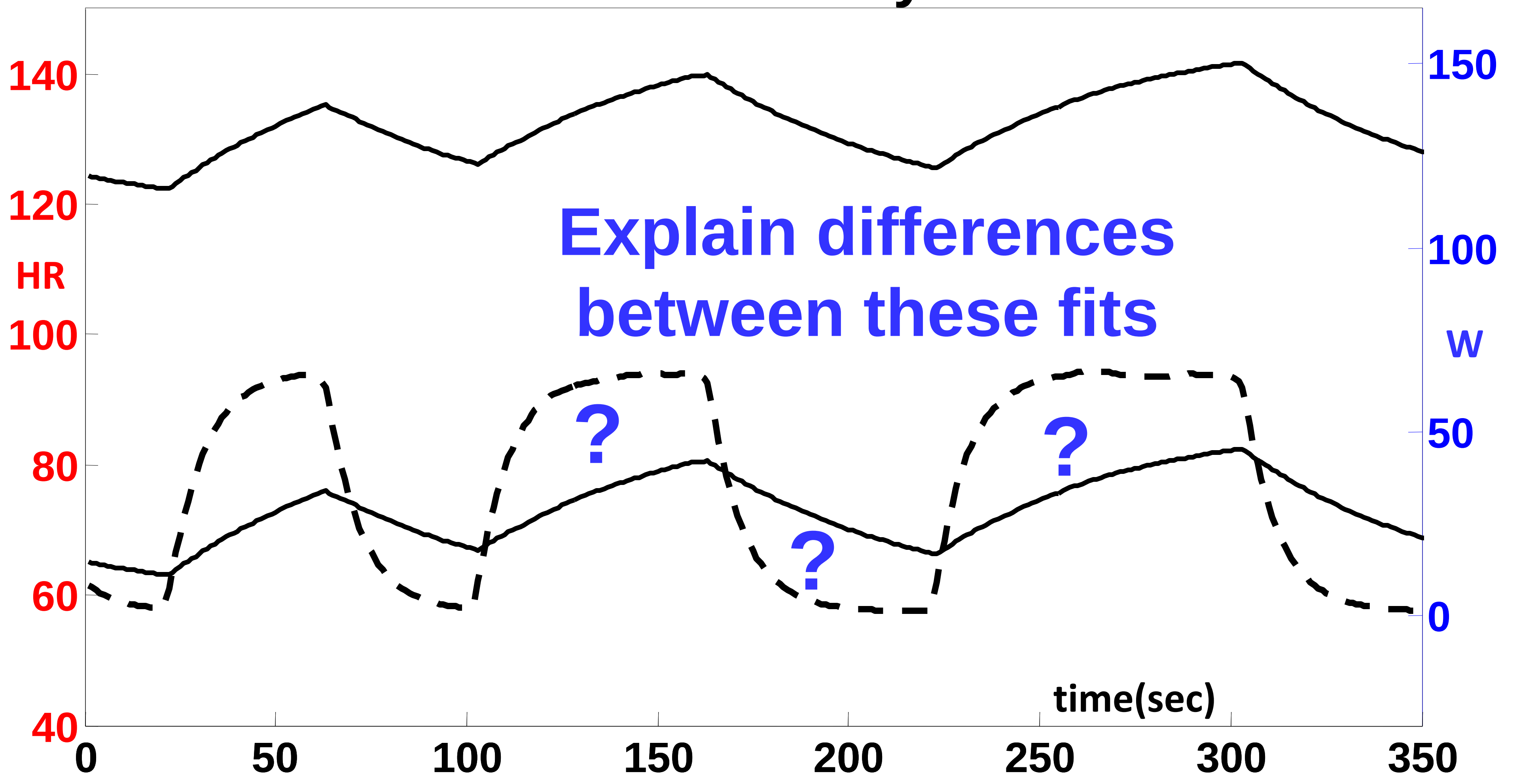


Two different 1st order linear fit(s)



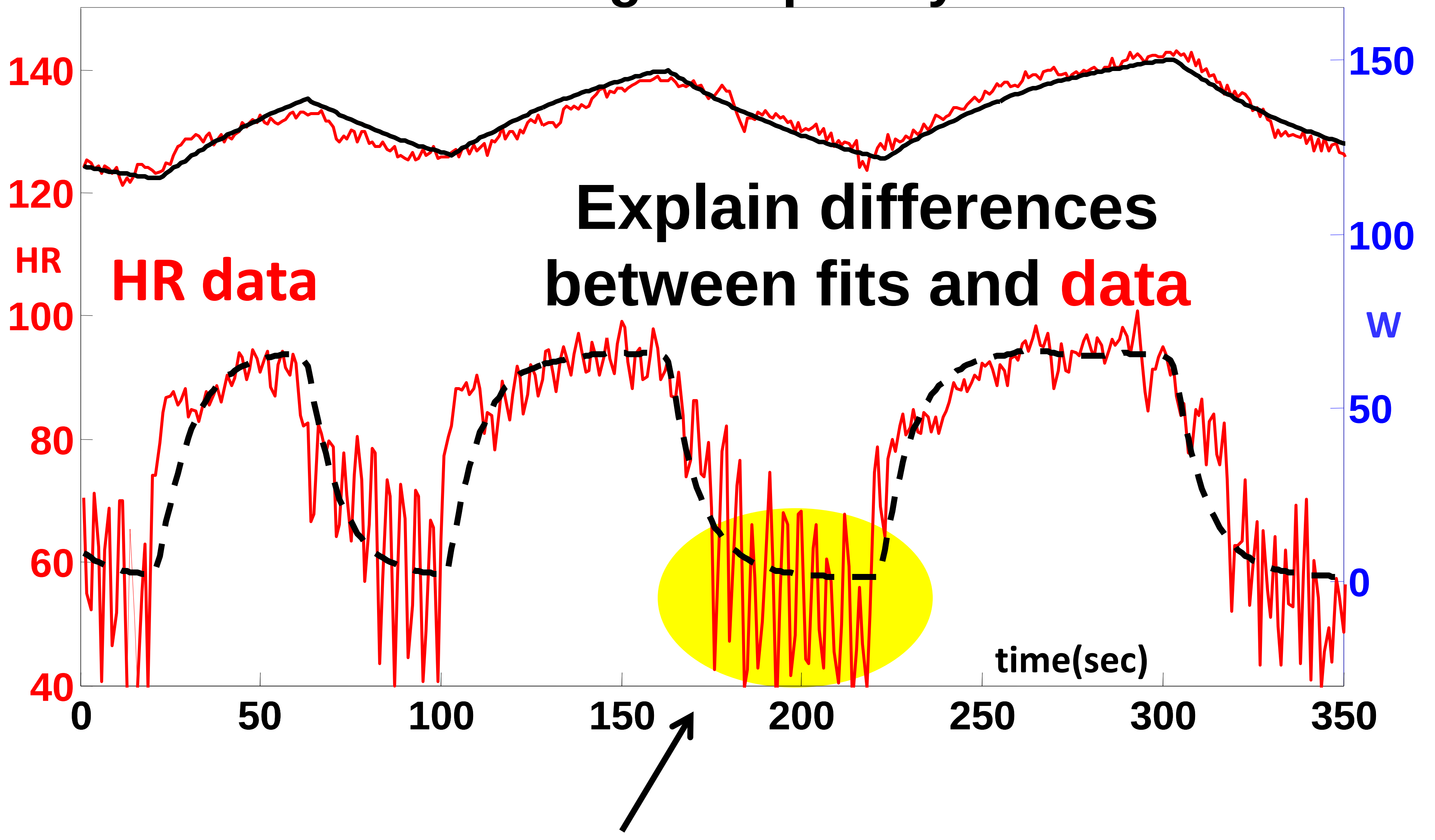
Two different 1st order linear fit(s)

Nonlinearity



Both static (steady state) and dynamic

High frequency



Lower mean, higher variability

Thanks to

Theory/tools

- Na Li (→Harvard)
- Jerry Cruz
- Somayeh Sojoudi
- Simon Chien
- Ben Recht (→UCB)

Equipment

- Philips

~~*Science Trans Med*~~ &

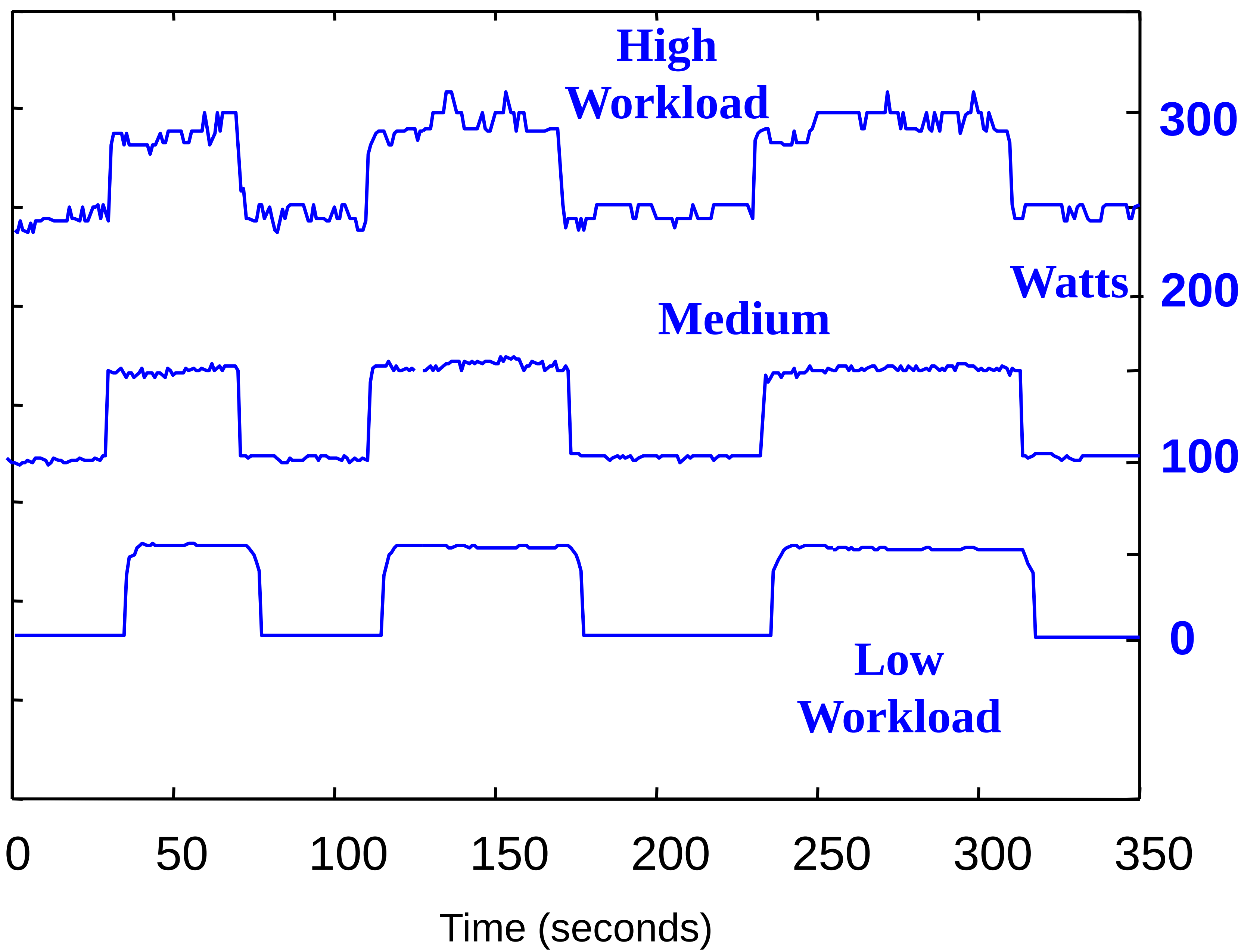
Anonymous reviewers

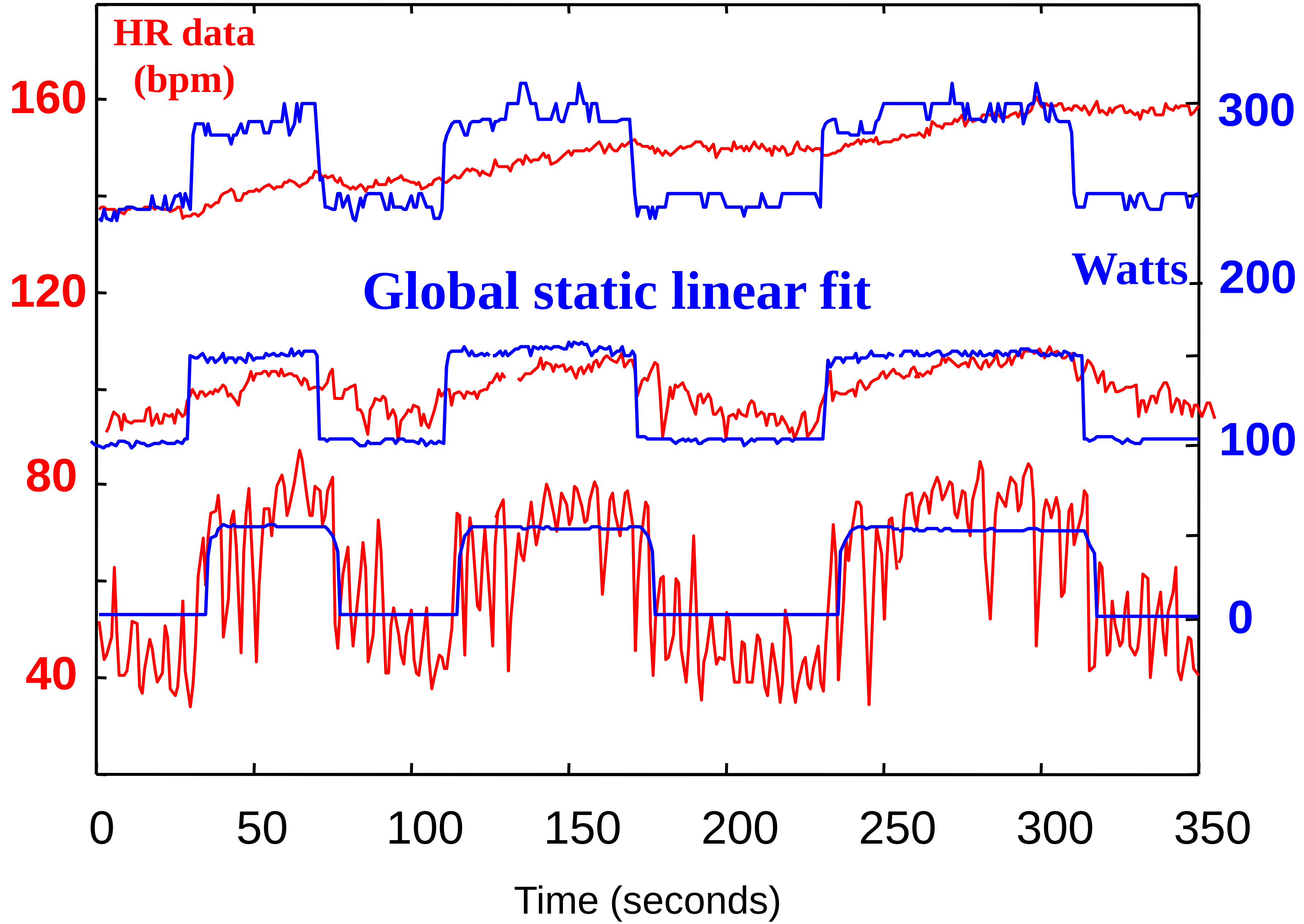
Medical

- Marie Csete MD PhD
- David Stone MD
- Dan Bahmiller MD
- SCAI and ICCAI

Funding

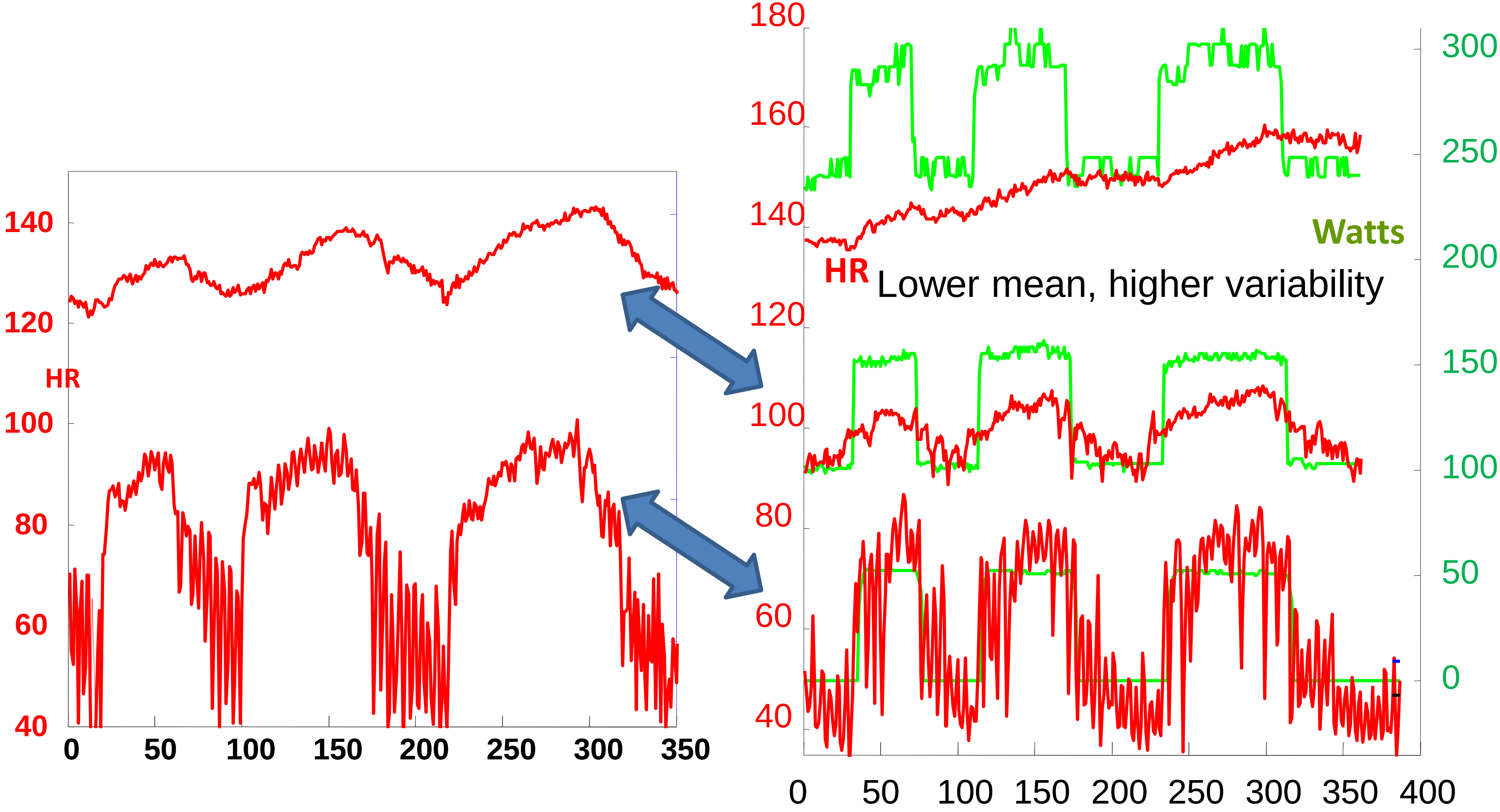
- ~~NIH~~
- ~~Army~~
- ~~Pfizer~~
- Braun family
- AFOSR/NSF


High
Workload
Medium
Low
Workload
Watts
300
200
100
0
0
50
100
150
200
250
300
350
Time (seconds)



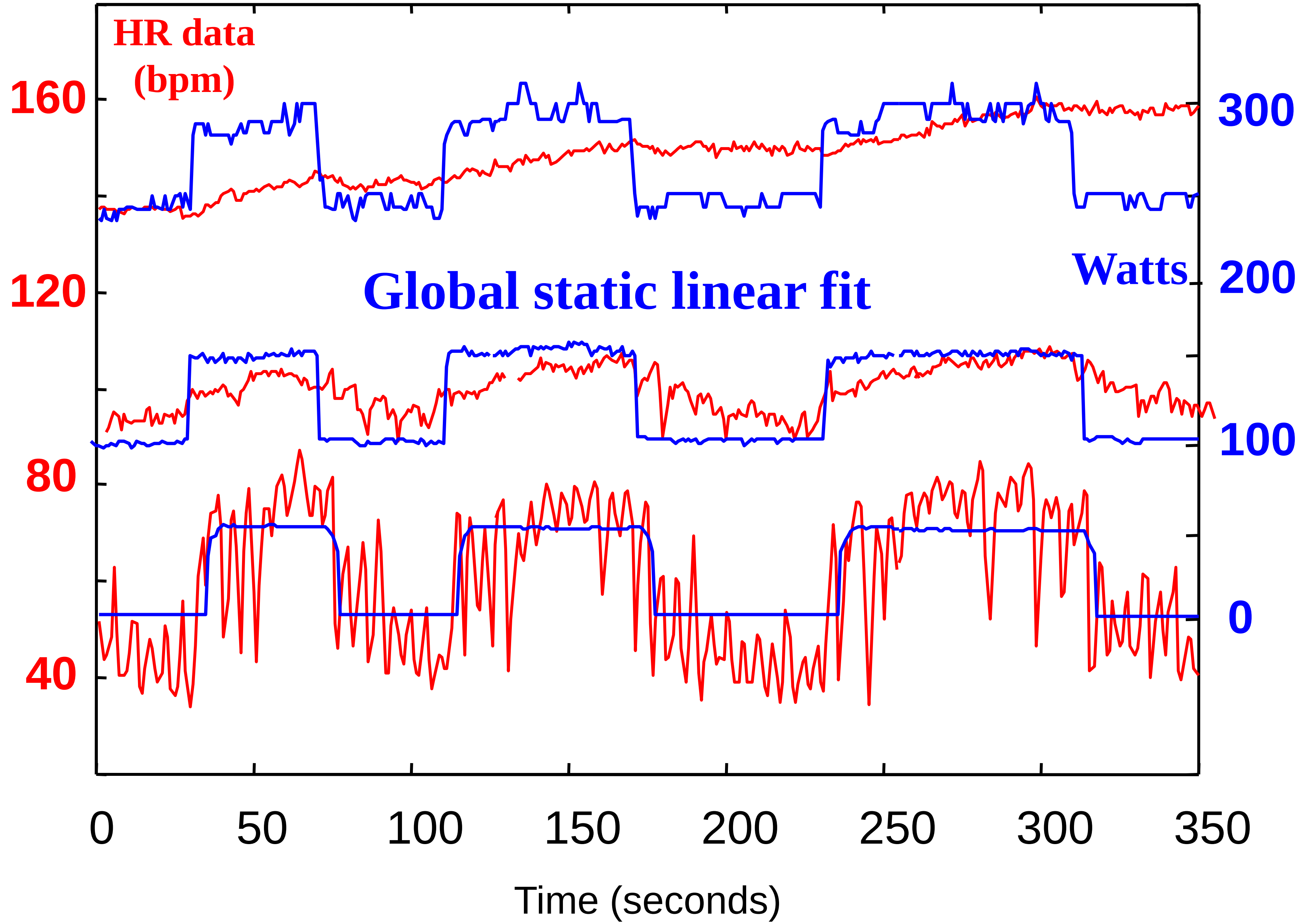
HR data (bpm)
160
120
80
40
Global static linear fit
Watts
300
200
100
0
0
50
100
150
200
250
300
350
Time (seconds)

Shift so HR units are same

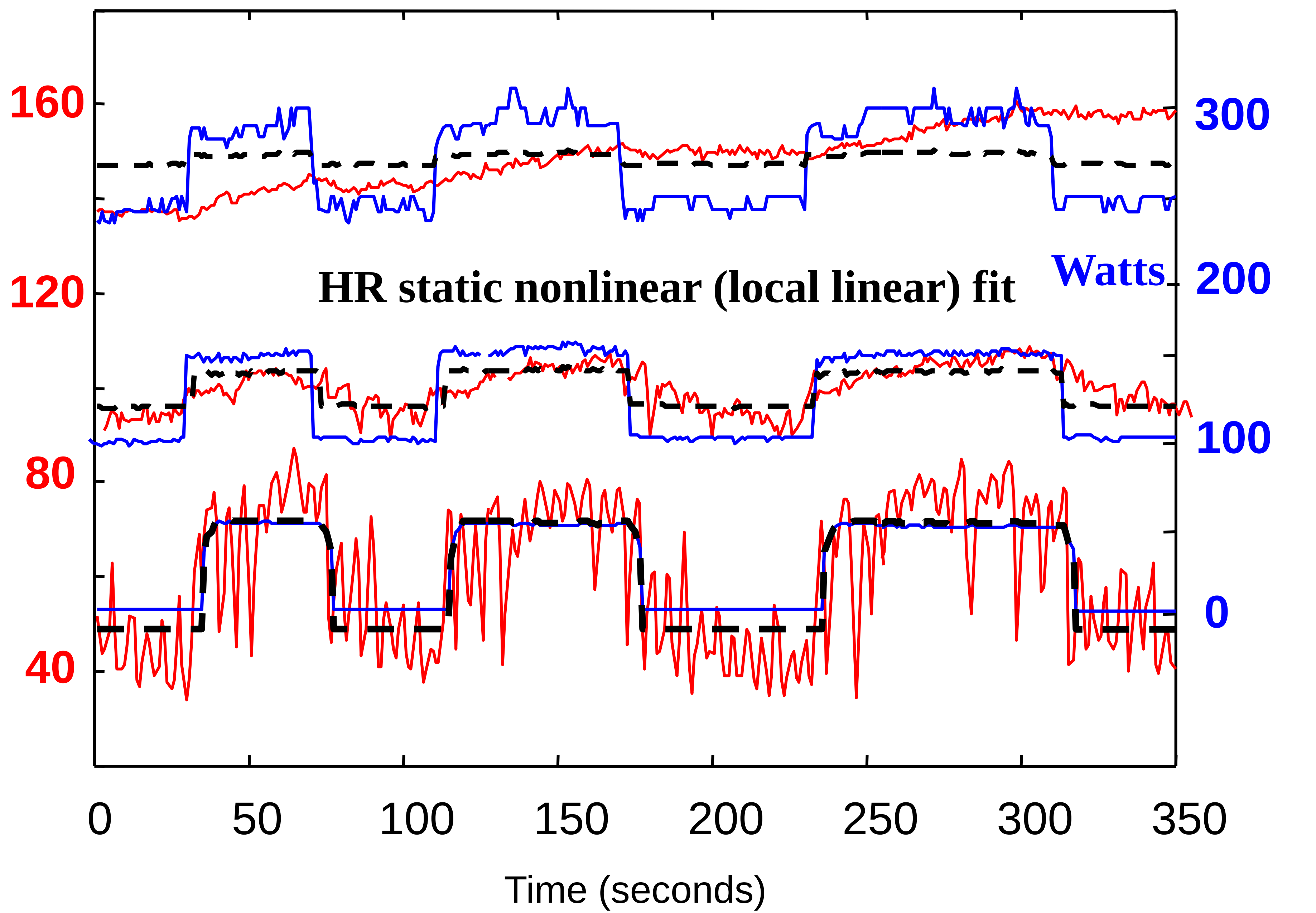


Subject 1

Subject 2

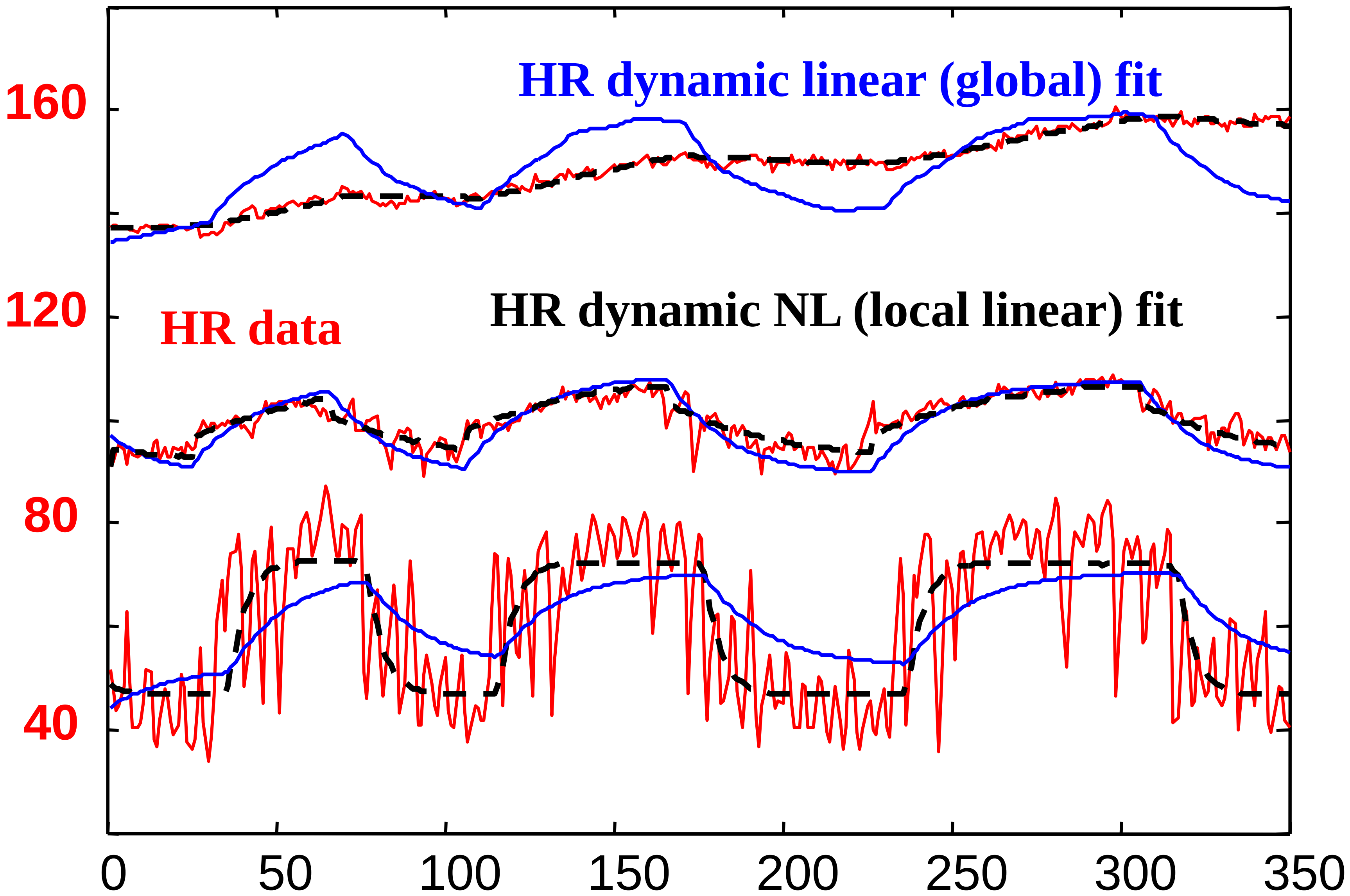


HR data
(bpm)
160
120
80
40
300
200
100
0
Watts
Global static linear fit
0
50
100
150
200
250
300
350
Time (seconds)

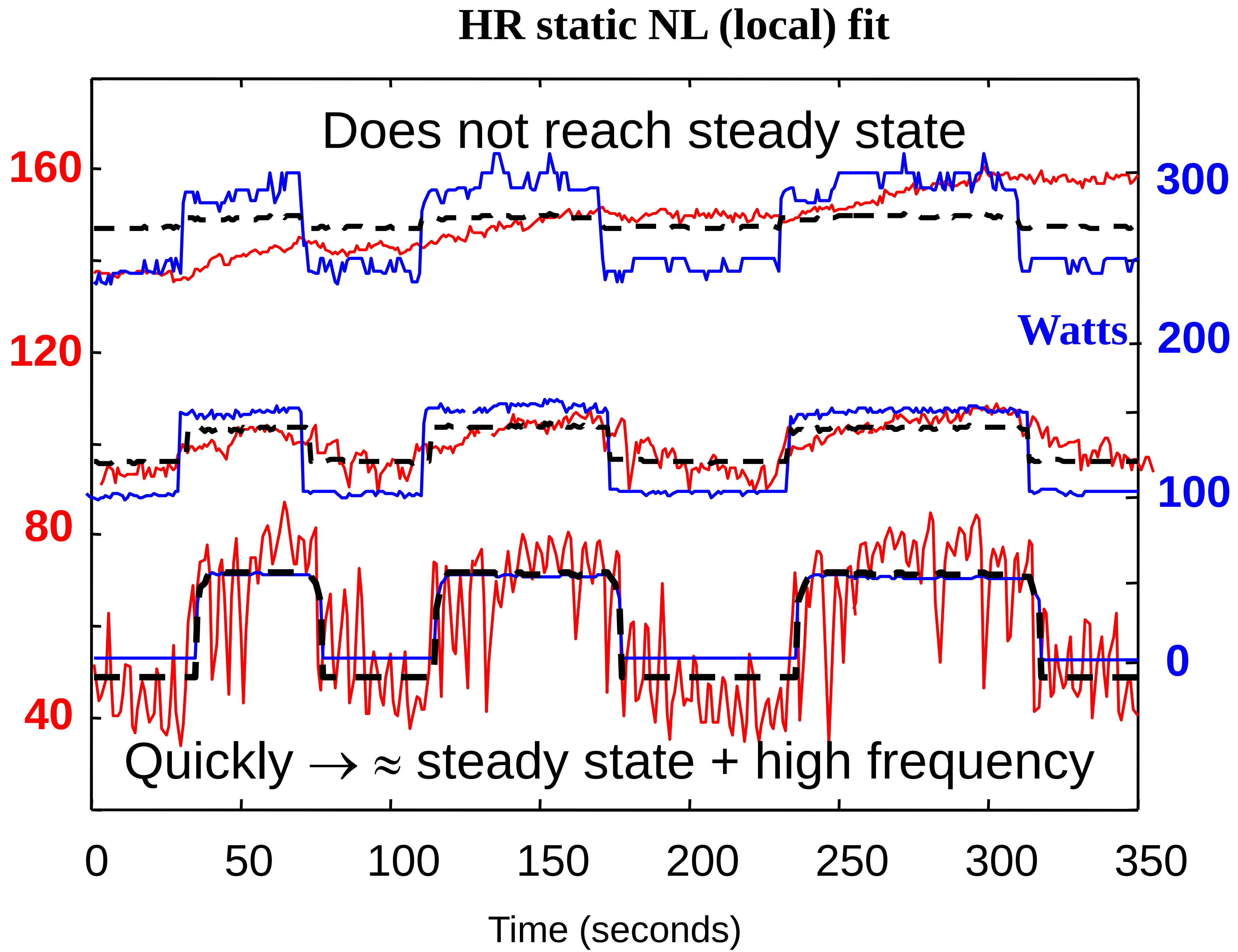


160
120
80
40
300
200
100
0
Watts
HR static nonlinear (local linear) fit
0
50
100
150
200
250
300
350
Time (seconds)

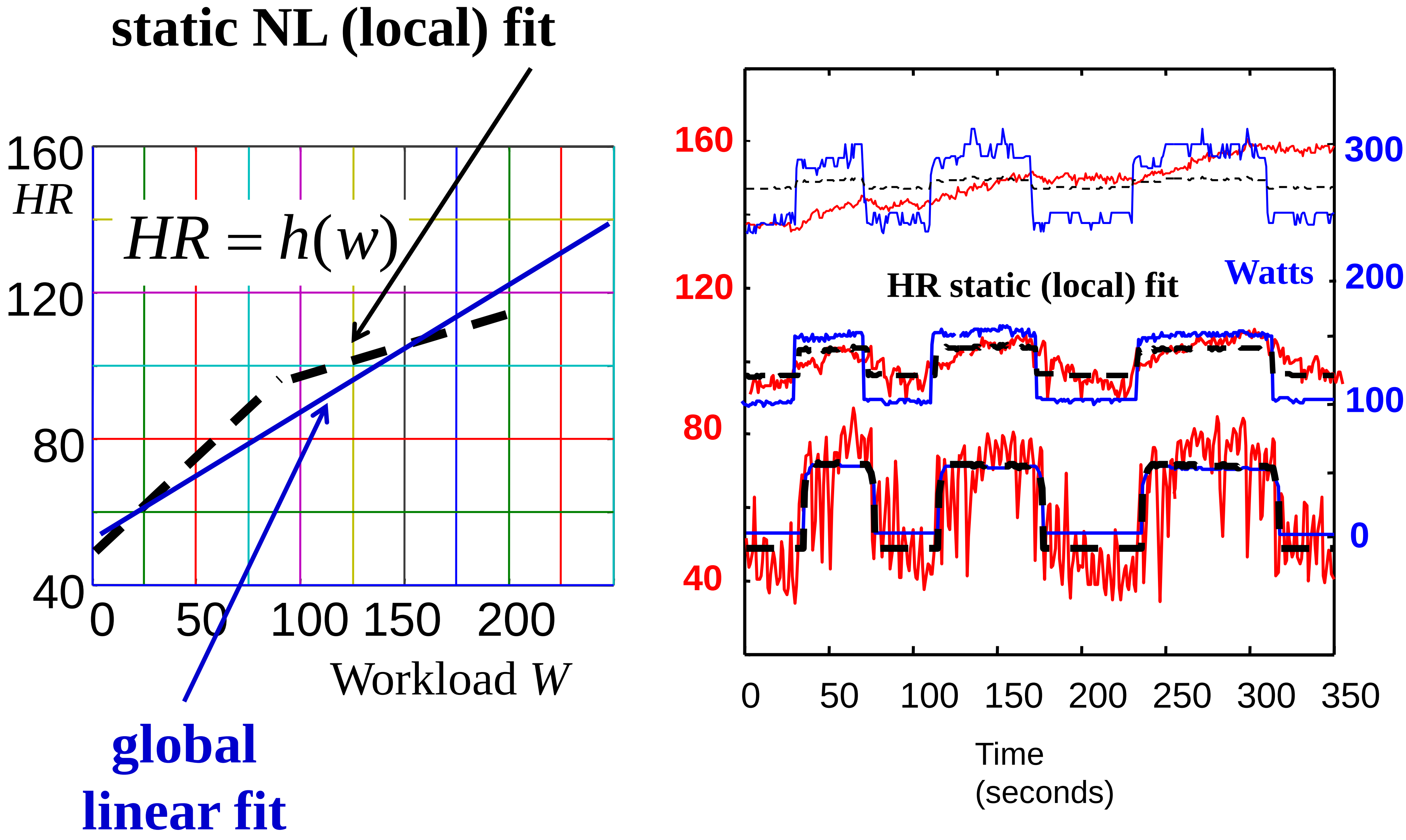
1st order linear model



$$\Delta h(t) = h(t+1) - h(t) = ah(t) + bw(t) + c$$

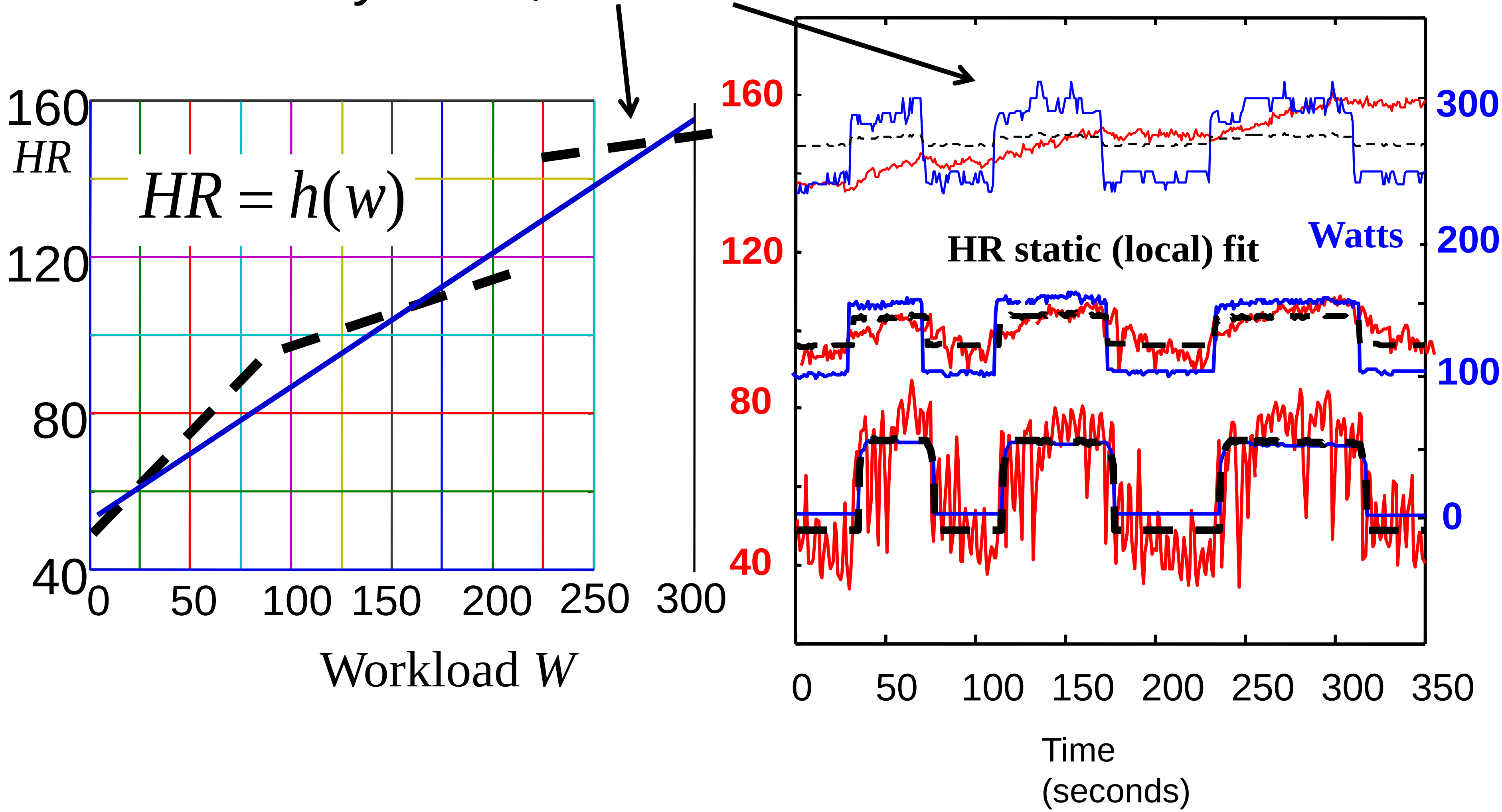


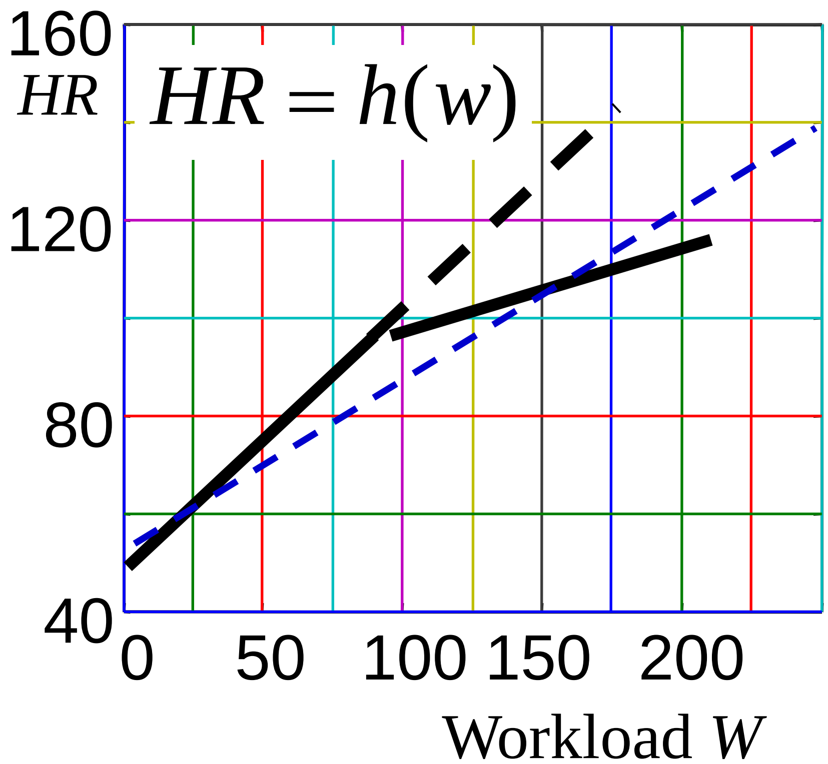
HR static NL (local) fit
Does not reach steady state
Quickly → ≈ steady state + high frequency
160
120
80
40
300
200
100
0
Watts
0
50
100
150
200
250
300
350
Time (seconds)

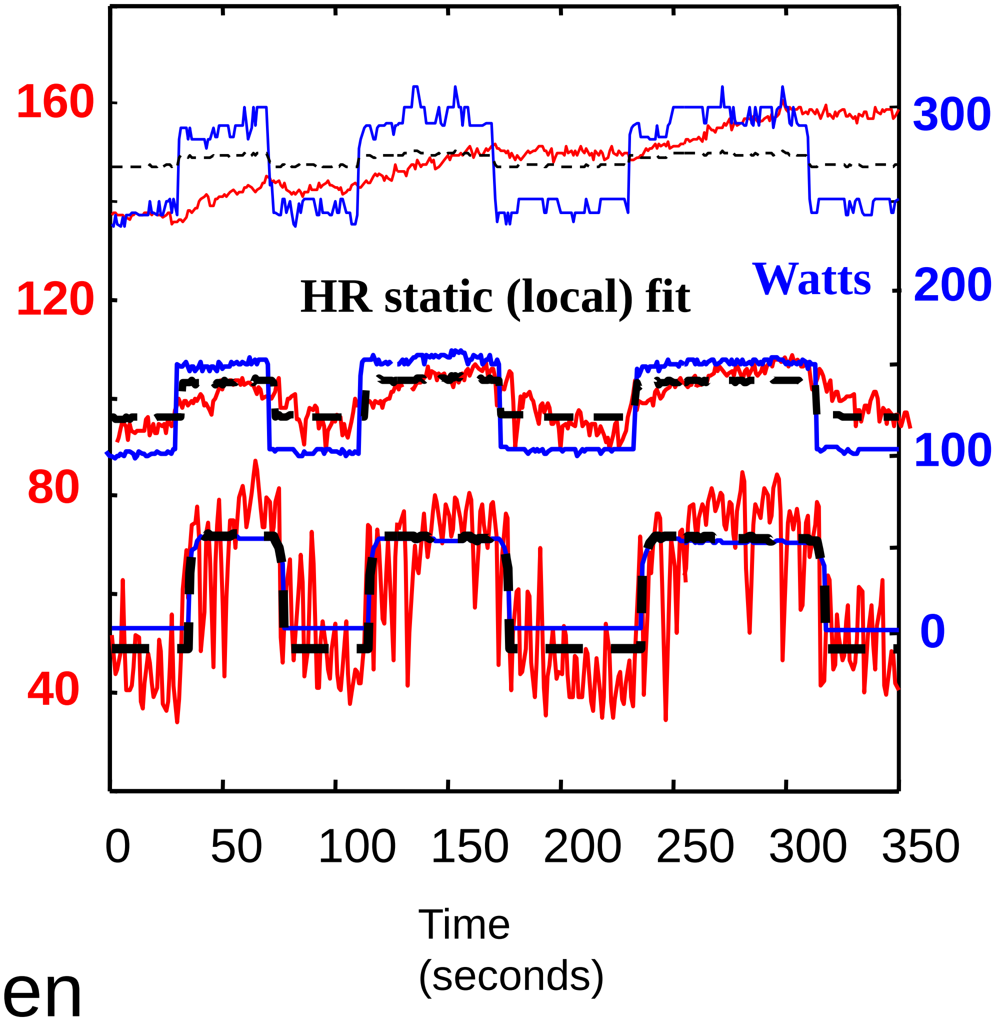


static NL (local) fit
160
HR
120
80
40
$HR = h(w)$
0
50
100 150
200
Workload W
global
linear fit
HR static (local) fit
Watts
160
120
80
40
300
200
100
0
0
50
100
150
200
250
300
350
Time
(seconds)

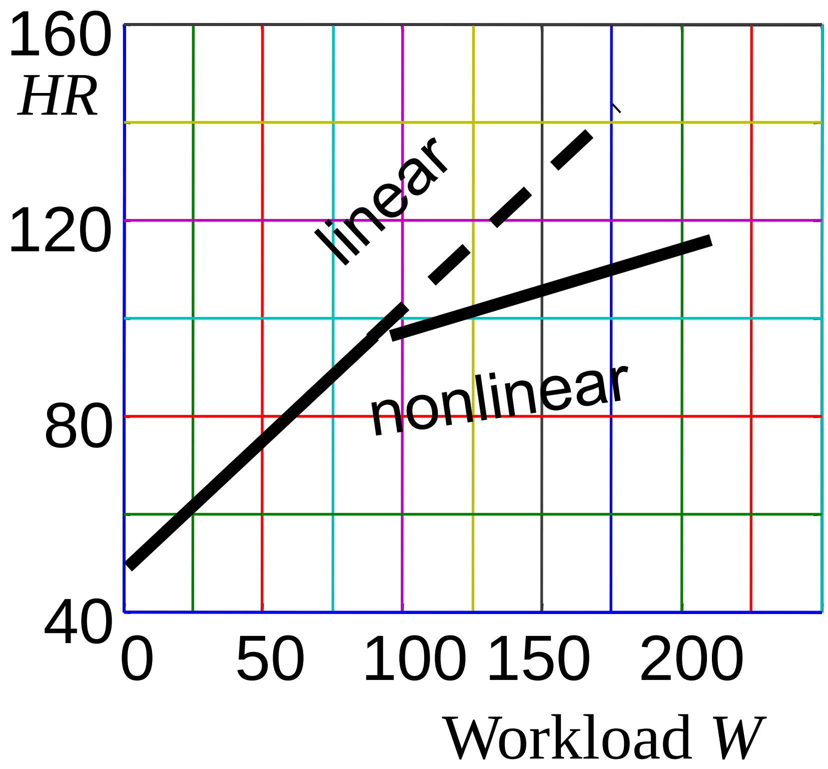
Not steady state, defer for now

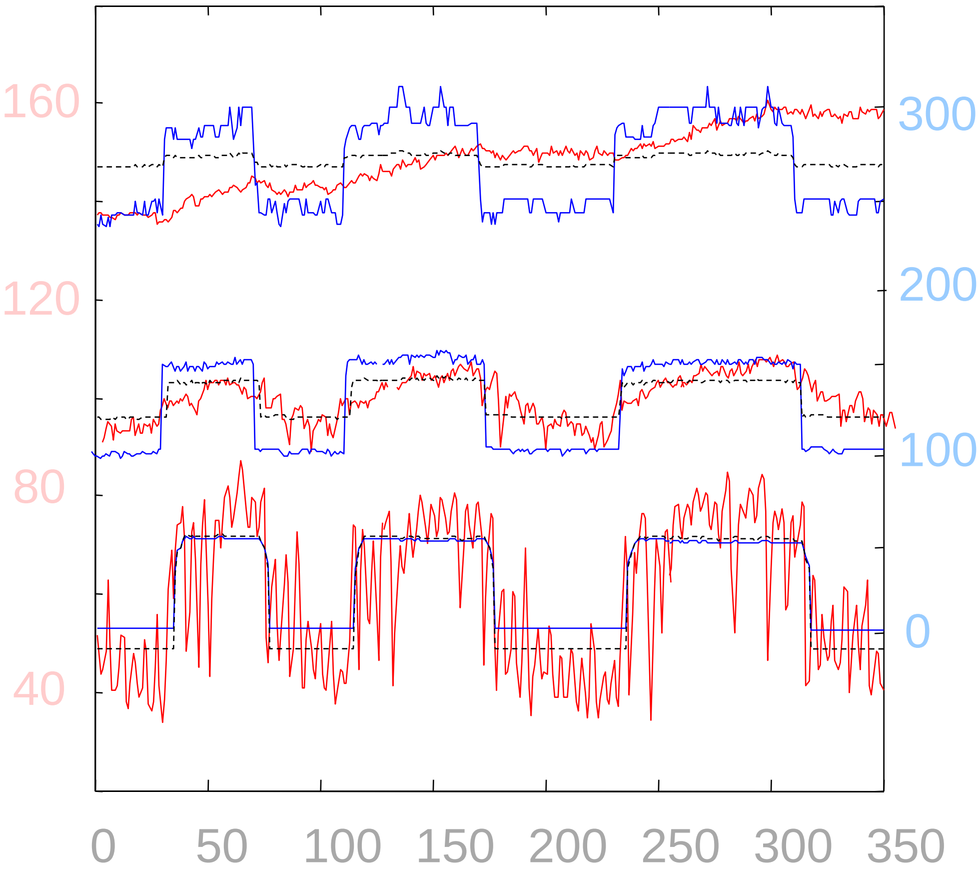




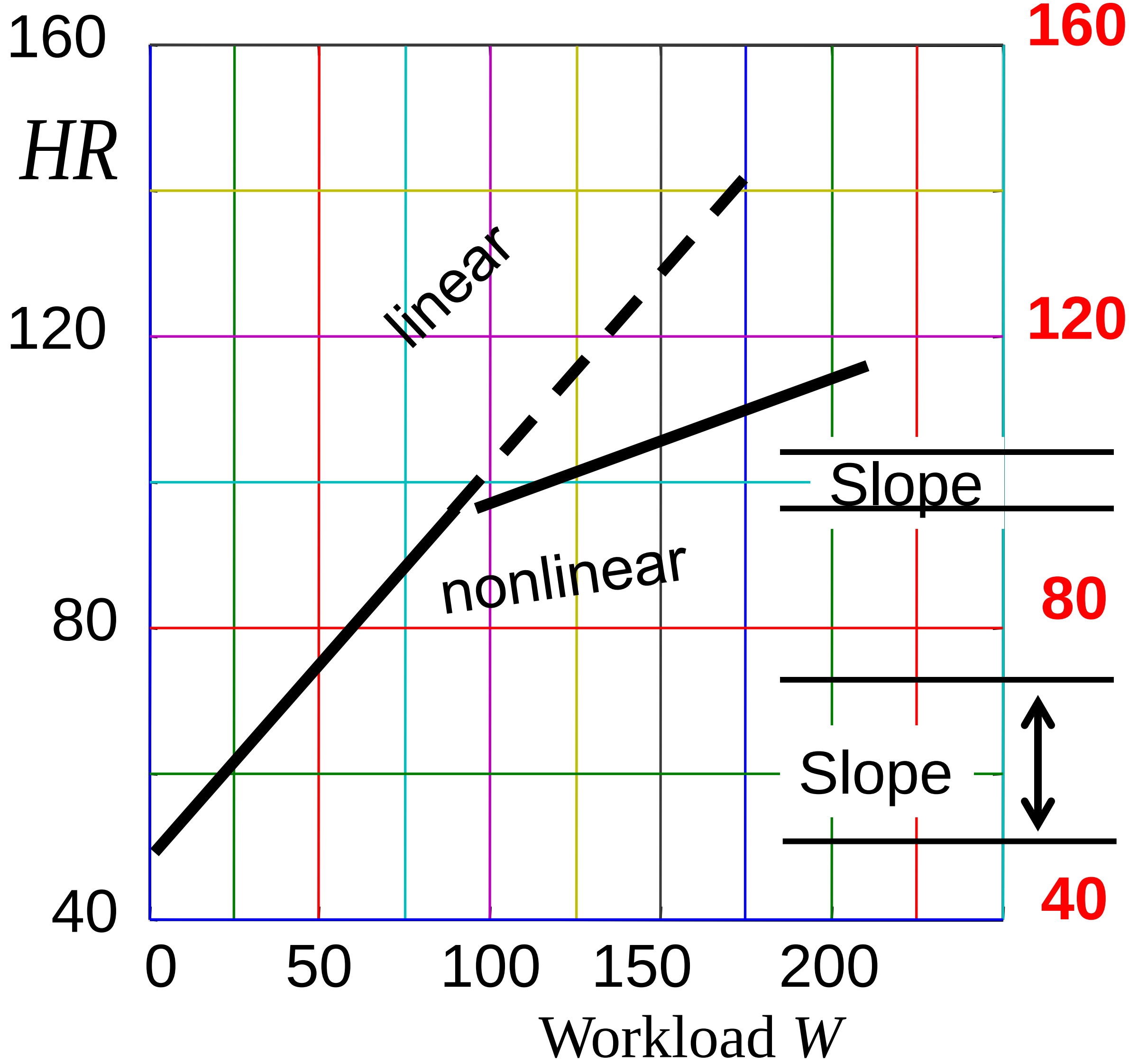


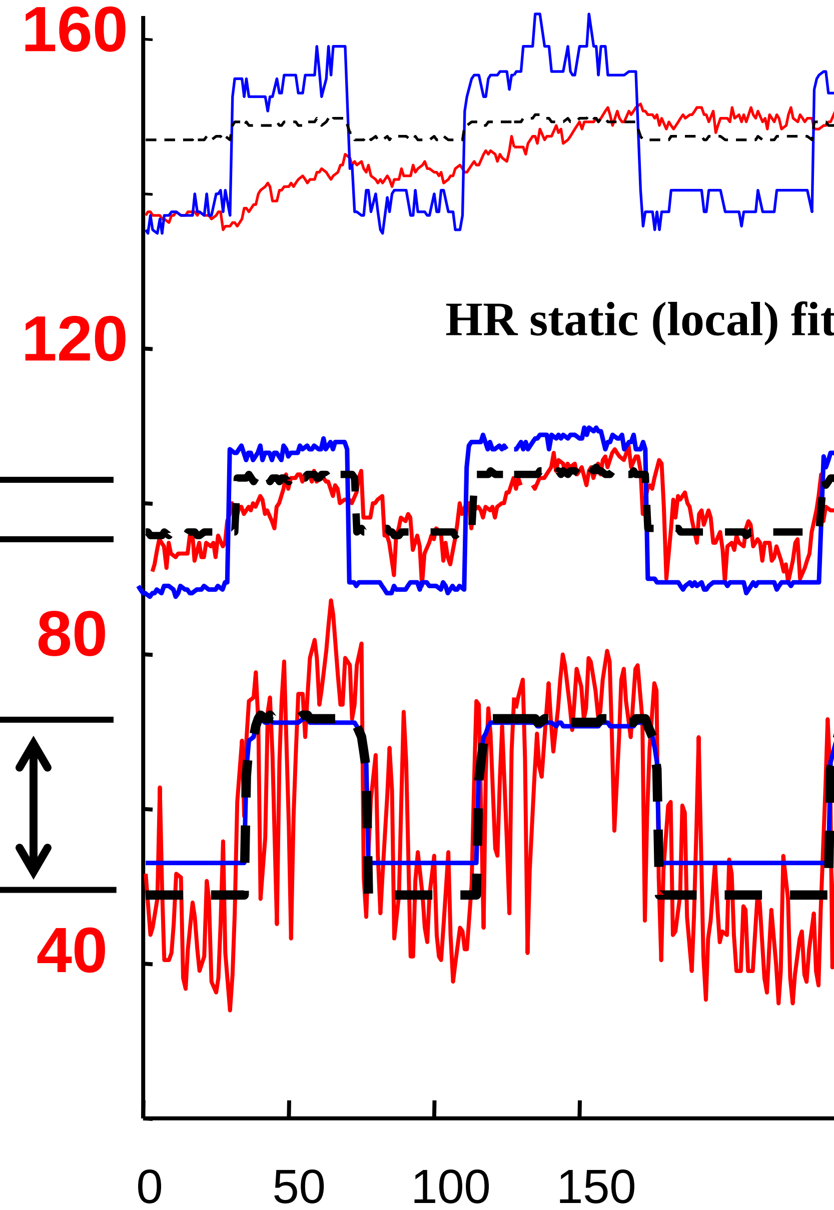
Focus on contrast between
linear and **nonlinear**



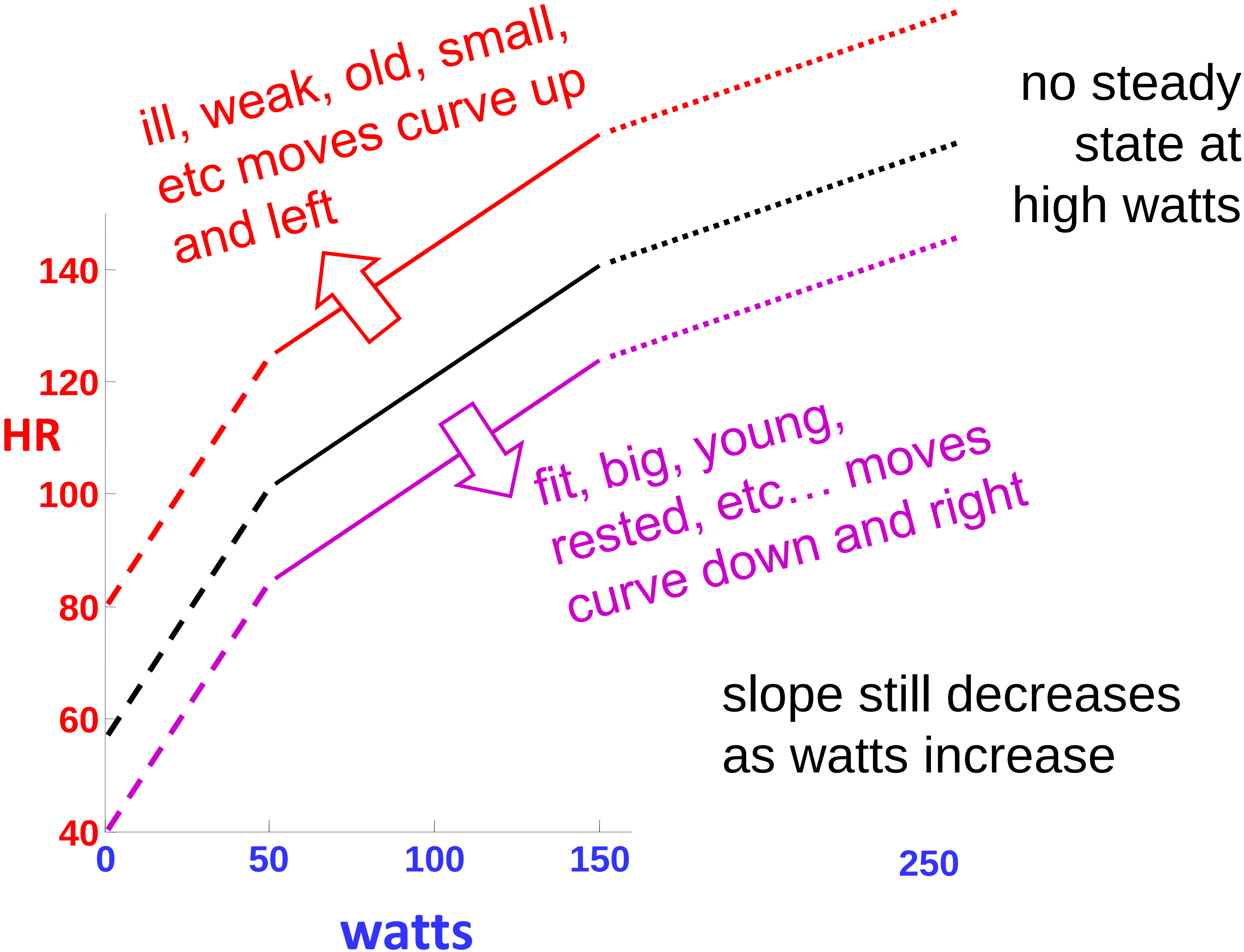


Focus on contrast between linear and nonlinear (which is a better fit to data)

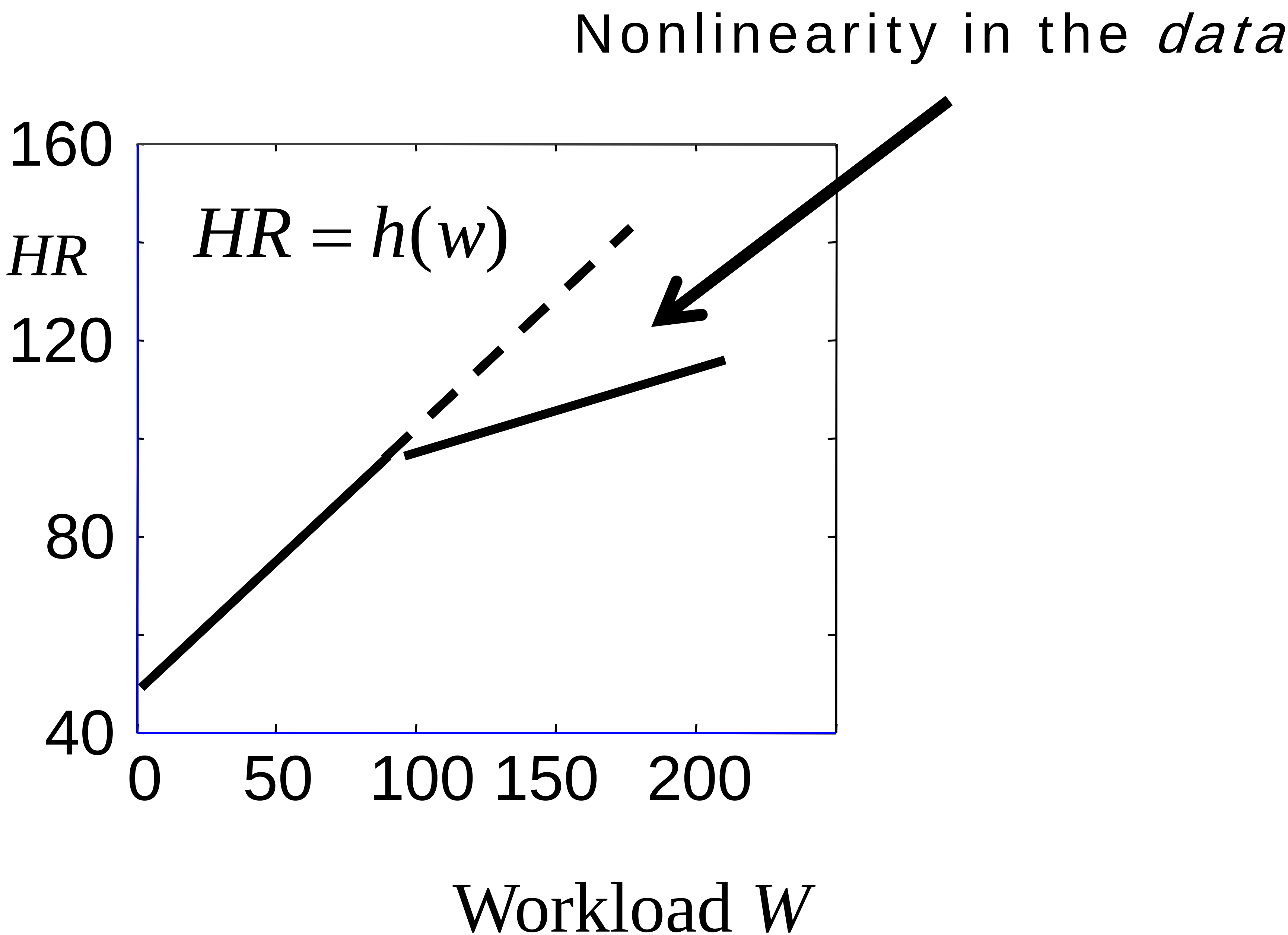




The simplest case of changing HRV, mean ↑ and variability ↓



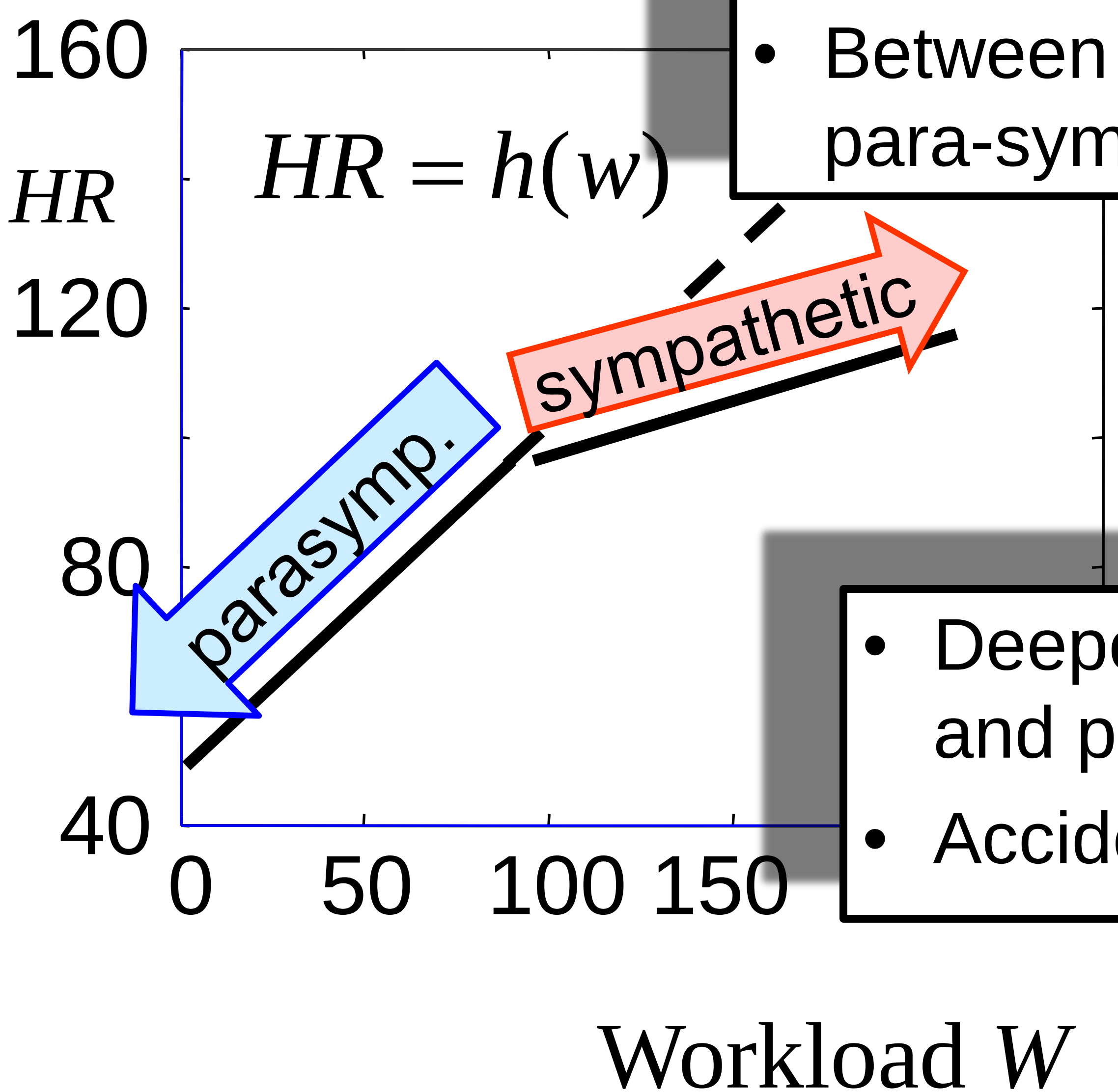
ill, weak, old, small, etc moves curve up and left
no steady state at high watts
fit, big, young, rested, etc… moves curve down and right
slope still decreases as watts increase
HR
140
120
100
80
60
40
0
50
100
150
250
watts



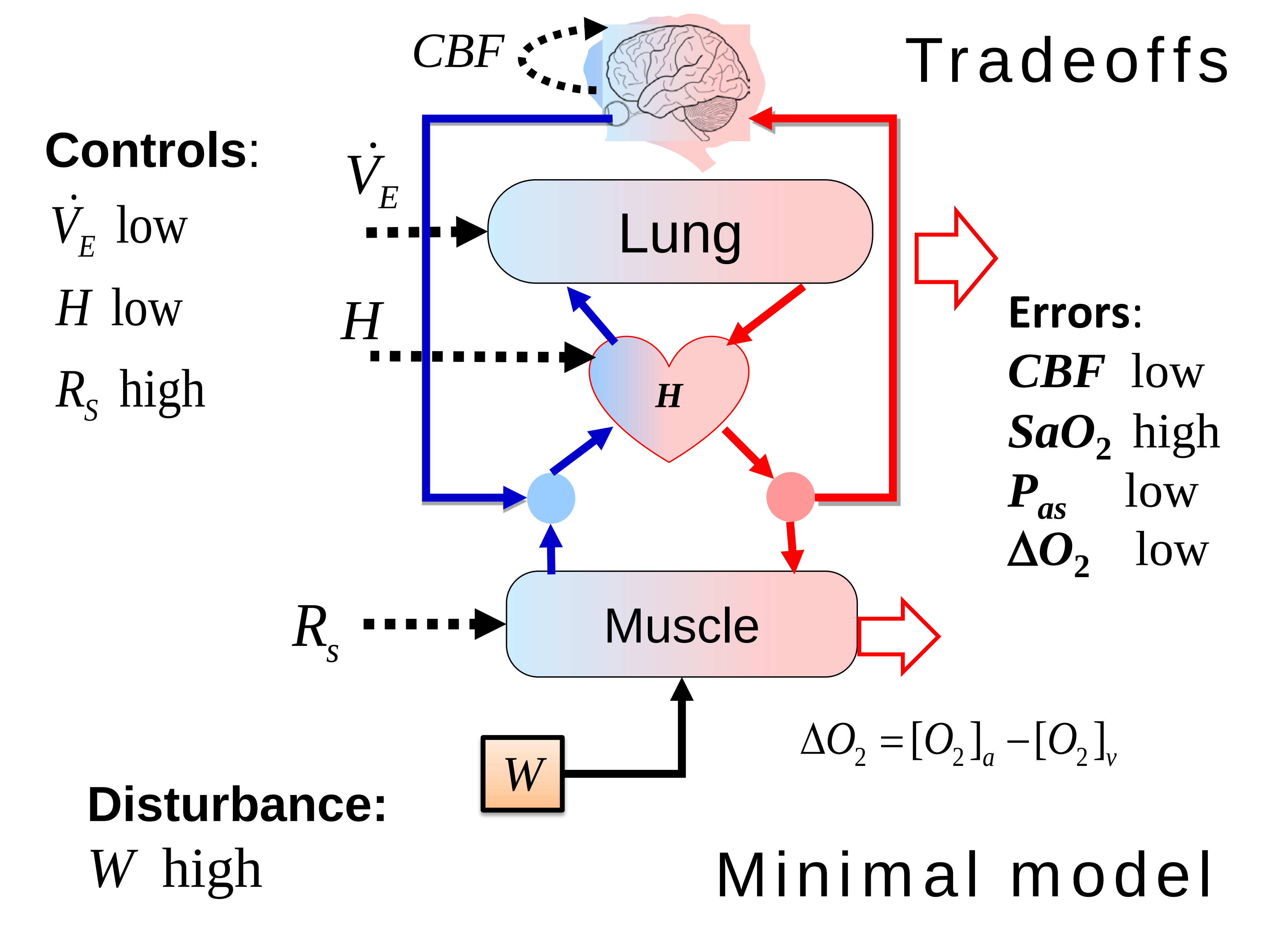
Nonlinearity in the *data*
160
HR
$HR = h(w)$
120
80
40
0
50
100
150
200
Workload W

Why?

- Proximal cause: Autonomic nervous system balance
- Between sympathetic and para-sympathetic



- Deeper why: evolution and physiology
- Accident or necessity?


Tradeoffs
CBF
Controls:
$\dot{V}_E$ low
H low
R_S high
$\dot{V}_E$
Lung
H
H
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
R_S
Muscle
W
$\Delta O_2 = [O_2]_a - [O_2]_v$
Disturbance:
W high
Minimal model

Heart as a control actuator (pump)

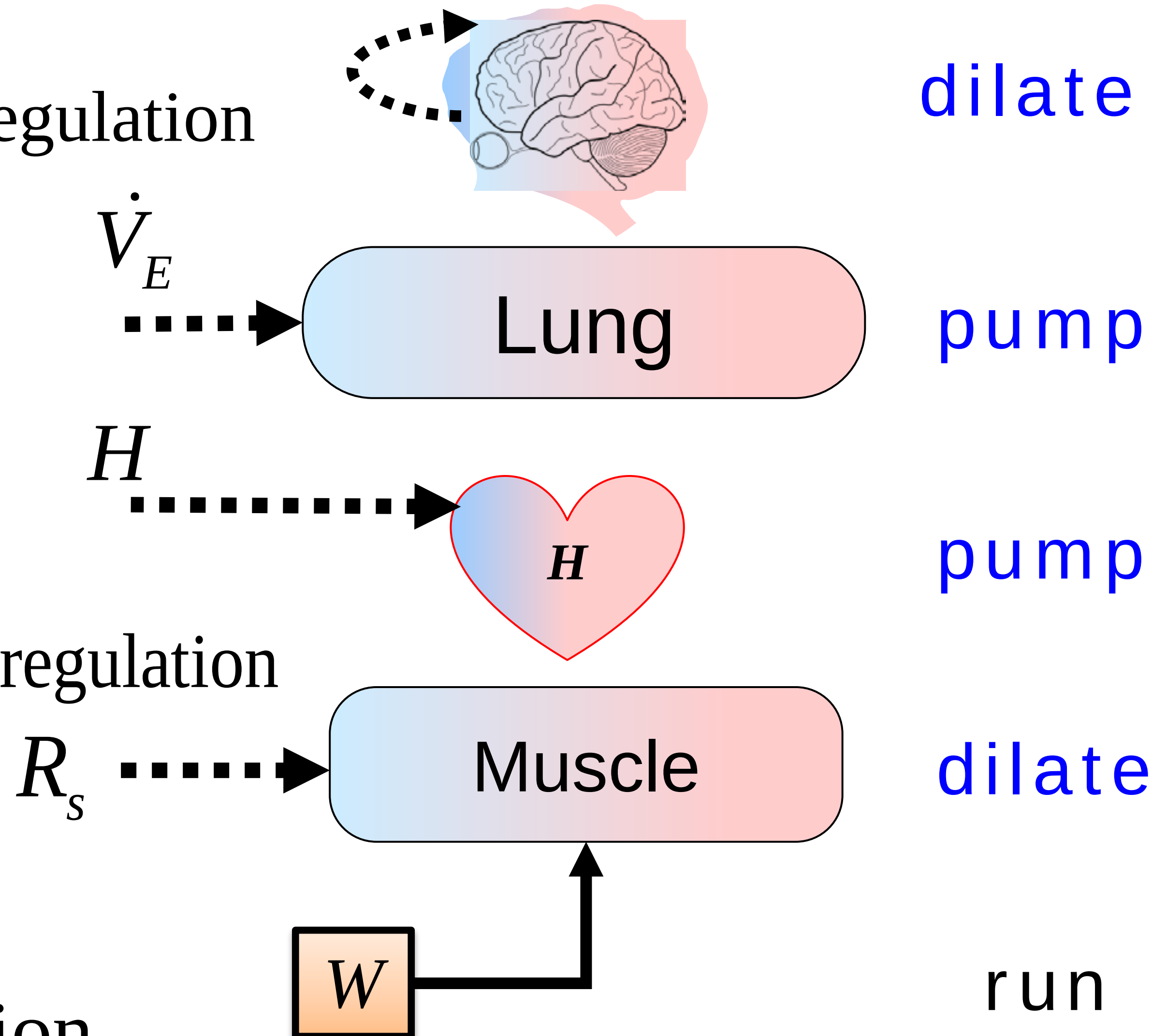
Controls:

CA cerebral autoregulation

$\dot{V}_E$ ventilation rate

H heart rate

R_S peripheral autoregulation



Disturbance:

W watt production

Healthy control = highly variable   Why?

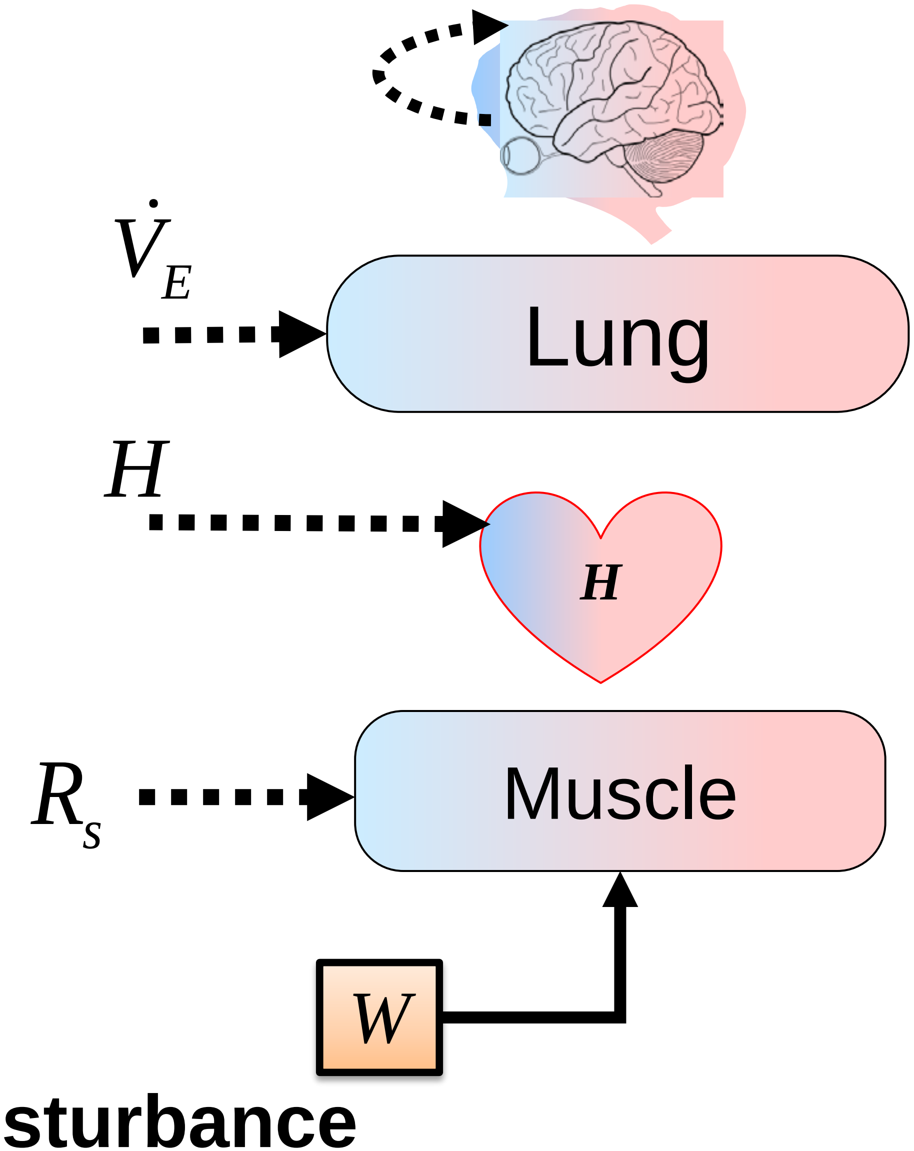
dilate

pump

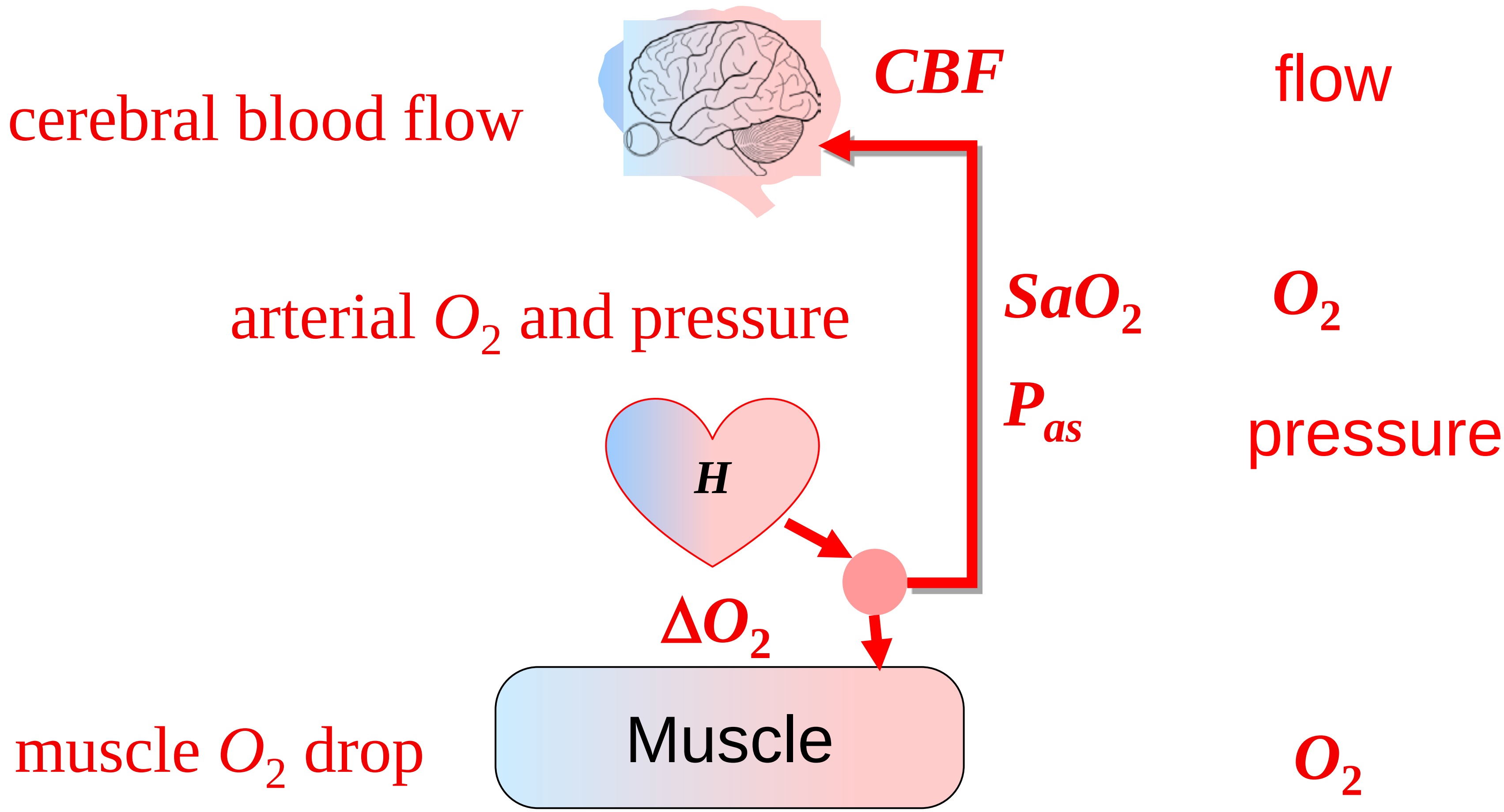
pump

dilate

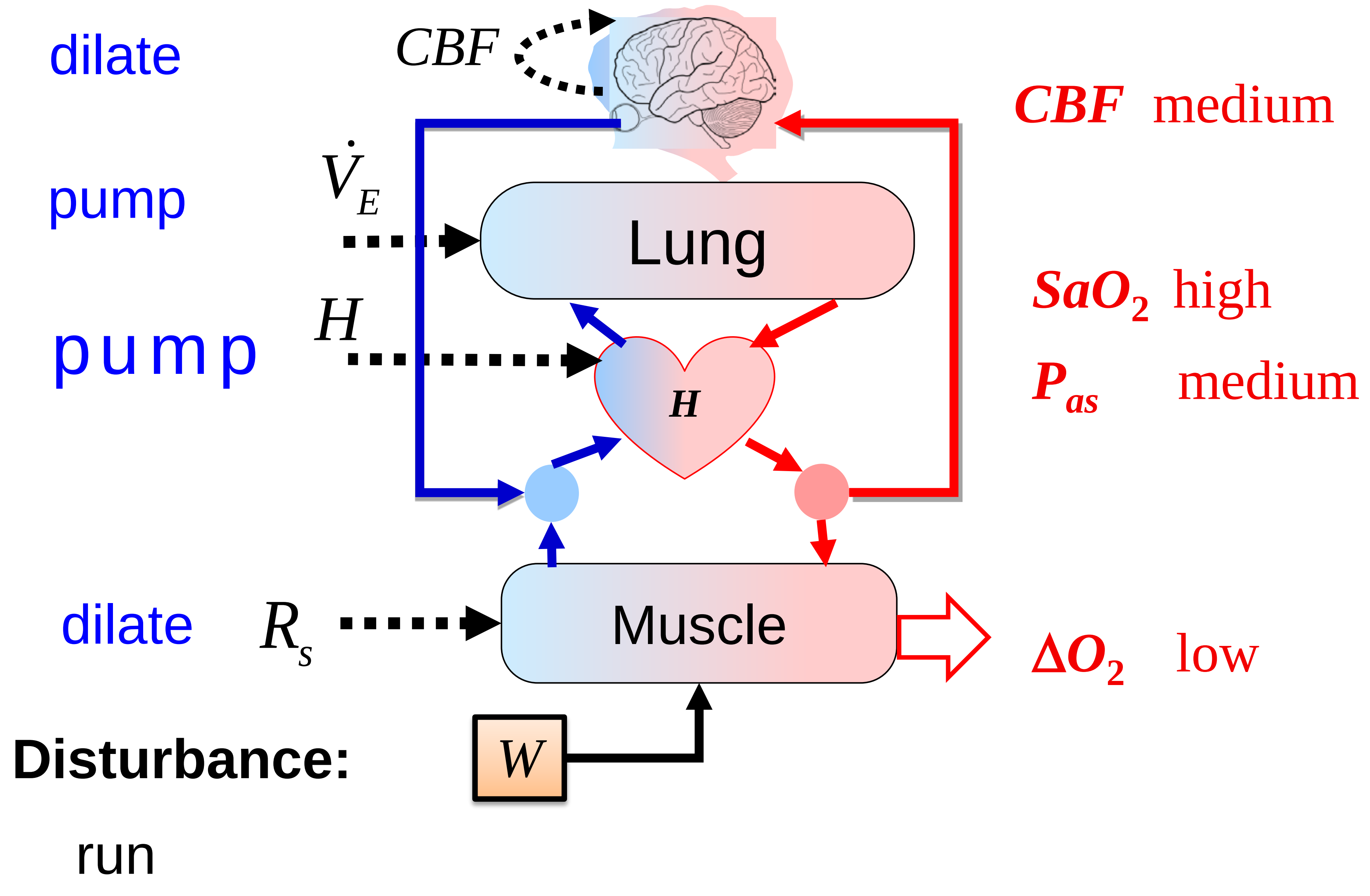
run



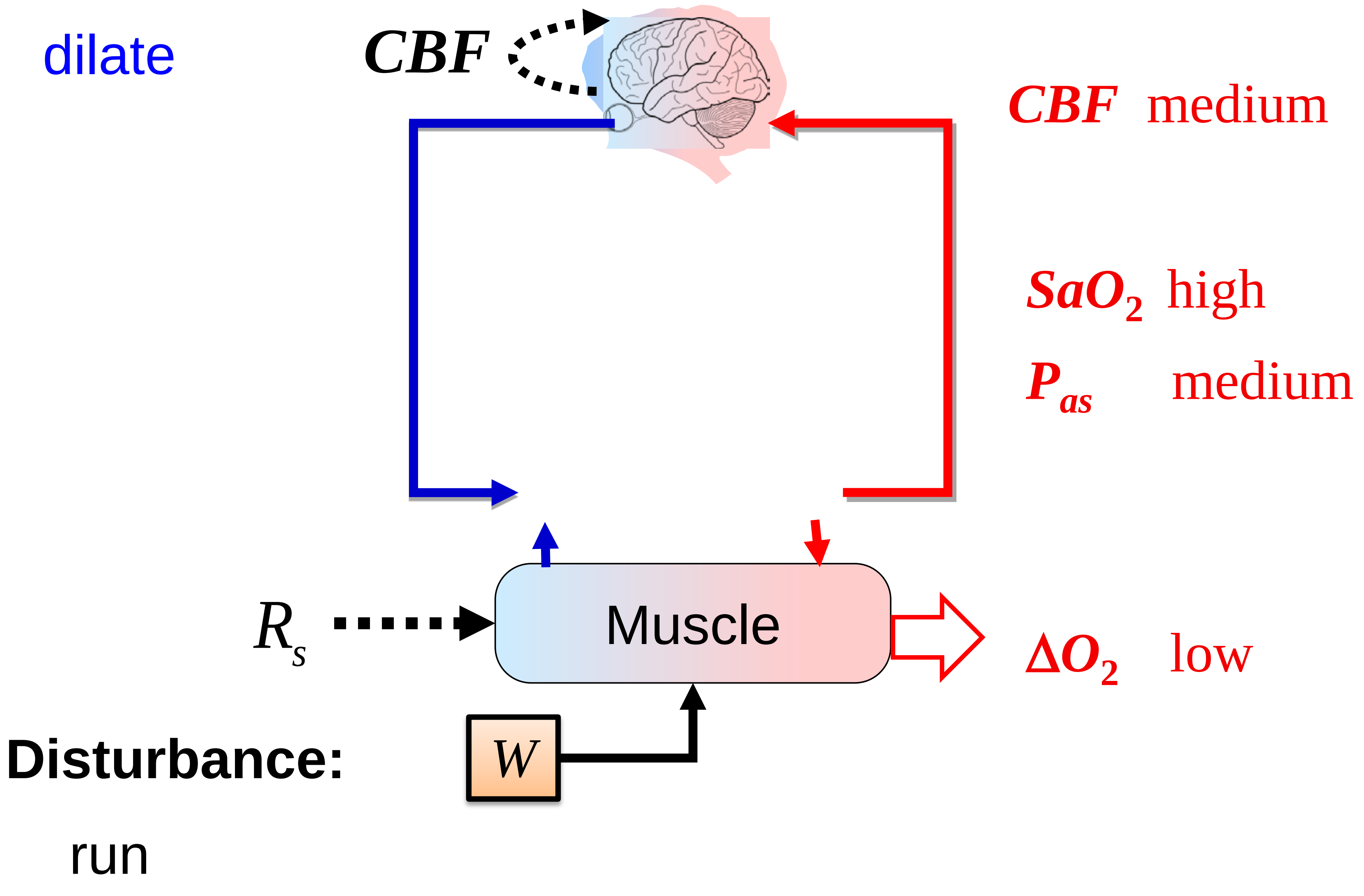
Healthy function = low variability (output)



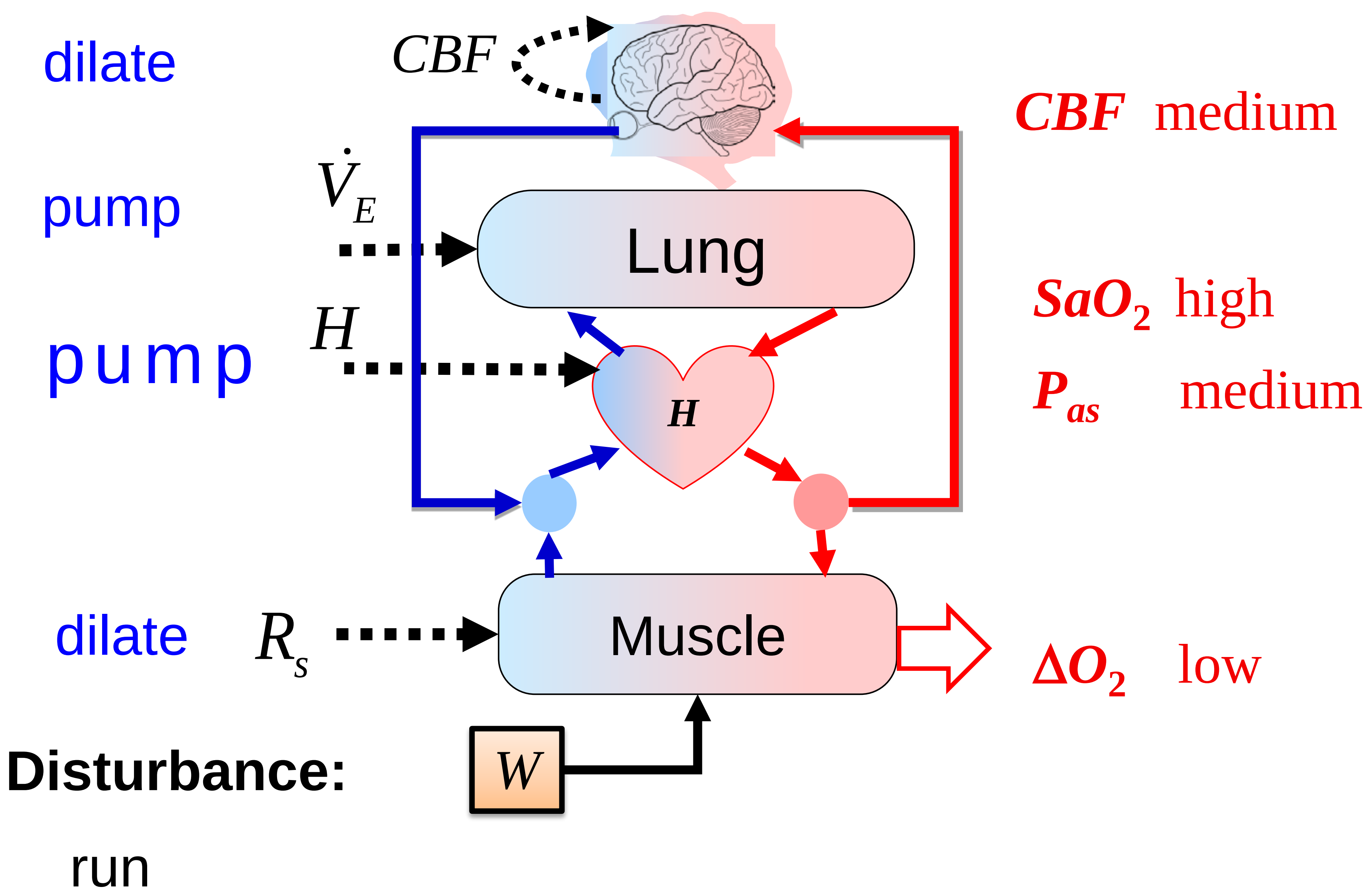
Minimal Physiology



Tradeoffs and saturations



Minimal Physiology

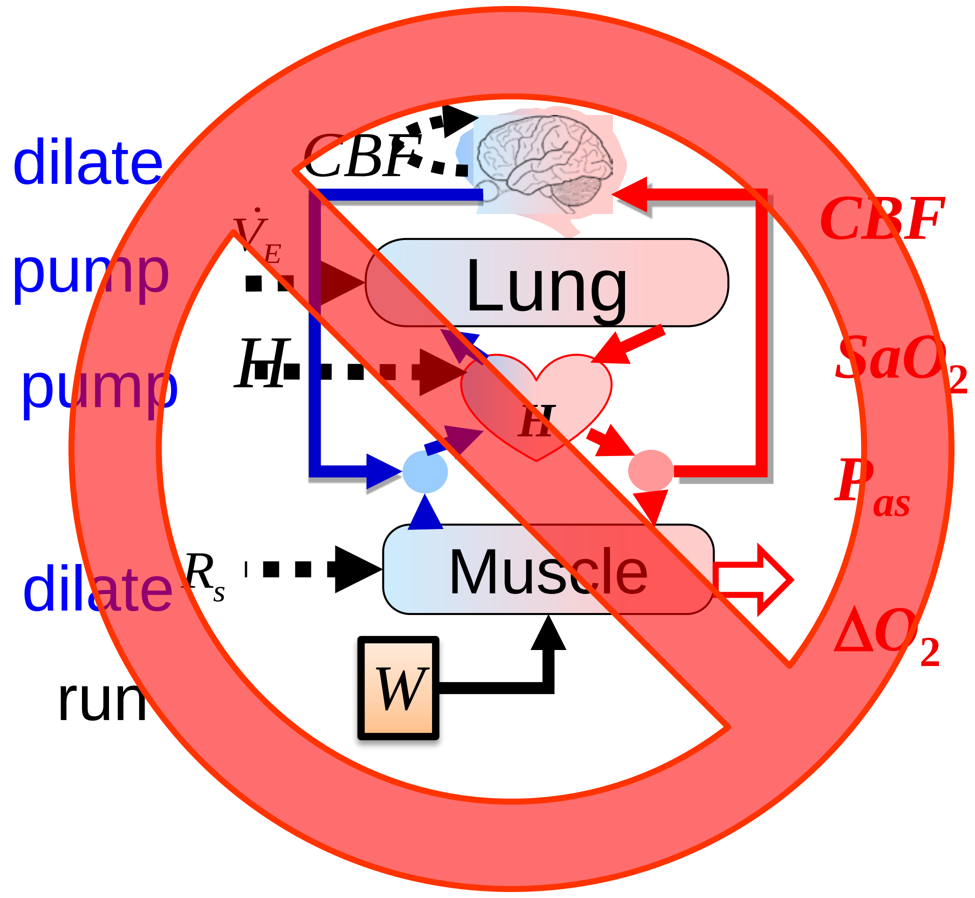


Avoiding Physiology and Math

Want a
- Nature paper
- NIH grant

Need a
- graph?
- power law?

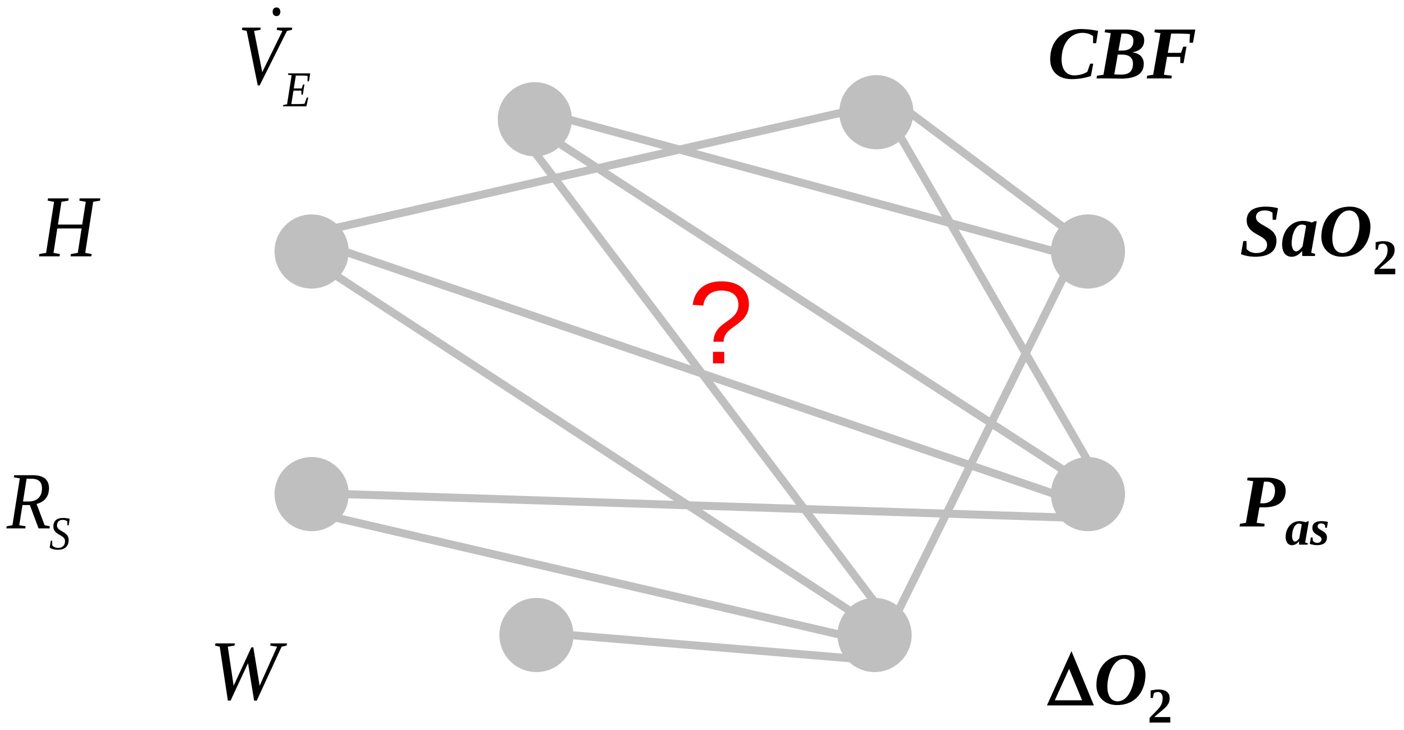
Avoid physiology
Avoid math



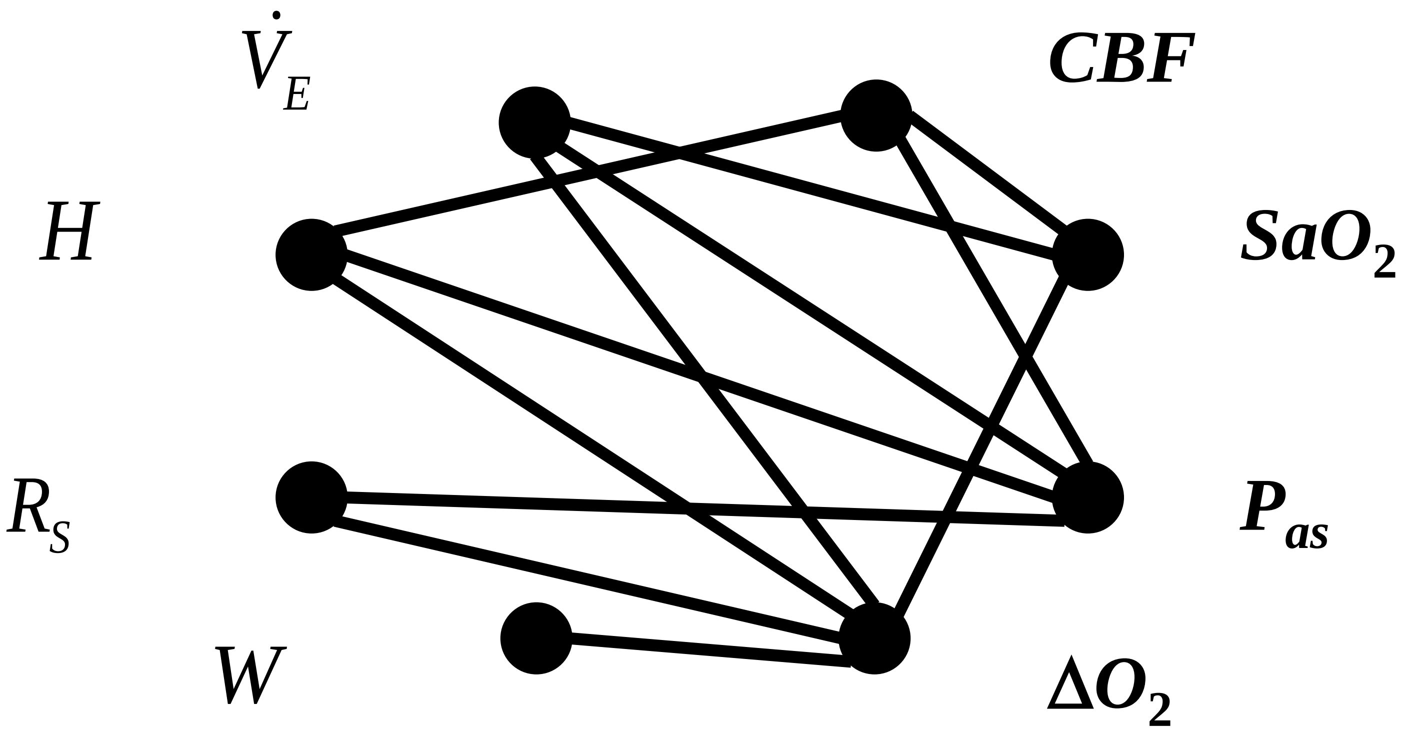
ideal

Want a
- Nature paper
- NIH grant

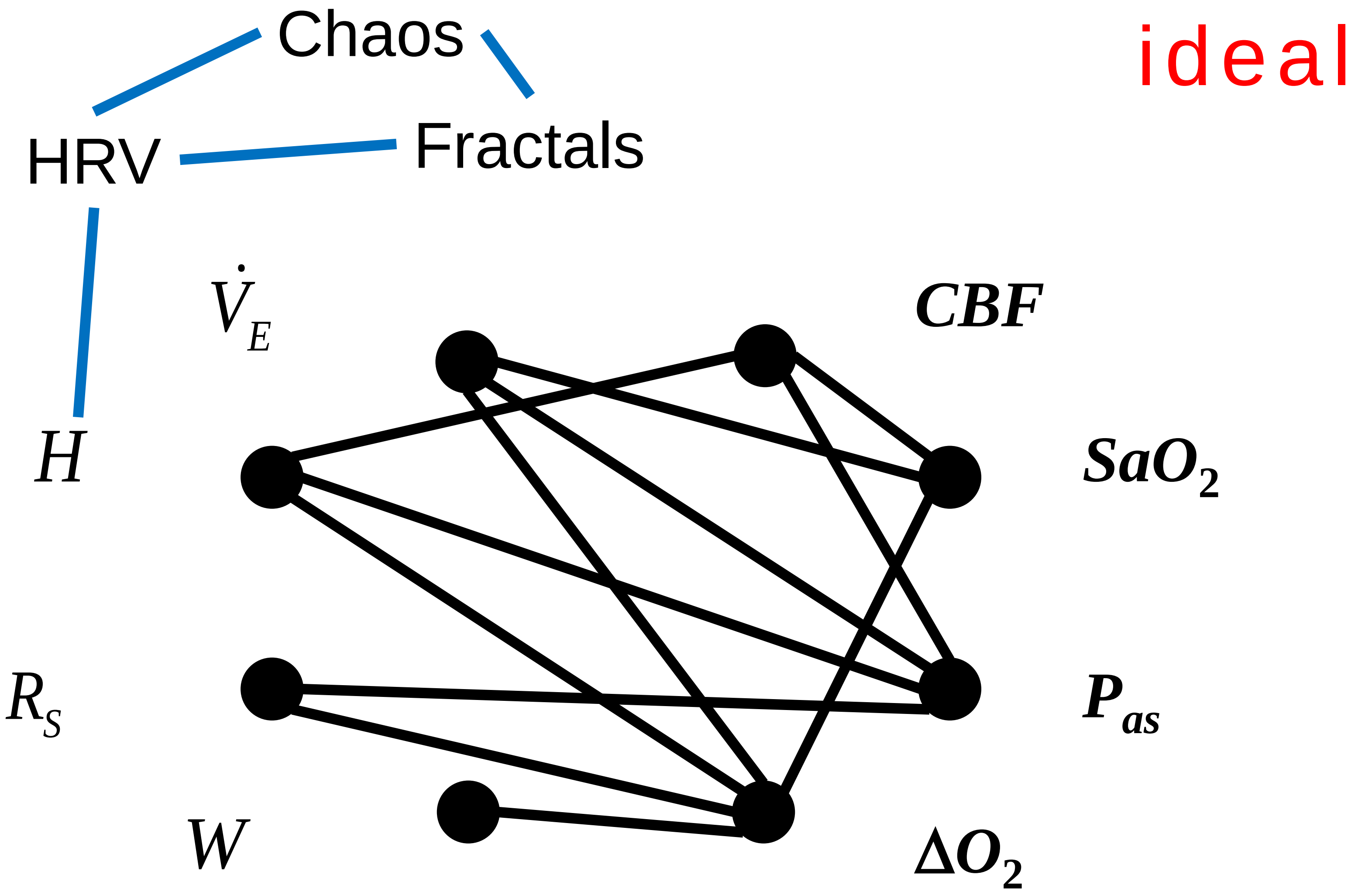
Need a
- graph?
- power law?



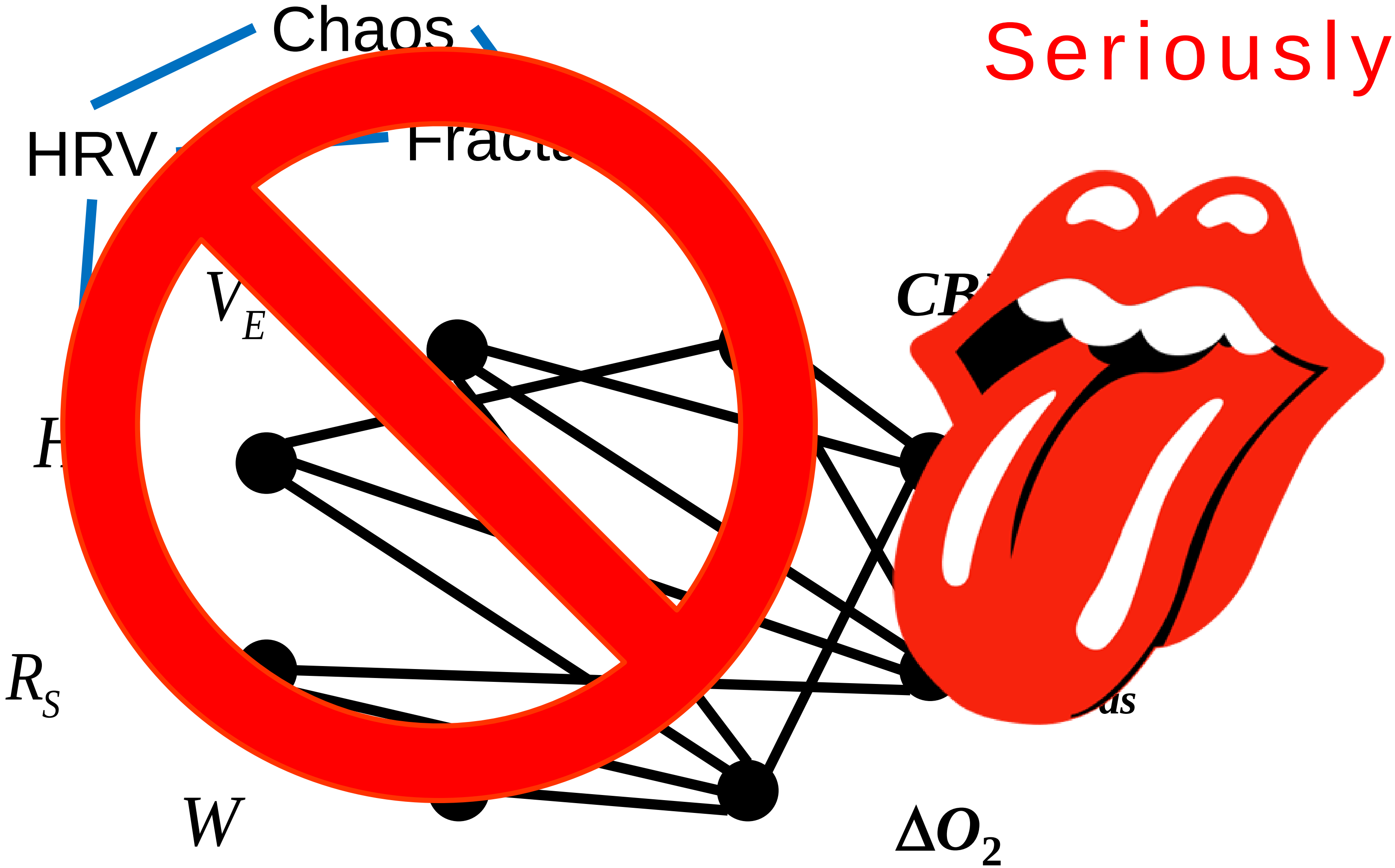
ideal



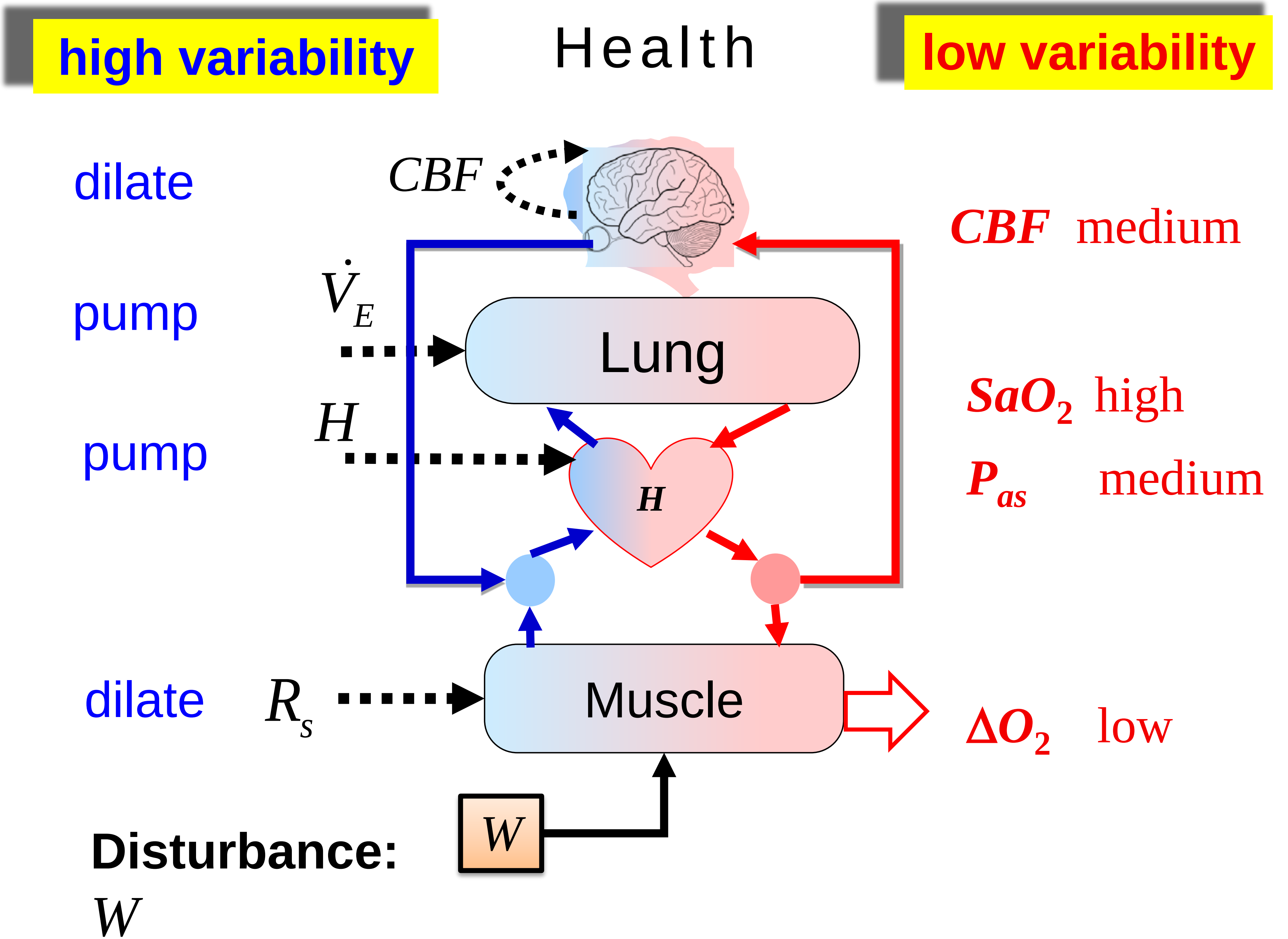
Analysis of 175,629 papers for word co-occurrence.



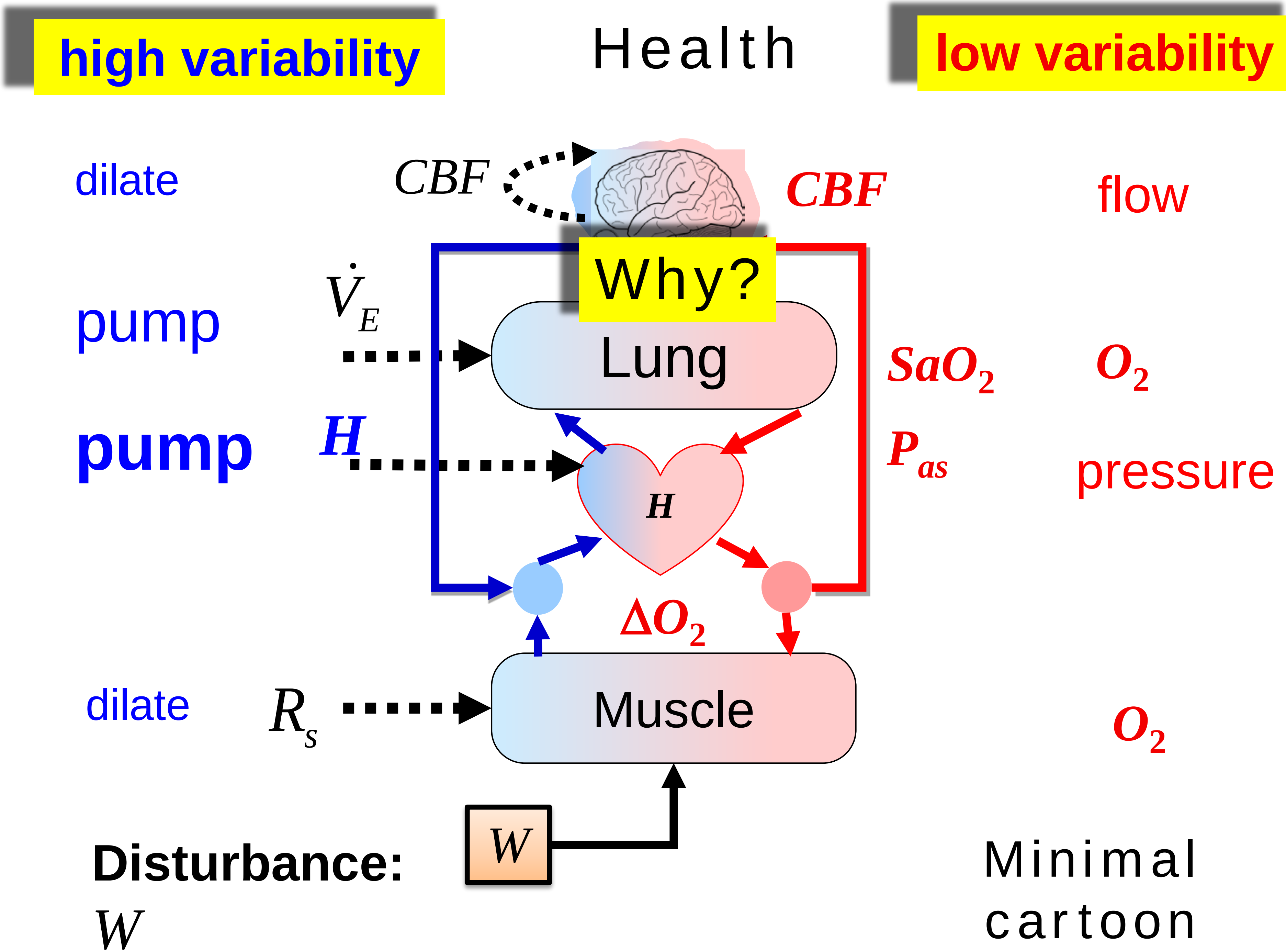
Analysis of 175,629 papers for word co-occurrence.



Analysis of 175,629 papers for word co-occurrence.



high variability
Health
low variability
dilate
CBF
CBF medium
pump
$\dot{V}_E$
Lung
SaO_2 high
pump
H
H
P_{as} medium
dilate
R_s
Muscle
ΔO_2 low
W
Disturbance:
W



high variability
Health
low variability
dilate
CBF
CBF
flow
Why?
pump
$\dot{V}_E$
Lung
SaO_2
O_2
pump
H
H
P_{as}
pressure
ΔO_2
dilate
R_s
Muscle
O_2
Disturbance:
W
W
Minimal
cartoon

high variability

Healthy homeostasis

low variability

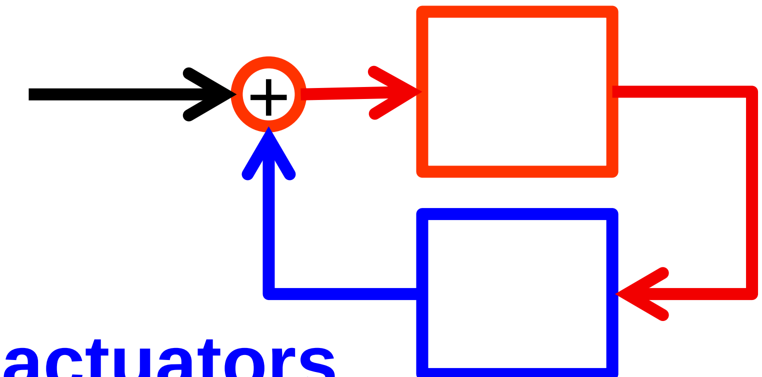
dilate

pump

pump

dilate

Disturbance



actuators

regulated variables

flow

O_2

pressure

O_2

Disturbance: run

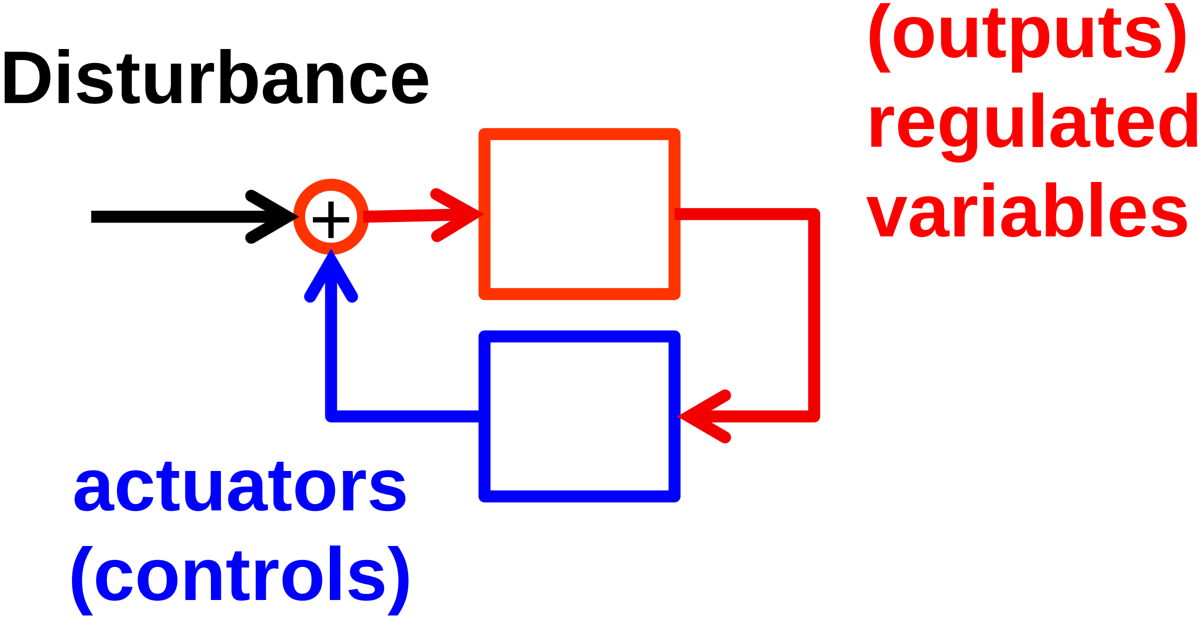
Minimal cartoon

Universals

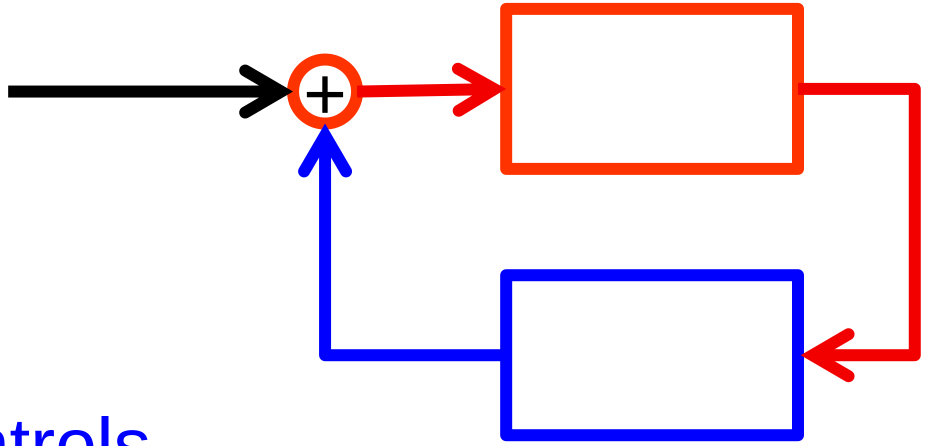
low variability outputs

\+ ***large*** disturbances

⇒ ***high*** variability controls



Universals



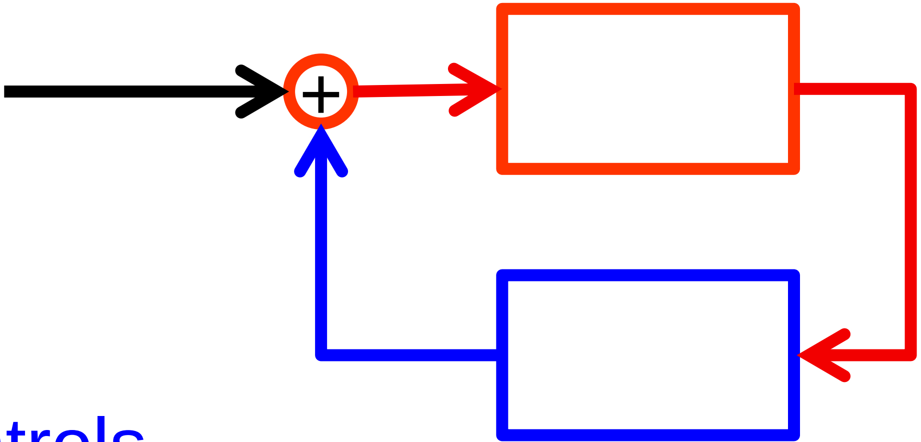
low variability outputs

+ ***large*** disturbances

⇒ ***high*** variability controls

- Independent of how variability is measured
- Universal across biology and technology
- Many theorems and case studies
- Arguably most basic idea in control theory
- Most important nonlinearity is actuator saturation

Universals



low variability outputs

+ ***large*** disturbances

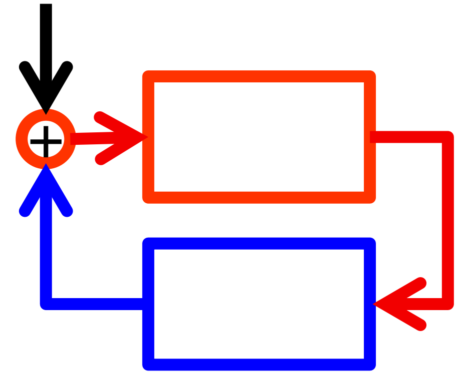
⇒ ***high*** variability controls

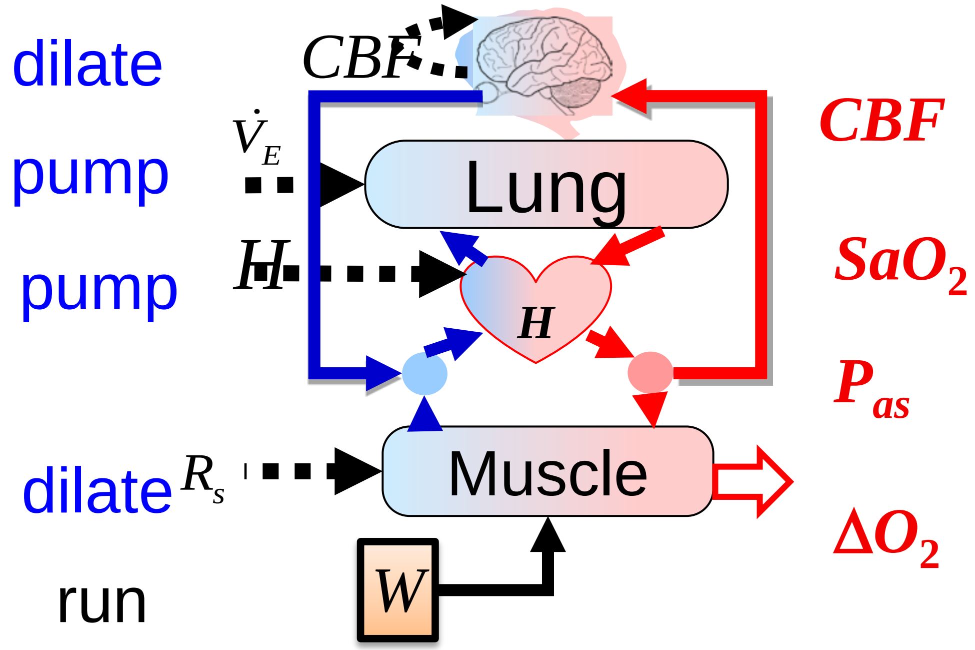
- Independent of how variability is measured
- Universal across biology and technology
- Many theorems and case studies

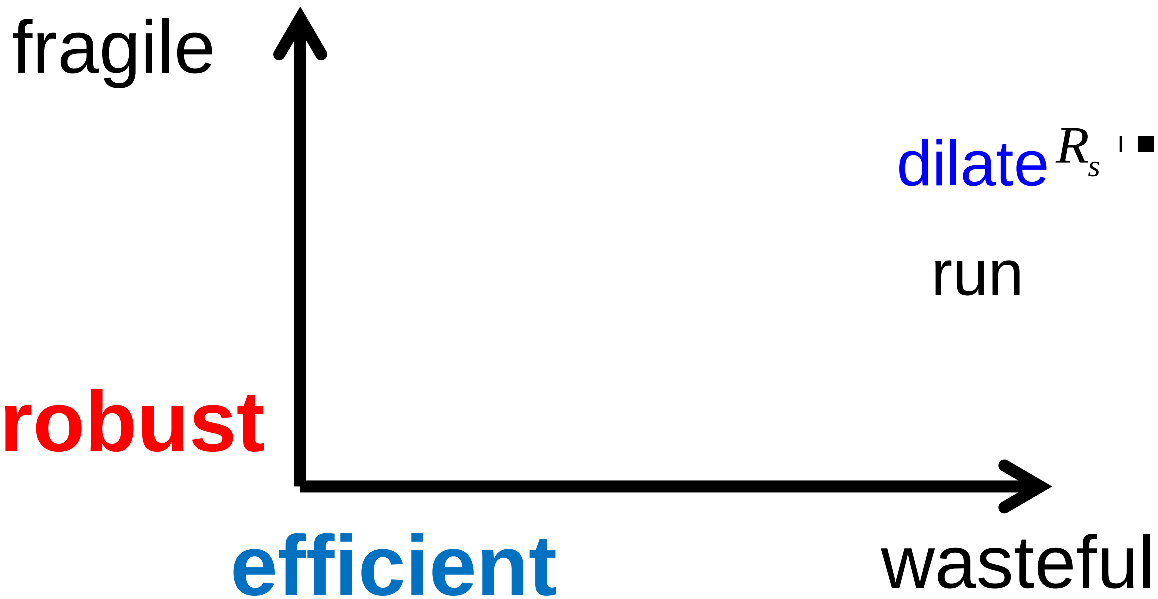
- You bet your life on it every time you fly
- (or walk or run or eat…)
- More precisely: you bet your life that engineers understand this (and doctors should too)

Other Universals

- ***Laws and architectures***
- Darwin and Turing
- Other case studies

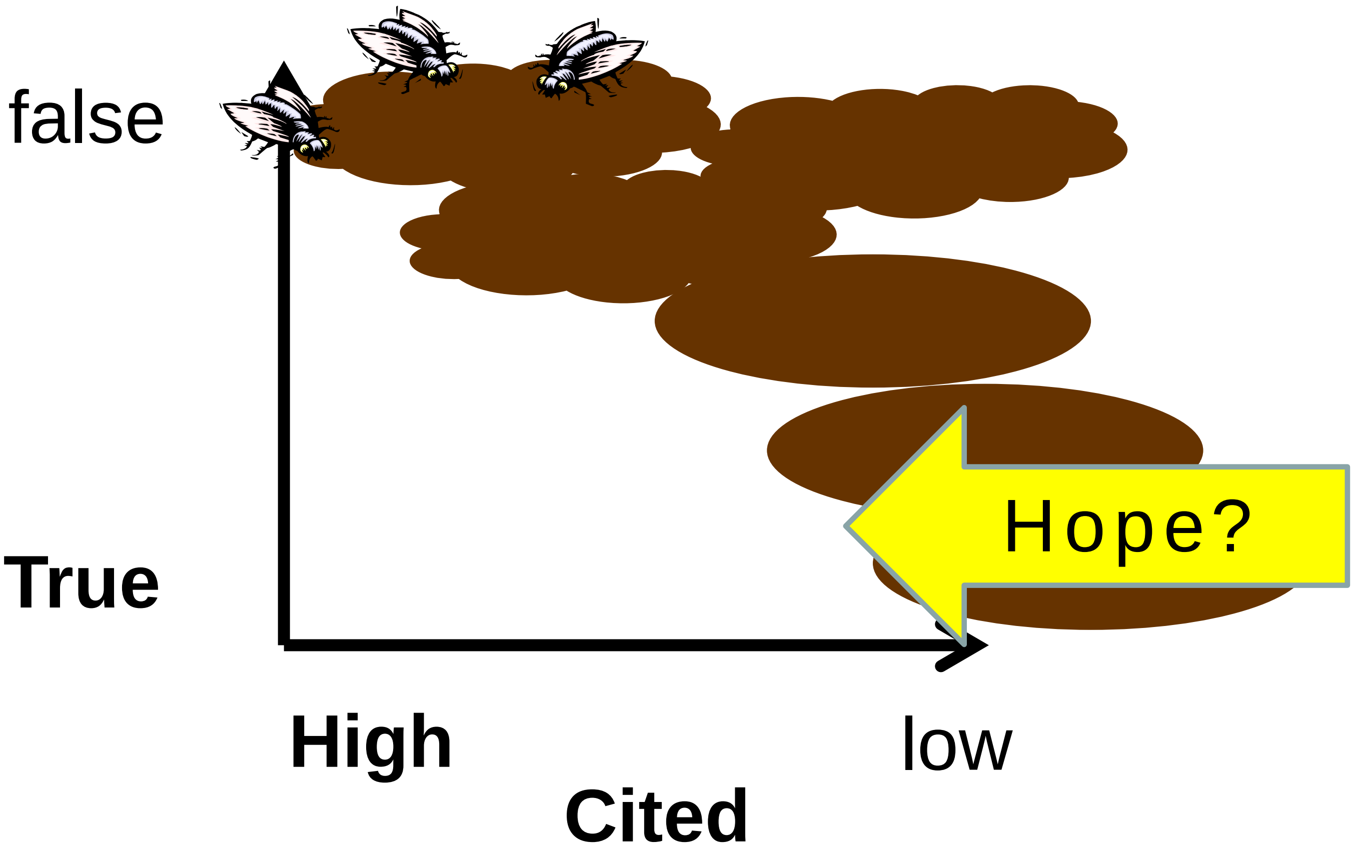


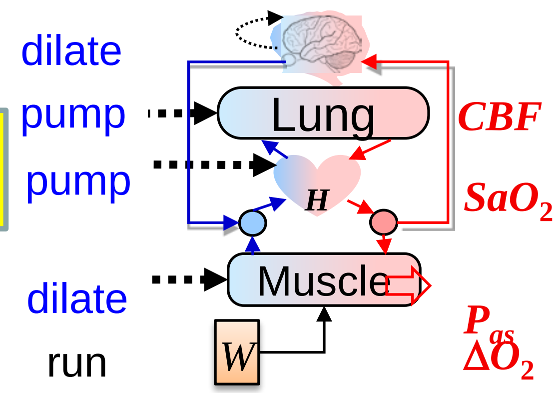




Other Universals

- Journals that love "new sciences"
- ….hate both math and physiology





Unpublishable?

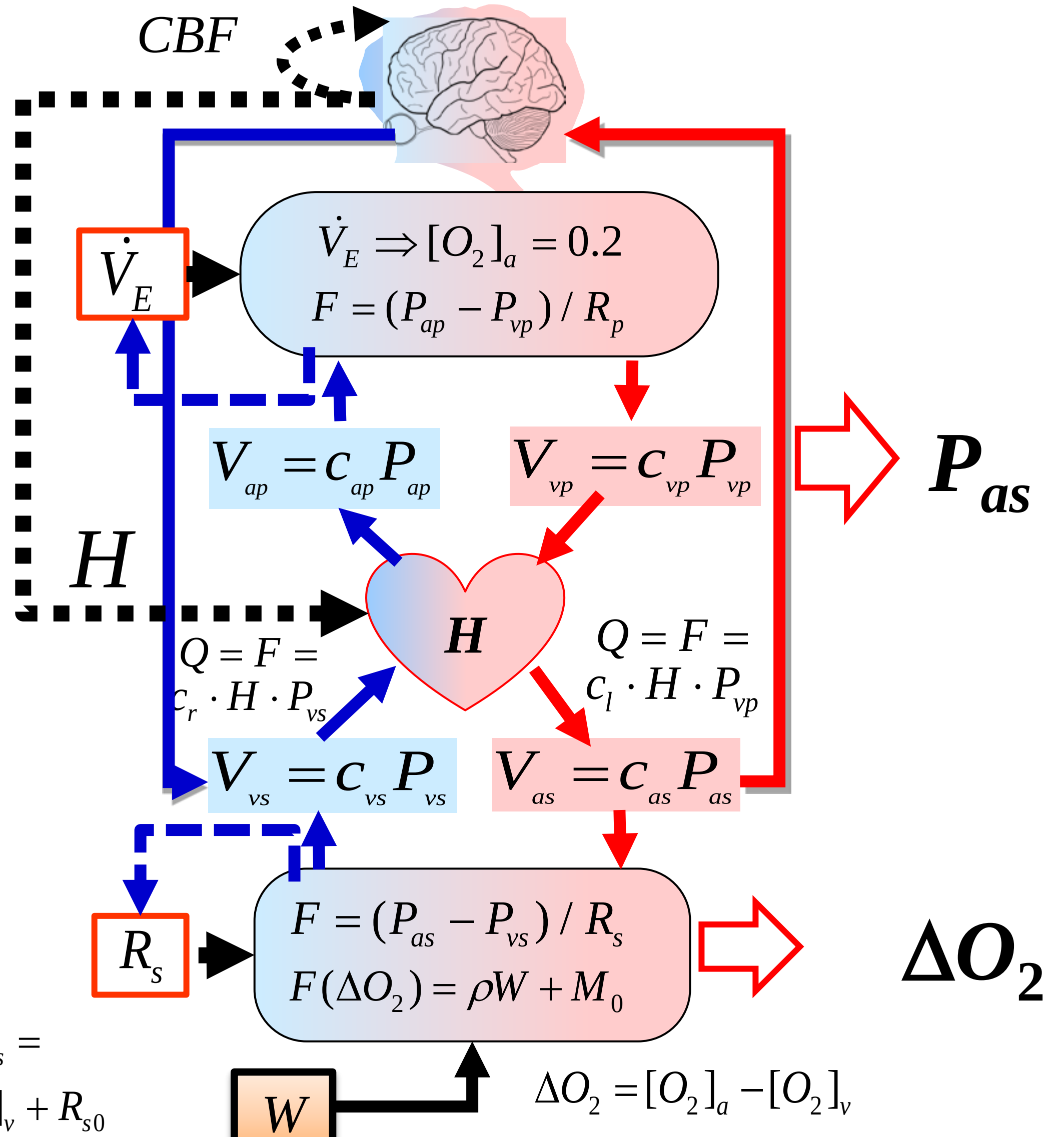
$$\min \int \left(q_P^2 \left(P_{as} - P_{as}^*\right)^2 + q_{o_2}^2 \left(\Delta O_2 - \Delta O_2^*\right)^2 + q_H^2 \left(H - H^*\right)^2 \right) dt$$

Optimal control

Local autoregulation

In each compartment:

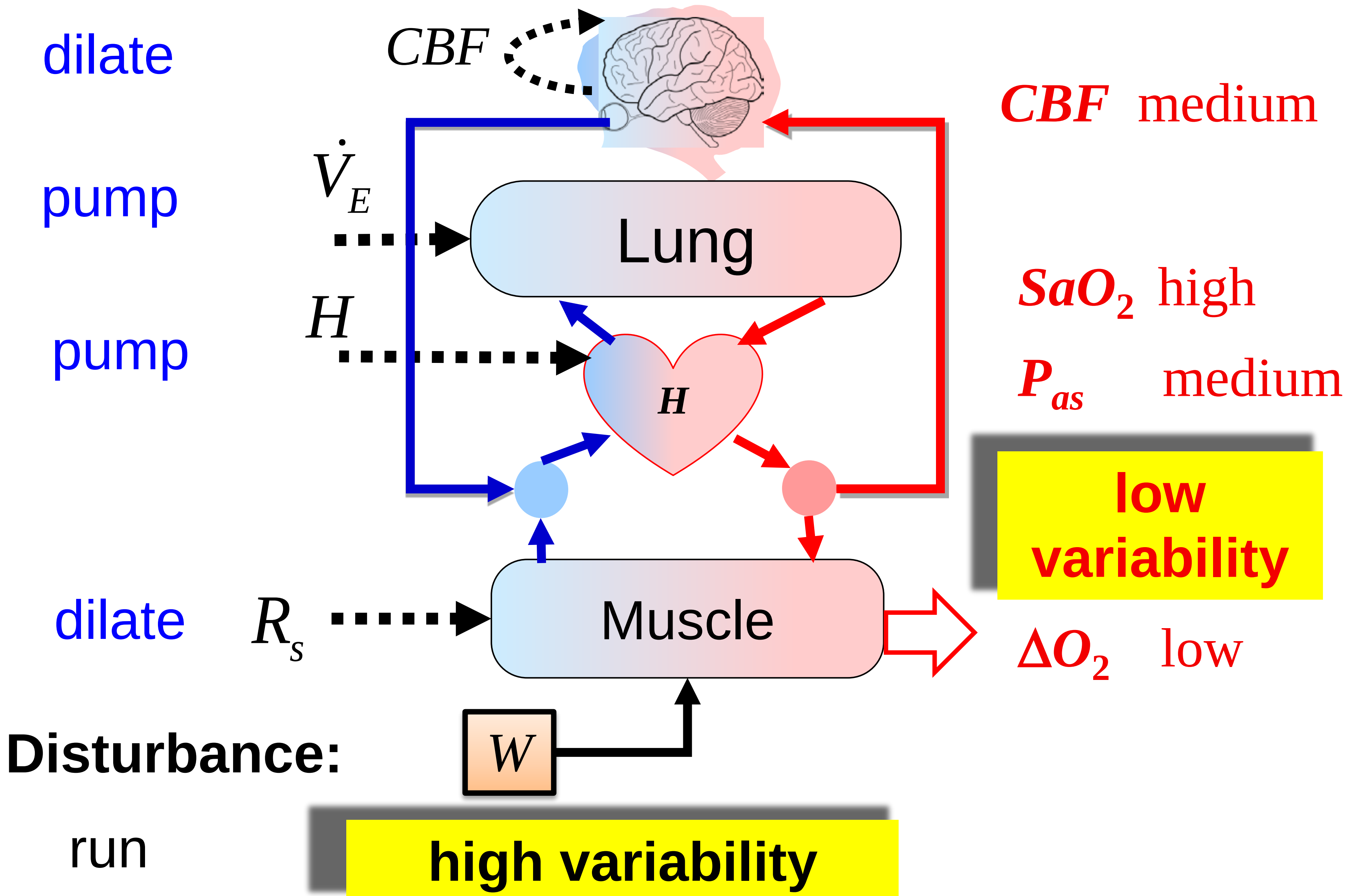
- Oxygen
- Pressure
- Flow



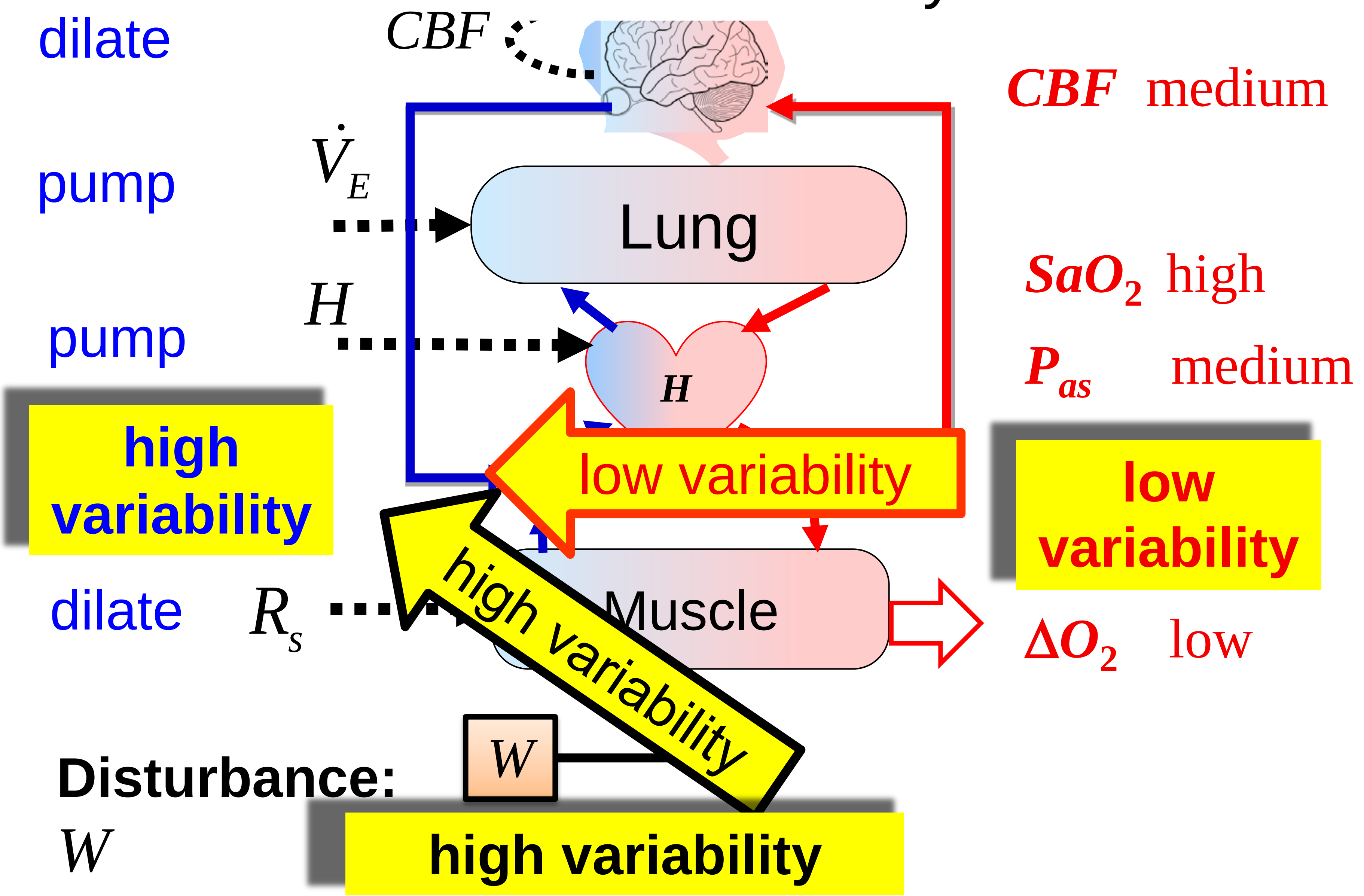
Local autoregulation

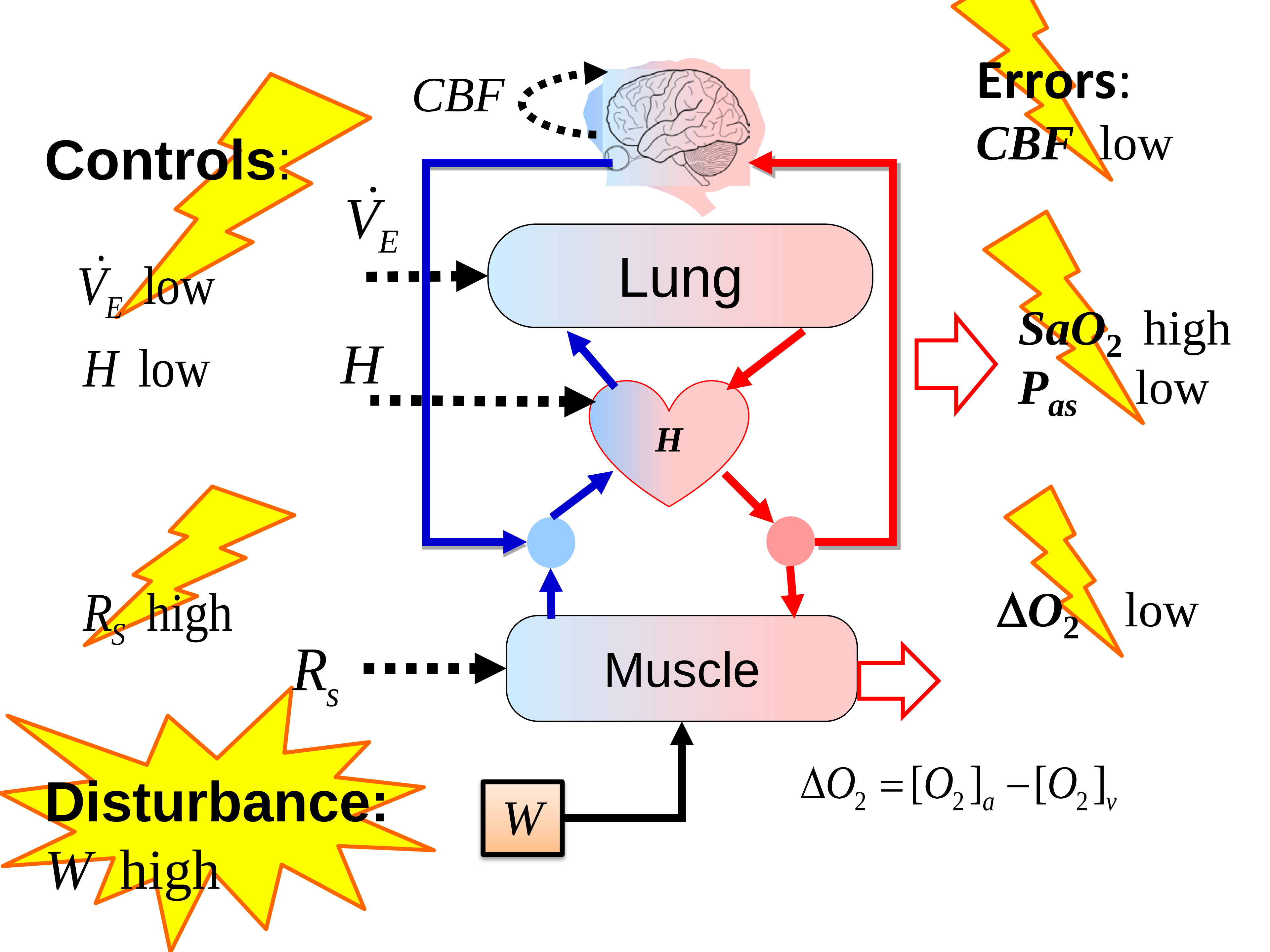
$R_s = A \cdot [O_2]_v + R_{s0}$

Physiological mechanism (cartoon)



Physiology + basic control theory = necessity





Controls:
$\dot{V}_E$ low
H low
R_S high
Disturbance:
W high
CBF
$\dot{V}_E$
H
R_s
Lung
H
Muscle
W
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
$\Delta O_2 = [O_2]_a - [O_2]_v$

Ideally

Controls:

$\dot{V}_E$ low

H low

R_S high

Controls vary −

Because

Disturbances vary +

Disturbance:

W high

To keep errors

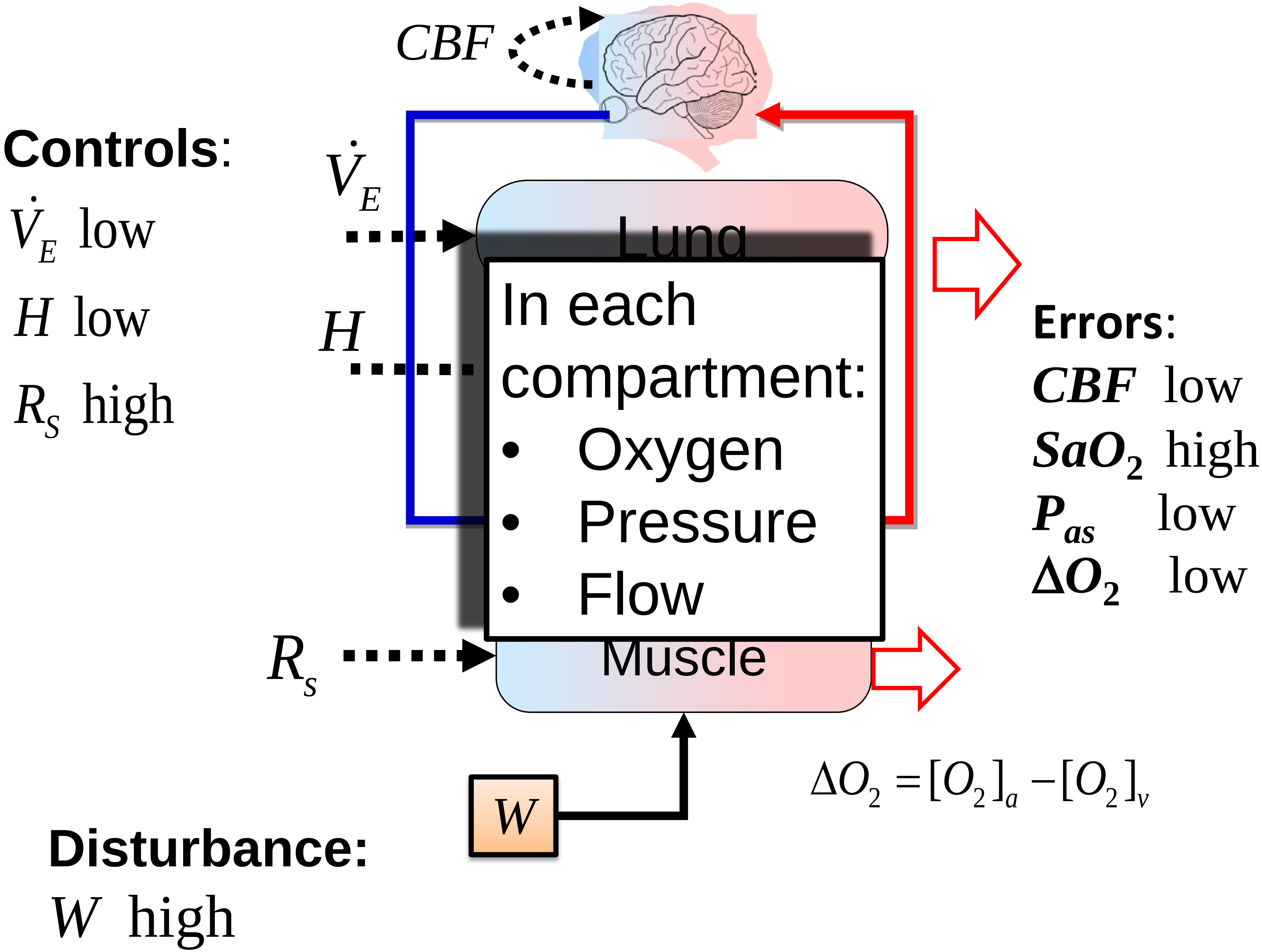
CBF low

SaO_2 high

P_{as} low

ΔO_2 low

small

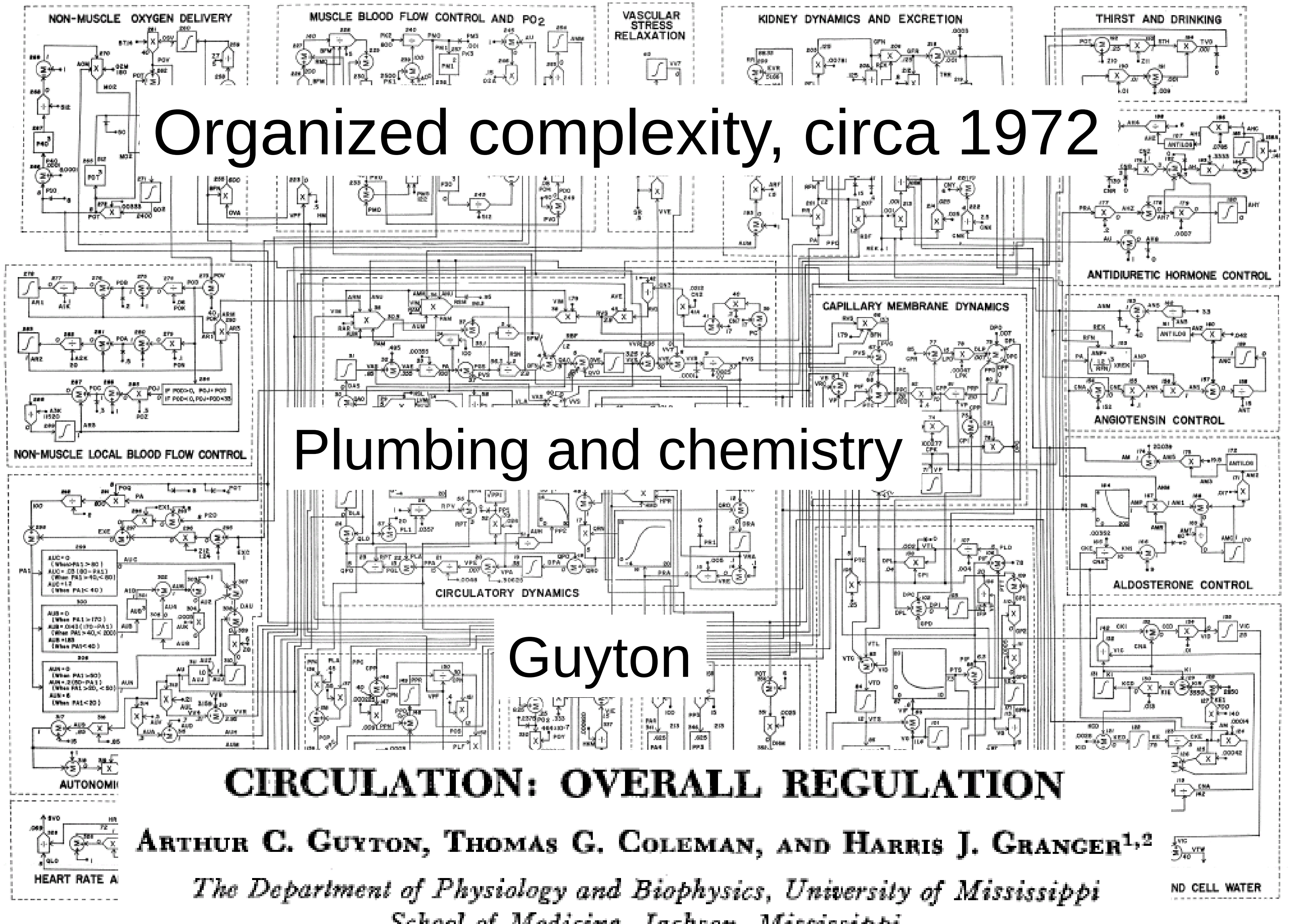


Controls:
$\dot{V}_E$ low
H low
R_S high
Disturbance:
W high
CBF
$\dot{V}_E$
H
R_S
Lung
In each compartment:
• Oxygen
• Pressure
• Flow
Muscle
W
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
$\Delta O_2 = [O_2]_a - [O_2]_v$

Organized complexity, circa 1972

Plumbing and chemistry

Guyton



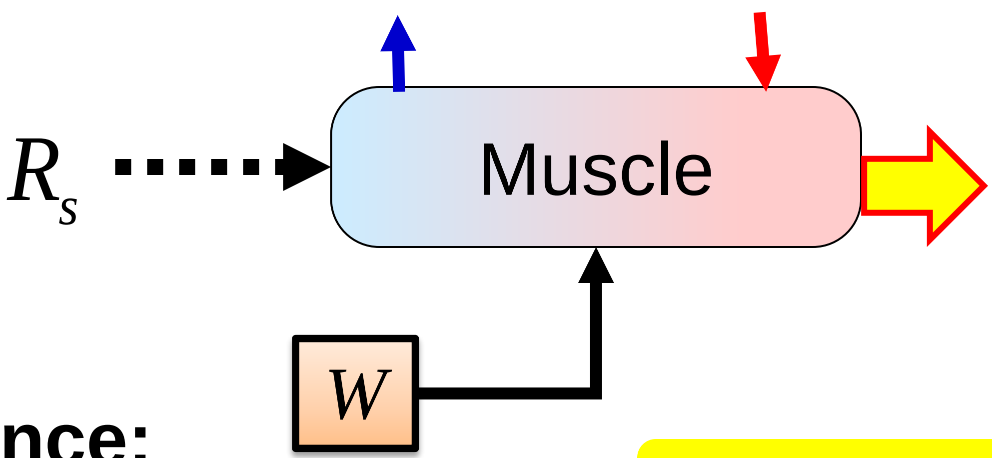
Controls:

R_s

Resistance, systemic

Oxygen drop across muscle

$$\Delta O_2 = [O_2]_a - [O_2]_v$$



Errors:

CBF low

SaO_2 high

P_{as} low

ΔO_2 low

Disturbance:

W high

W high $\Rightarrow$ ΔO_2 low

Local vasodilation

Controls:

$\dot{V}_E$ low

H low

R_S high

R_S low $\Leftarrow$ ΔO_2 low

Errors:

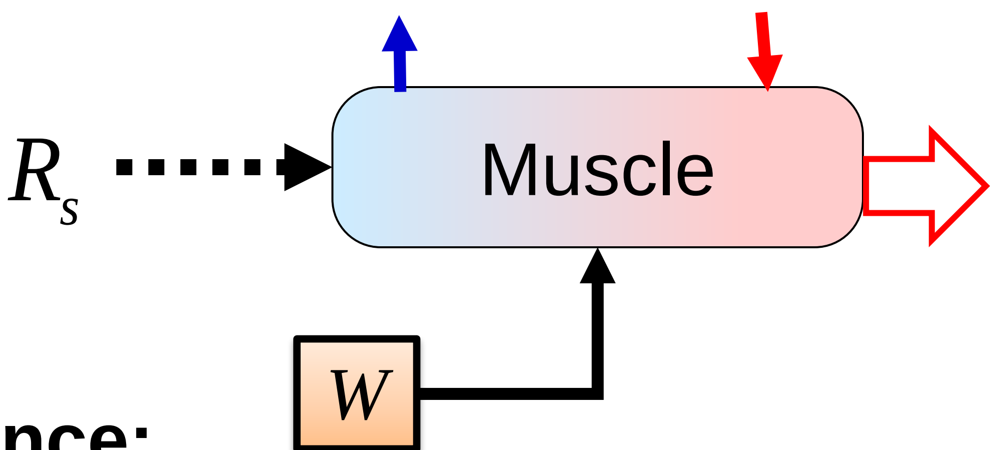
CBF low

$\boldsymbol{SaO_2}$ high

$\boldsymbol{P_{as}}$ low

$\boldsymbol{\Delta O_2}$ low

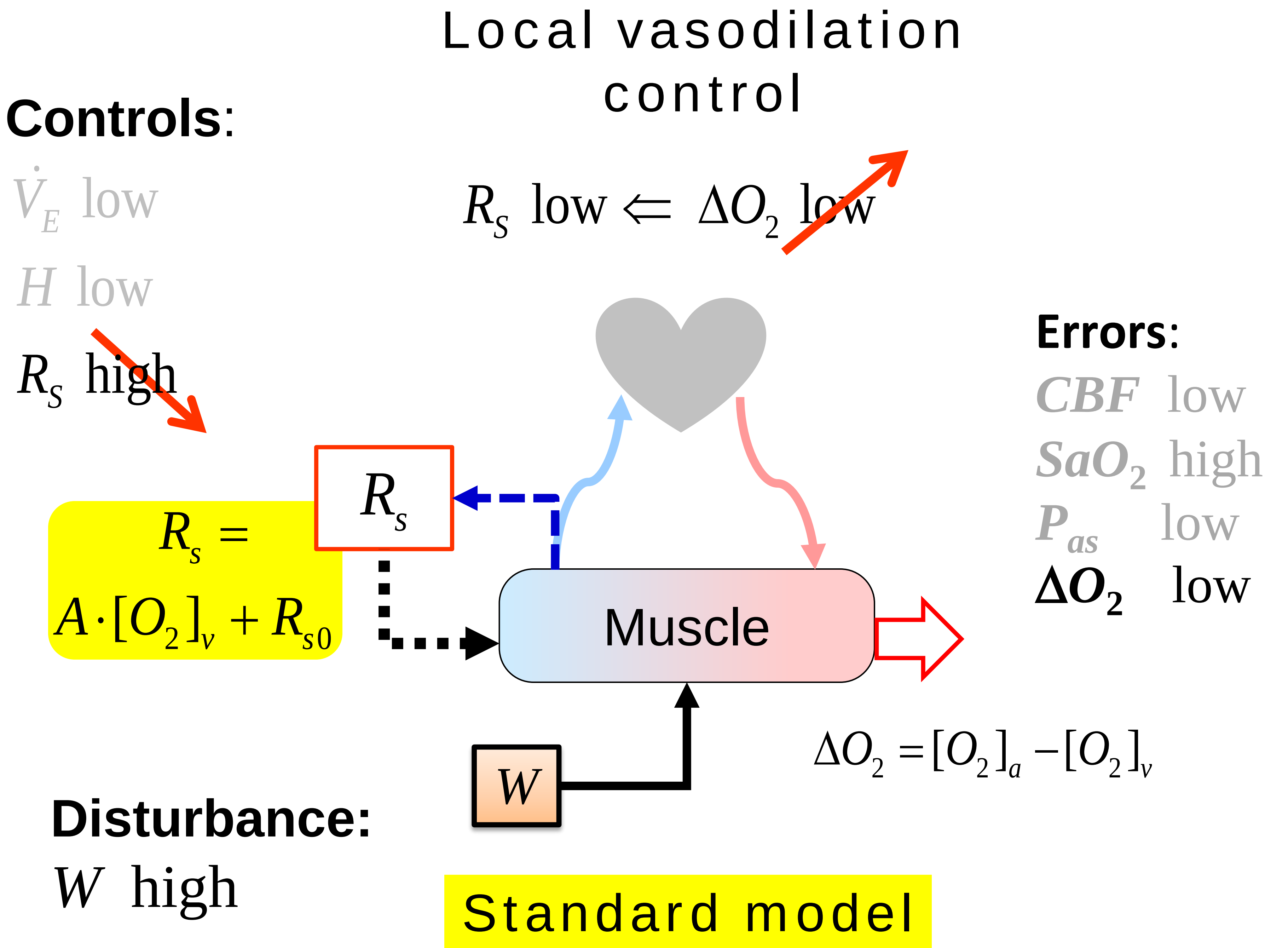
$$\Delta O_2 = [O_2]_a - [O_2]_v$$



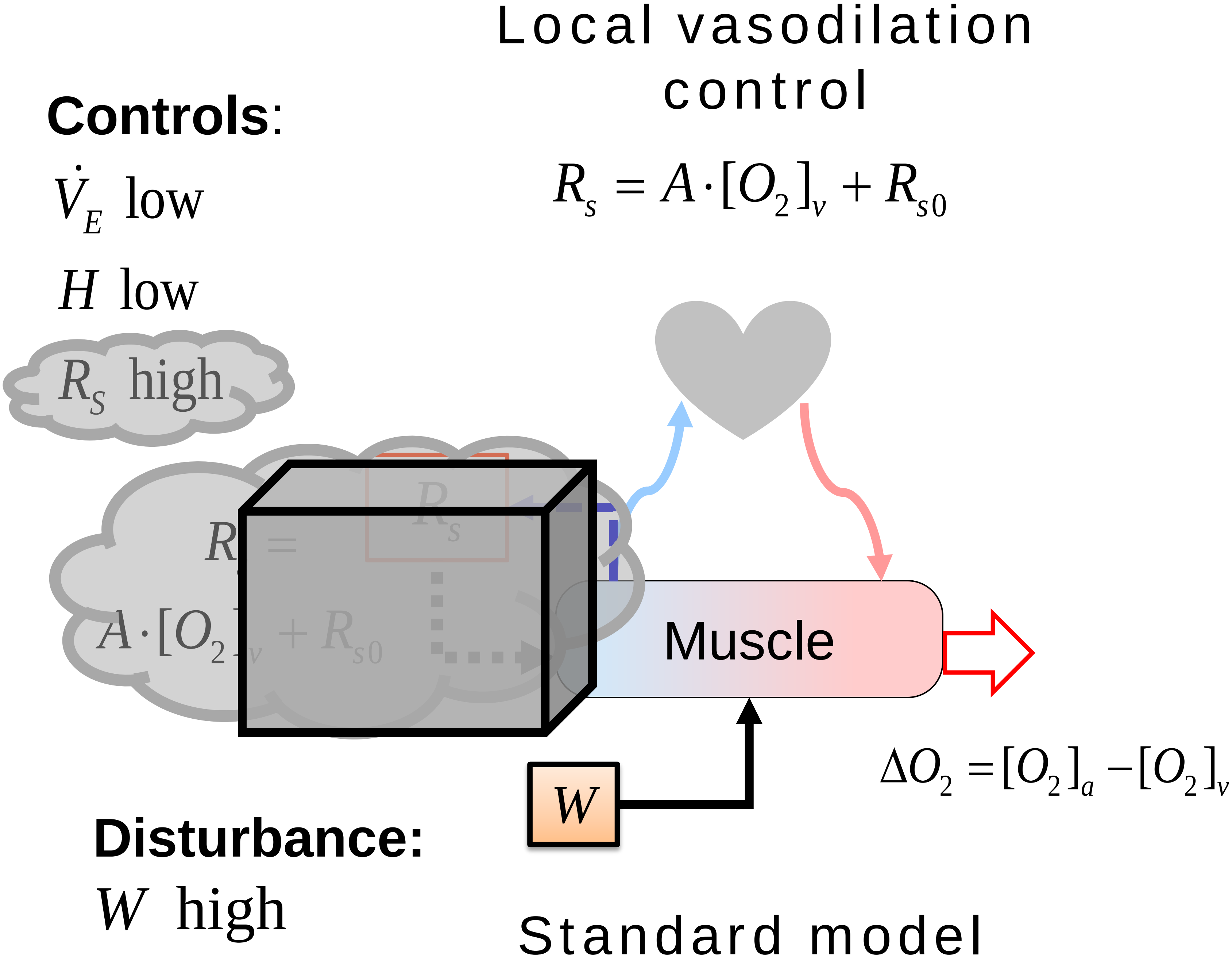
Disturbance:

W high

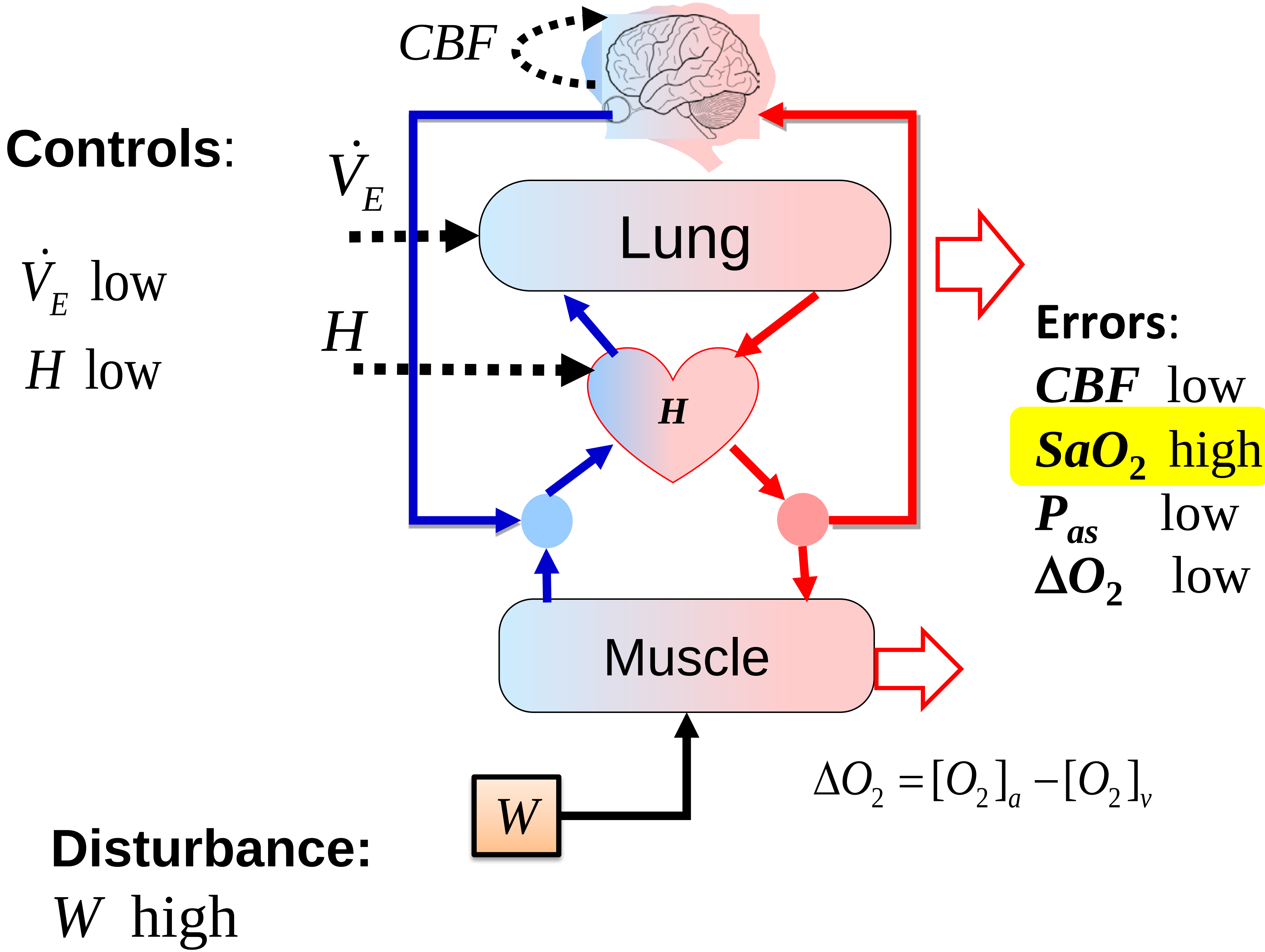
W high $\Rightarrow$ ΔO_2 low



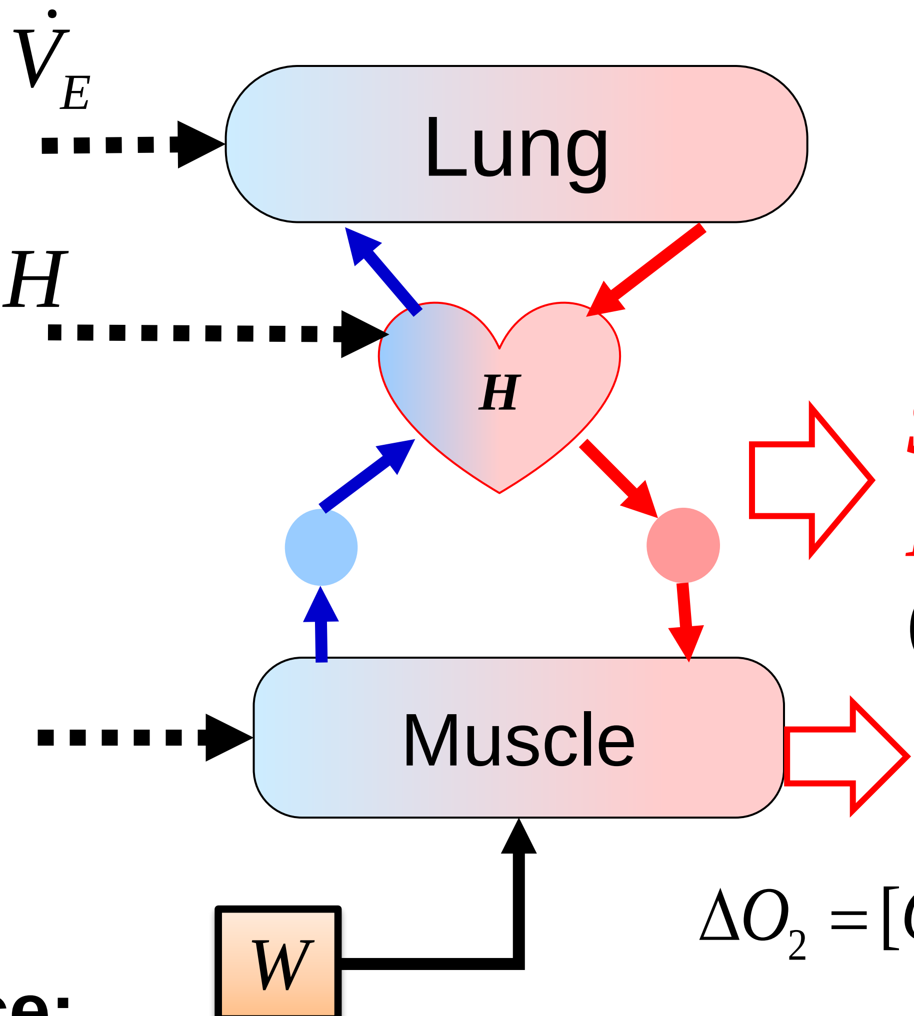
Local vasodilation control
Controls:
$\dot{V}_E$ low
H low
R_s high
R_s low $\Leftarrow$ ΔO_2 low
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
R_s
$R_s = A \cdot [O_2]_v + R_{s0}$
Muscle
W
$\Delta O_2 = [O_2]_a - [O_2]_v$
Disturbance:
W high
Standard model



Local vasodilation control
$R_s = A \cdot [O_2]_v + R_{s0}$
Controls:
$\dot{V}_E$ low
H low
R_S high
$R_s =$
$A \cdot [O_2]_v + R_{s0}$
R_s
Muscle
W
$\Delta O_2 = [O_2]_a - [O_2]_v$
Disturbance:
W high
Standard model



CBF
Controls:
$\dot{V}_E$
$\dot{V}_E$ low
H low
H
Lung
H
Muscle
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
$\Delta O_2 = [O_2]_a - [O_2]_v$
W
Disturbance:
W high



ce:

SaO_2 Arterial $\boldsymbol{O_2}$ saturation

P_{as} Mean Arterial Pressure
(Pressure, arterial, systemic)

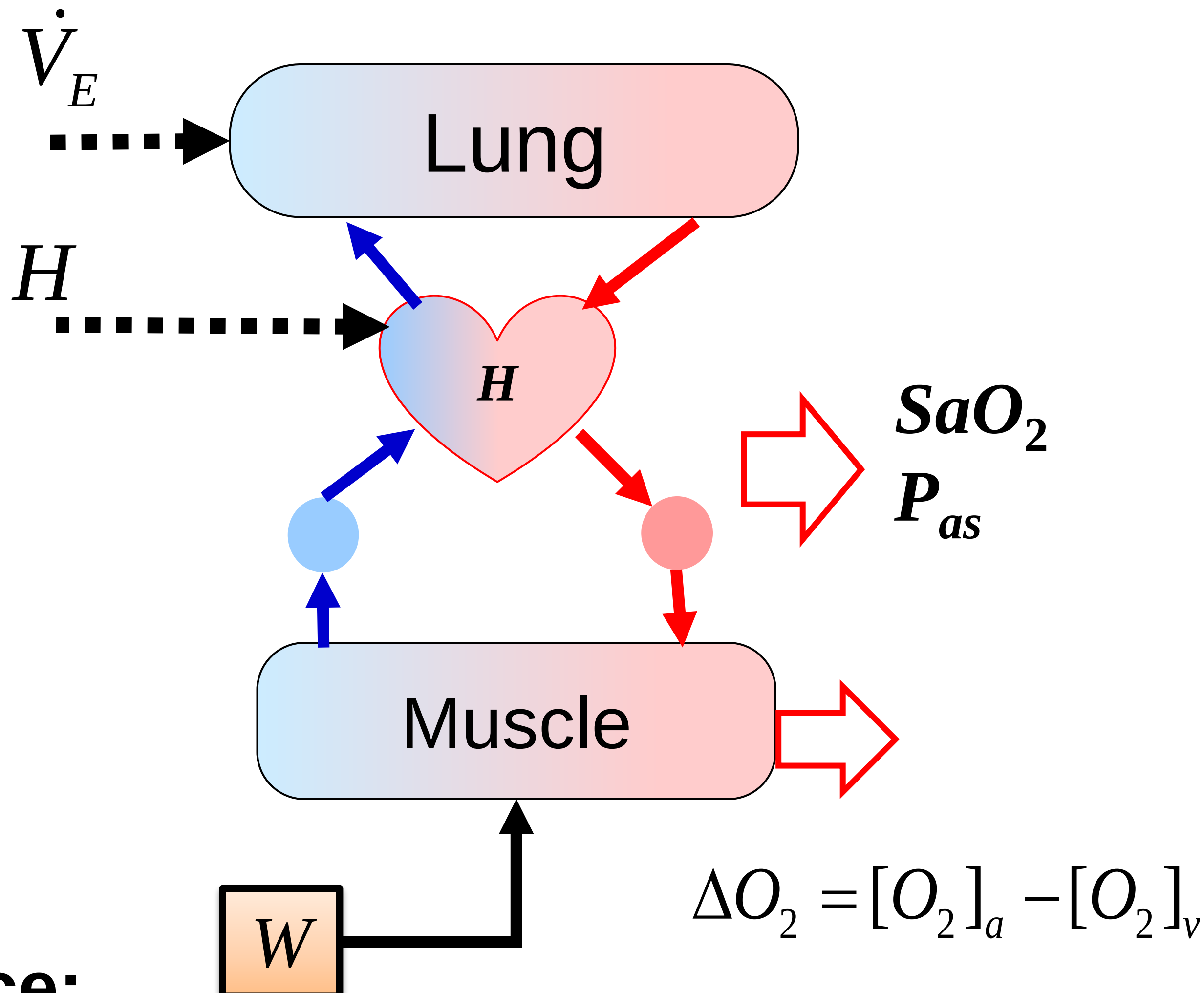
$$\Delta O_2 = [O_2]_a - [O_2]_v$$

Oxygen drop across muscle

Controls:

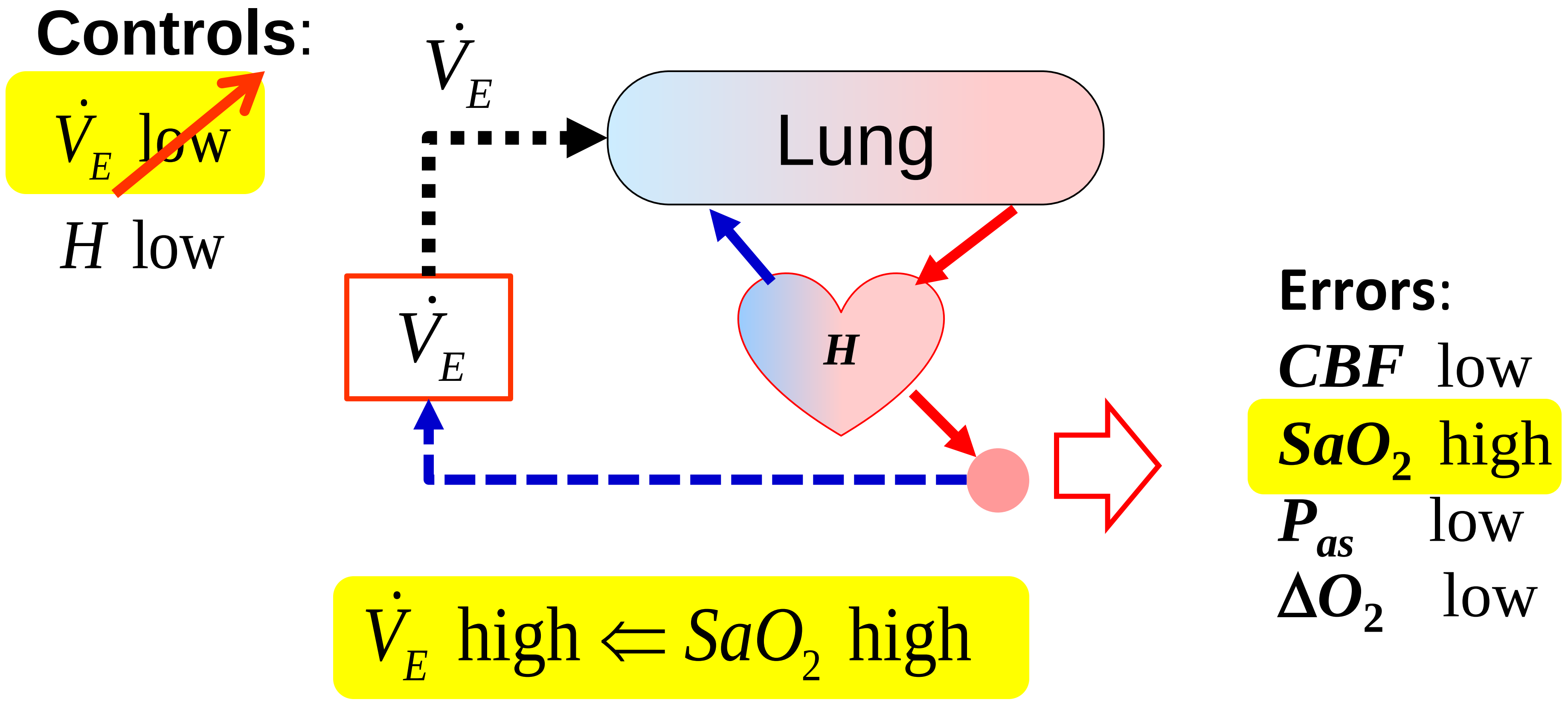
$\dot{V}_E$ low

H low



Disturbance:

W high

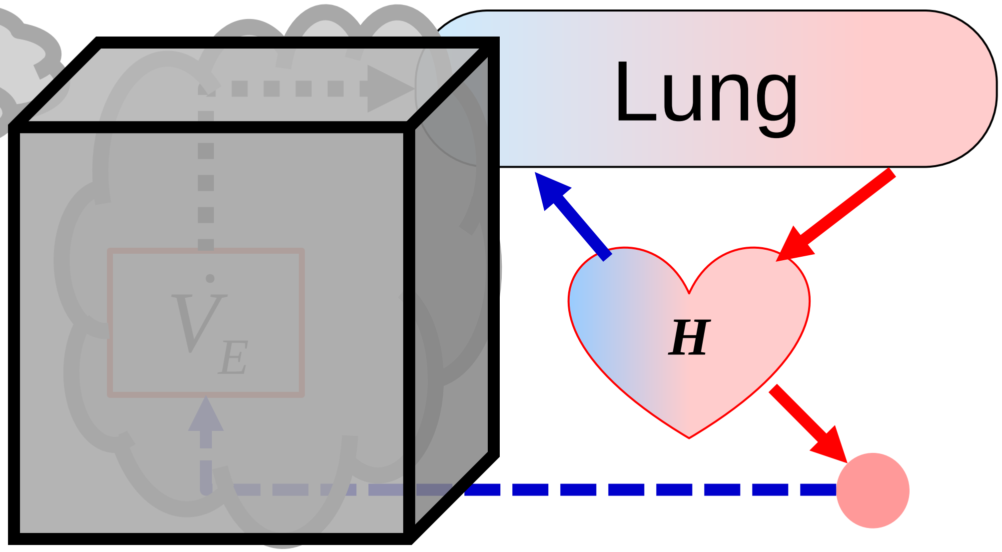


Local ventilation control

Controls:

$\dot{V}_E$ low

H low



Errors:

CBF low

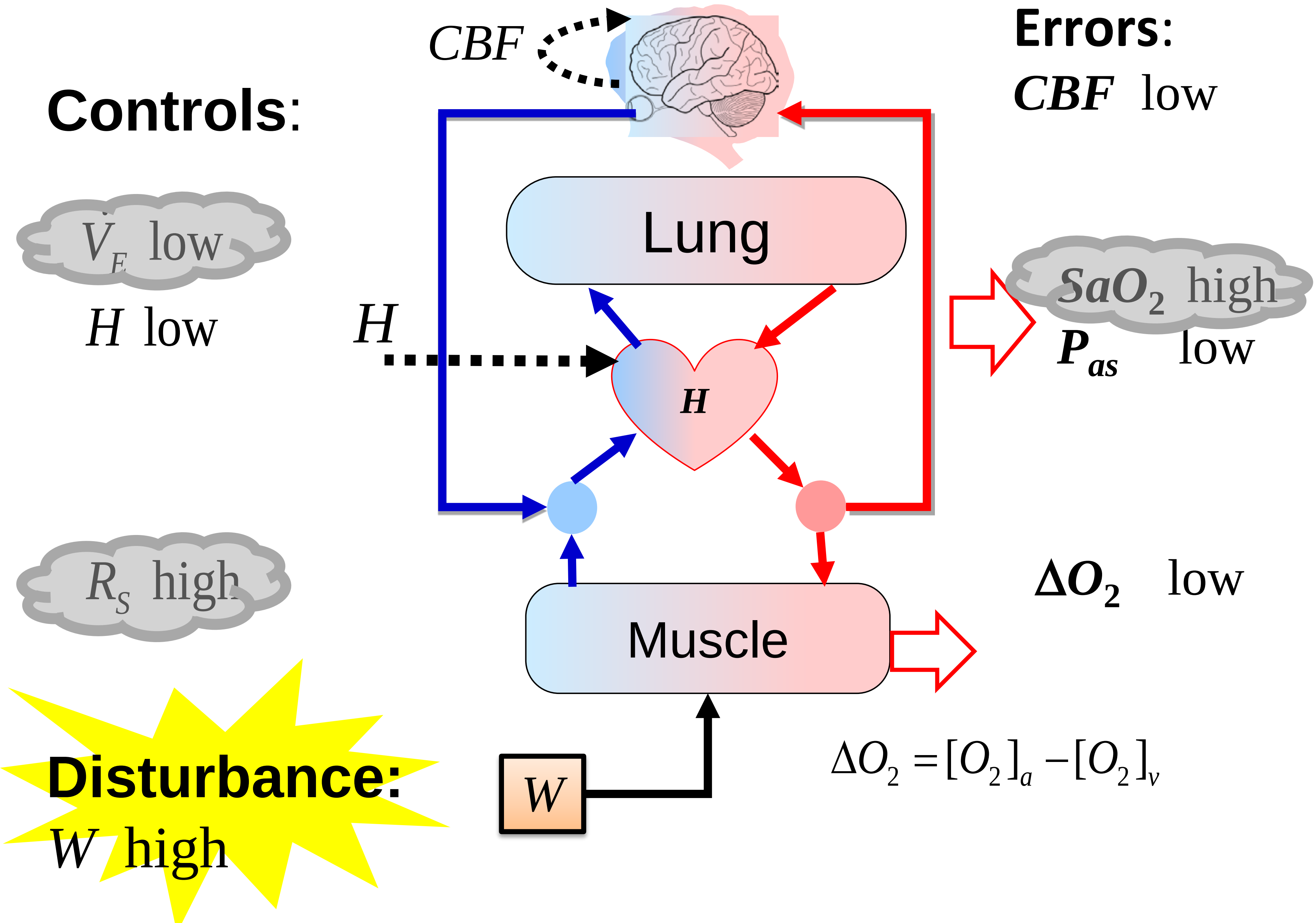
SaO_2 high

P_{as} low

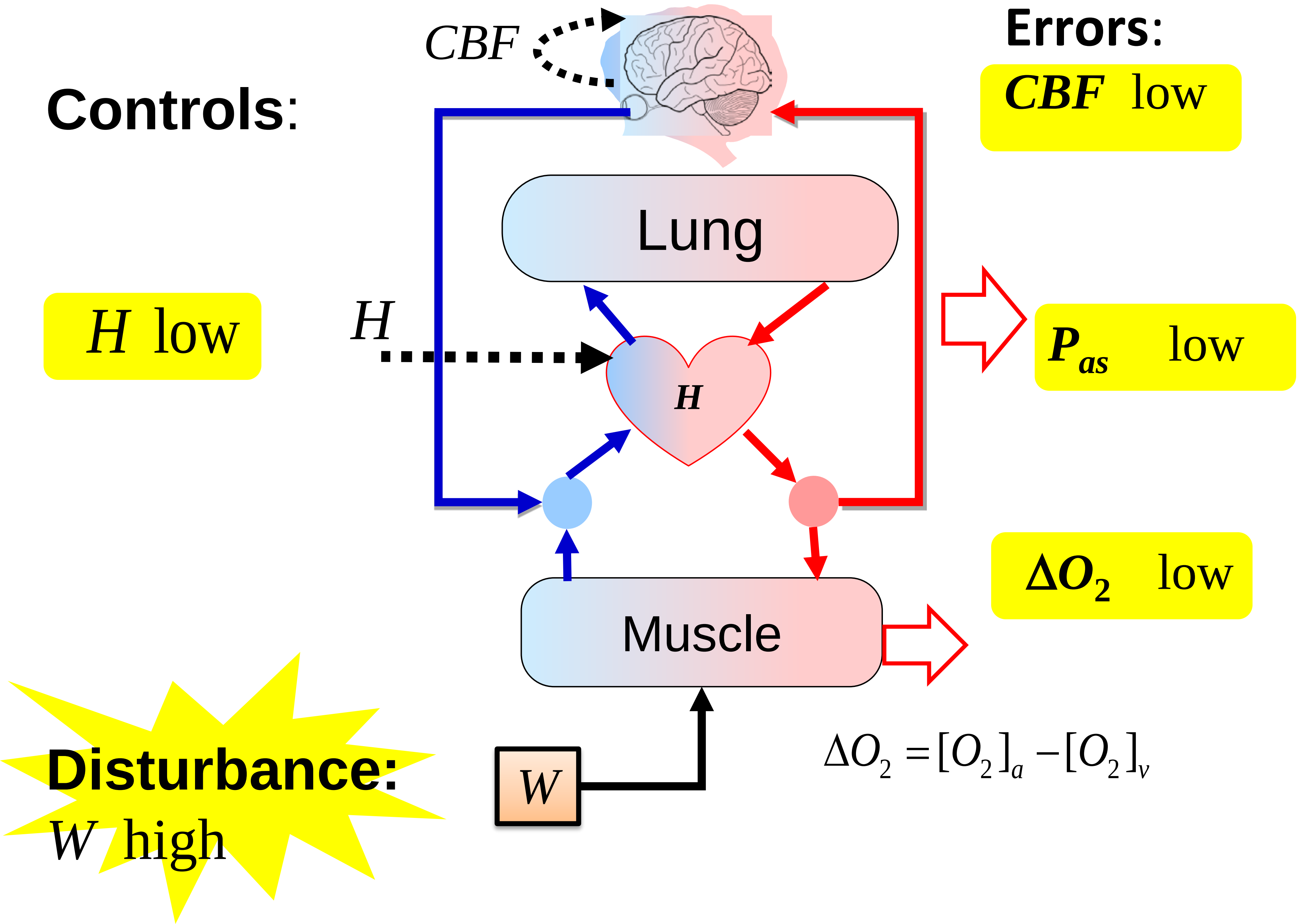
ΔO_2 low

$$\dot{V}_E \text{ high} \Leftarrow SaO_2 \text{ high}$$

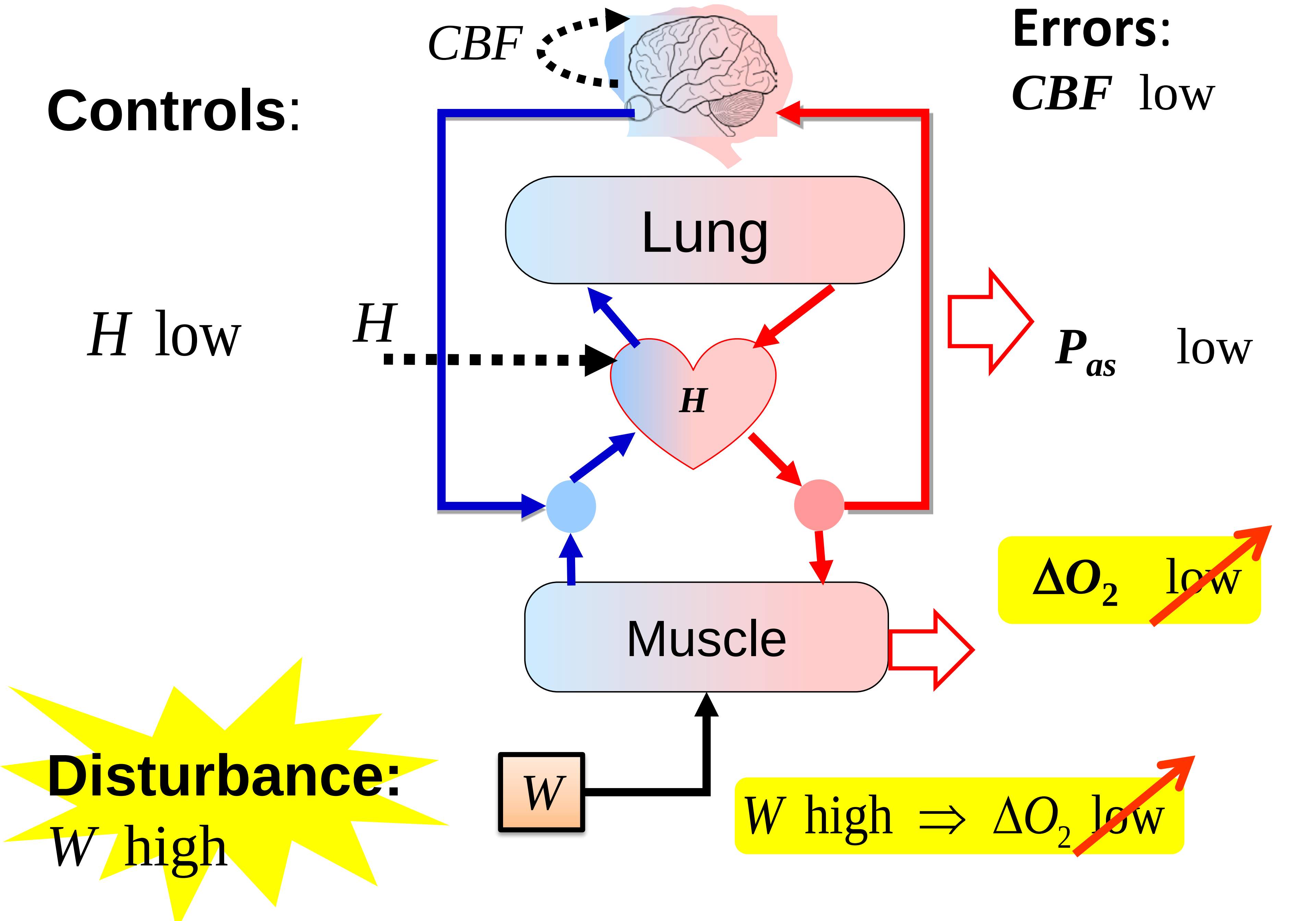
Local ventilation control



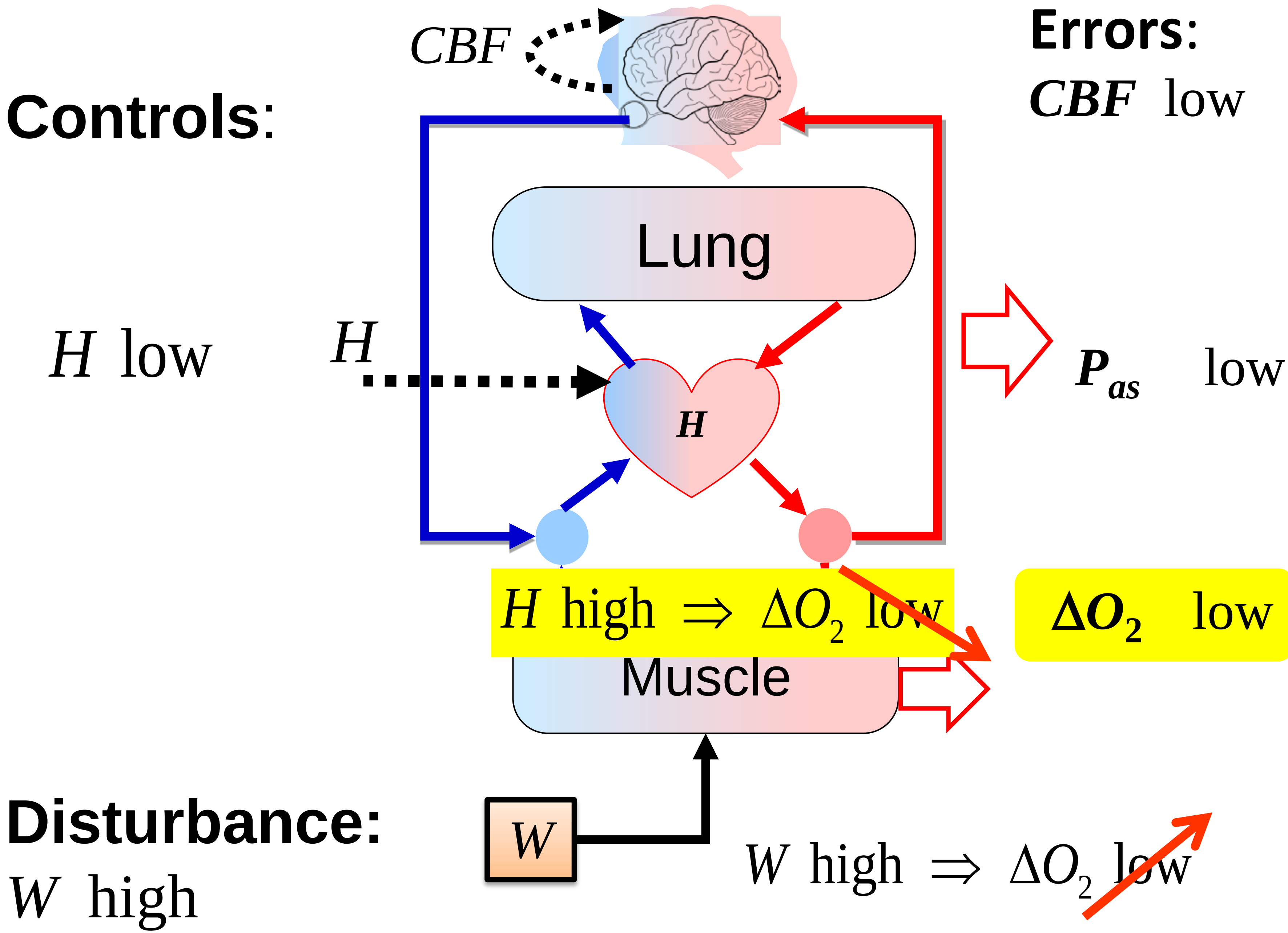
Controls:
$\dot{V}_E$ low
H low
R_S high
Disturbance:
W high
CBF
H
Lung
H
Muscle
W
Errors:
CBF low
SaO_2 high
P_{as} low
ΔO_2 low
$\Delta O_2 = [O_2]_a - [O_2]_v$



Controls:
H low
H
CBF
Errors:
CBF low
Lung
H
Pas low
ΔO2 low
Muscle
W
Disturbance:
W high
ΔO2 = [O2]a − [O2]v



Controls:
H low
H
CBF
Errors:
CBF low
Lung
H
P_{as} low
ΔO_2 low
Muscle
Disturbance:
W high
W
W high ⇒ ΔO_2 low



Controls:
H low
Errors:
$\boldsymbol{CBF}$ low
$\boldsymbol{P_{as}}$ low
$\boldsymbol{\Delta O_2}$ low
Disturbance:
W high
CBF
Lung
H
H
H high $\Rightarrow$ ΔO_2 low
Muscle
W
W high $\Rightarrow$ ΔO_2 low

Controls:

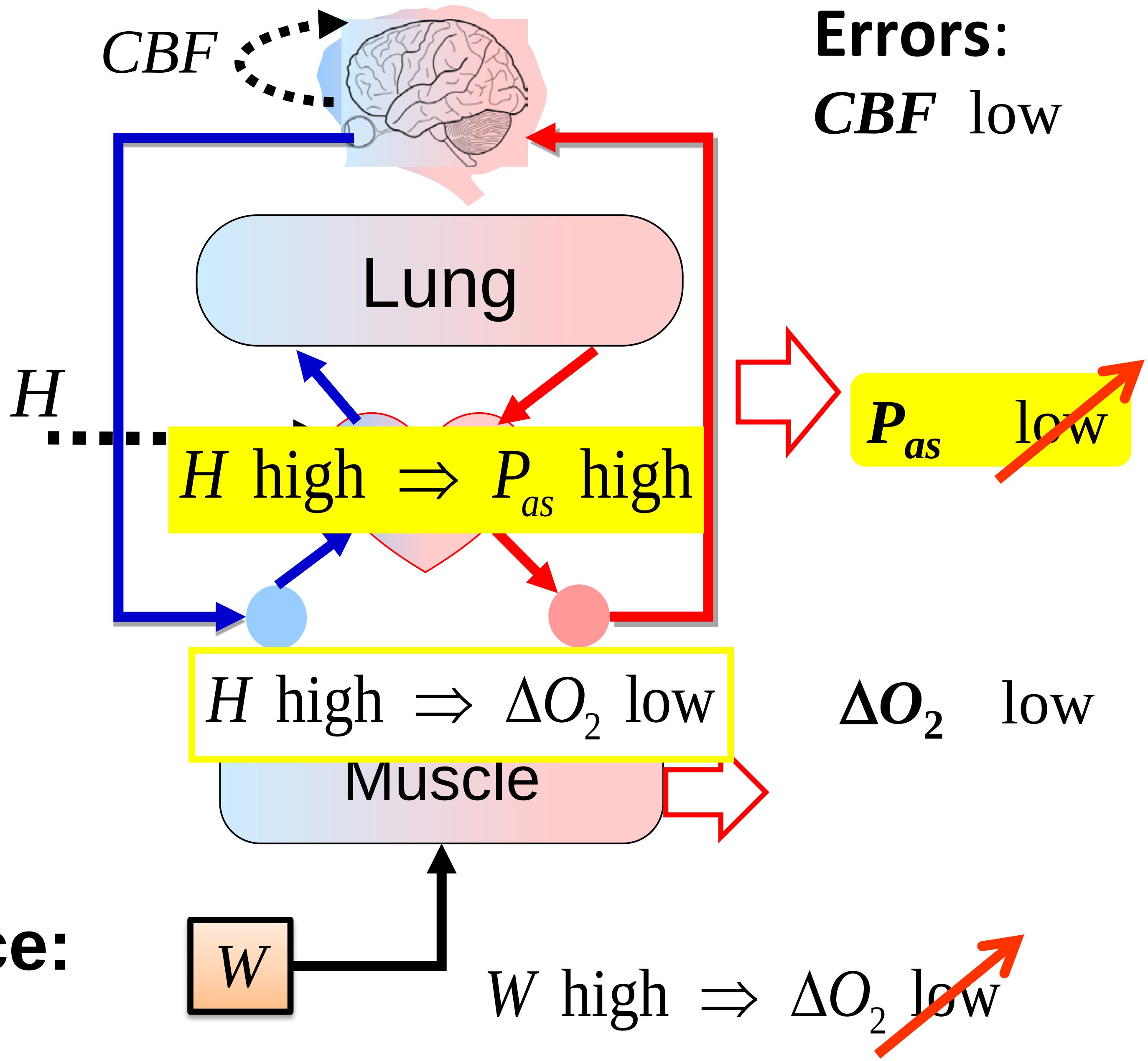
H low

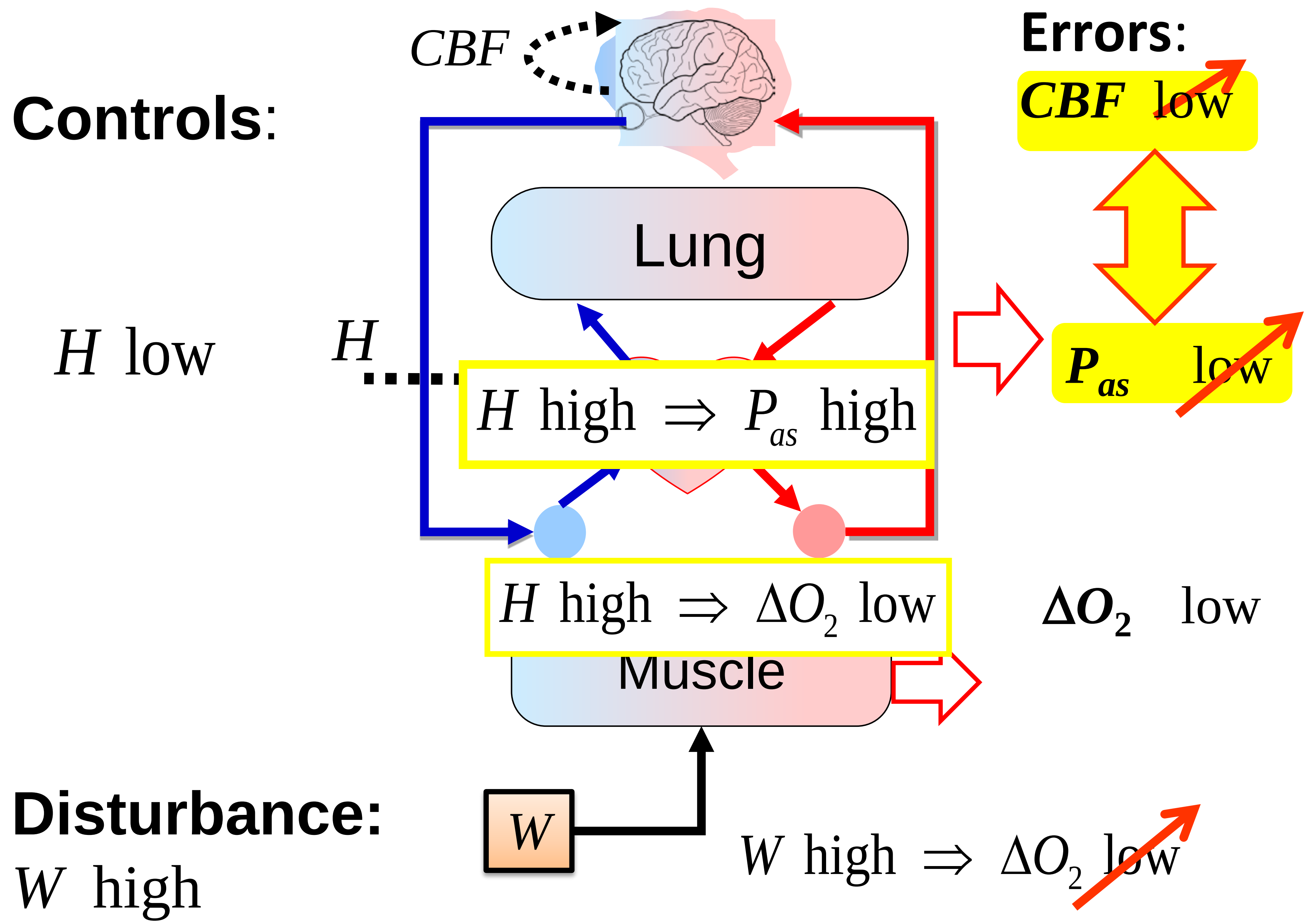
Disturbance:

W high

Errors:

$\boldsymbol{CBF}$ low




Controls:
H low
Disturbance:
W high
CBF
H
Lung
H high ⇒ P_{as} high
H high ⇒ ΔO_2 low
Muscle
W
W high ⇒ ΔO_2 low
Errors:
CBF low
P_{as} low
ΔO_2 low

Controls:

Tradeoffs?

Errors:

H low

$\boldsymbol{P_{as}}$ low

H high $\Rightarrow$ P_{as} high

H high $\Rightarrow$ ΔO_2 low

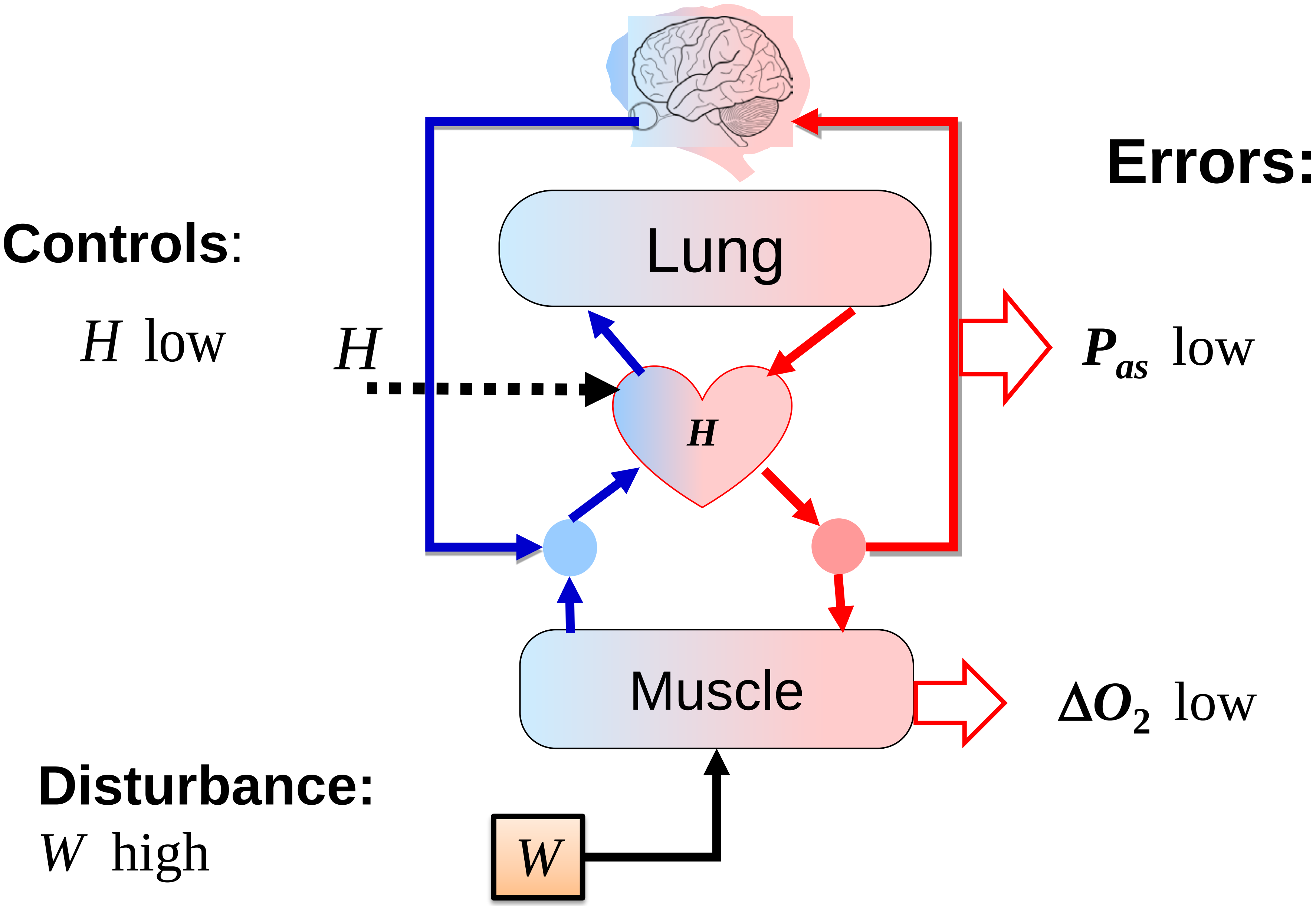
$\boldsymbol{\Delta O_2}$ low

Disturbance:

W high

W high $\Rightarrow$ ΔO_2 low

Tradeoffs?



Errors:
Controls:
H low
H
Lung
H
Pas low
Muscle
ΔO2 low
Disturbance:
W high
W

Tradeoffs?

Errors:

Controls:

H low

P_{as} low

Greatly
simplified

ΔO_2 low

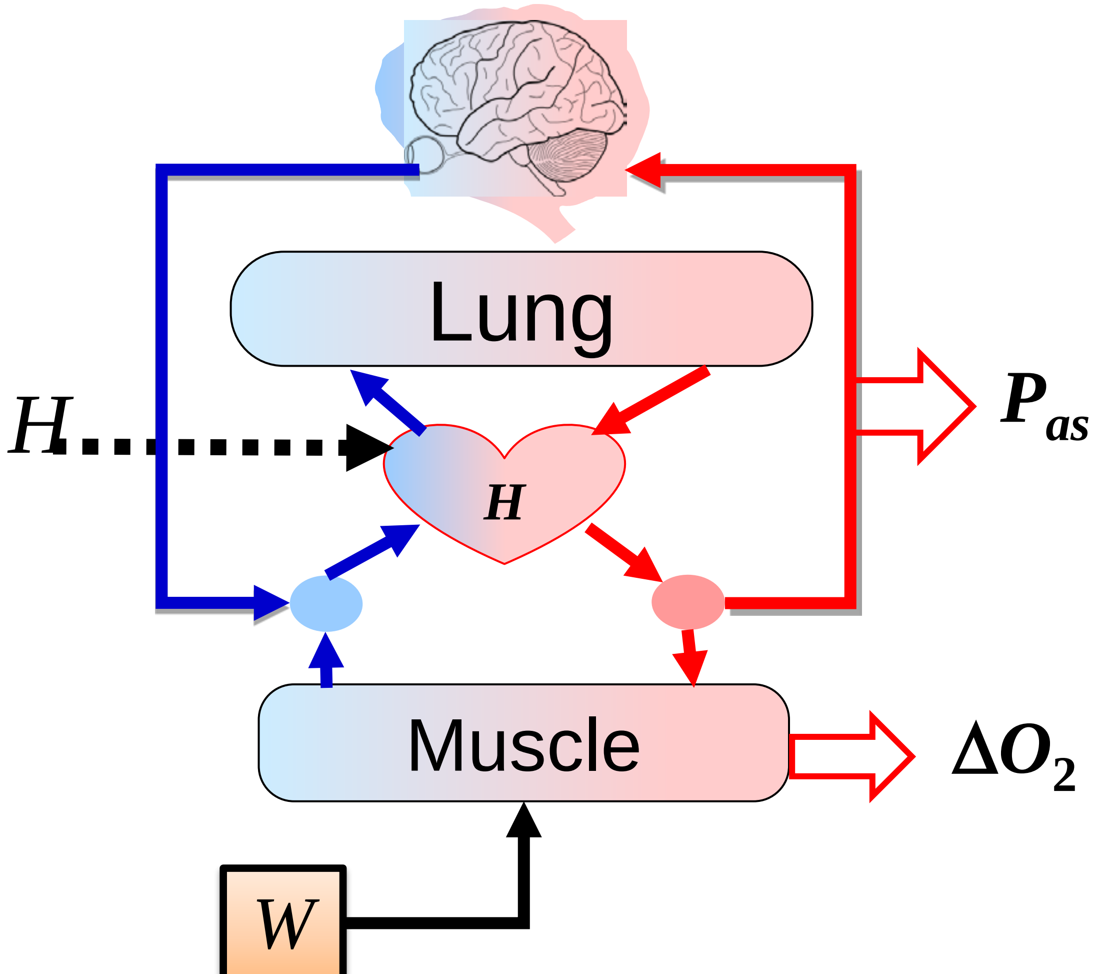
Disturbance:

W high

Math model?

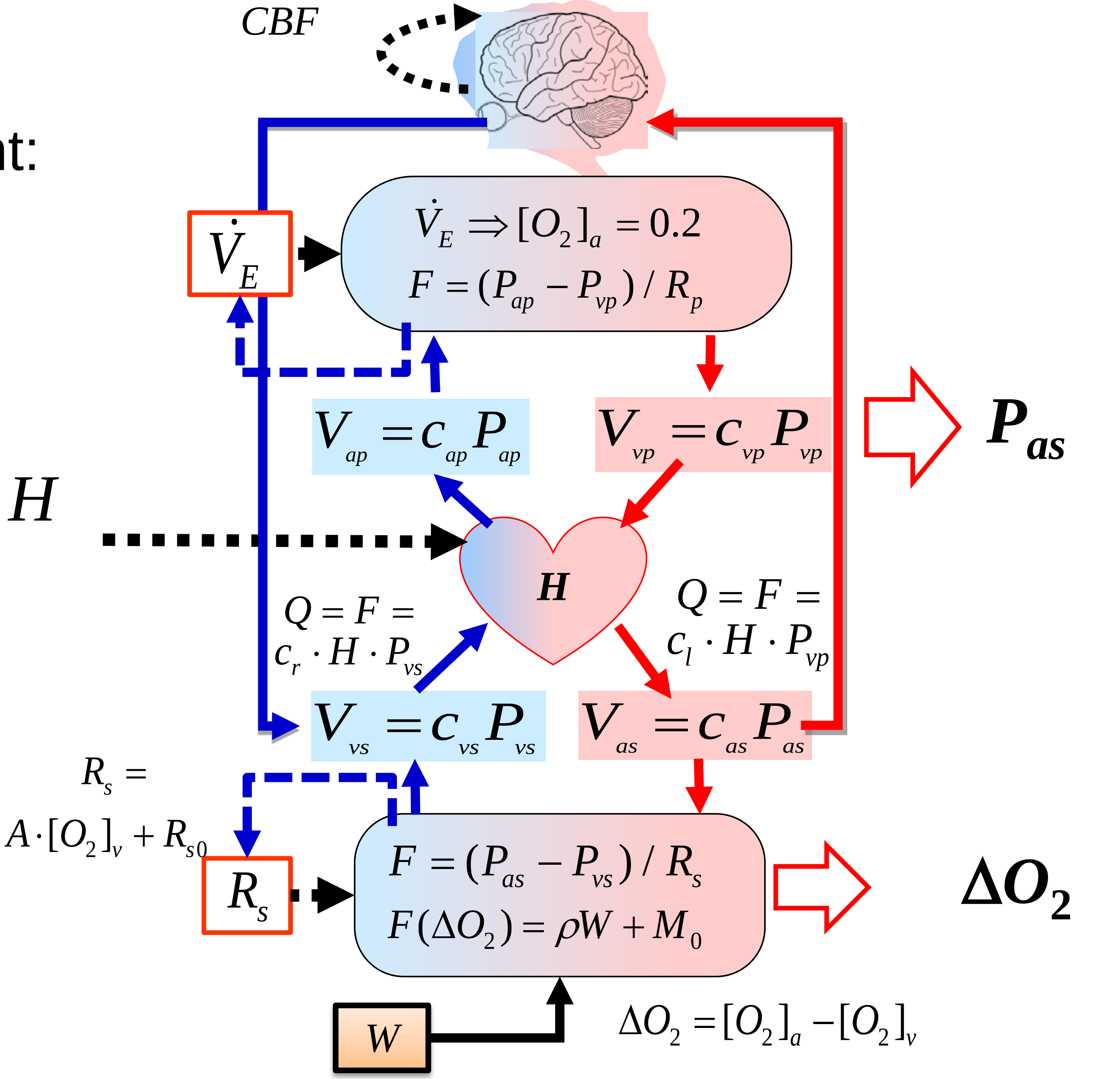
In each compartment:

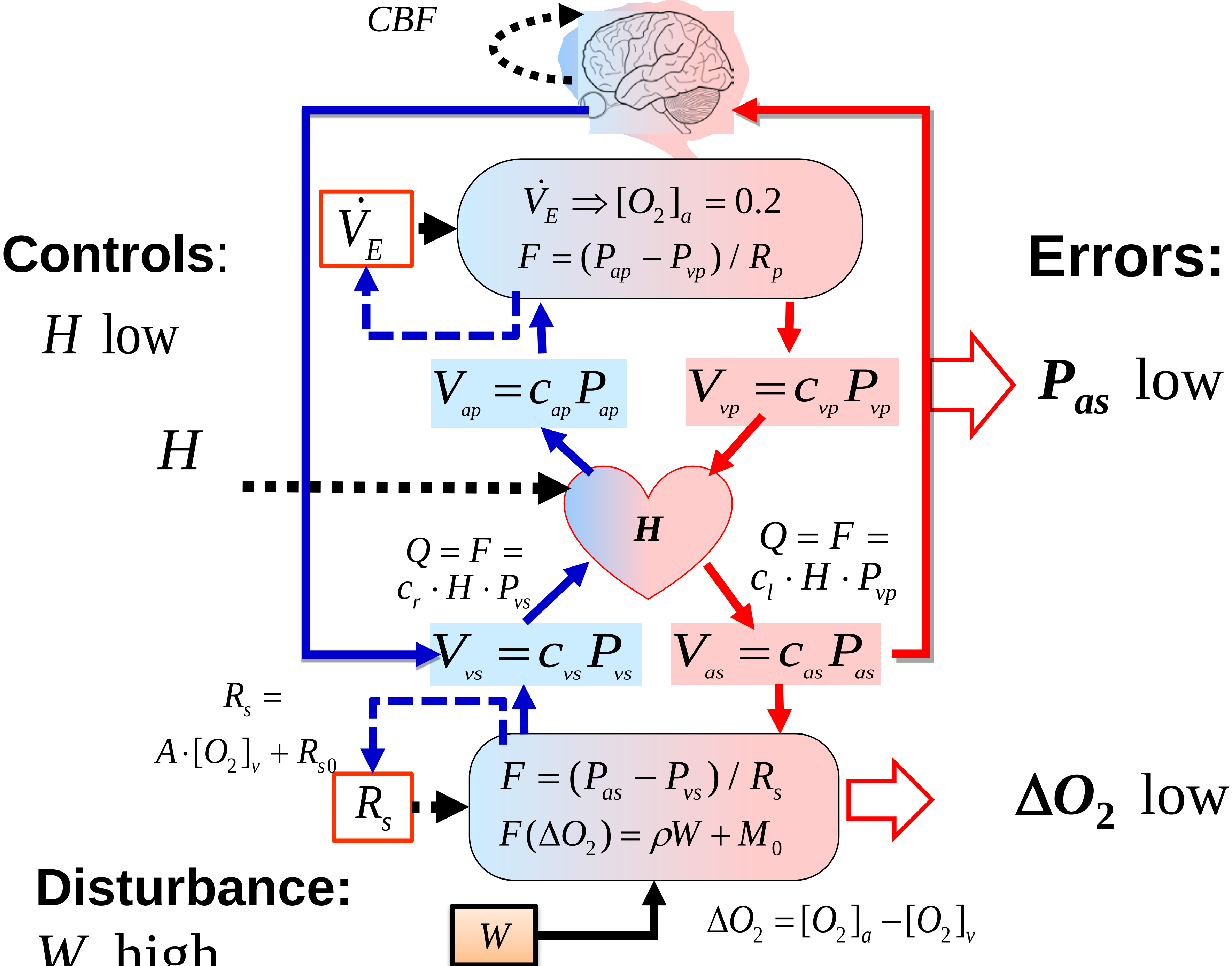
- Oxygen
- Pressure
- Flow



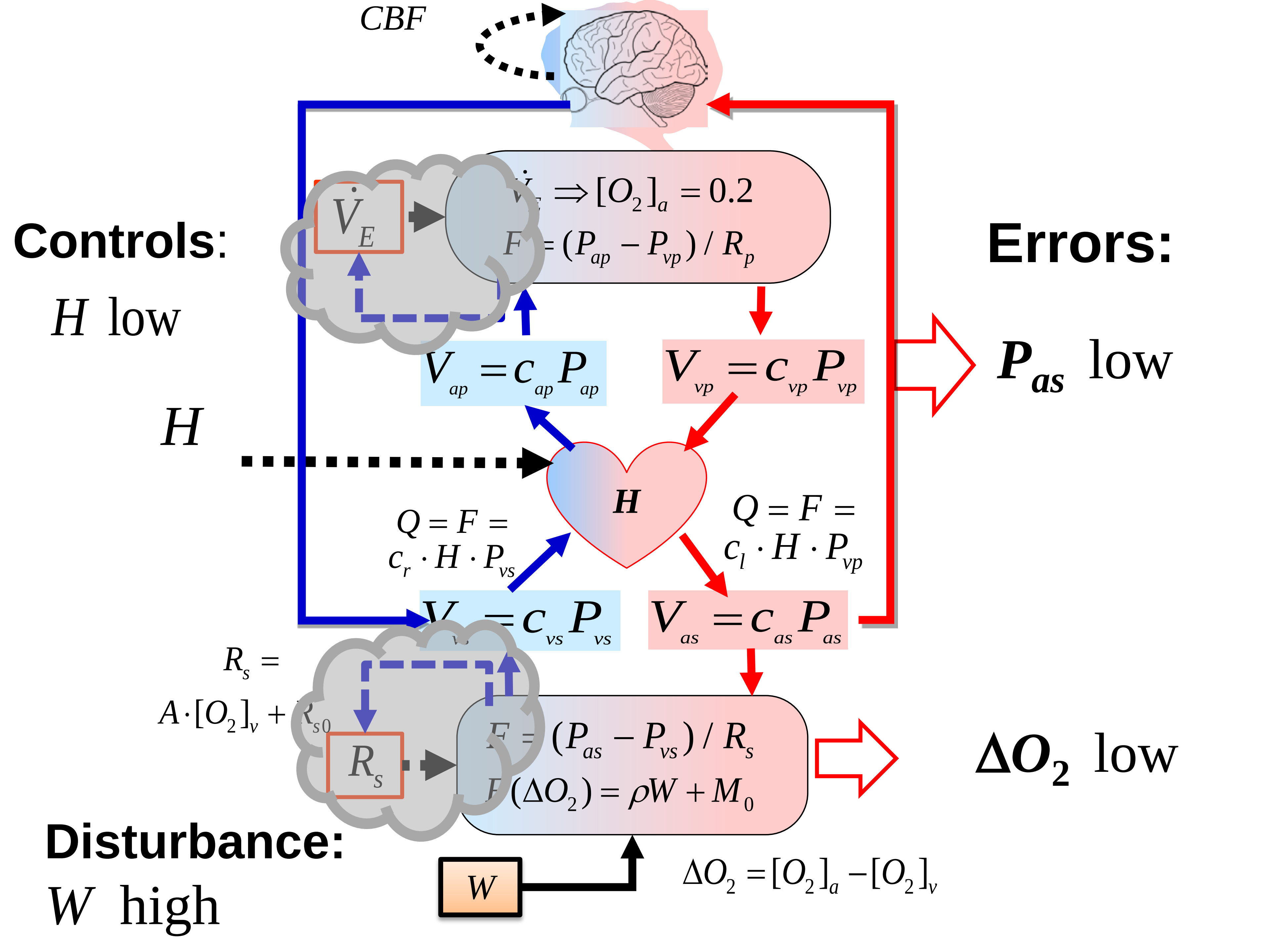
In each compartment:

- Oxygen
- Pressure
- Flow

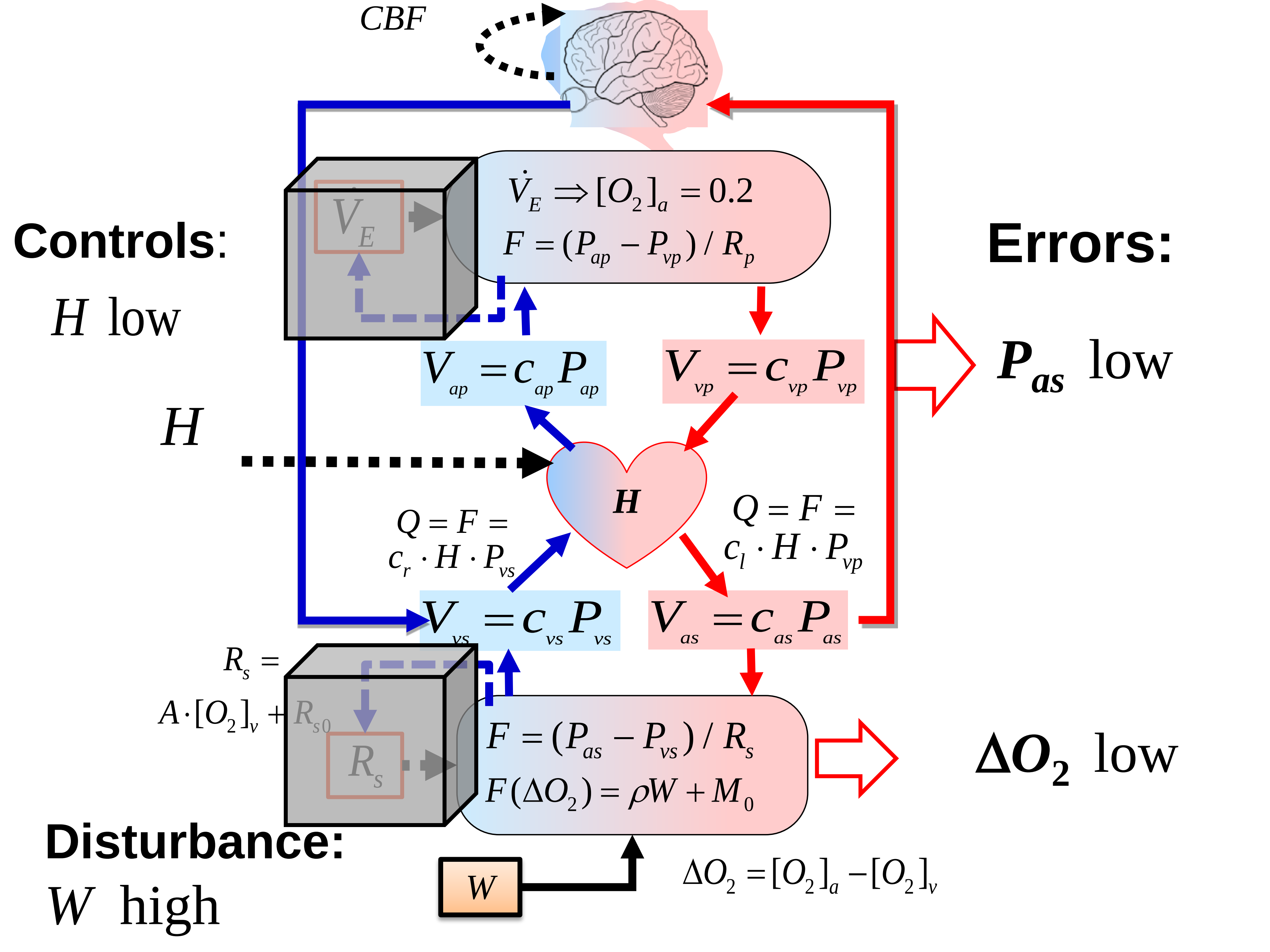




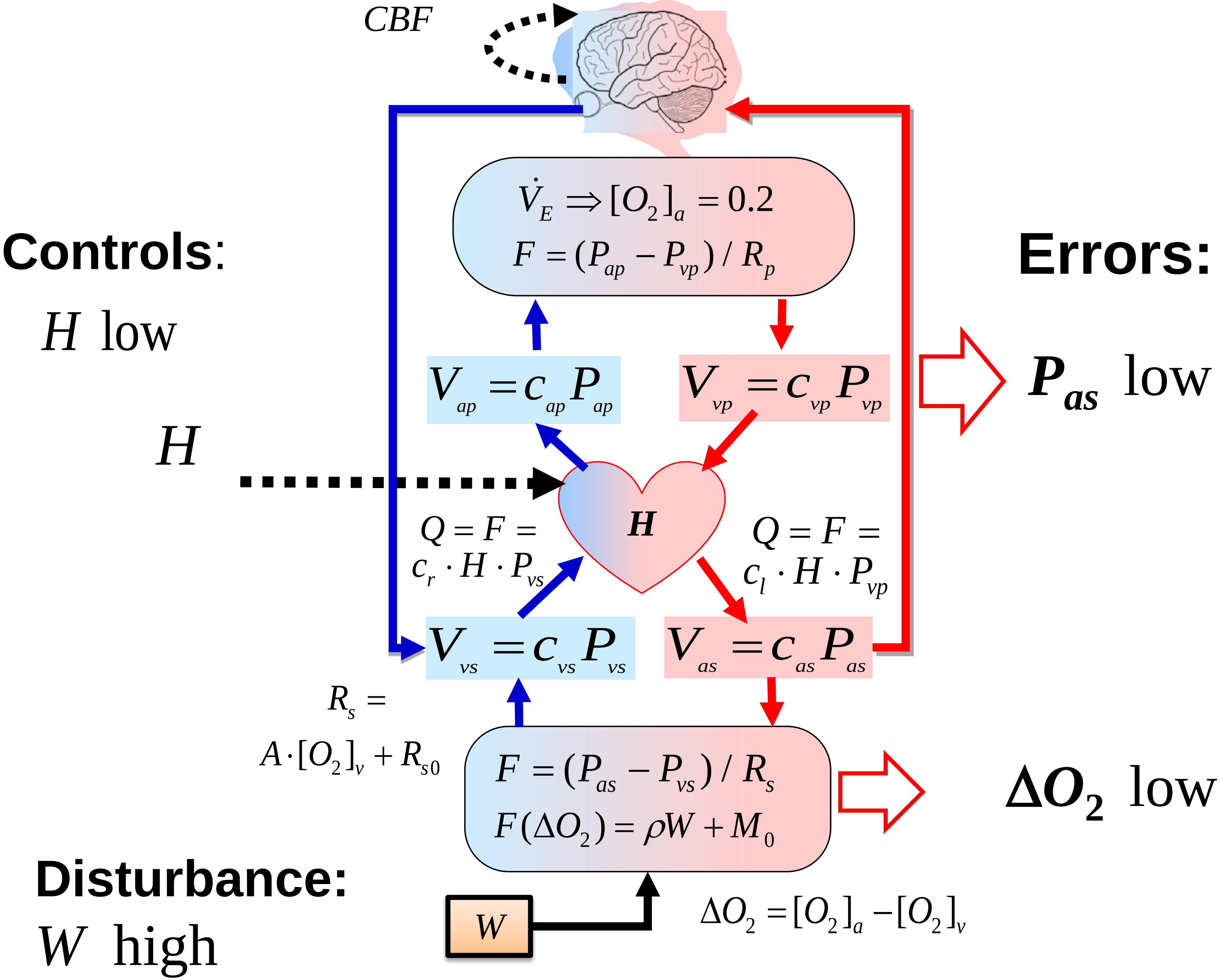
CBF
Controls:
H low
$\dot{V}_E$
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$



CBF
Controls:
H low
H
Errors:
P_as low
ΔO_2 low
Disturbance:
W high
W
Q = F = c_r · H · P_vs
Q = F = c_l · H · P_vp
R_s = A·[O_2]_v + R_s0
ΔO_2 = [O_2]_a − [O_2]_v



CBF
Controls:
H low
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
V_E
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$



CBF
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
Controls:
H low
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$

Controls:

H low

$$\dot{V}_E \Rightarrow [O_2]_a = 0.2$$
$$F = (P_{ap} - P_{vp}) / R_p$$

Errors:

$$V_{ap} = c_{ap} P_{ap} \qquad V_{vp} = c_{vp} P_{vp}$$

$\boldsymbol{P_{as}}$ low

H

$$Q = F = c_r \cdot H \cdot P_{vs} \qquad Q = F = c_l \cdot H \cdot P_{vp}$$

$$V_{vs} = c_{vs} P_{vs} \qquad V_{as} = c_{as} I$$

$$R_s = A \cdot [O_2]_v + R_{s0}$$

$$F = (P_{as} - P_{vs}) / R_s$$
$$F(\Delta O_2) = \rho W + M_0$$

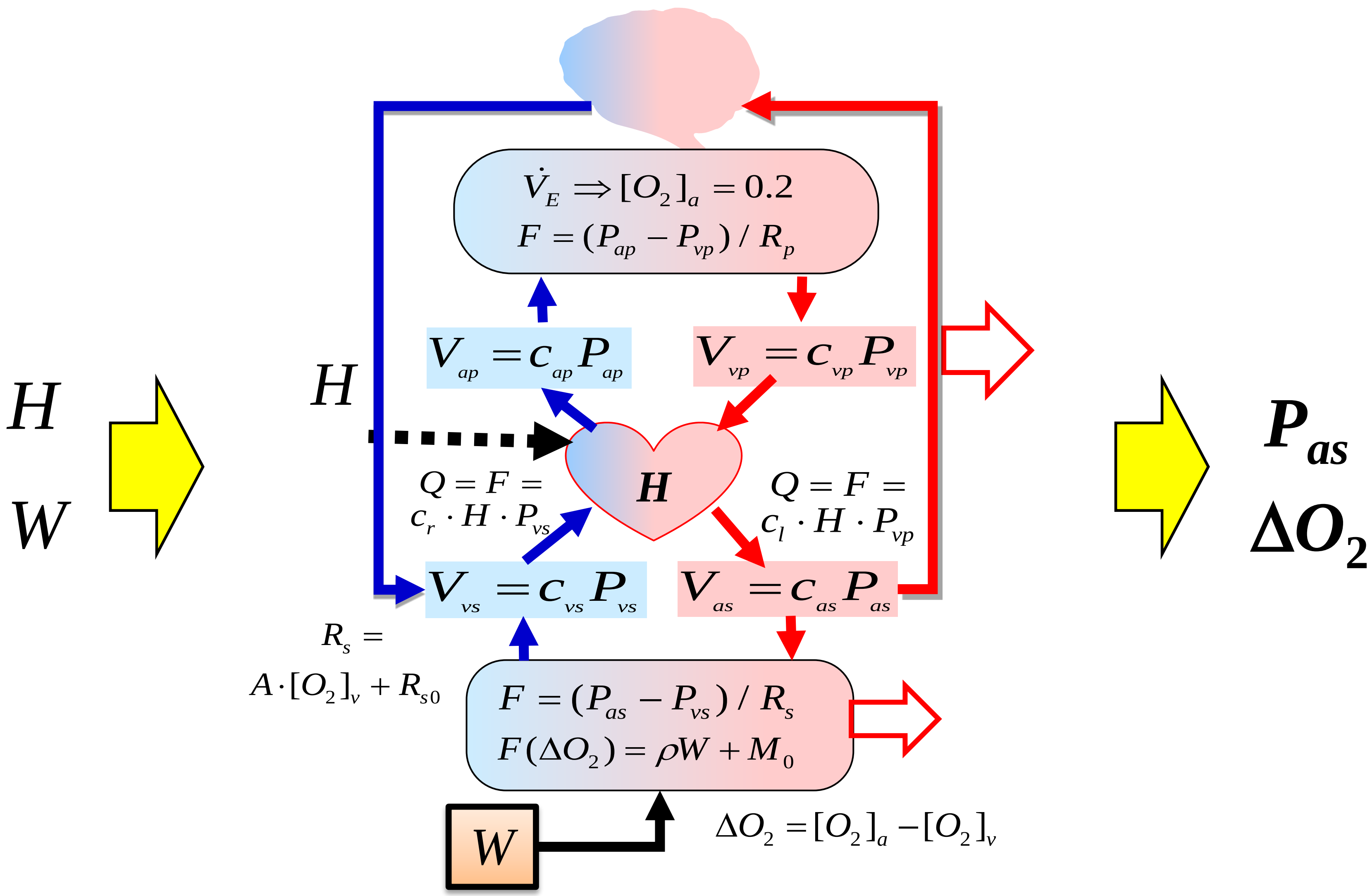
$\boldsymbol{\Delta O_2}$ low

Disturbance:

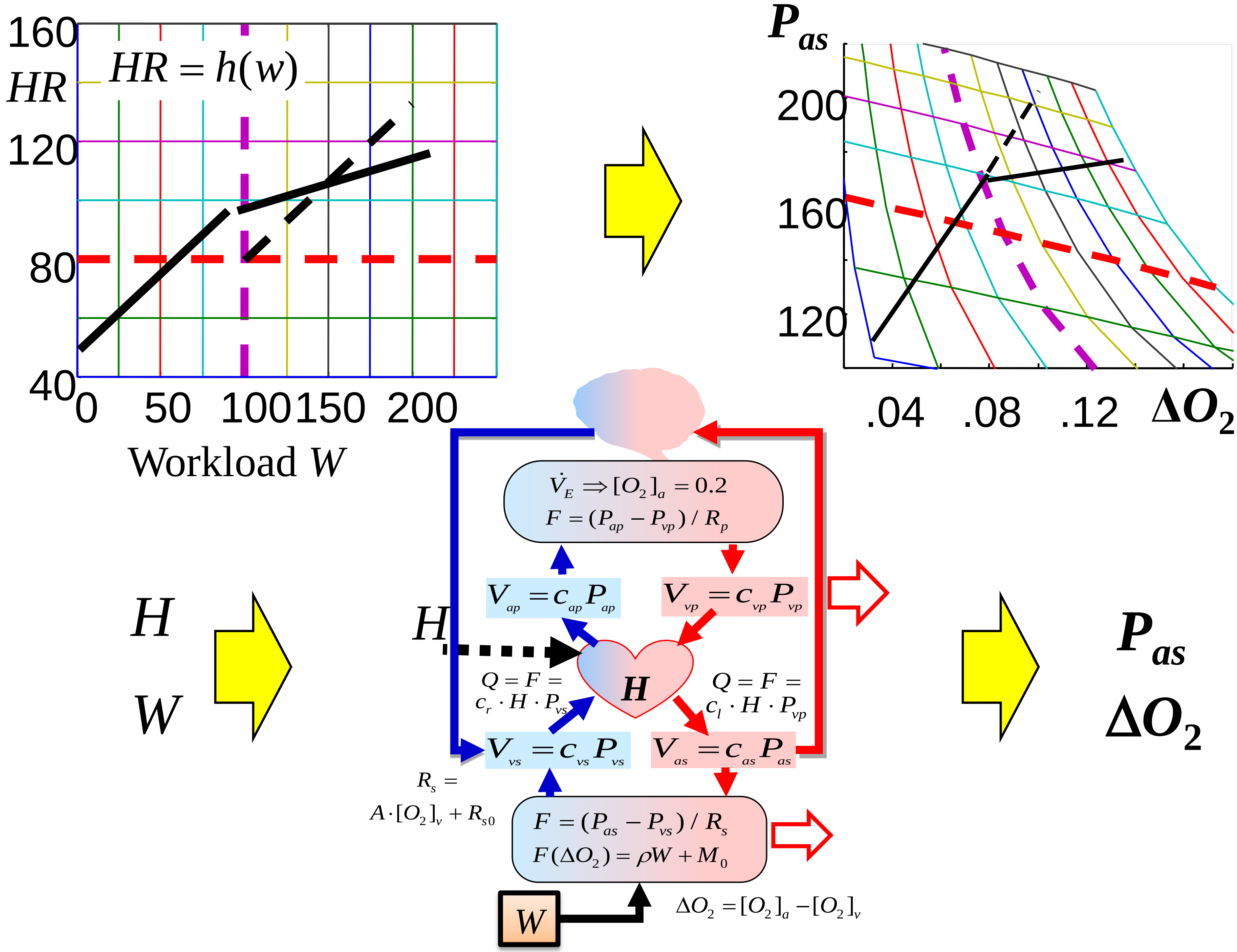
W high

W

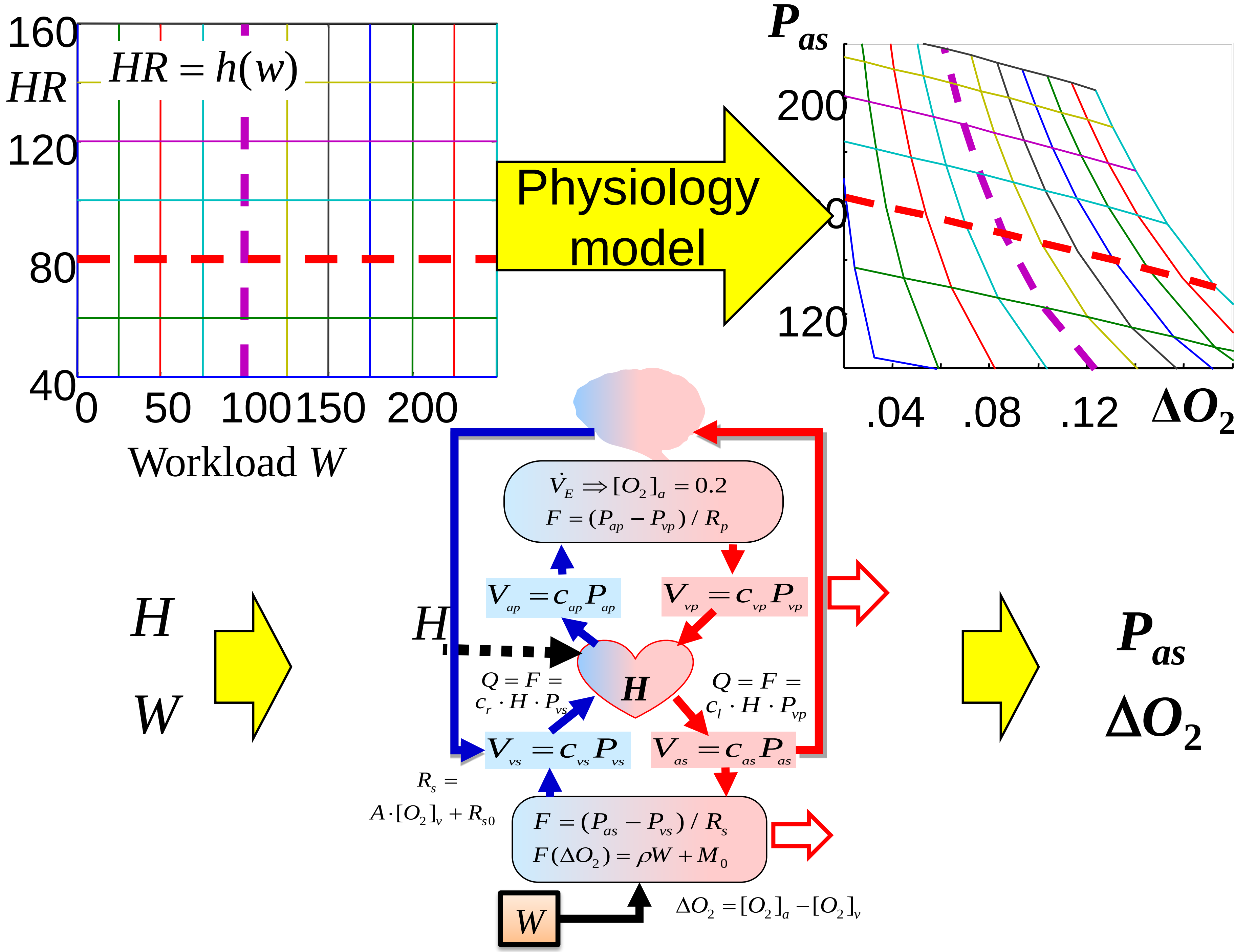
$$\Delta O_2 = [O_2]_a - [O_2]_v$$



H
W
H
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
W
$\Delta O_2 = [O_2]_a - [O_2]_v$
P_{as}
ΔO_2

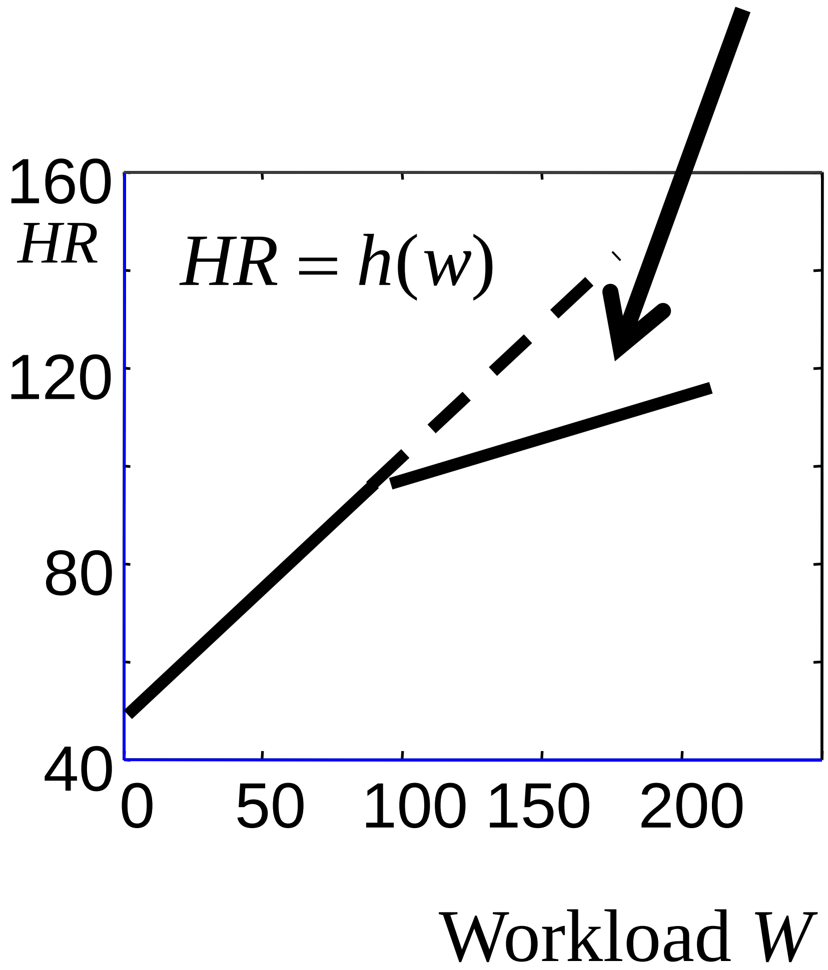


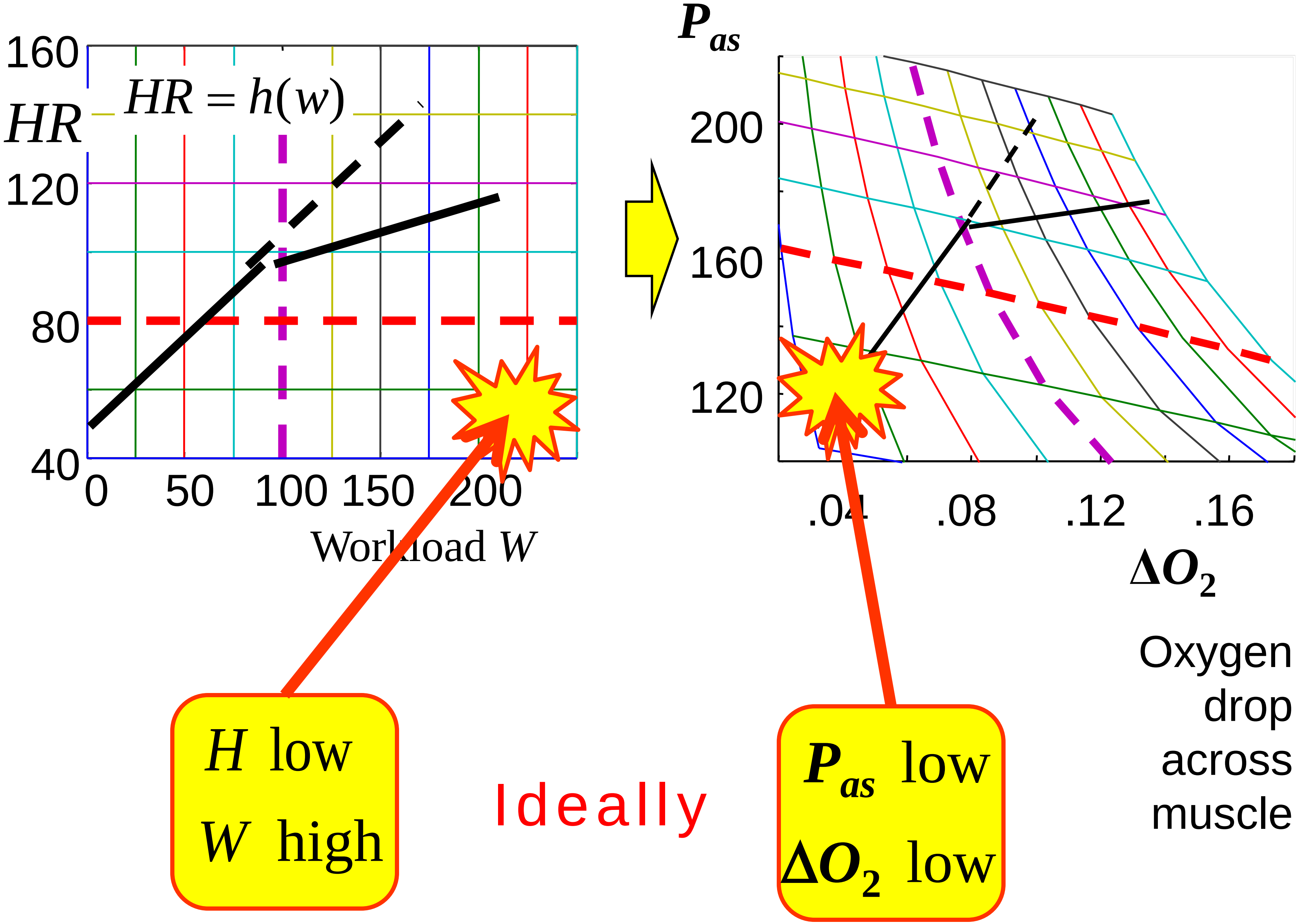
160
HR
120
80
40
HR = h(w)
0
50
100
150
200
Workload W
P_as
200
160
120
.04
.08
.12
ΔO_2
V̇_E ⇒ [O_2]_a = 0.2
F = (P_ap − P_vp) / R_p
V_ap = c_ap P_ap
V_vp = c_vp P_vp
H
W
H
H
Q = F = c_r · H · P_vs
Q = F = c_l · H · P_vp
V_vs = c_vs P_vs
V_as = c_as P_as
R_s = A · [O_2]_v + R_s0
F = (P_as − P_vs) / R_s
F(ΔO_2) = ρW + M_0
W
ΔO_2 = [O_2]_a − [O_2]_v
P_as
ΔO_2



160
HR
120
80
40
$HR = h(w)$
0
50
100
150
200
Workload W
Physiology model
P_{as}
200
120
.04
.08
.12
ΔO_2
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
H
W
H
$Q = F = c_r \cdot H \cdot P_{vs}$
H
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
W
$\Delta O_2 = [O_2]_a - [O_2]_v$
P_{as}
ΔO_2

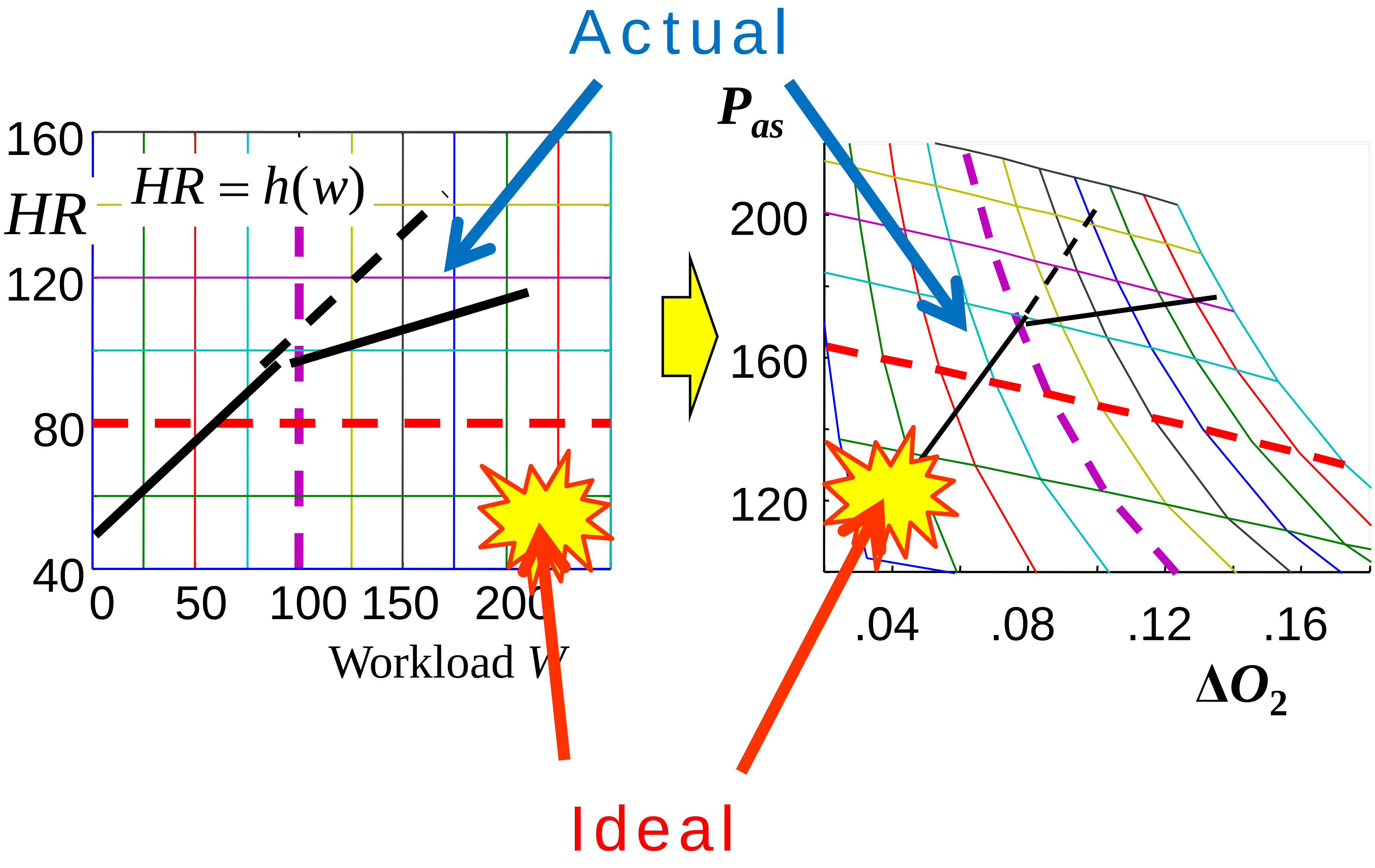
Nonlinearity in the *data*





HR
HR = h(w)
160
120
80
40
0
50
100
150
200
Workload W
P_as
200
160
120
.04
.08
.12
.16
ΔO_2
Oxygen drop across muscle
H low
W high
Ideally
P_as low
ΔO_2 low

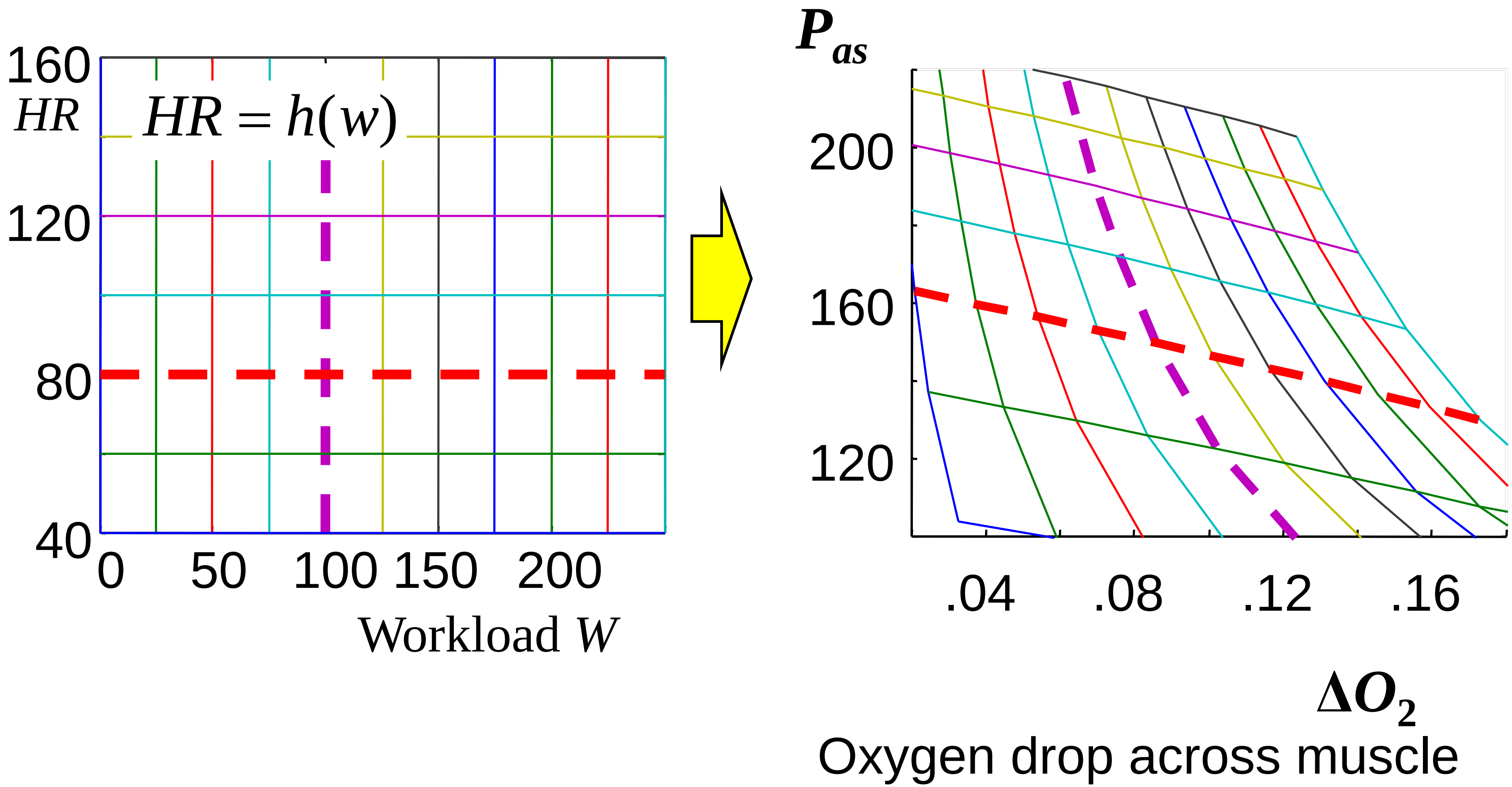
Necessary?


Actual
Ideal
HR
HR = h(w)
160
120
80
40
0
50
100
150
200
Workload W
P_as
200
160
120
.04
.08
.12
.16
ΔO2

Physiological *model*

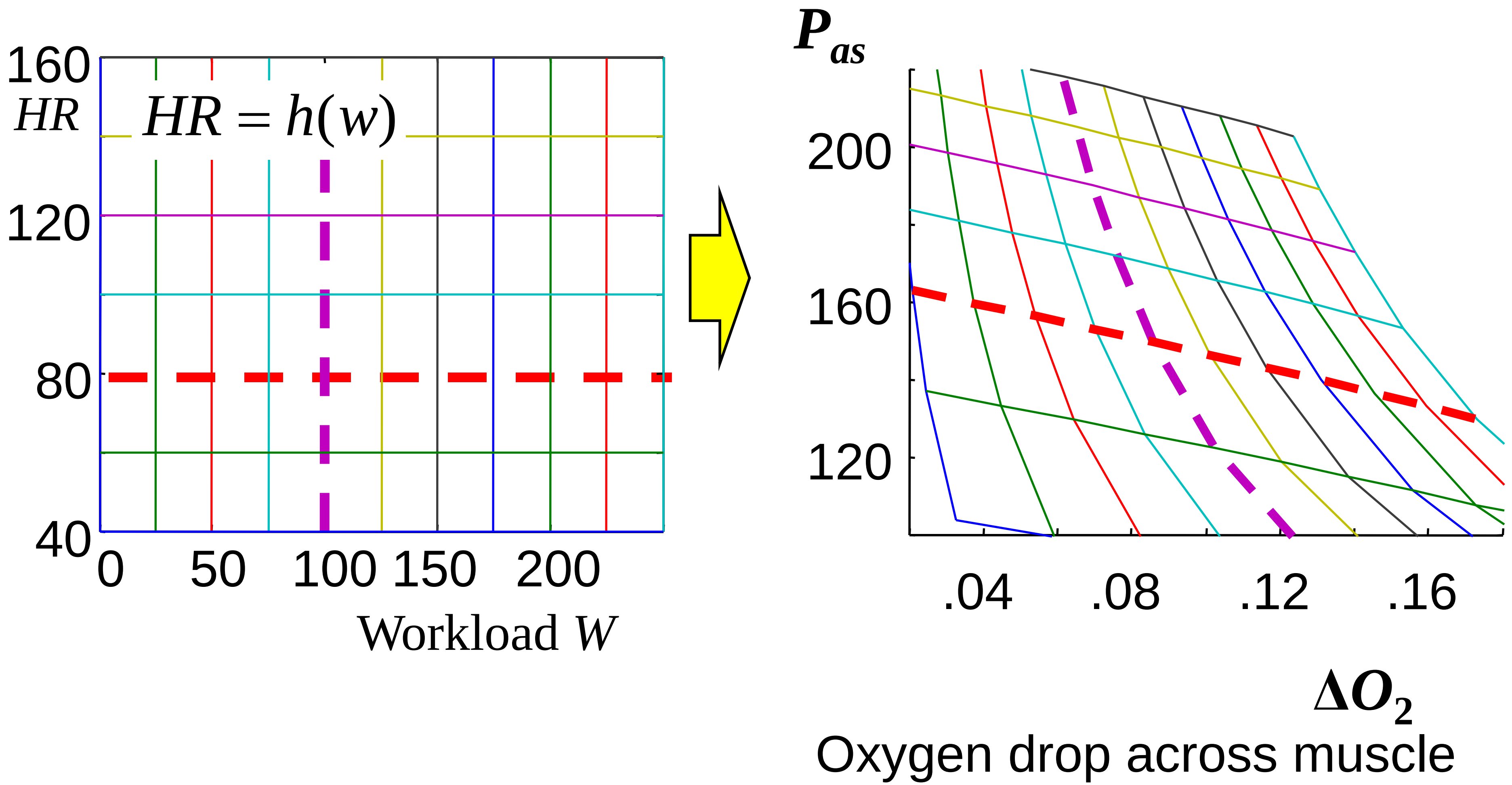
Mean Arterial Blood Pressure (MAP)

= $\boldsymbol{P_{as}}$ Pressure, Arterial, Systemic



Intuition

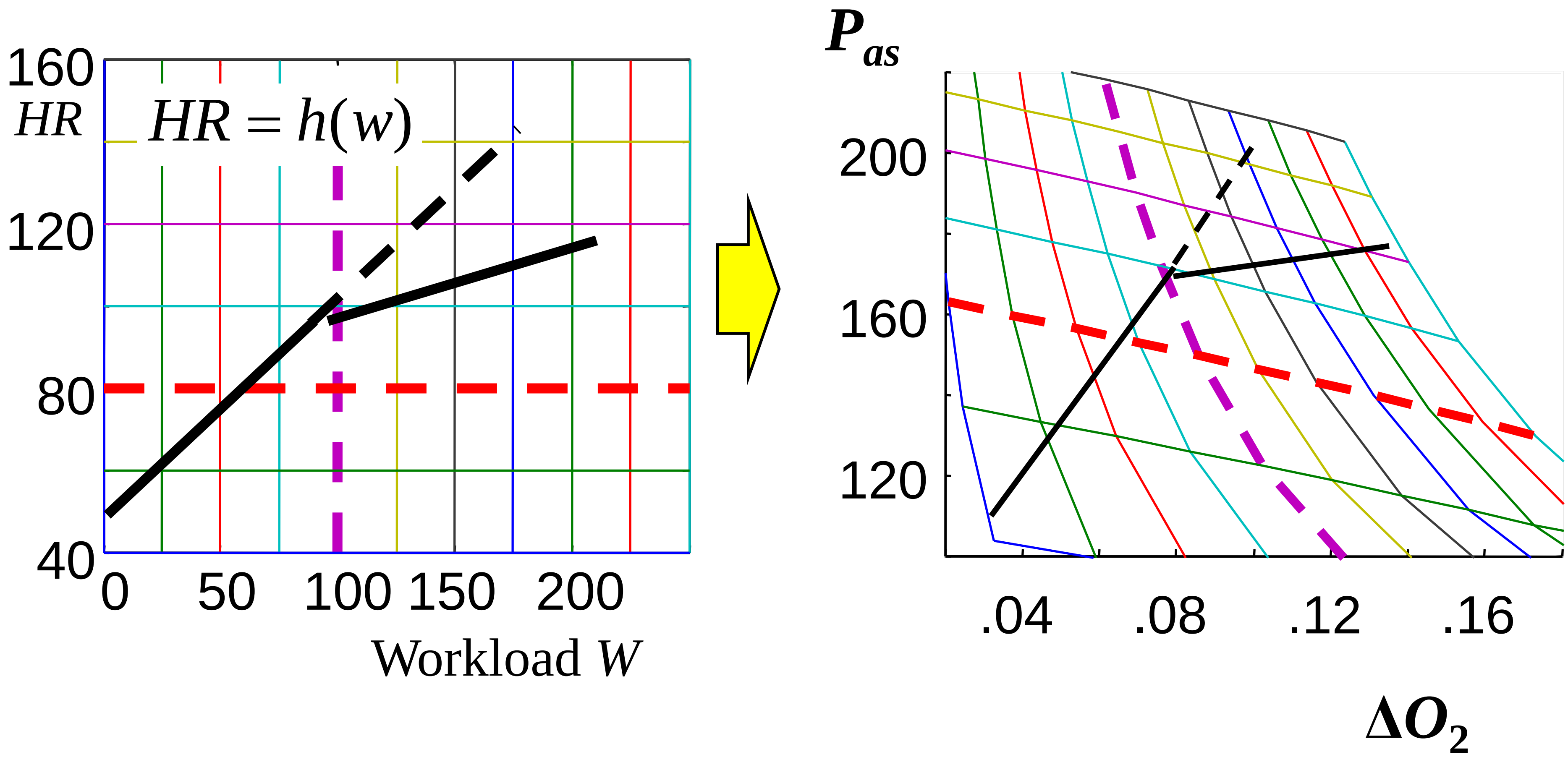
Mean Arterial Blood Pressure (MAP)
= P_{as} Pressure, Arterial, Systemic



Physiological model + *data*

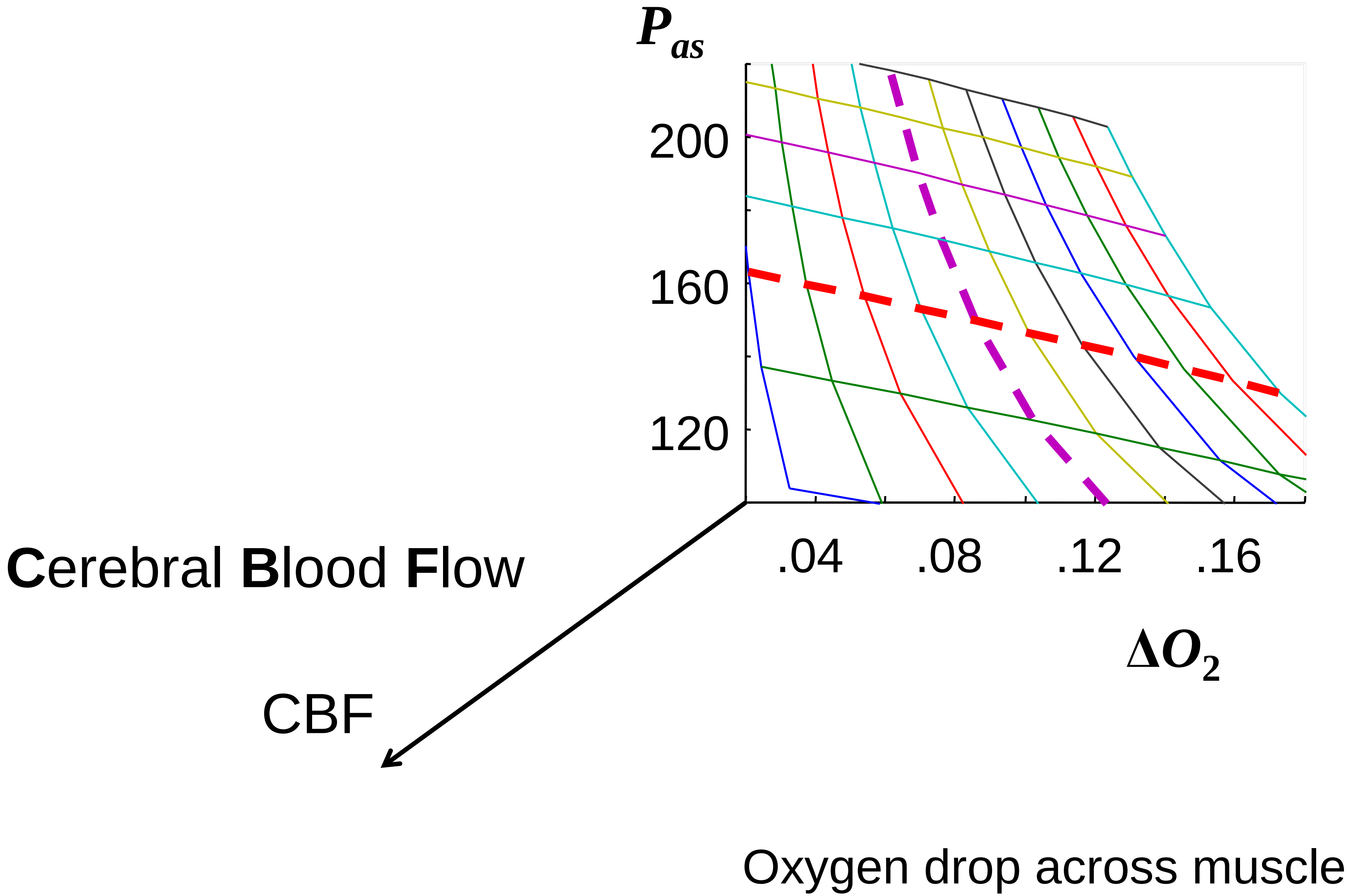
Mean Arterial Blood Pressure (MAP)

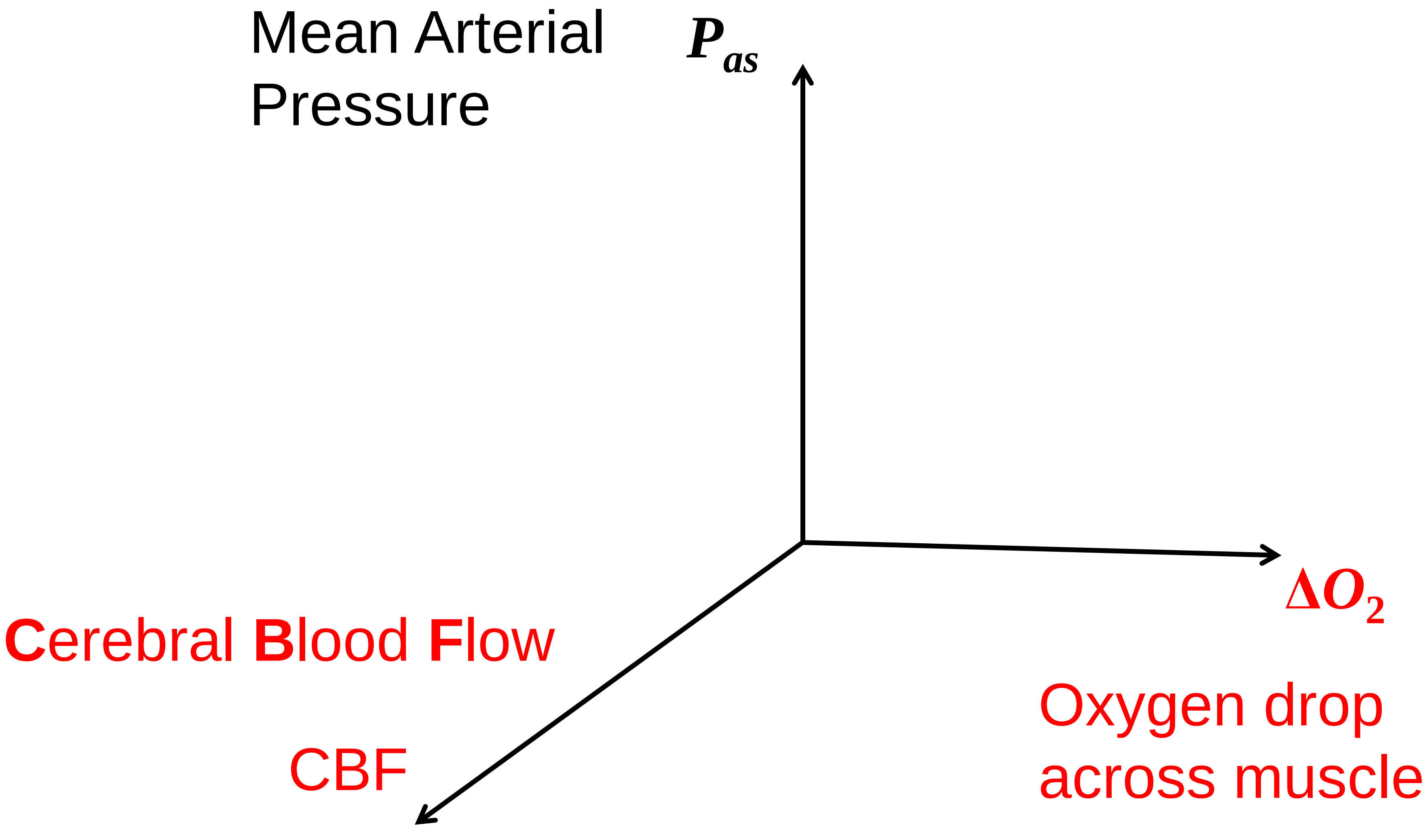
= P_{as} Pressure, Arterial, Systemic

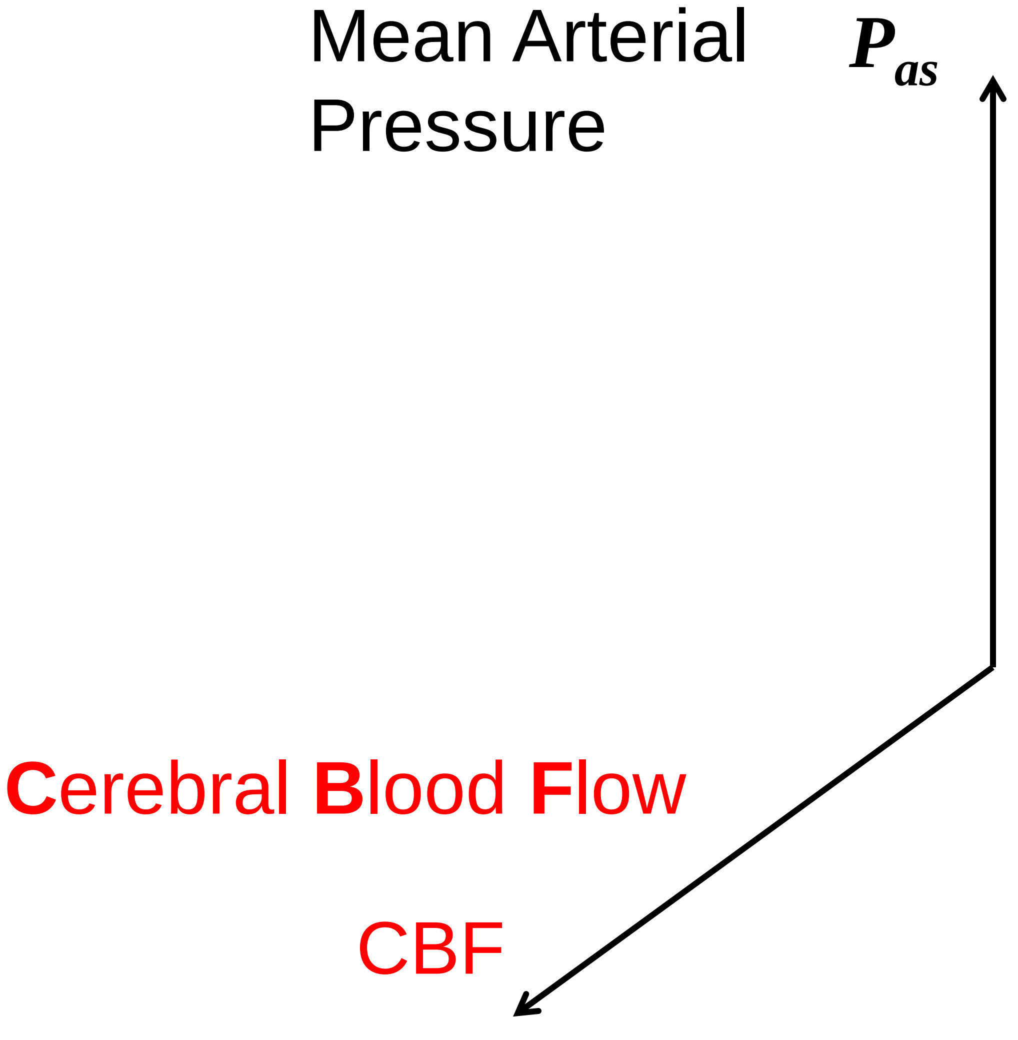


Oxygen drop across muscle

Intuition


P_{as}
200
160
120
.04
.08
.12
.16
ΔO_2
Cerebral **B**lood **F**low
CBF
Oxygen drop across muscle

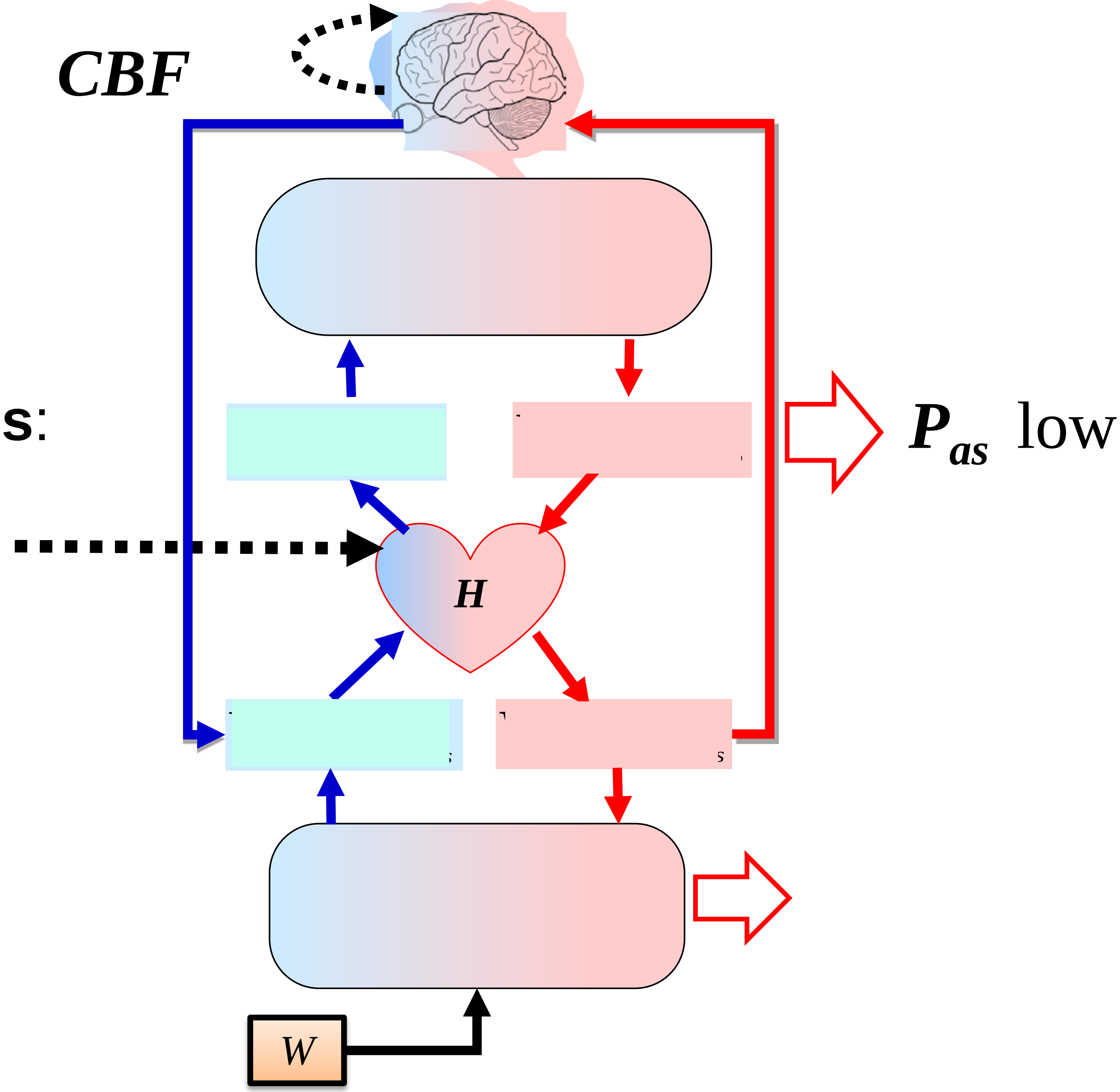

Mean Arterial Pressure
P_{as}
ΔO_2
Oxygen drop across muscle
Cerebral Blood Flow
CBF

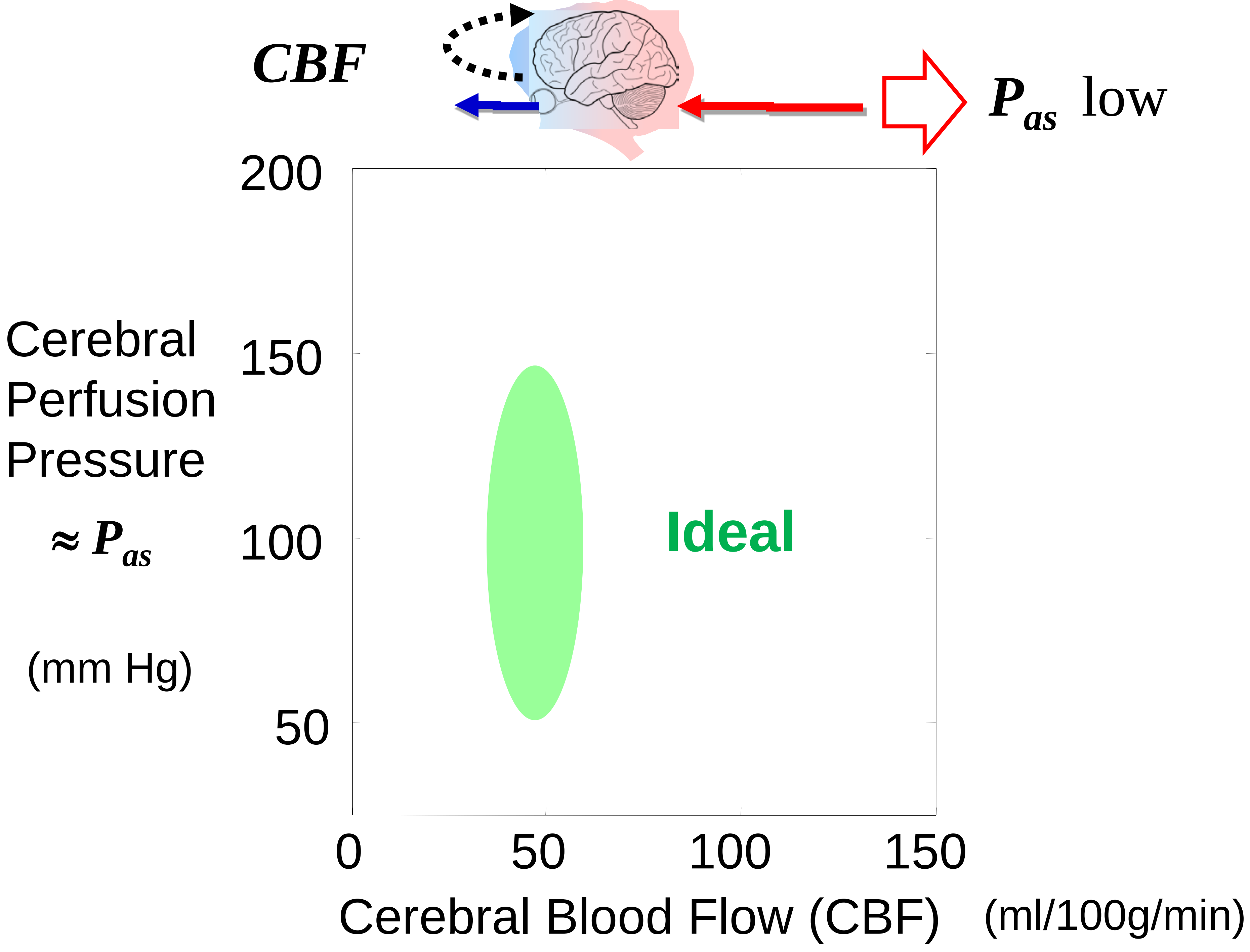

Mean Arterial
Pressure
P_{as}
Cerebral **B**lood **F**low
CBF

Cerebral Blood Flow

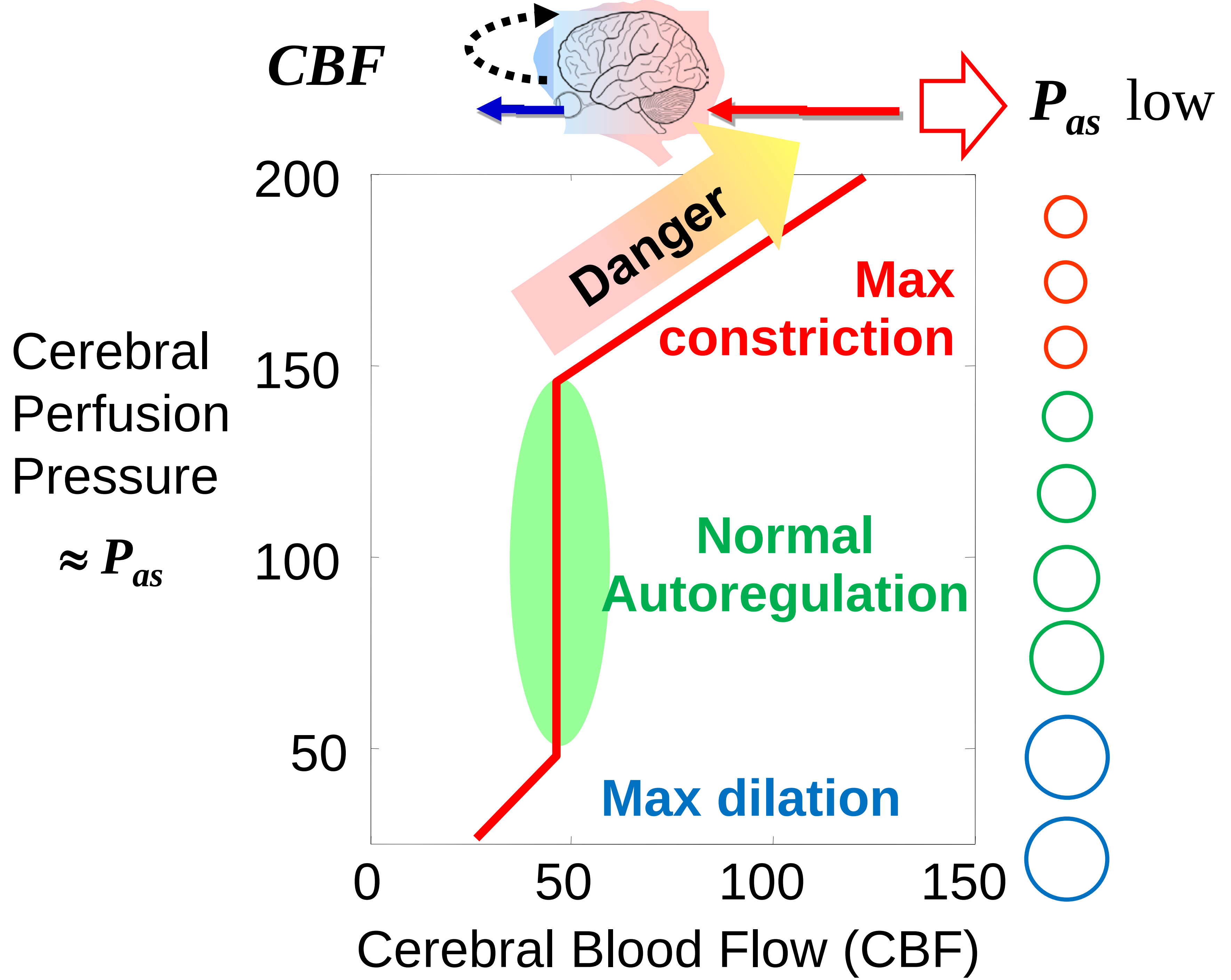
Controls:

H

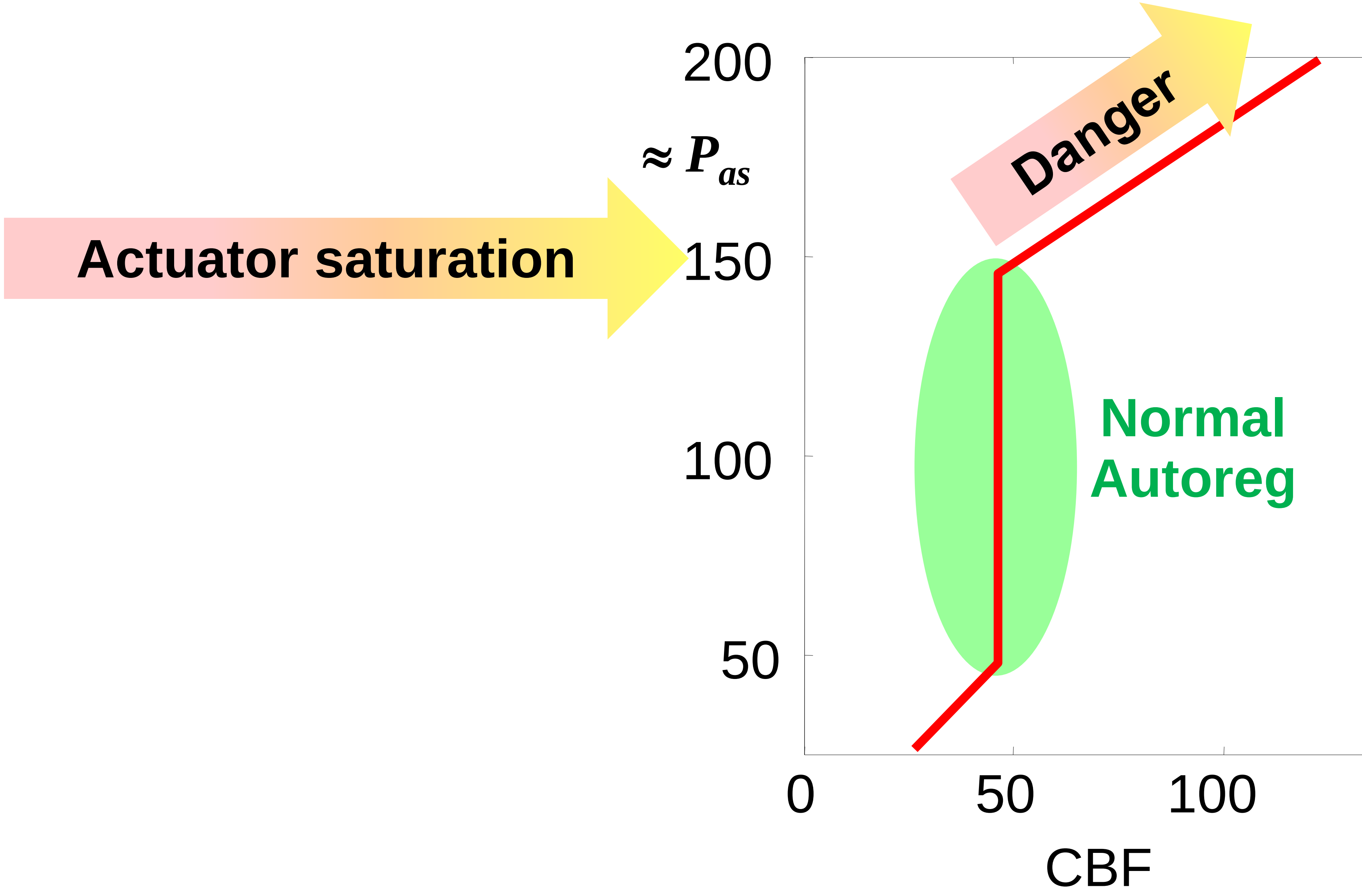




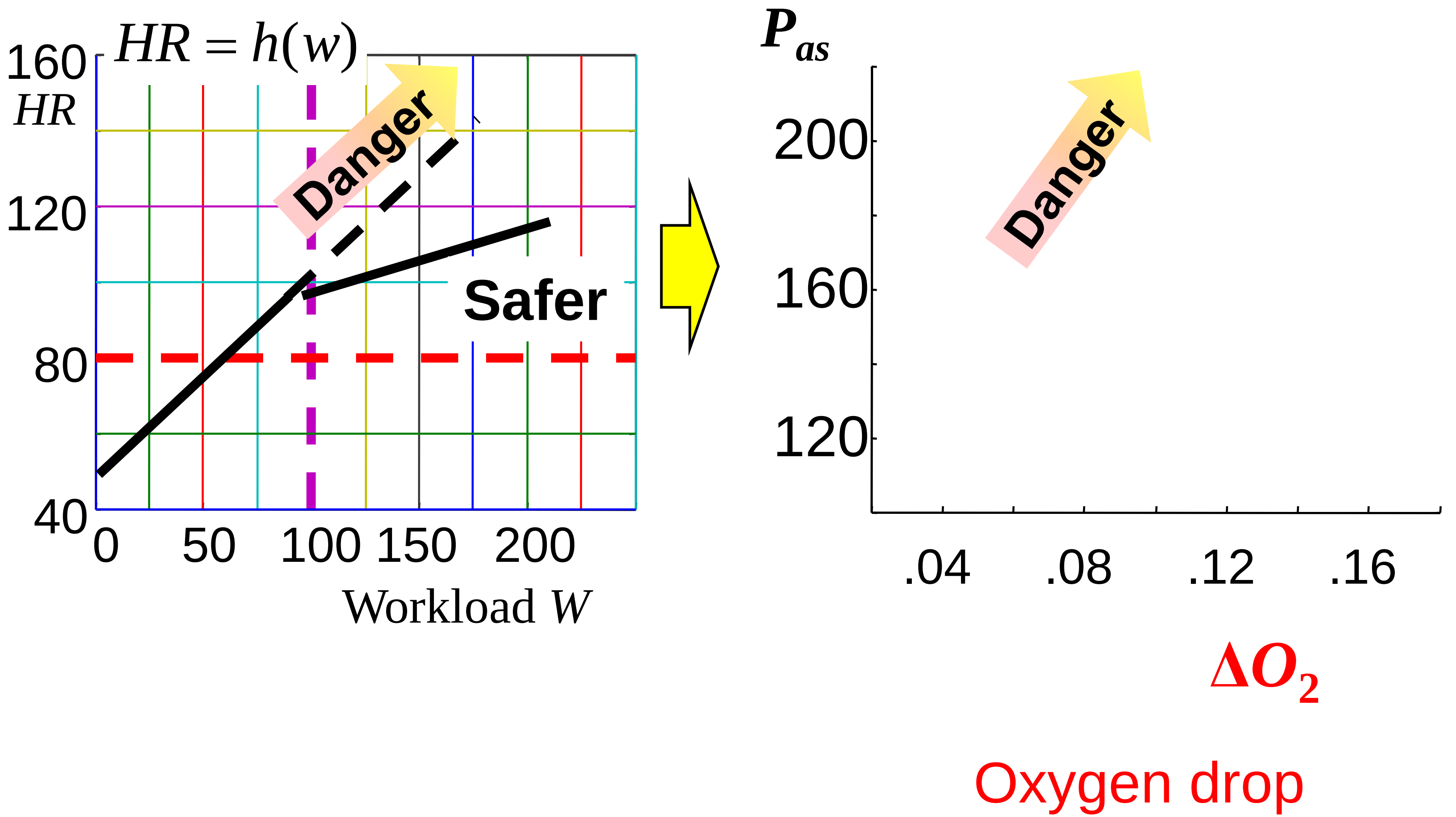
CBF
P_{as} low
Cerebral Perfusion Pressure
$\approx P_{as}$
(mm Hg)
200
150
100
50
Ideal
0
50
100
150
Cerebral Blood Flow (CBF)
(ml/100g/min)



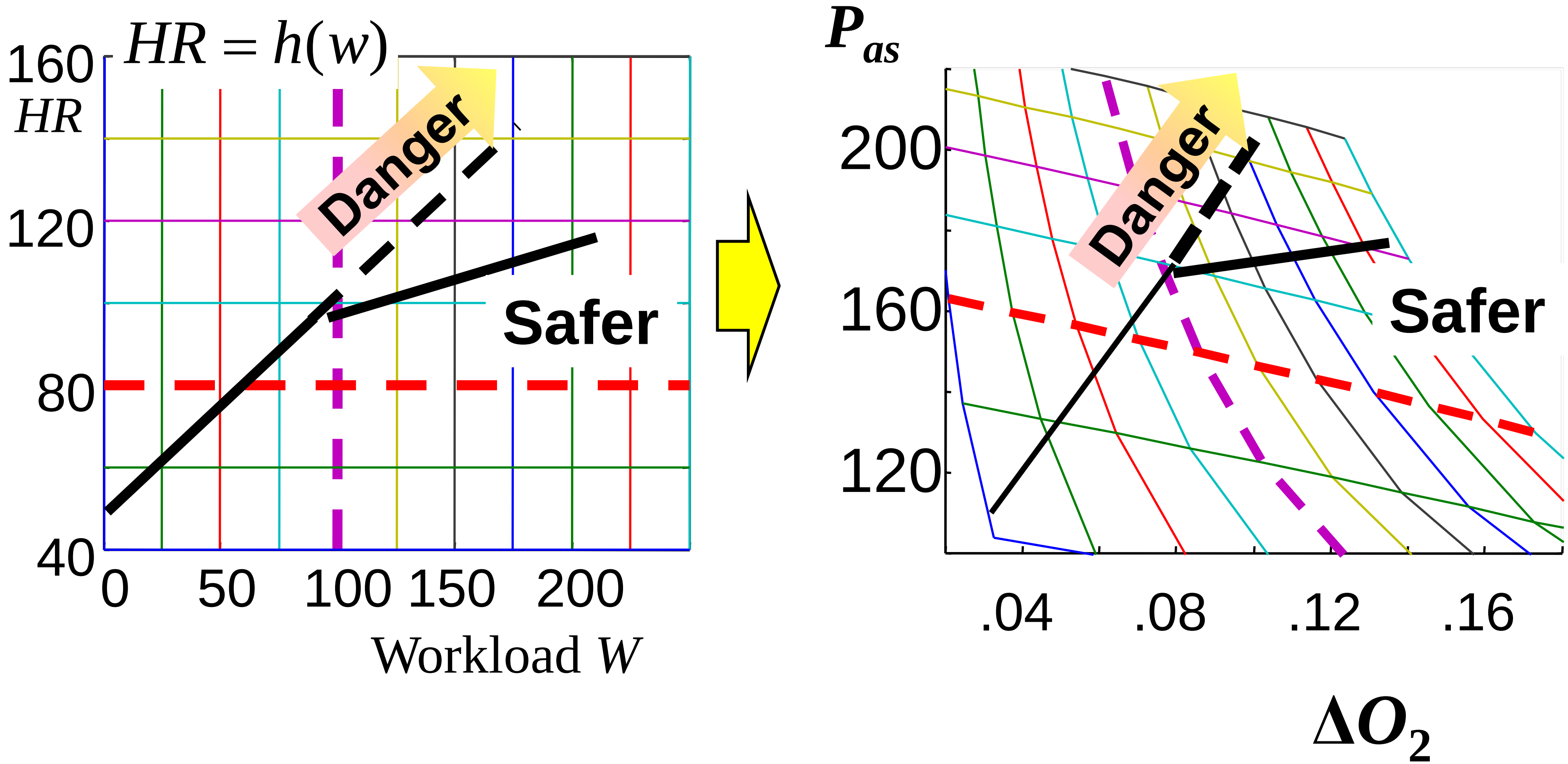
CBF
P_{as} low
200
150
100
50
Danger
Max constriction
Normal Autoregulation
Max dilation
Cerebral Perfusion Pressure
$\approx P_{as}$
0
50
100
150
Cerebral Blood Flow (CBF)



Actuator saturation
≈ P_{as}
Danger
Normal
Autoreg
200
150
100
50
0
50
100
CBF



$HR = h(w)$
160
HR
120
80
40
0
50
100
150
200
Workload W
Danger
Safer
P_{as}
200
160
120
.04
.08
.12
.16
Danger
ΔO_2
Oxygen drop
across muscle

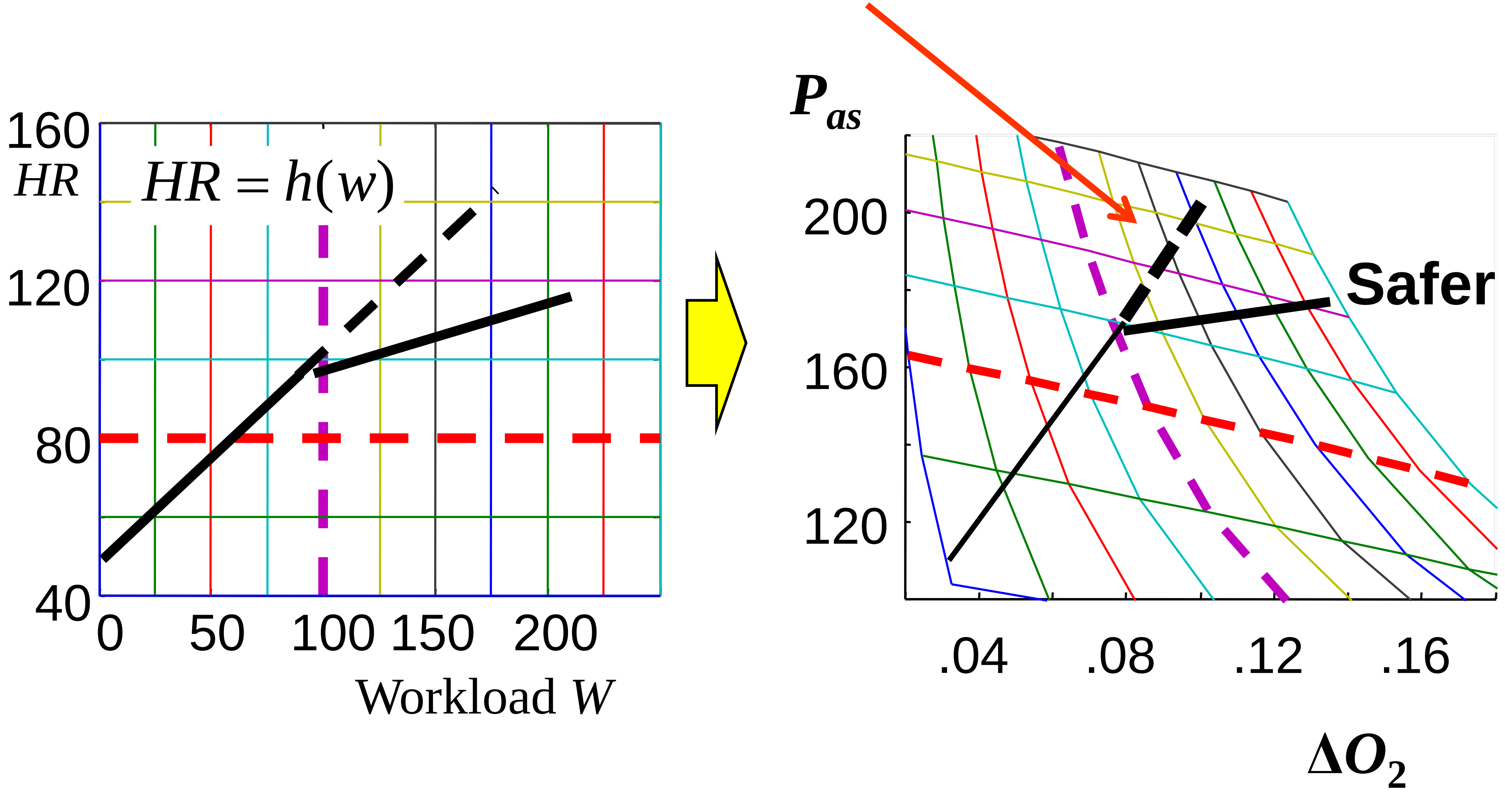


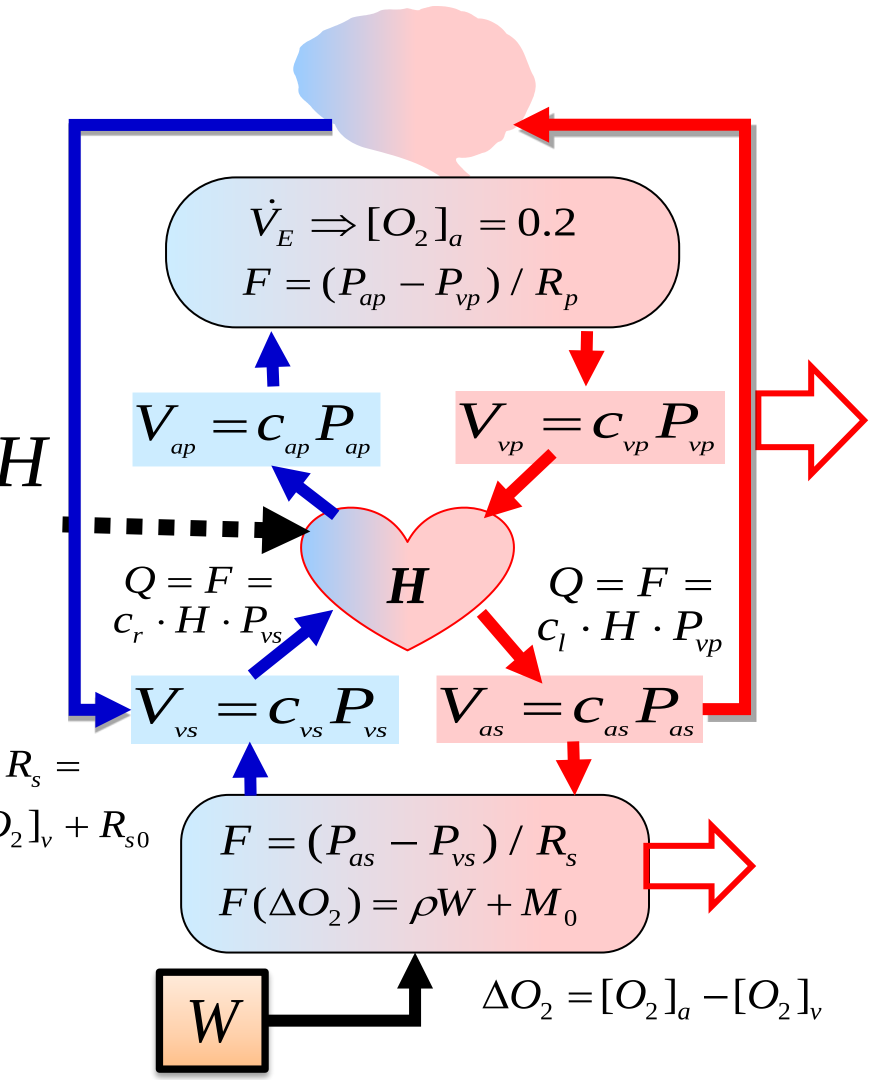
Safer ⇒ worse ΔO_2

⇒ metabolic cost

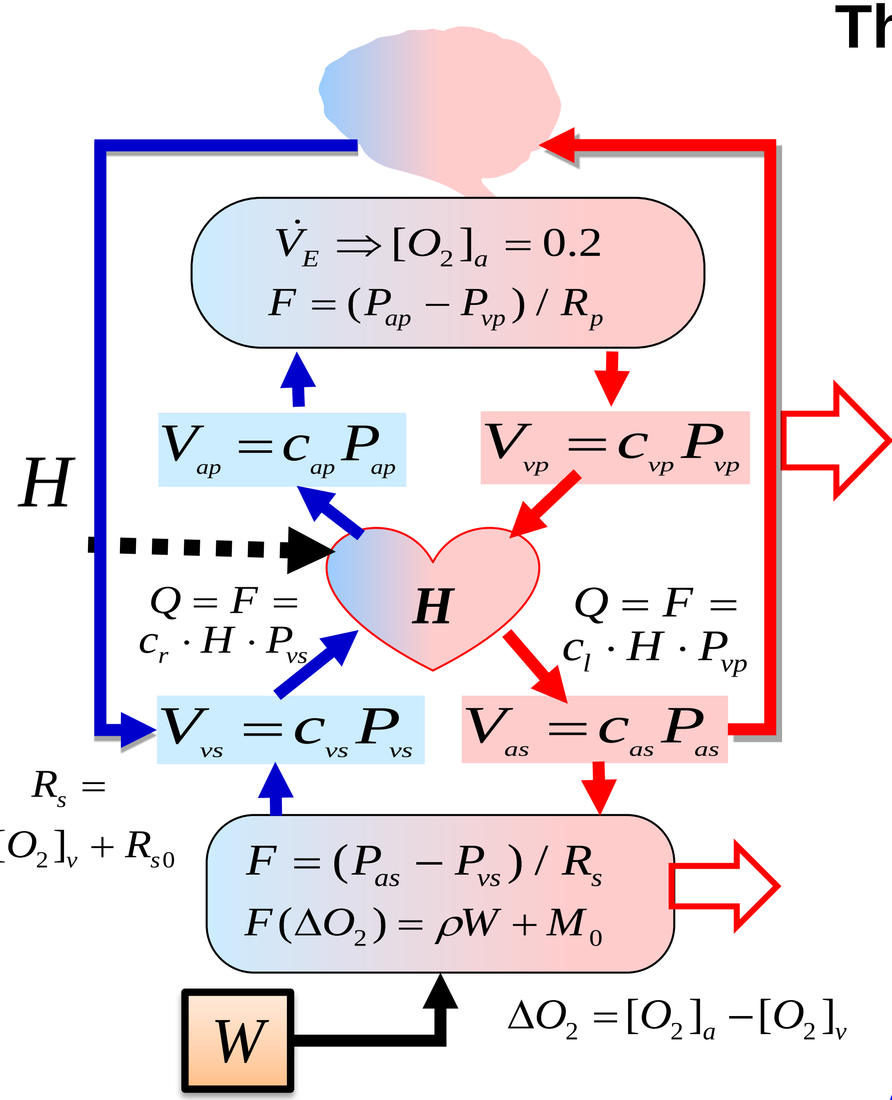
Dangerous

MAP= P_{as}





$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s =$
$O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
W
$\Delta O_2 = [O_2]_a - [O_2]_v$



The simplified model:

$$F_p = (P_{ap} - P_{vp}) / R_p$$
$$F_s = (P_{as} - P_{vs}) / R_s$$
$$Q_r = c_r \cdot H \cdot P_{vs}$$
$$Q_l = c_l \cdot H \cdot P_{vp}$$
$$F_p = F_s = Q_r = Q_l$$

$$V_{vs} = c_{vs} P_{vs}$$
$$V_{as} = c_{as} P_{as}$$
$$V_{ap} = c_{ap} P_{ap}$$
$$V_{vp} = c_{vp} P_{vp}$$

$$V_{tot} = V_{as} + V_{vs} + V_{ap} + V_{vp}$$
$$F_s([O_2]_a - [O_2]_v) = \rho w + M_0$$
$$R_s = A \cdot [O_2]_v + R_{s0}$$
$$[O_2]_a = 0.2$$

$$(BP, \Delta O_2) = F(w, H)$$

$$\Delta O_2 = [O_2]_a - [O_2]_v$$

Flow

$$F_p = (P_{ap} - P_{vp}) / R_p$$

$$F_s = (P_{as} - P_{vs}) / R_s$$

$$Q_r = c_r \cdot H \cdot P_{vs}$$

$$Q_l = c_l \cdot H \cdot P_{vp}$$

HR

$$F_p = F_s = Q_r = Q_l$$

static

Volume

$$V_{vs} = c_{vs} P_{vs}$$

$$V_{as} = c_{as} P_{as}$$

$$V_{ap} = c_{ap} P_{ap}$$

$$V_{vp} = c_{vp} P_{vp}$$

Pressure

$$V_{tot} = V_{as} + V_{vs} + V_{ap} + V_{vp}$$

Oxygen

$$F_s([O_2]_a - [O_2]_v) = \rho w + M_0$$

Metabolism

$$R_s = A \cdot [O_2]_v + R_{s0}$$

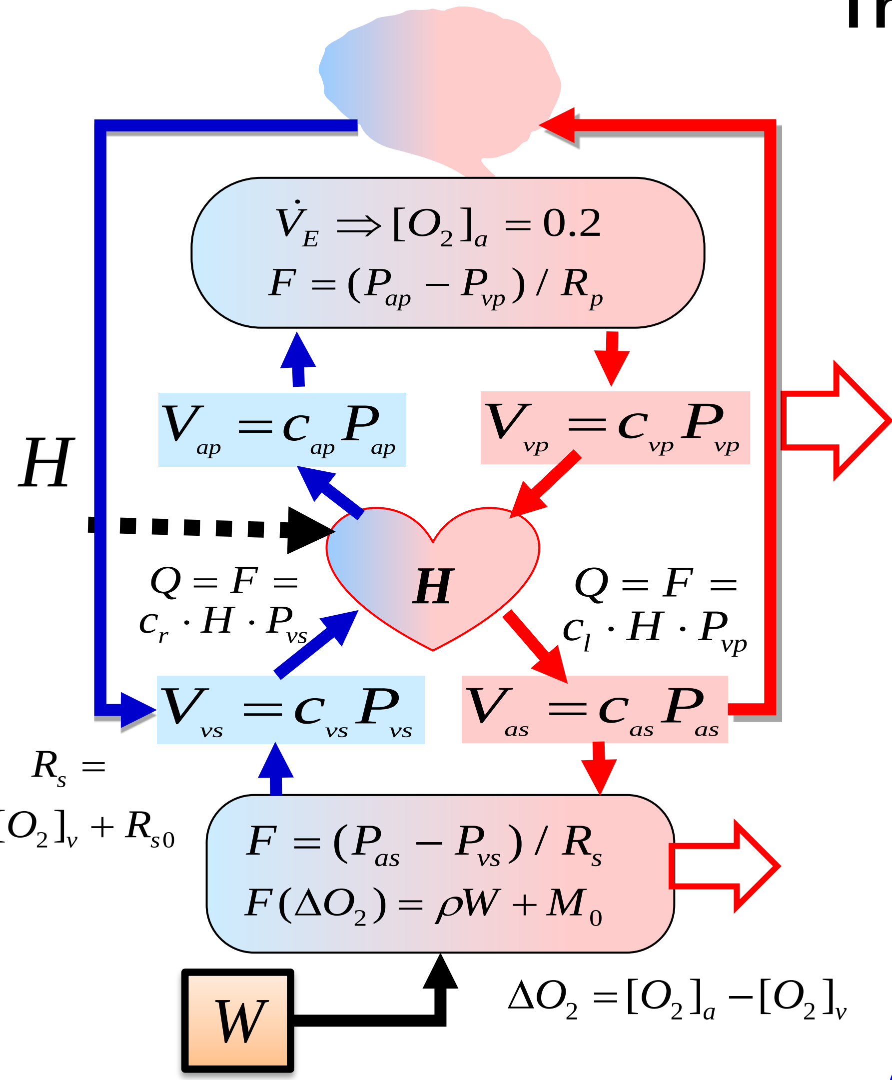
Vasodilation

$$[O_2]_a = 0.2$$

Ventilation

$$(BP, \Delta O_2) = F(w, H)$$

$$\Delta O_2 = [O_2]_a - [O_2]_v$$



The simplified model:

$$F_p = (P_{ap} - P_{vp}) / R_p$$

$$F_s = (P_{as} - P_{vs}) / R_s$$

$$Q_r = c_r \cdot H \cdot P_{vs}$$

$$Q_l = c_l \cdot H \cdot P_{vp}$$

$$F_p = F_s = Q_r = Q_l$$

$$V_{vs} = c_{vs} P_{vs}$$

$$V_{as} = c_{as} P_{as}$$

$$V_{ap} = c_{ap} P_{ap}$$

$$V_{vp} = c_{vp} P_{vp}$$

$$V_{tot} = V_{as} + V_{vs} + V_{ap} + V_{vp}$$

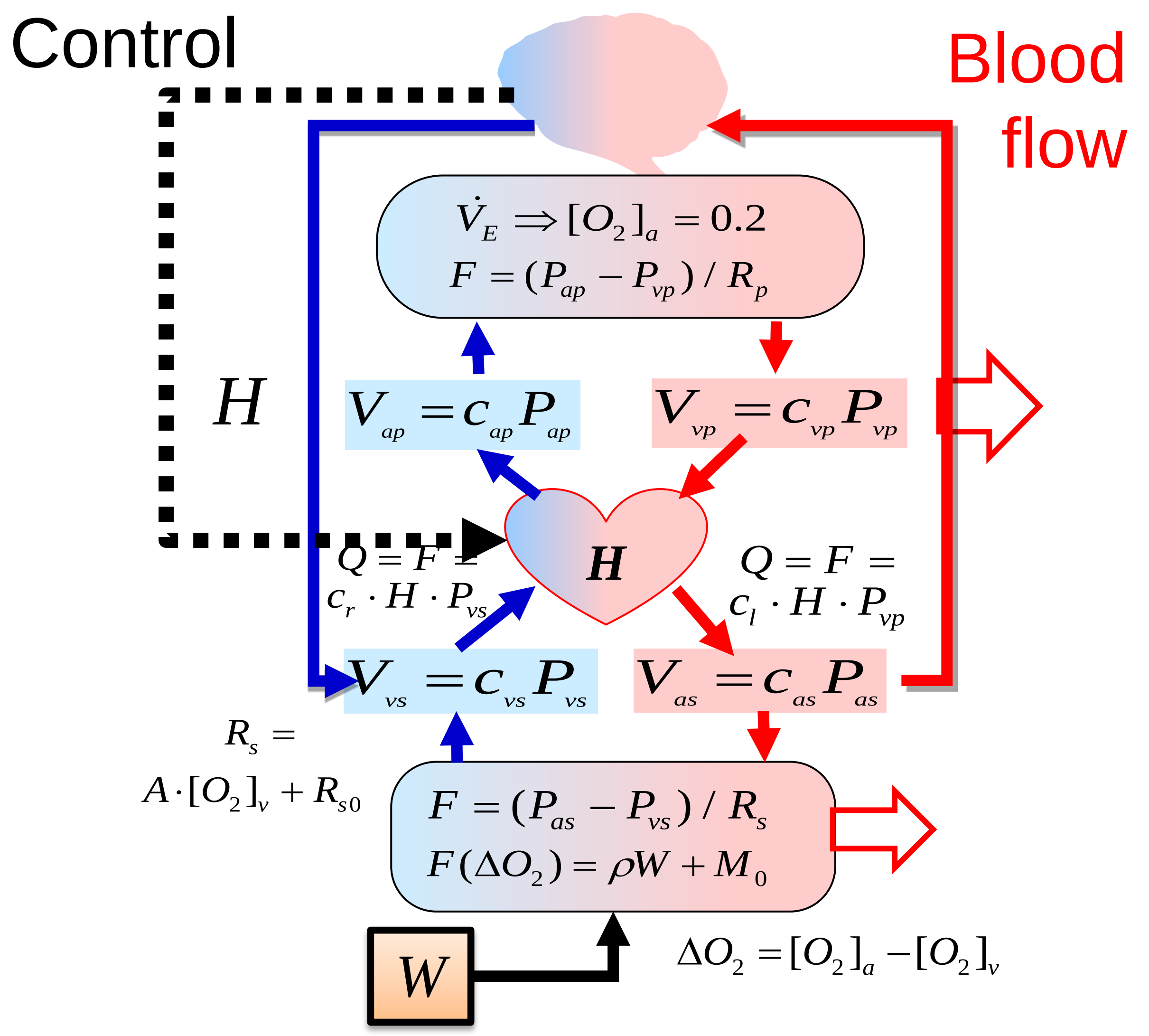
$$F_s([O_2]_a - [O_2]_v) = \rho w + M_0$$

$$R_s = A \cdot [O_2]_v + R_{s0}$$

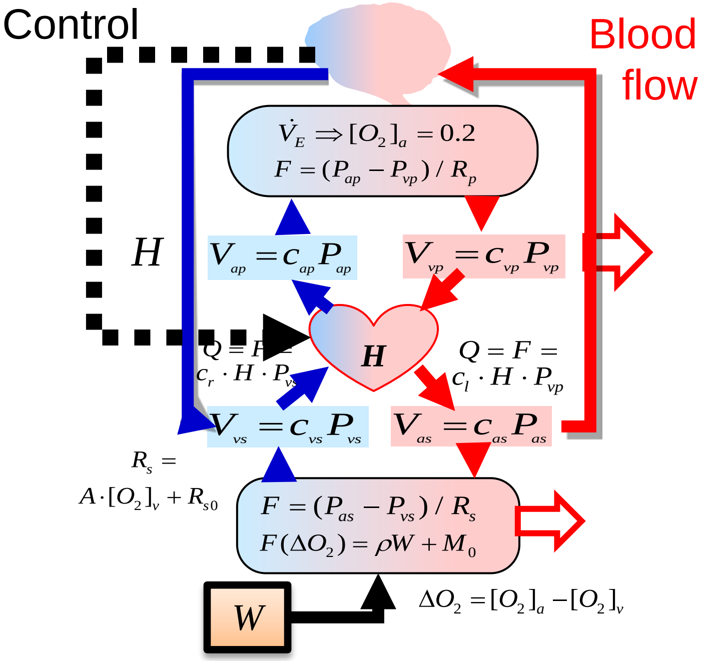
$$[O_2]_a = 0.2$$

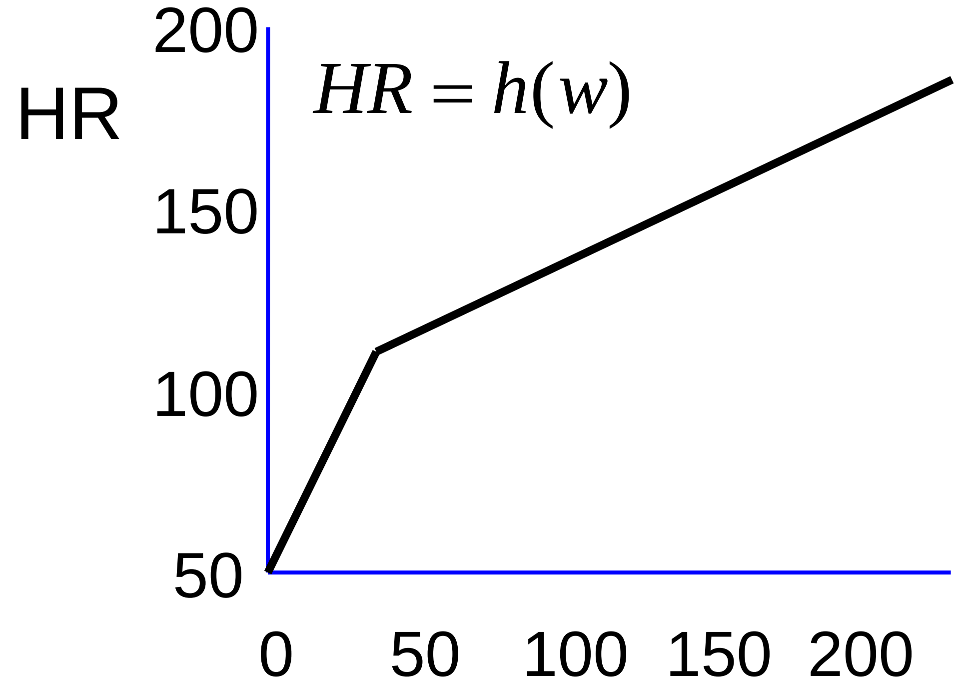
$$(BP, \Delta O_2) = F(w, H)$$

$$\Delta O_2 = [O_2]_a - [O_2]_v$$



Control
Blood
flow
H
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
W
$\Delta O_2 = [O_2]_a - [O_2]_v$





$$\left(BP, \Delta O2t\right) = F\left(w, HR\right)$$

Watts

static optimization problem

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right.$$

$$\left. \middle| HR = h(w) \;\; \left(BP, \Delta O2t\right) = F\left(w, HR\right) \right\}$$

static optimization problem

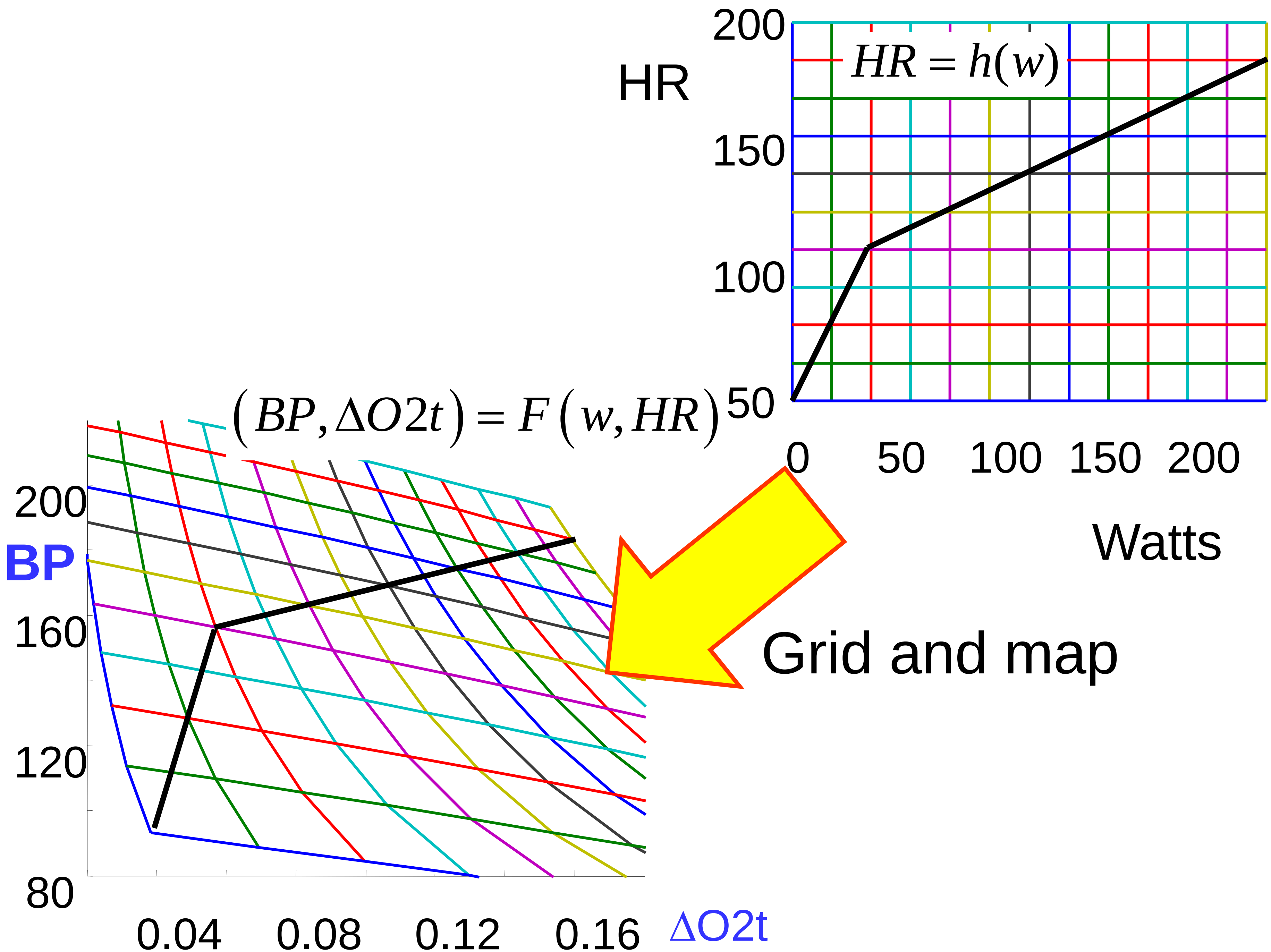
optimization objective

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right.$$

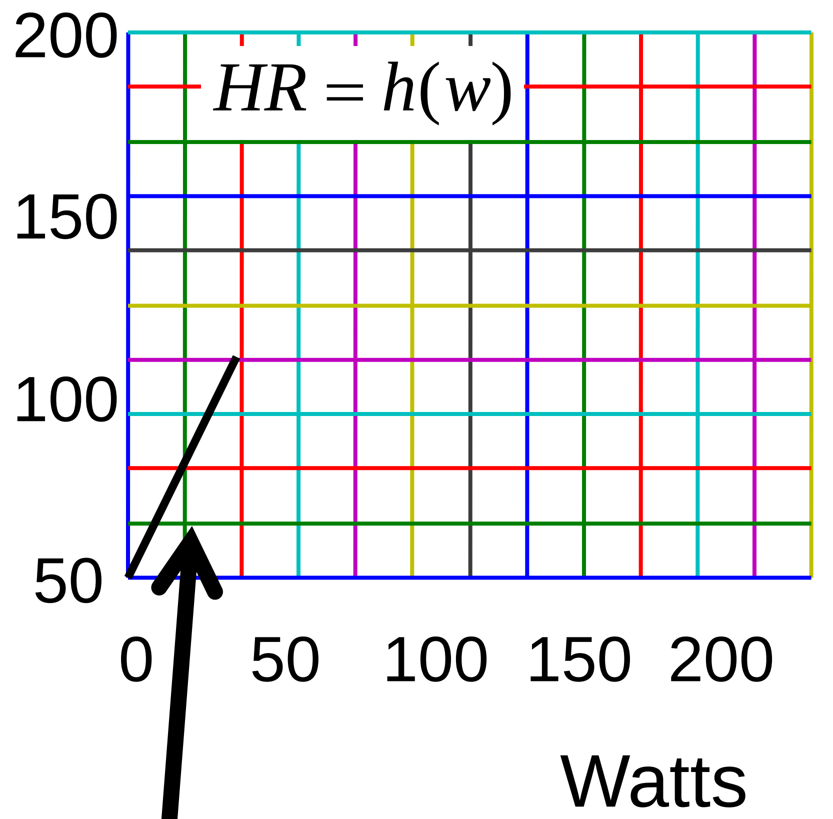
$$\left. \middle| HR = h(w) \;\; \left(BP, \Delta O2t\right) = F\left(w, HR\right) \right\}$$

optimal HR

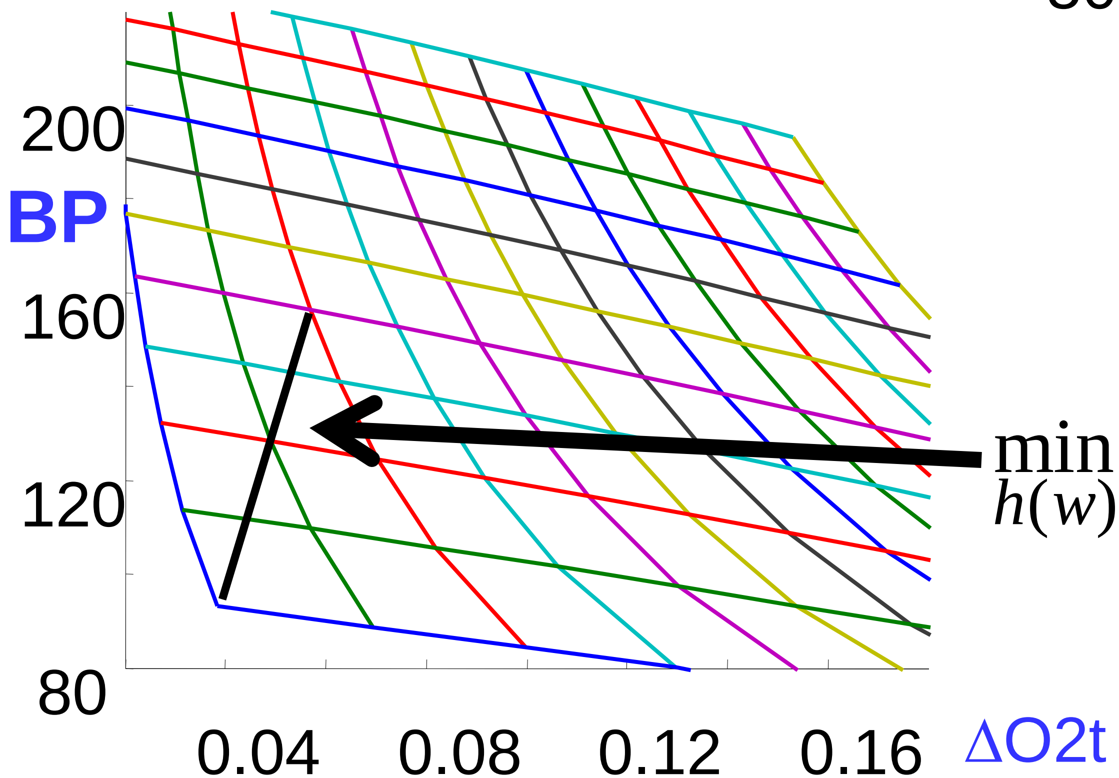
plumbing and chemistry constraints gives static model

HR
200
150
100
50
$HR = h(w)$
0
50
100
150
200
Watts
$(BP, \Delta O2t) = F(w, HR)$
BP
200
160
120
80
0.04
0.08
0.12
0.16
ΔO2t
Grid and map

At low watts and HR, high BP is not an issue, so only metabolism matters.



$$\min_{h(w)}\left\{\left(q\left(\Delta O2t\right)^{2}+r\left(HR\right)^{2}\right)\right\}$$

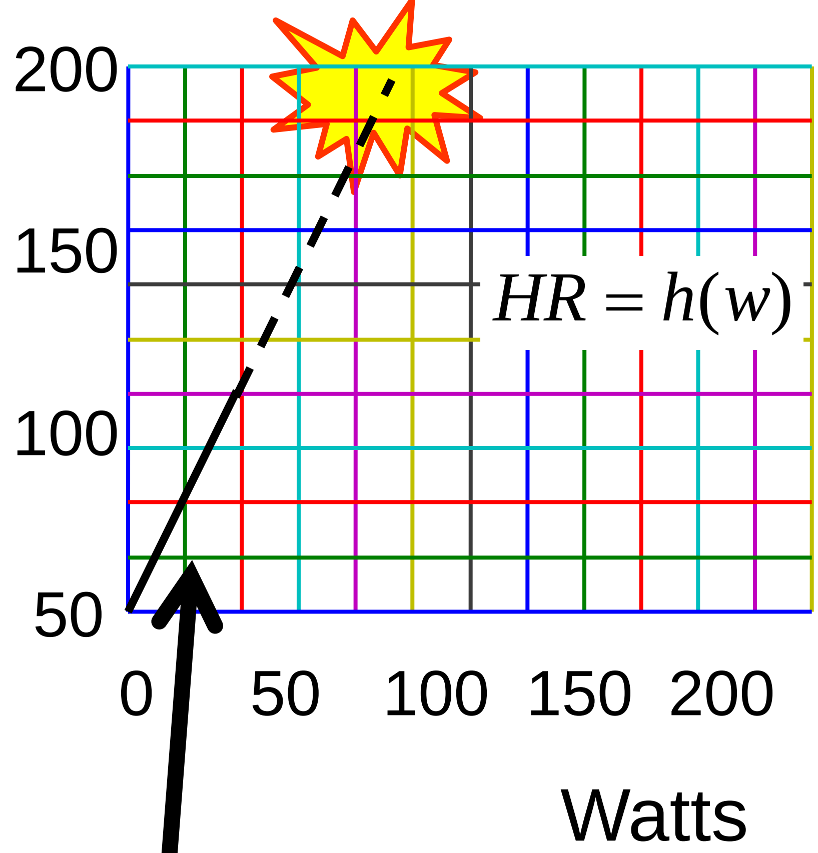


Architecture

Low watts and HR

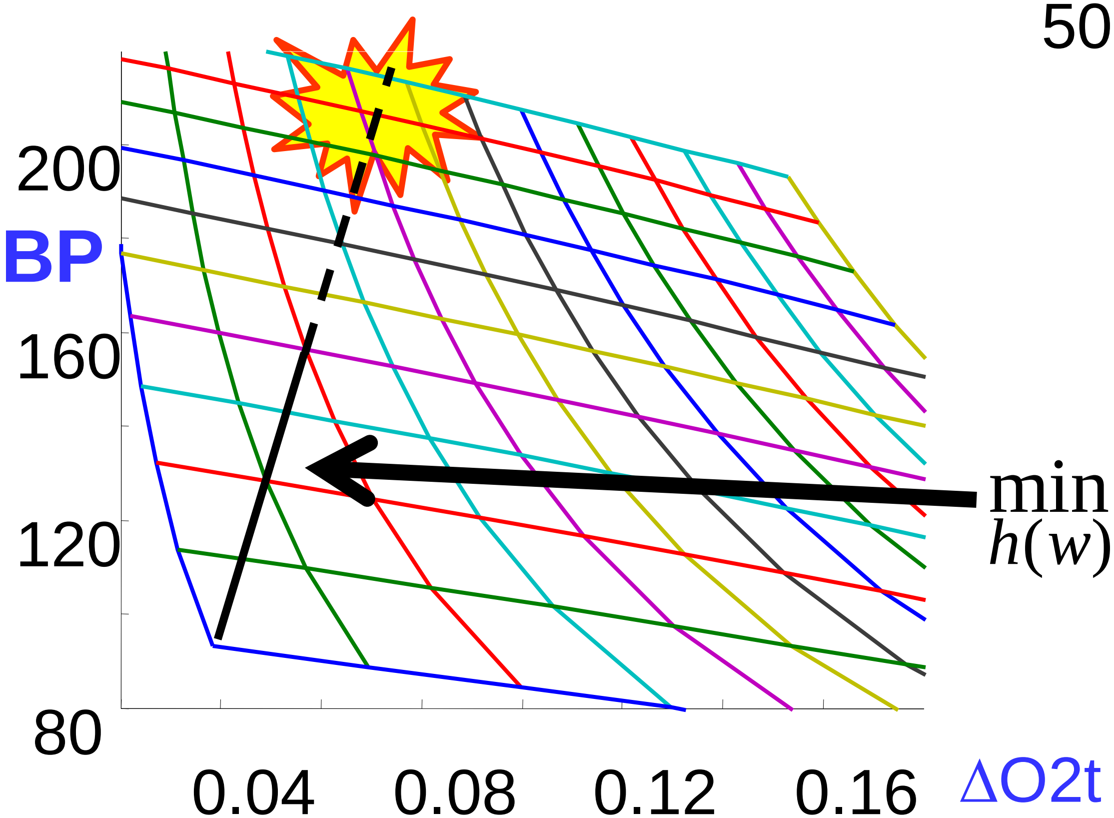
Not sustainable

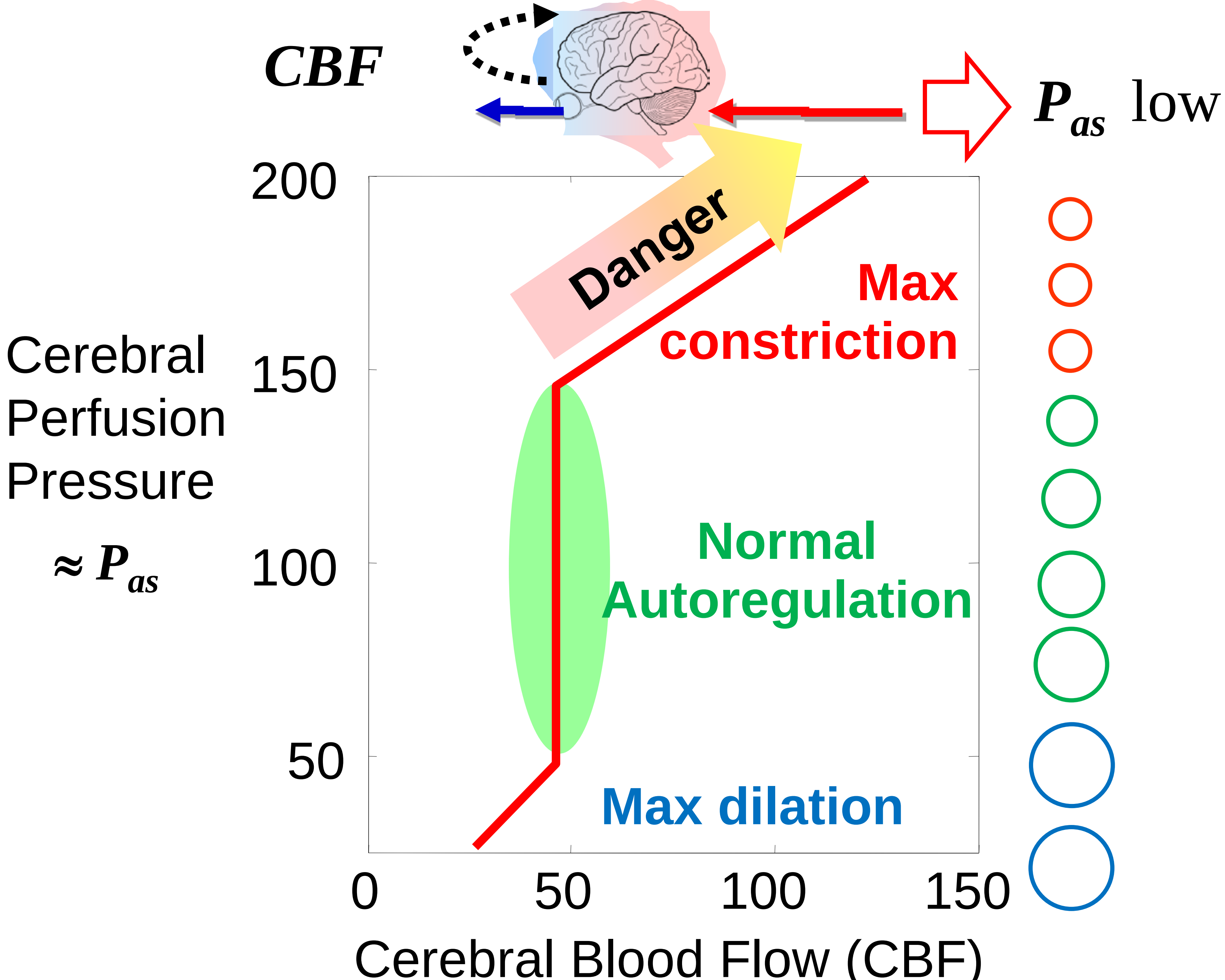
High BP >160 matters,
as does HR > 100



$$HR = h(w)$$

$$\min_{h(w)} \left\{ \left(q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right\}$$

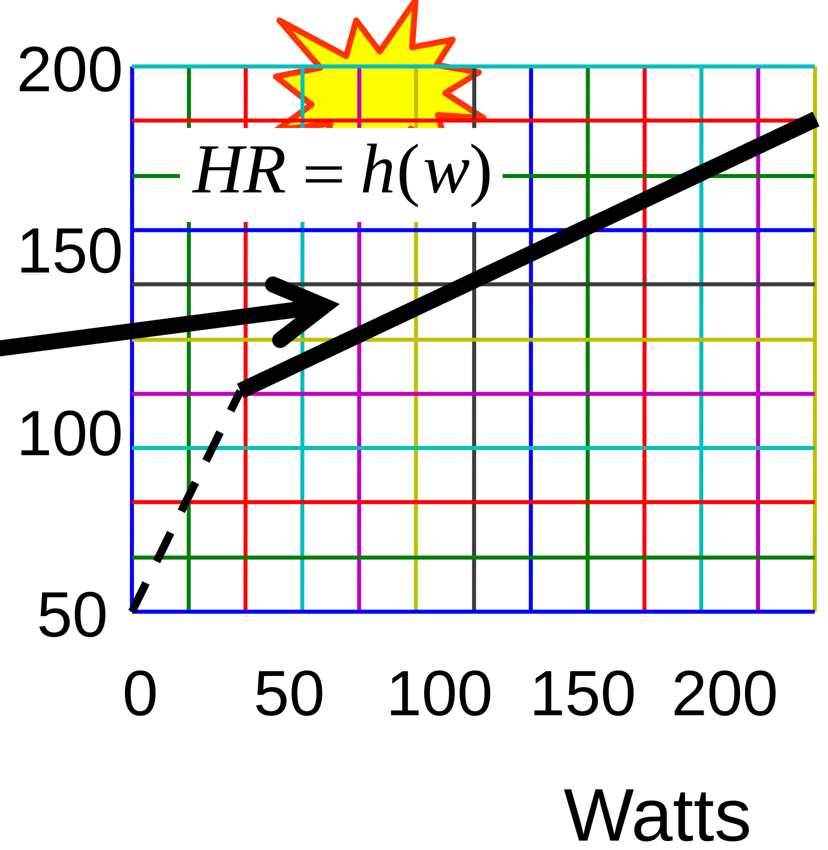




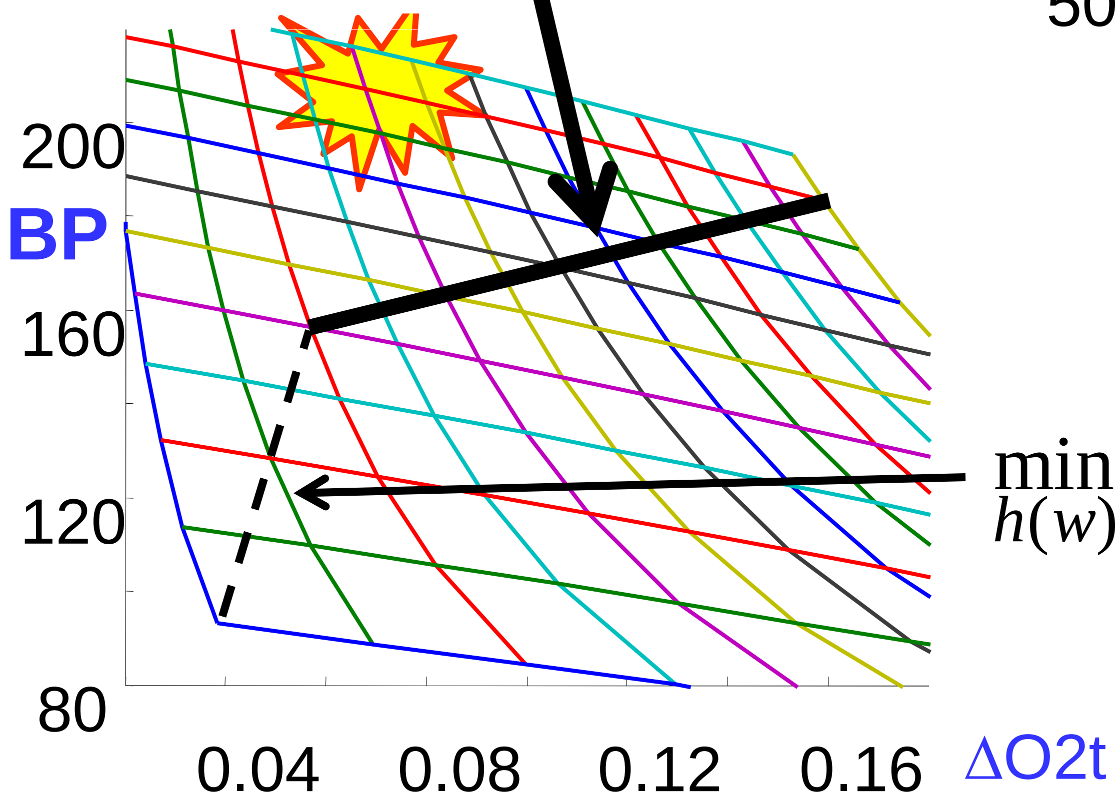
CBF
P_{as} low
200
150
100
50
Danger
Max constriction
Normal Autoregulation
Max dilation
Cerebral Perfusion Pressure
$\approx P_{as}$
0
50
100
150
Cerebral Blood Flow (CBF)

So penalizing BP and HR more here

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2 \right) \right\}$$



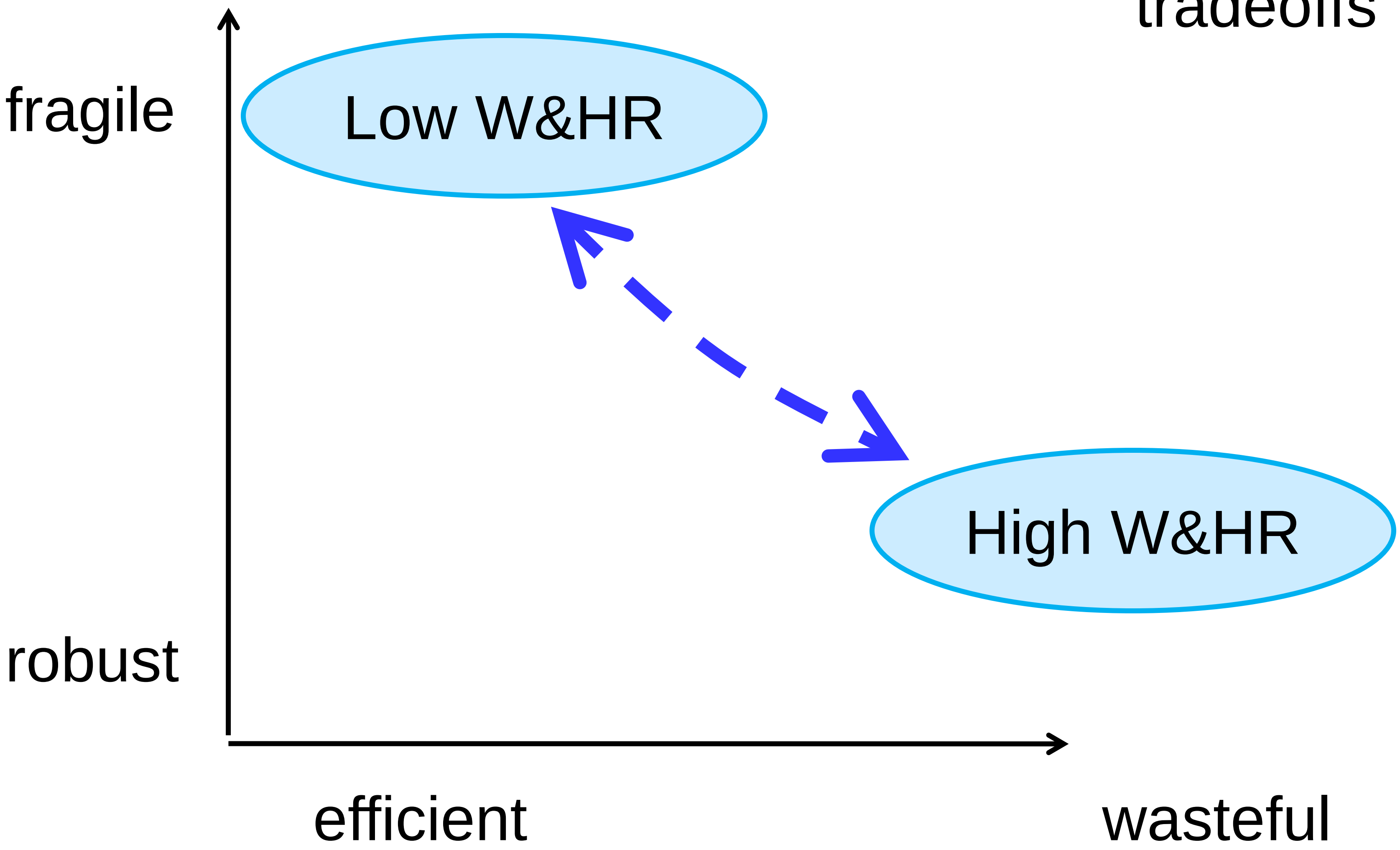
$p > 0$ $\hat{r} > r$

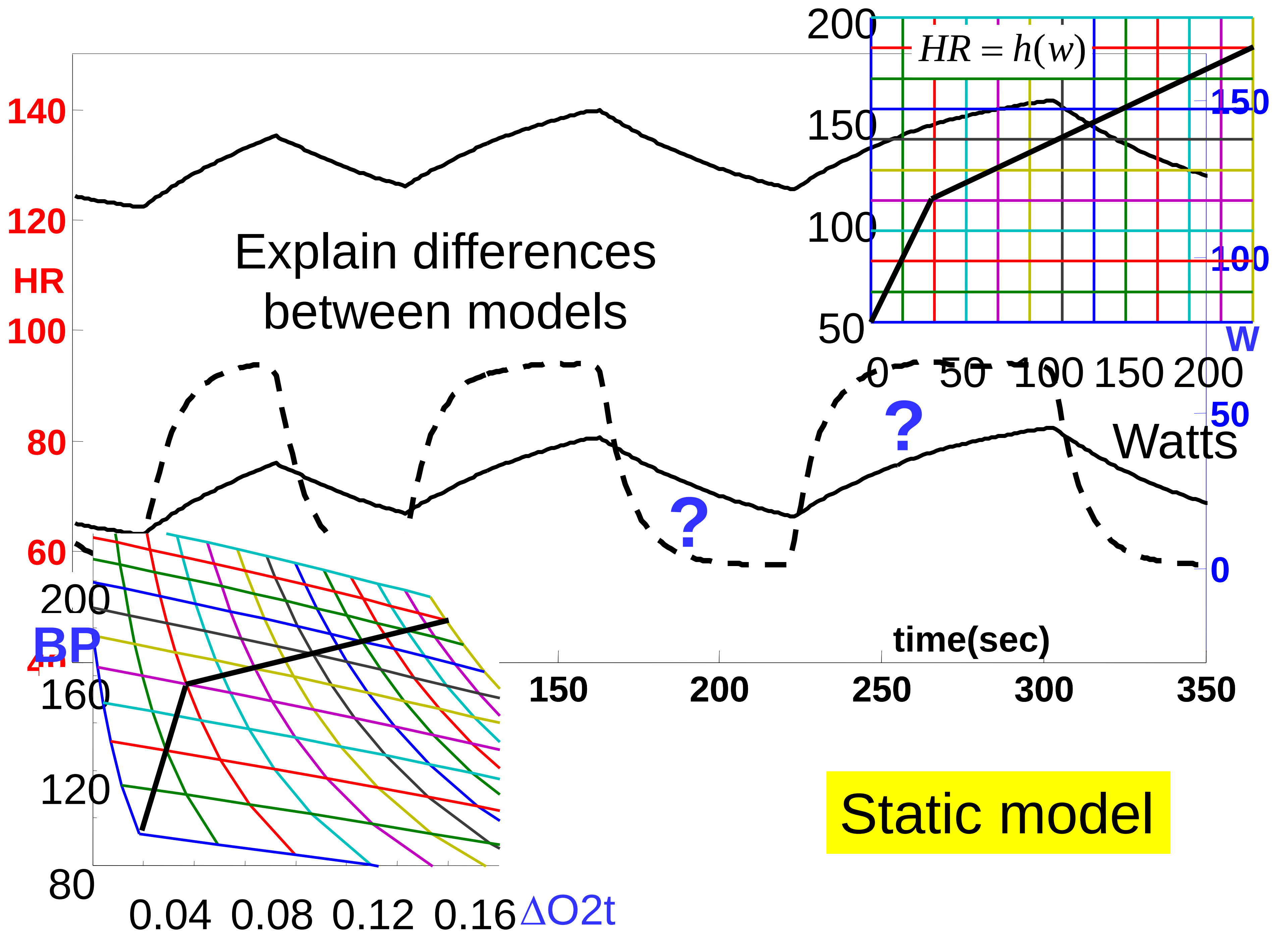


$$\min_{h(w)} \left\{ \left(q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right\}$$

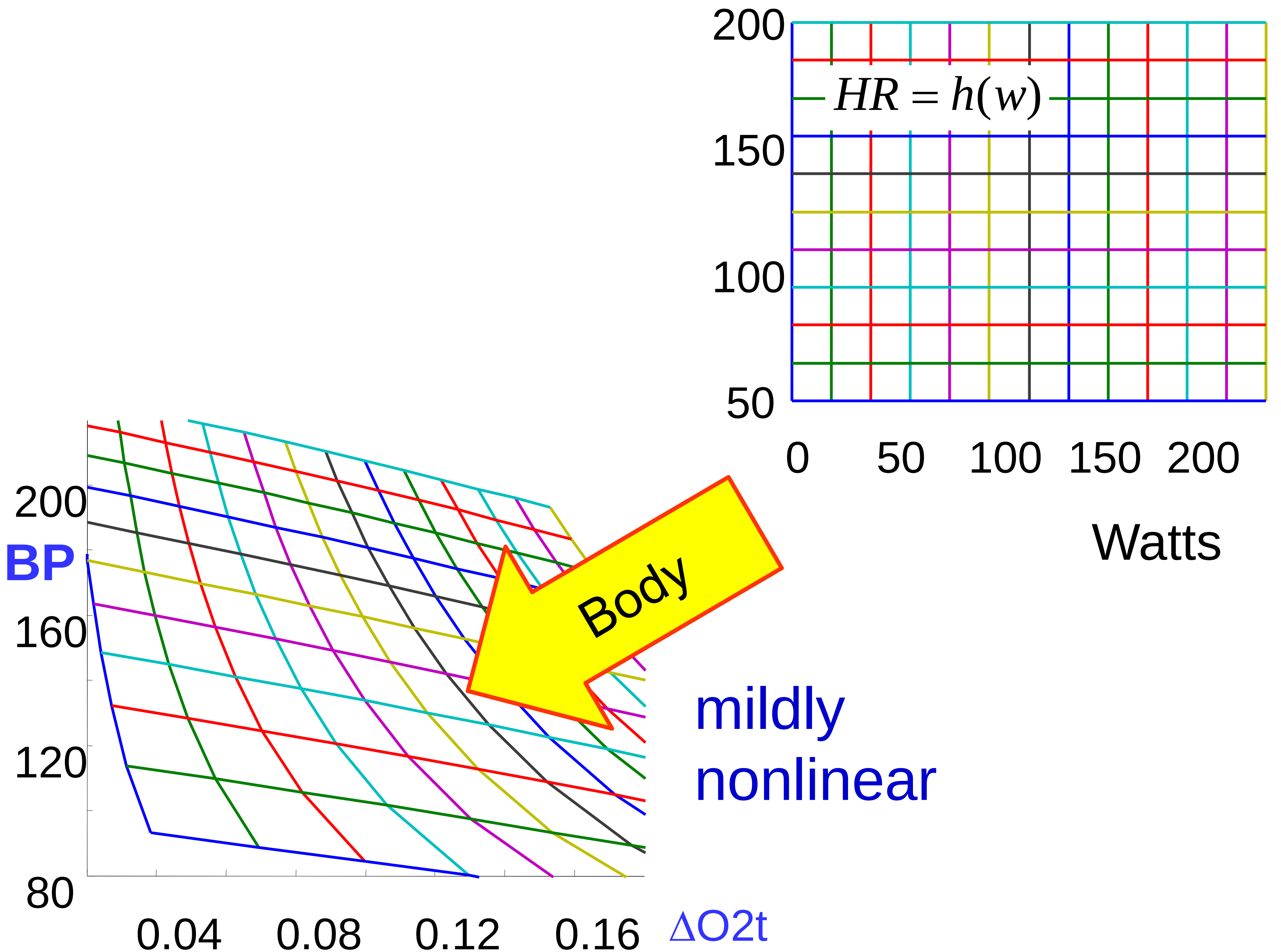
Architecture

Good architectures allow for effective tradeoffs

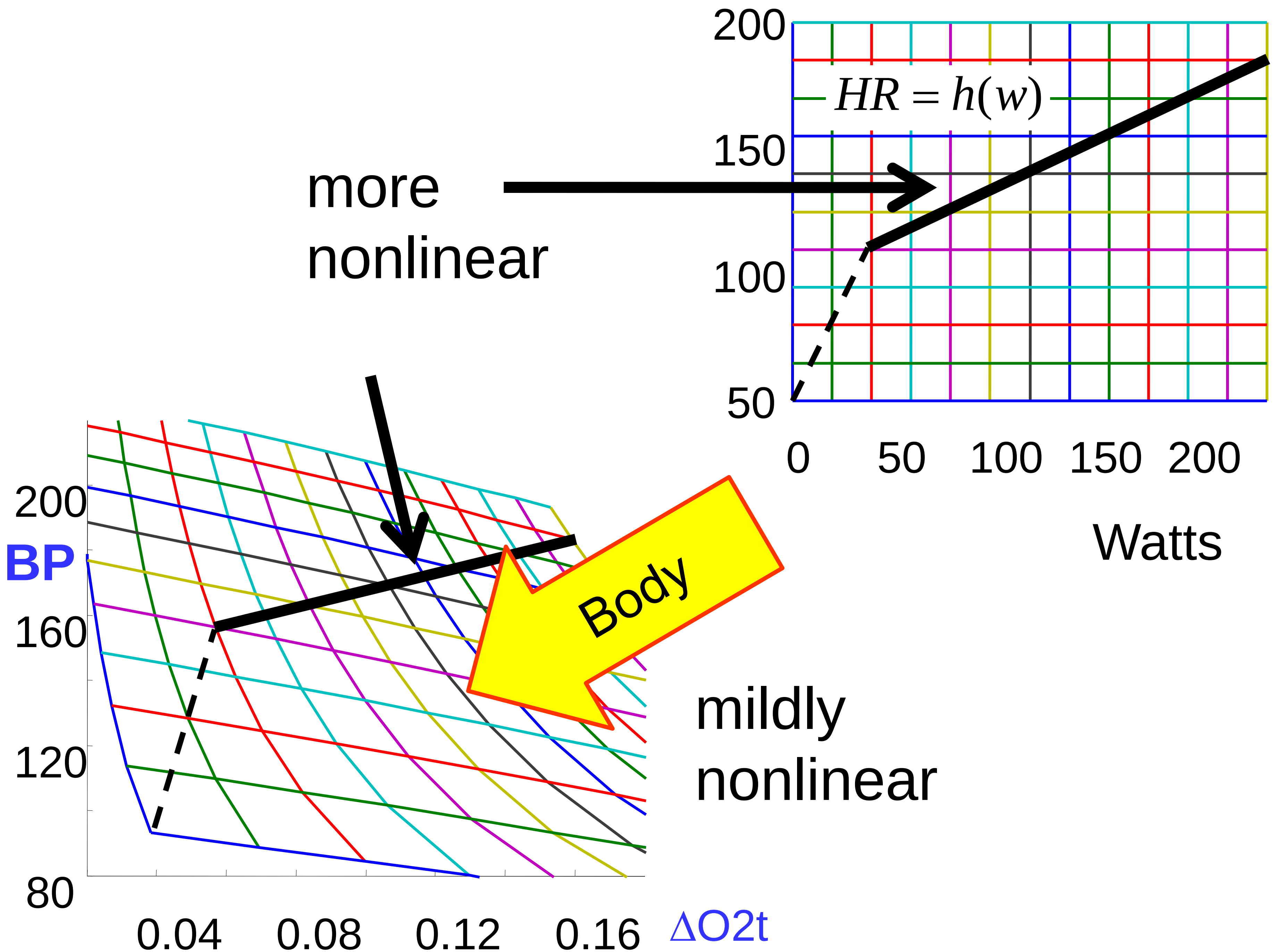


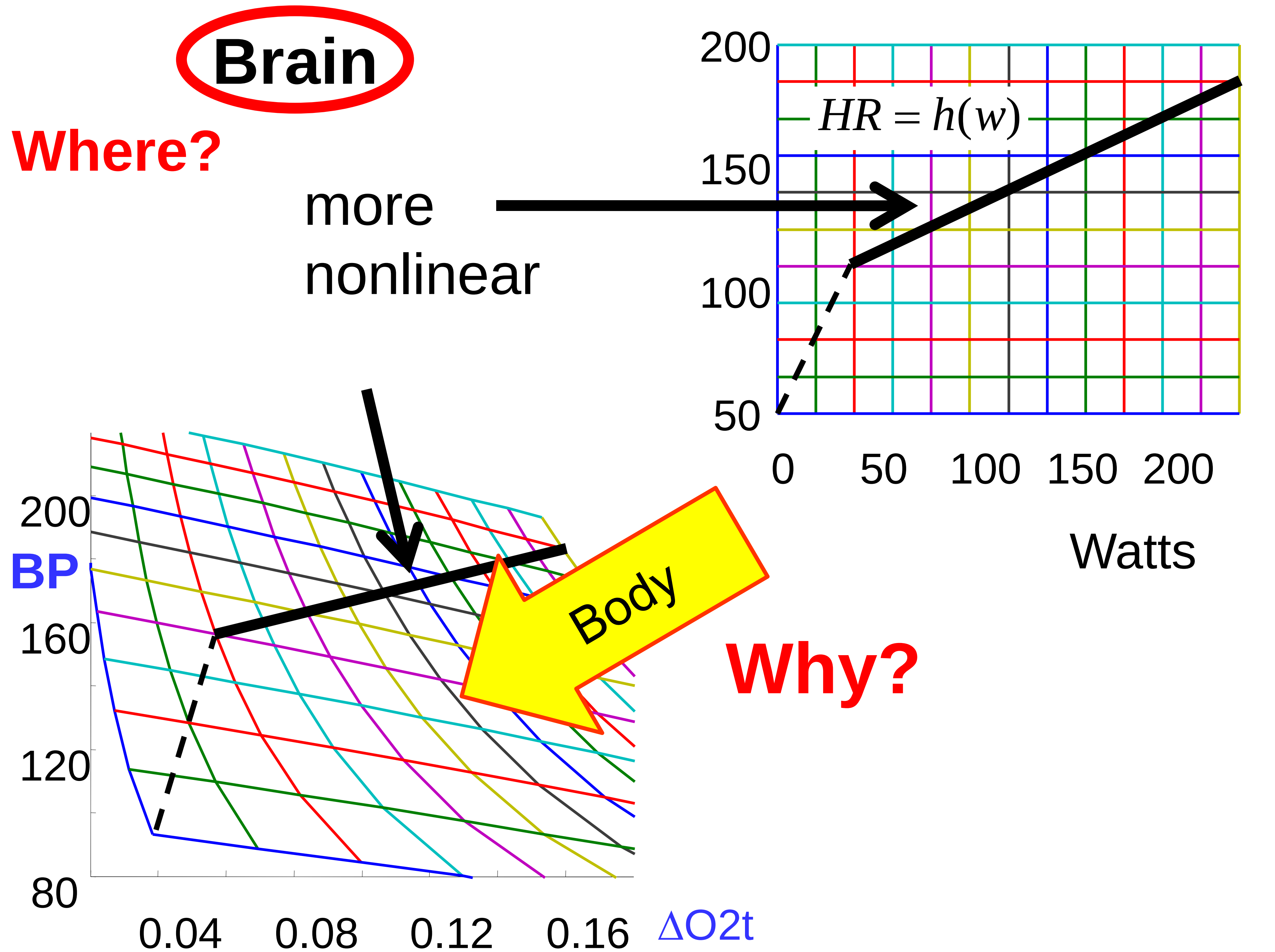


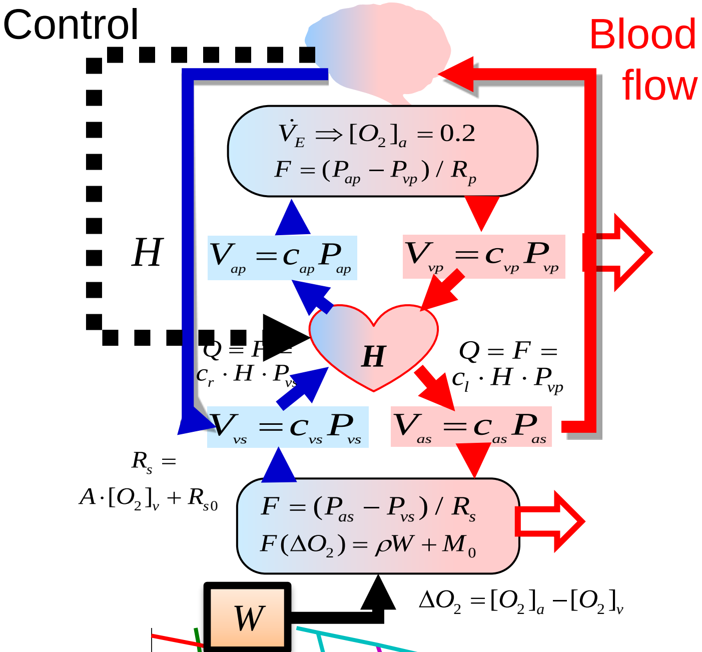
140
120
HR
100
80
60
Explain differences
between models
200
150
100
50
$HR = h(w)$
0 50 100 150 200
150
100
50
0
W
Watts
?
?
time(sec)
150 200 250 300 350
200
BP
160
120
80
0.04 0.08 0.12 0.16
ΔO2t
Static model



200
150
100
50
$HR = h(w)$
0
50
100
150
200
Watts
Body
BP
200
160
120
80
0.04
0.08
0.12
0.16
ΔO2t
mildly
nonlinear


200
150
100
50
$HR = h(w)$
0
50
100
150
200
Watts
more
nonlinear
BP
200
160
120
80
0.04
0.08
0.12
0.16
ΔO2t
Body
mildly
nonlinear

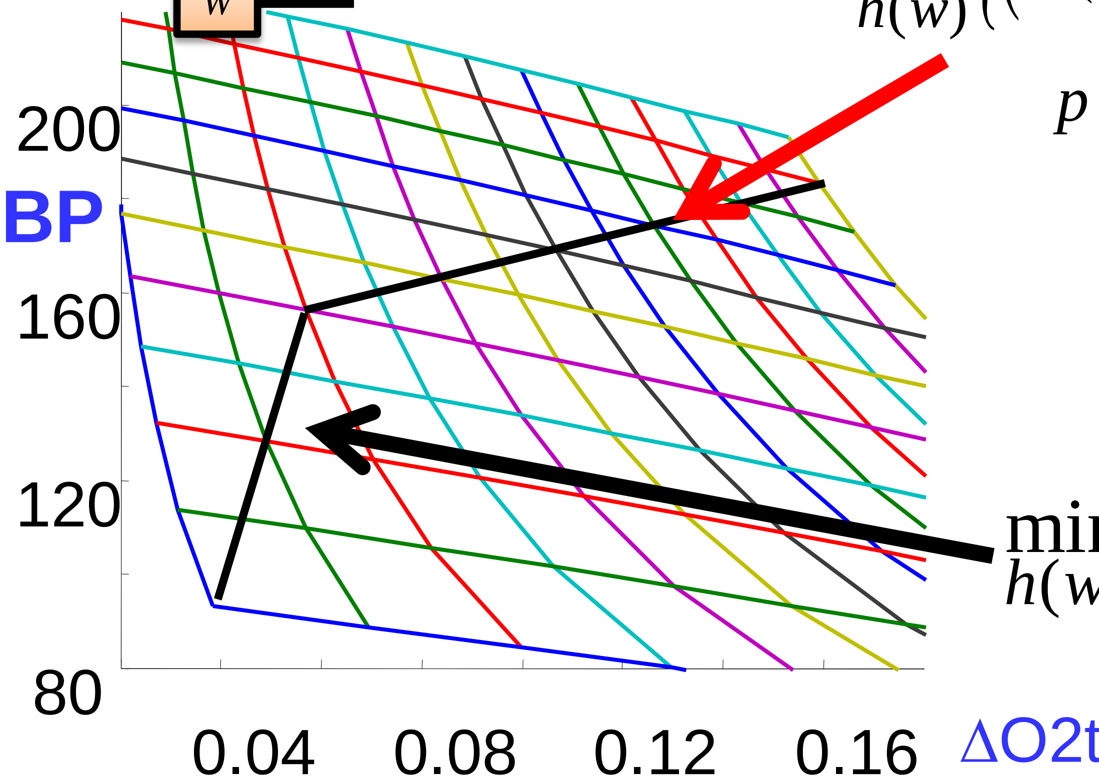

Brain
Where?
more
nonlinear
$HR = h(w)$
200
150
100
50
0
50
100
150
200
Watts
BP
200
160
120
80
0.04
0.08
0.12
0.16
ΔO2t
Body
Why?



Use same weights but add ***dynamics***

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2 \right) \right\}$$

$$p > 0 \qquad \hat{r} > r$$



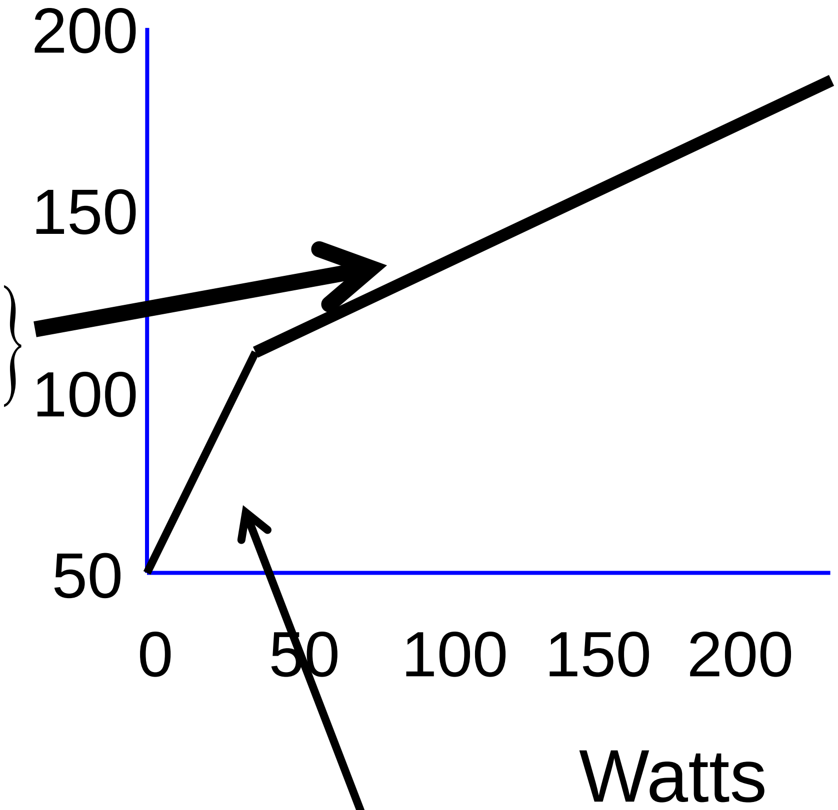
$$\min_{h(w)} \left\{ \left(q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right\}$$

This idea can be used directly with a dynamic model

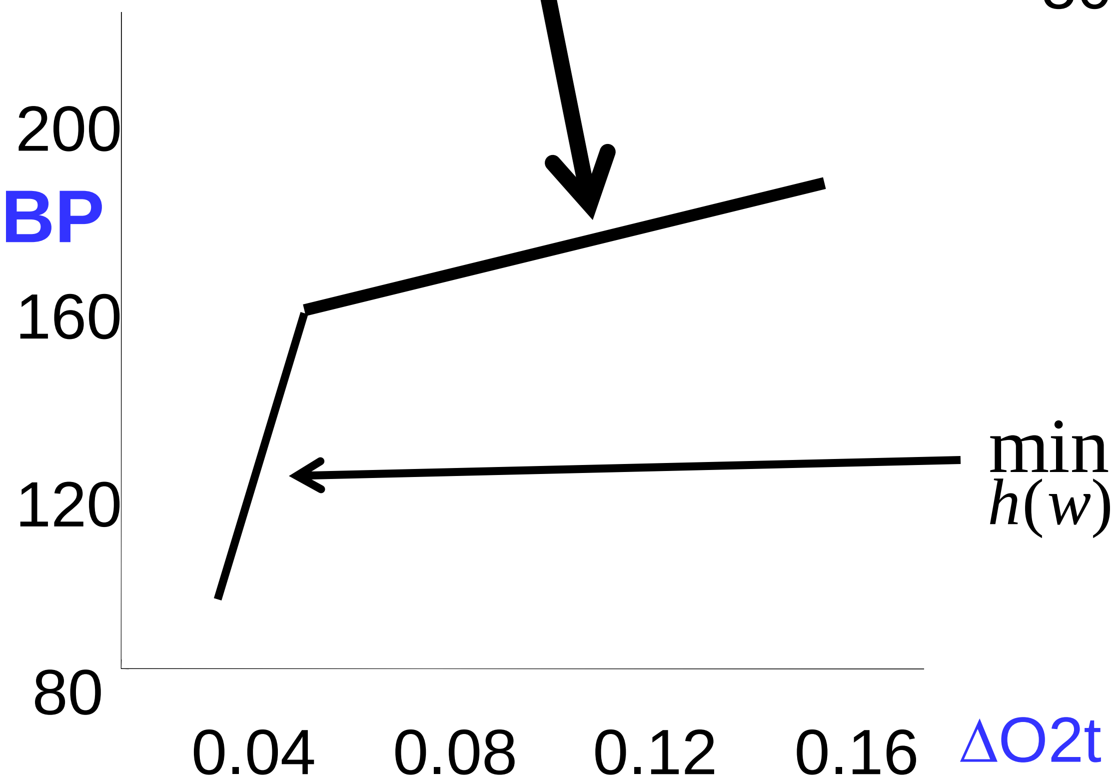
$$HR = h(w)$$

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2 \right) \right\}$$

$p > 0$ $\quad$ $\hat{r} > r$



$$\min_{h(w)} \left\{ \left(q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right\}$$



This idea can be used directly with a dynamic model

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2 \right) \right\}$$

$$p > 0 \qquad\qquad \hat{r} > r$$

$$\min \int \left(q_P^2 \left(P_{as} - P_{as}^*\right)^2 + q_{o_2}^2 \left(\Delta O_2 - \Delta O_2^*\right)^2 + q_H^2 \left(H - H^*\right)^2 \right) dt$$

s

$$\min_{h(w)} \left\{ \left(q\left(\Delta O2t\right)^2 + r\left(HR\right)^2 \right) \right\}$$

Recall:

The simplified *static* model:

$$F_p = (P_{ap} - P_{vp}) / R_p$$

$$F_s = (P_{as} - P_{vs}) / R_s$$

$$Q_r = c_r \cdot H \cdot P_{vs}$$

$$Q_l = c_l \cdot H \cdot P_{vp}$$

$$F_p = F_s = Q_r = Q_l$$

$$V_{vs} = c_{vs} P_{vs}$$

$$V_{as} = c_{as} P_{as}$$

$$V_{ap} = c_{ap} P_{ap}$$

$$V_{vp} = c_{vp} P_{vp}$$

$$V_{tot} = V_{as} + V_{vs} + V_{ap} + V_{vp}$$

$$F_s([O_2]_a - [O_2]_v) = \rho w + M_0$$

$$R_s = A \cdot [O_2]_v + R_{s0}$$

$$[O_2]_a = 0.2$$

$$\Delta O_2 = [O_2]_a - [O_2]_v$$

The simplified model:

$$F_p = (P_{ap} - P_{vp}) / R_p$$

$$F_s = (P_{as} - P_{vs}) / R_s$$

$$Q_r = c_r \cdot H \cdot P_{vs}$$

$$Q_l = c_l \cdot H \cdot P_{vp}$$

$$F_p = F_s = Q_r = Q_l$$

$$V_{vs} = c_{vs} P_{vs}$$

$$V_{as} = c_{as} P_{as}$$

$$V_{ap} = c_{ap} P_{ap}$$

$$V_{vp} = c_{vp} P_{vp}$$

$$V_{tot} = V_{as} + V_{vs} + V_{ap} + V_{vp}$$

$$F_s([O_2]_a - [O_2]_v) = \rho w + M_0$$

$$R_s = A \cdot [O_2]_v + R_{s0}$$

$$[O_2]_a = 0.2$$

$$\Delta O_2 = [O_2]_a - [O_2]_v$$

Dynamics:

$$c_{as} \dot{P}_{as} = Q_l - F_s$$

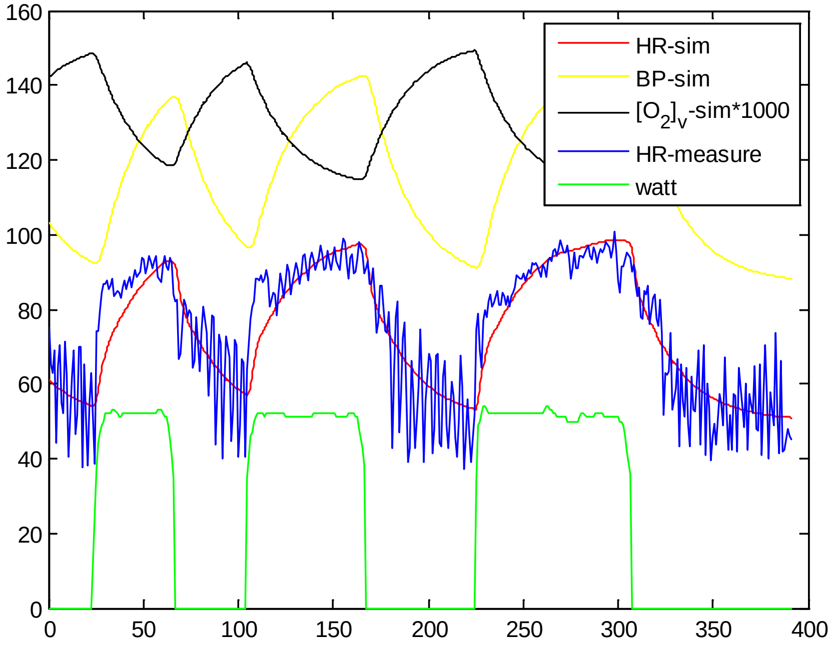
$$c_{vs} \dot{P}_{vs} = F_s - Q_r$$

$$c_{ap} \dot{P}_{ap} = Q_r - F_p$$

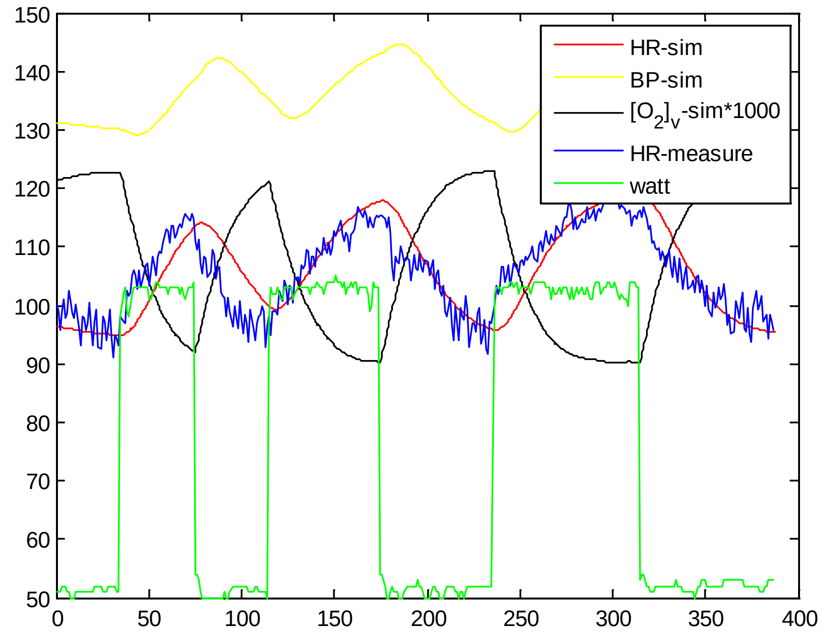
$$c_{vp} P_{vp} = V_{total} - \left(c_{as} P_{as} + c_{vs} P_{vs} + c_{ap} P_{ap} \right)$$

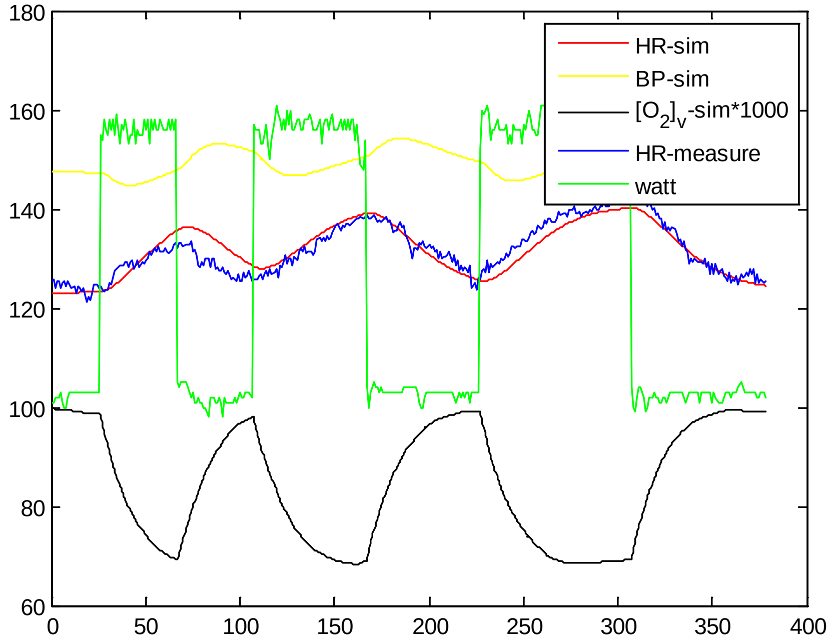
$$v_{T,O_2} [\dot{O}_2]_v = -M + F_s \cdot \left([O_2]_a - [O_2]_v \right)$$

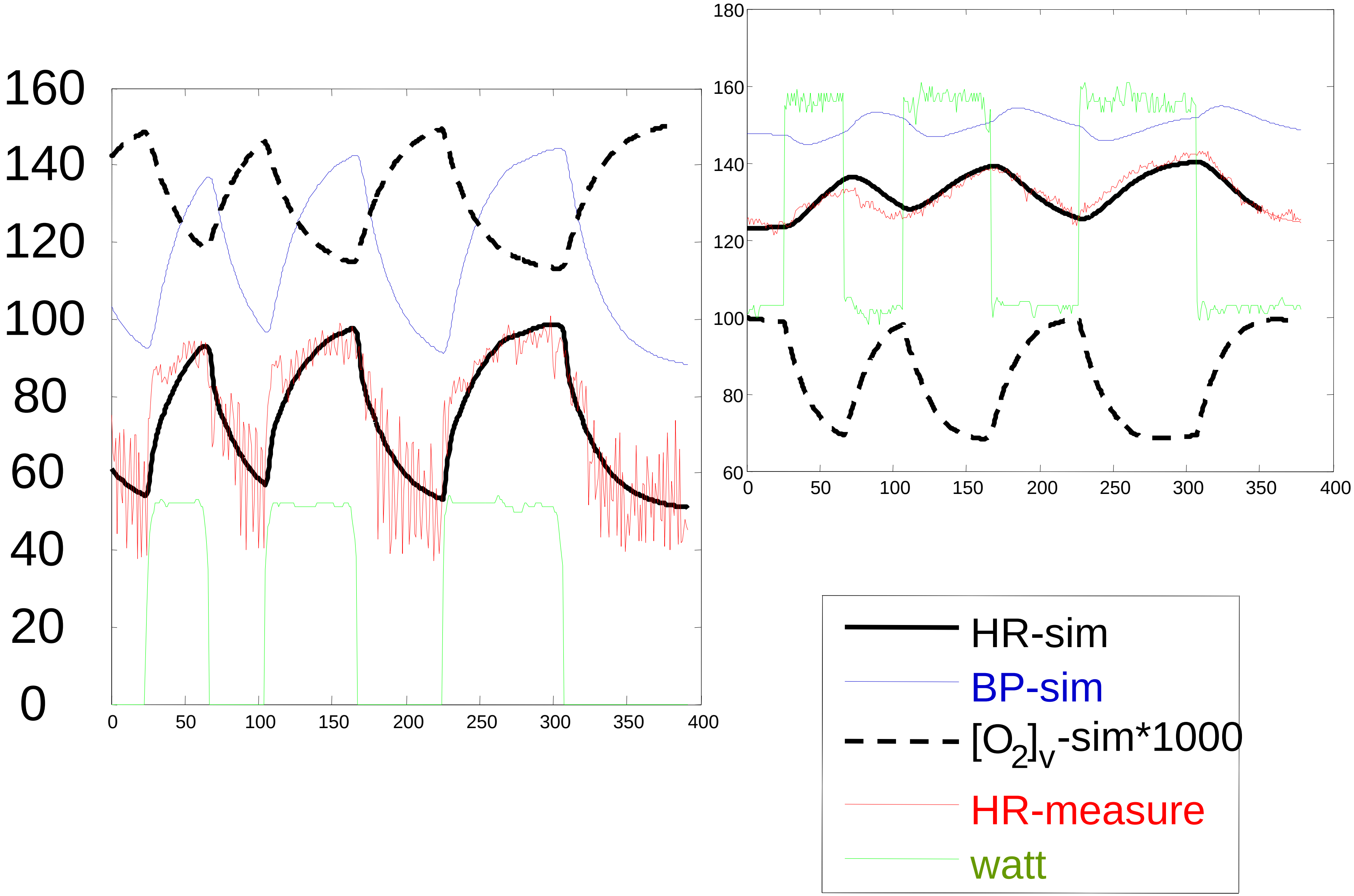
$$\min \int \left(q_P^2 \left(P_{as} - P_{as}^* \right)^2 + q_{o_2}^2 \left(\Delta O_2 - \Delta O_2^* \right)^2 + q_H^2 \left(H - H^* \right)^2 \right) dt$$


HR-sim
BP-sim
$[O_2]_v$-sim*1000
HR-measure
watt
0
20
40
60
80
100
120
140
160
0
50
100
150
200
250
300
350
400

It works!

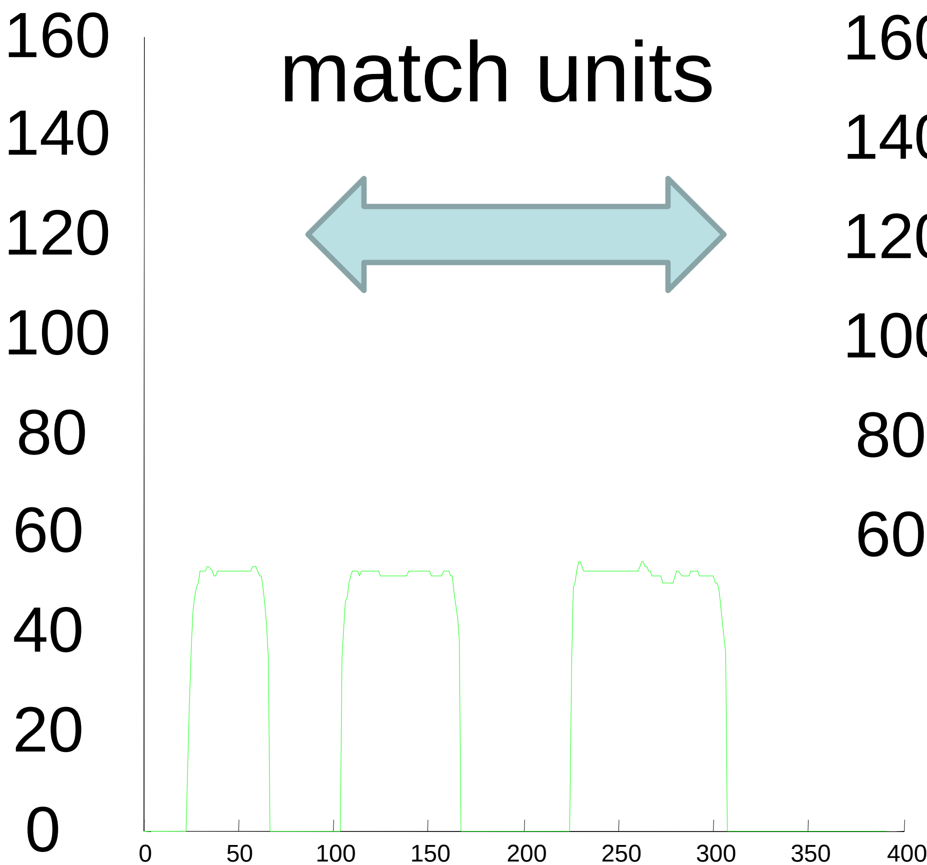

HR-sim
BP-sim
$[O_2]_v$-sim*1000
HR-measure
watt
50
60
70
80
90
100
110
120
130
140
150
0
50
100
150
200
250
300
350
400

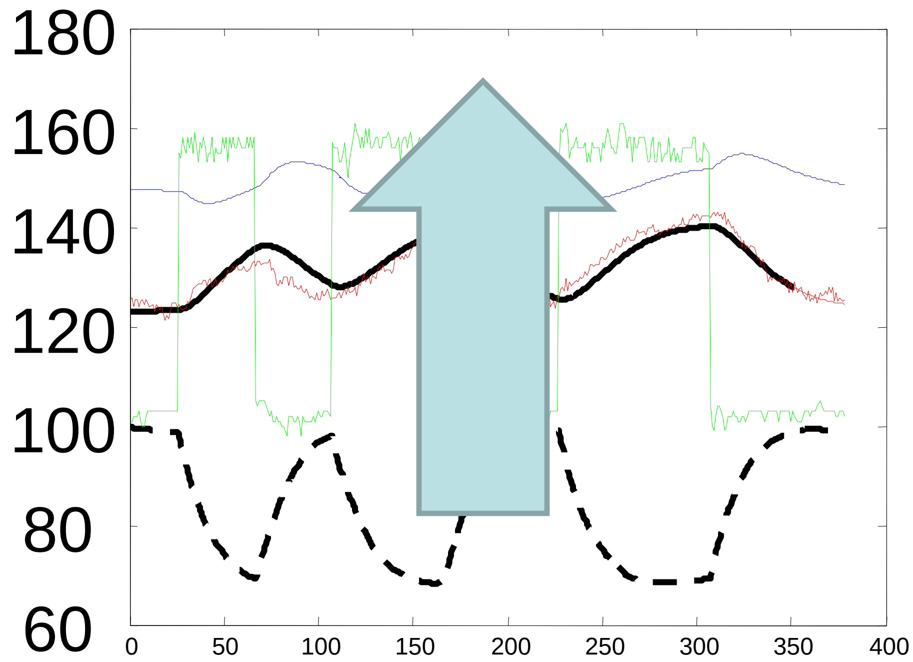

HR-sim
BP-sim
$[O_2]_v$-sim*1000
HR-measure
watt
60
80
100
120
140
160
180
0
50
100
150
200
250
300
350
400

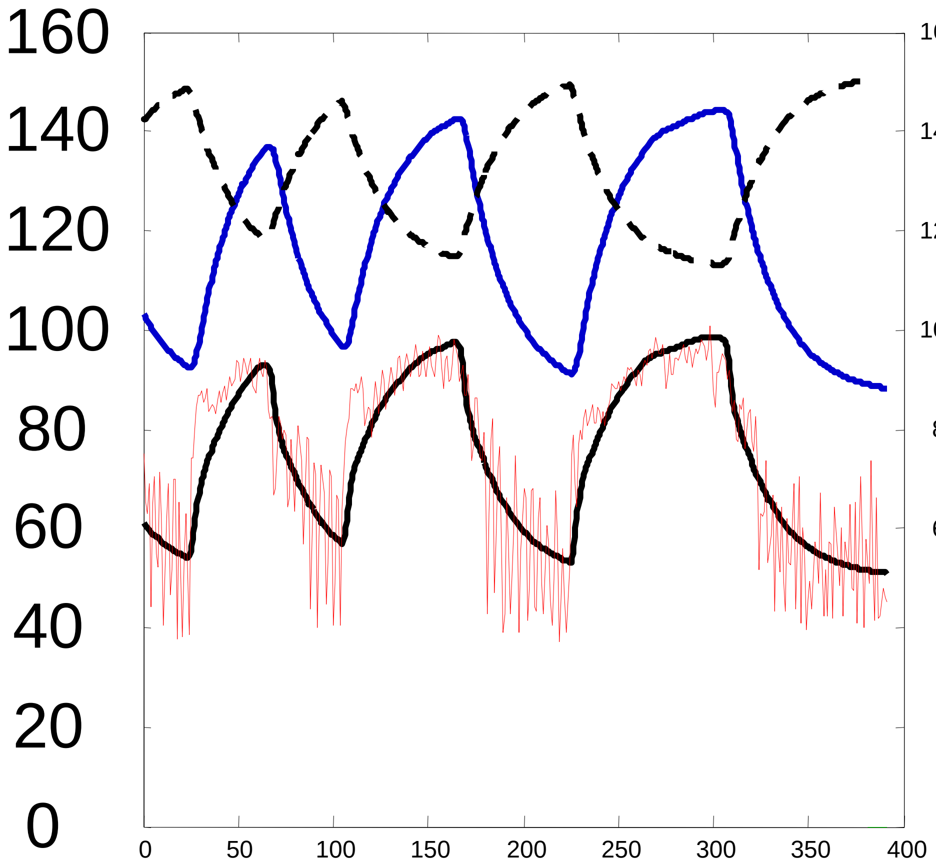


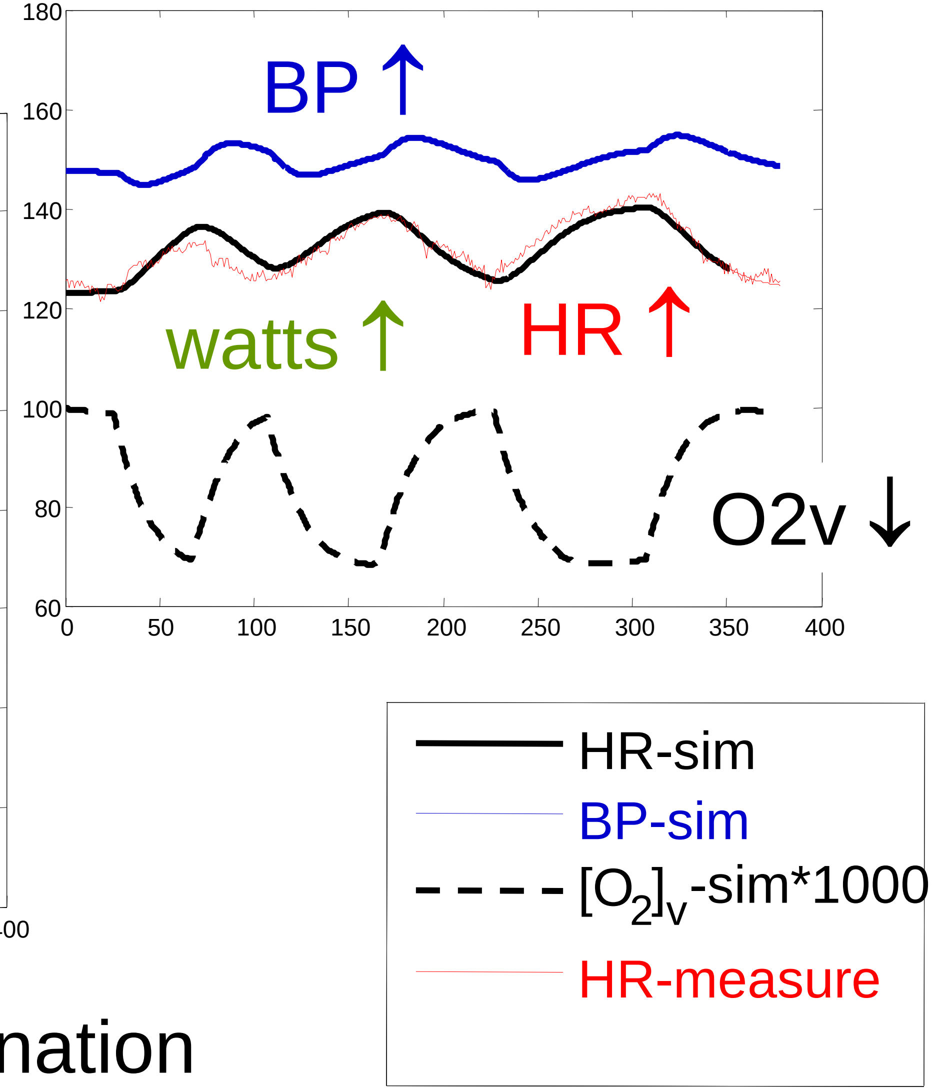
Data and model

note shift to match units



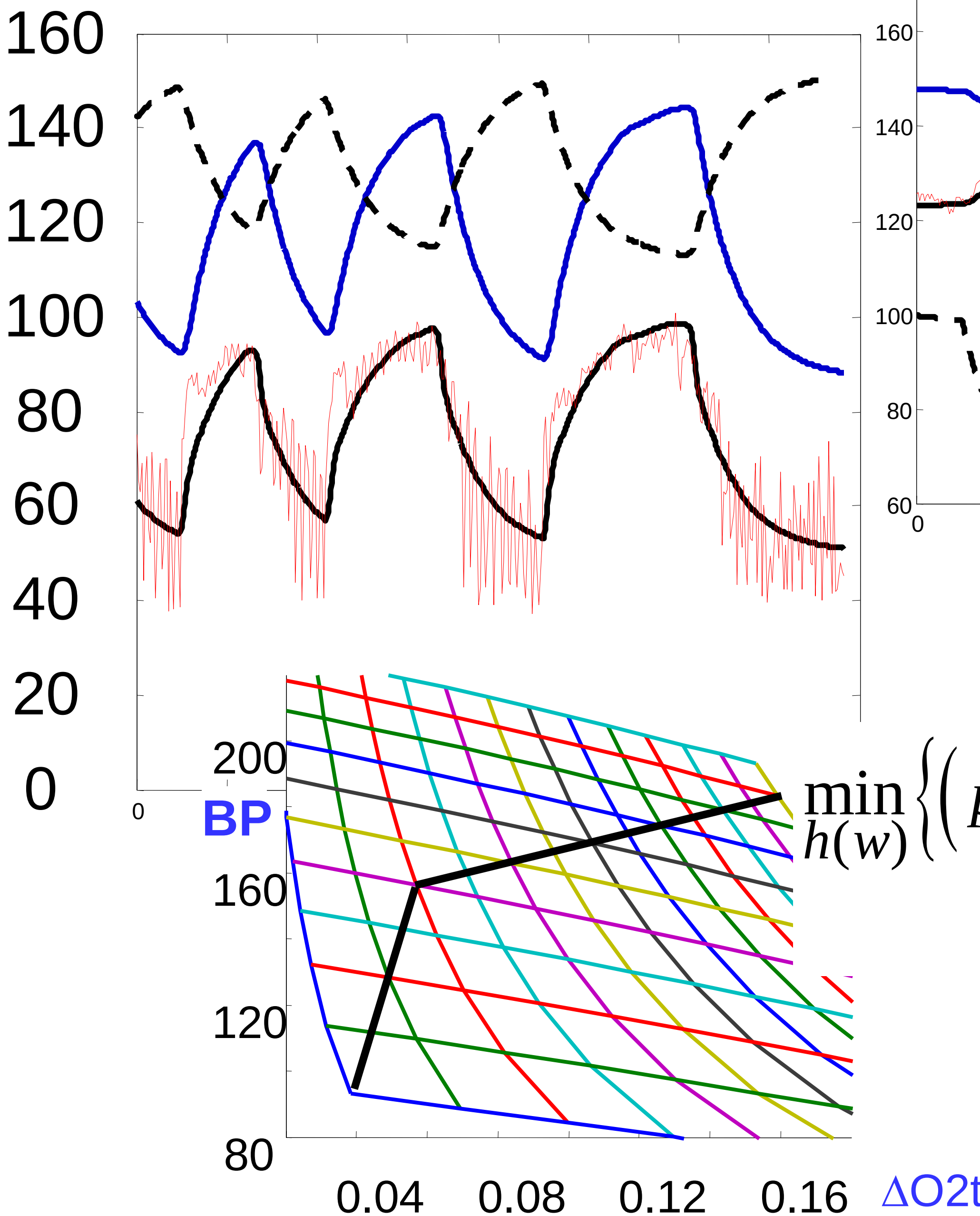


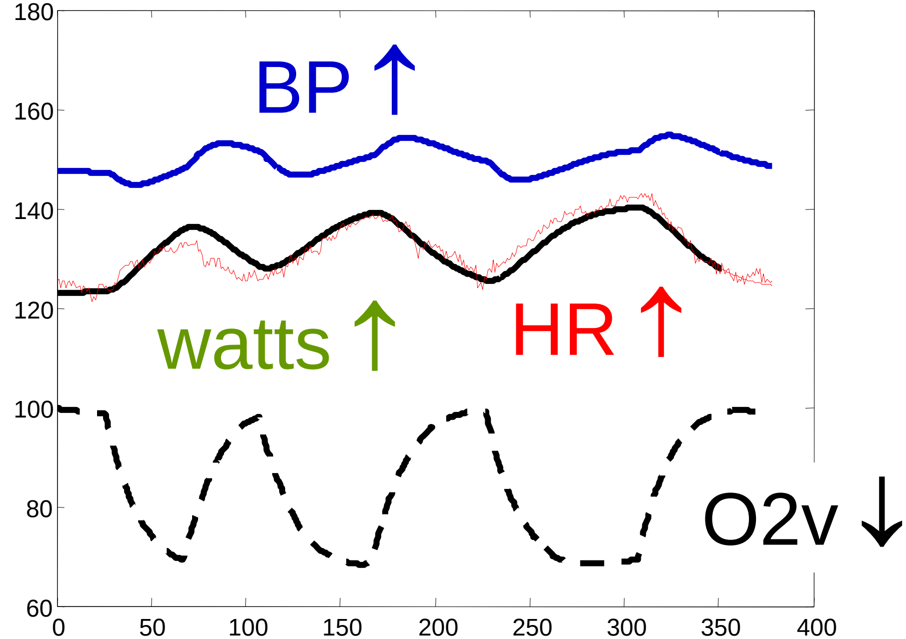




Mechanistic explanation for differences between models

$$\Delta O_2 = [O_2]_a - [O_2]_v$$

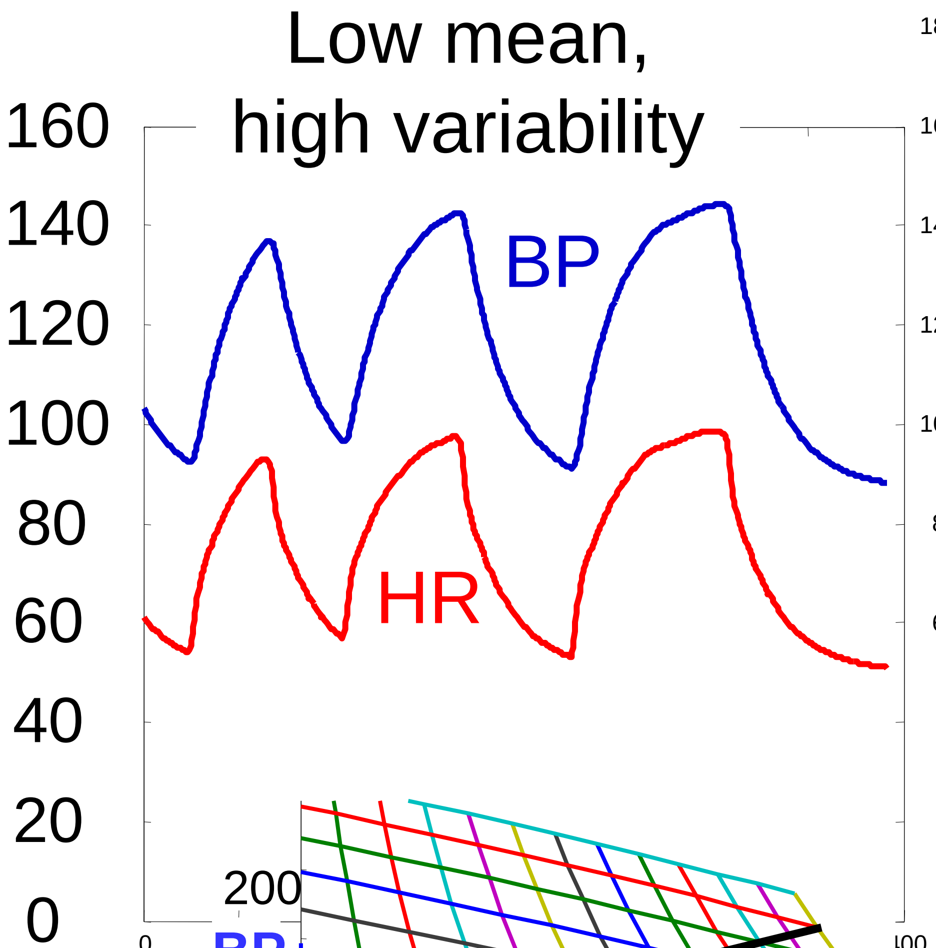


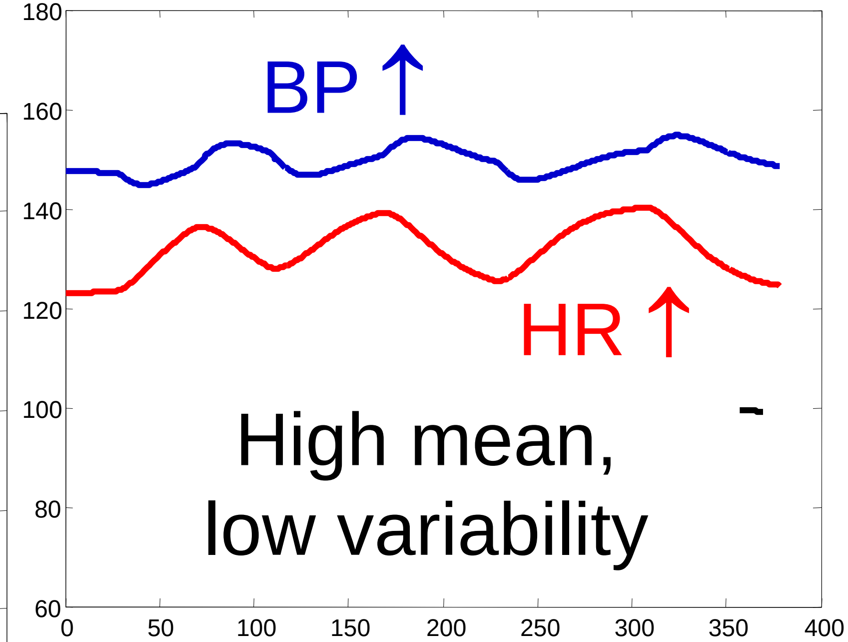


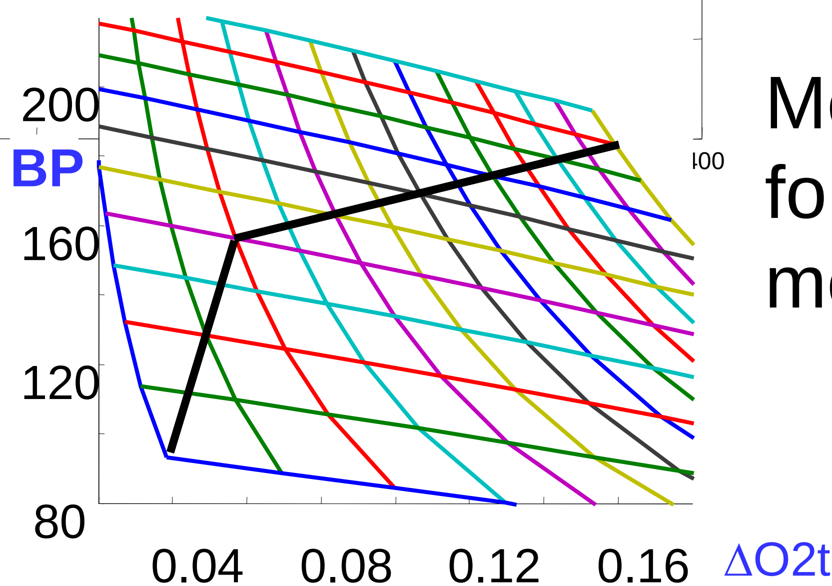
Penalize BP and HR more

$$\min_{h(w)} \left\{ \left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2 \right) \right\}$$

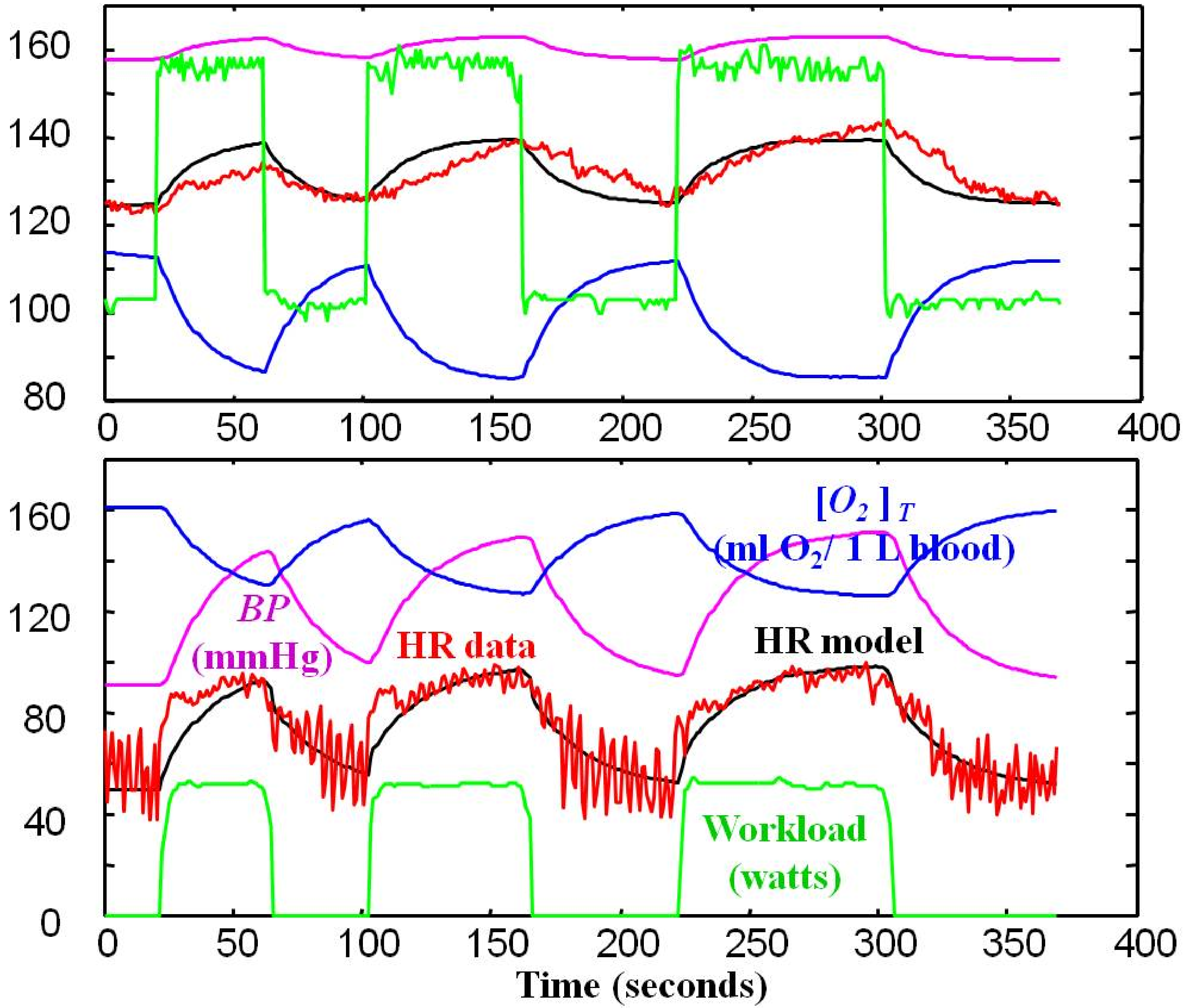
$$p > 0 \qquad \hat{r} > r$$



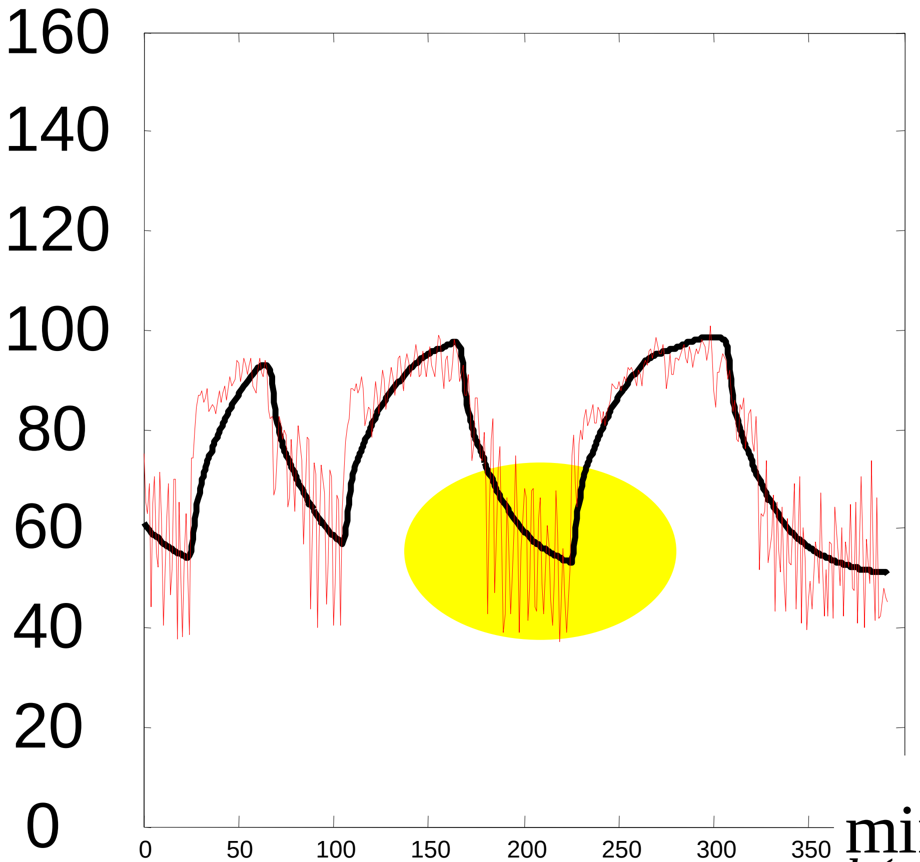


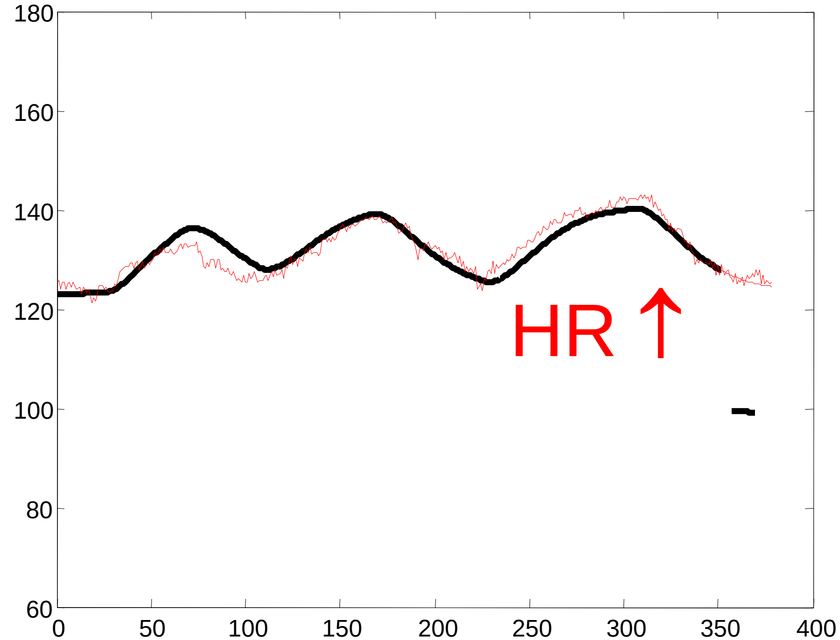


Mechanistic explanation for differences between models



160
140
120
100
80
0
50
100
150
200
250
300
350
400
$[O_2]_T$
(ml O_2/ 1 L blood)
BP
(mmHg)
HR data
HR model
Workload
(watts)
160
120
80
40
0
0
50
100
150
200
250
300
350
400
Time (seconds)



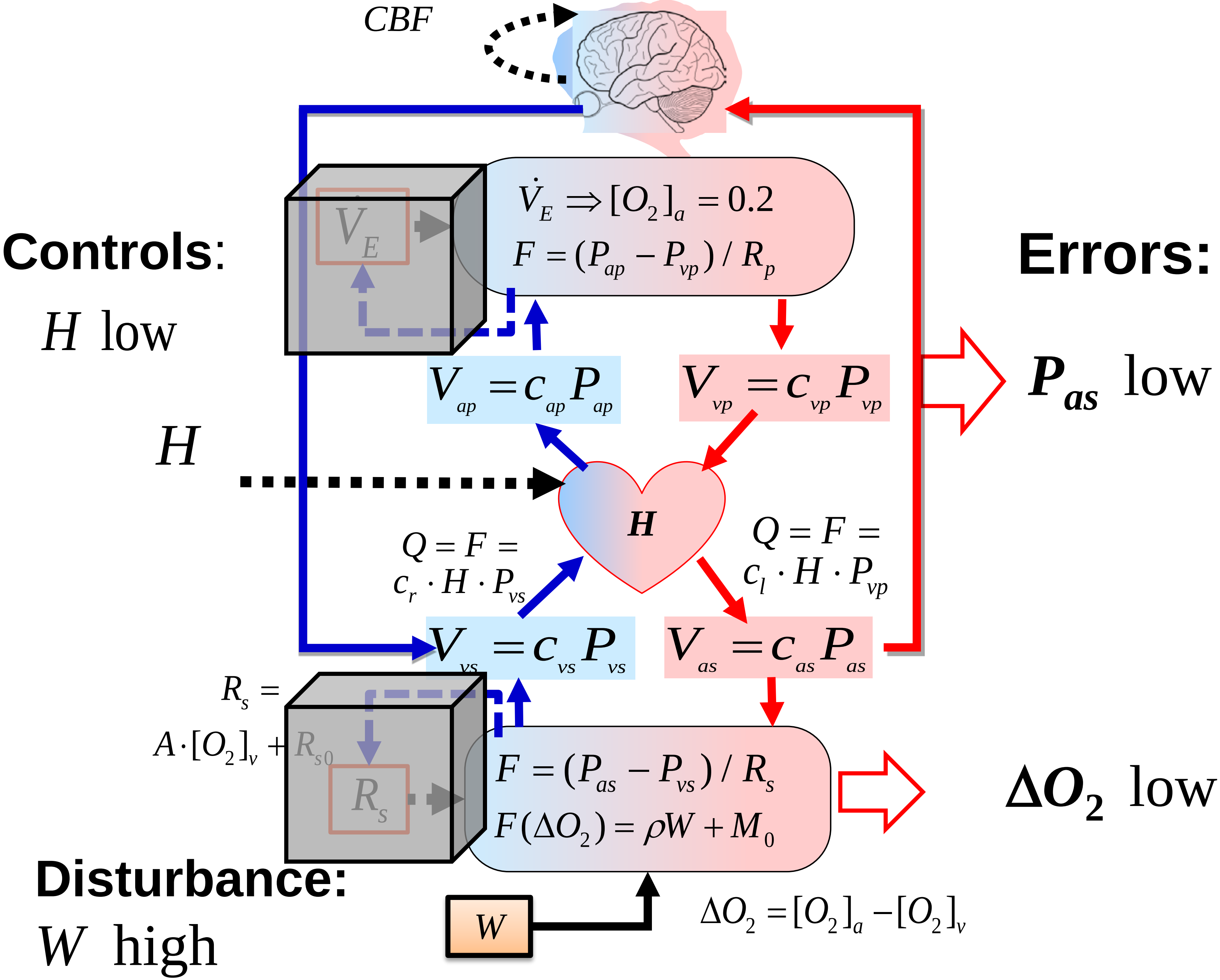


Penalize BP and HR more

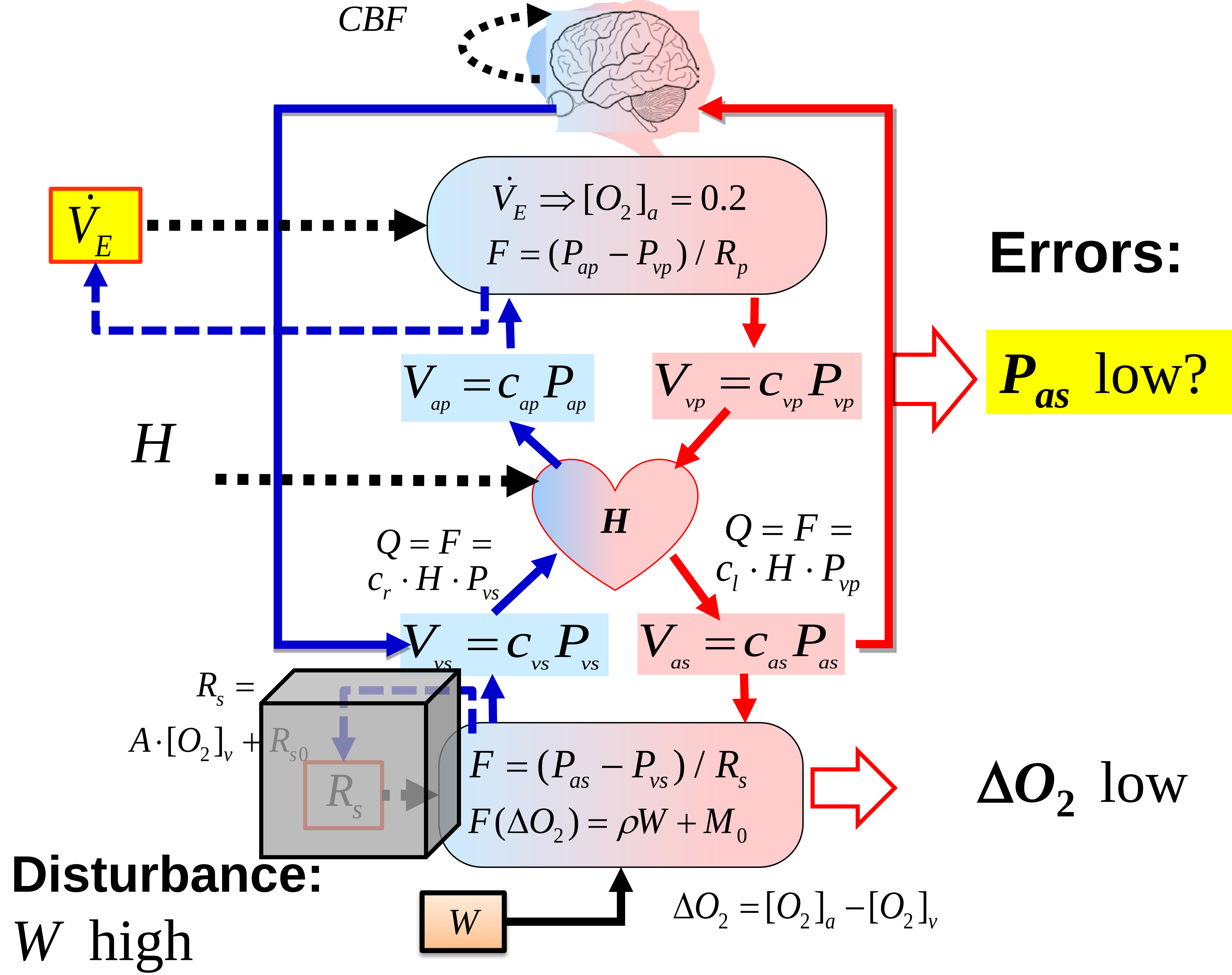
$$\min_{h(w)}\left\{\left(p\left(BP\right)^2 + q\left(\Delta O2t\right)^2 + \hat{r}\left(HR\right)^2\right)\right\}$$

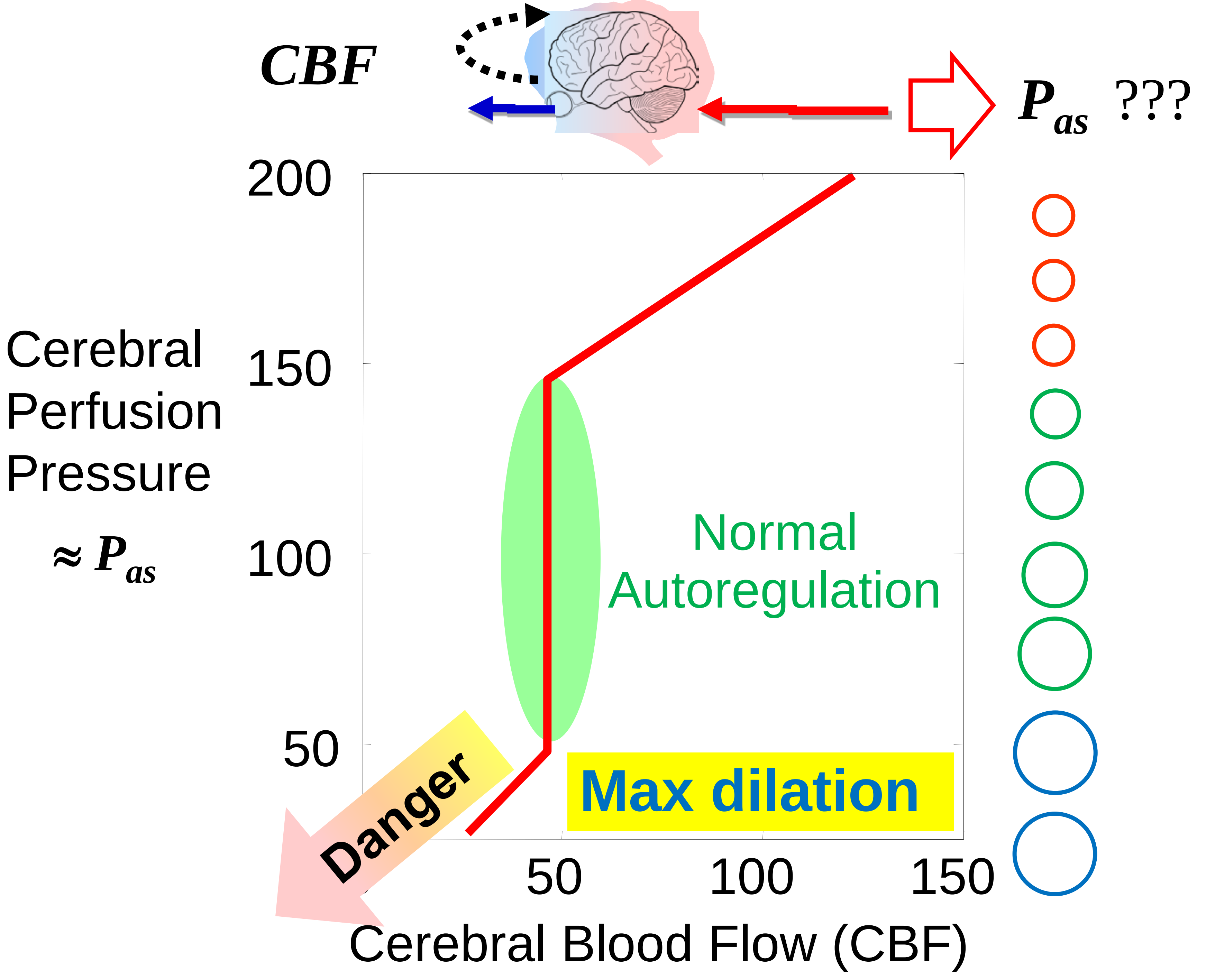
$p > 0$ $\hat{r} > r$

Explain differences between models and data?

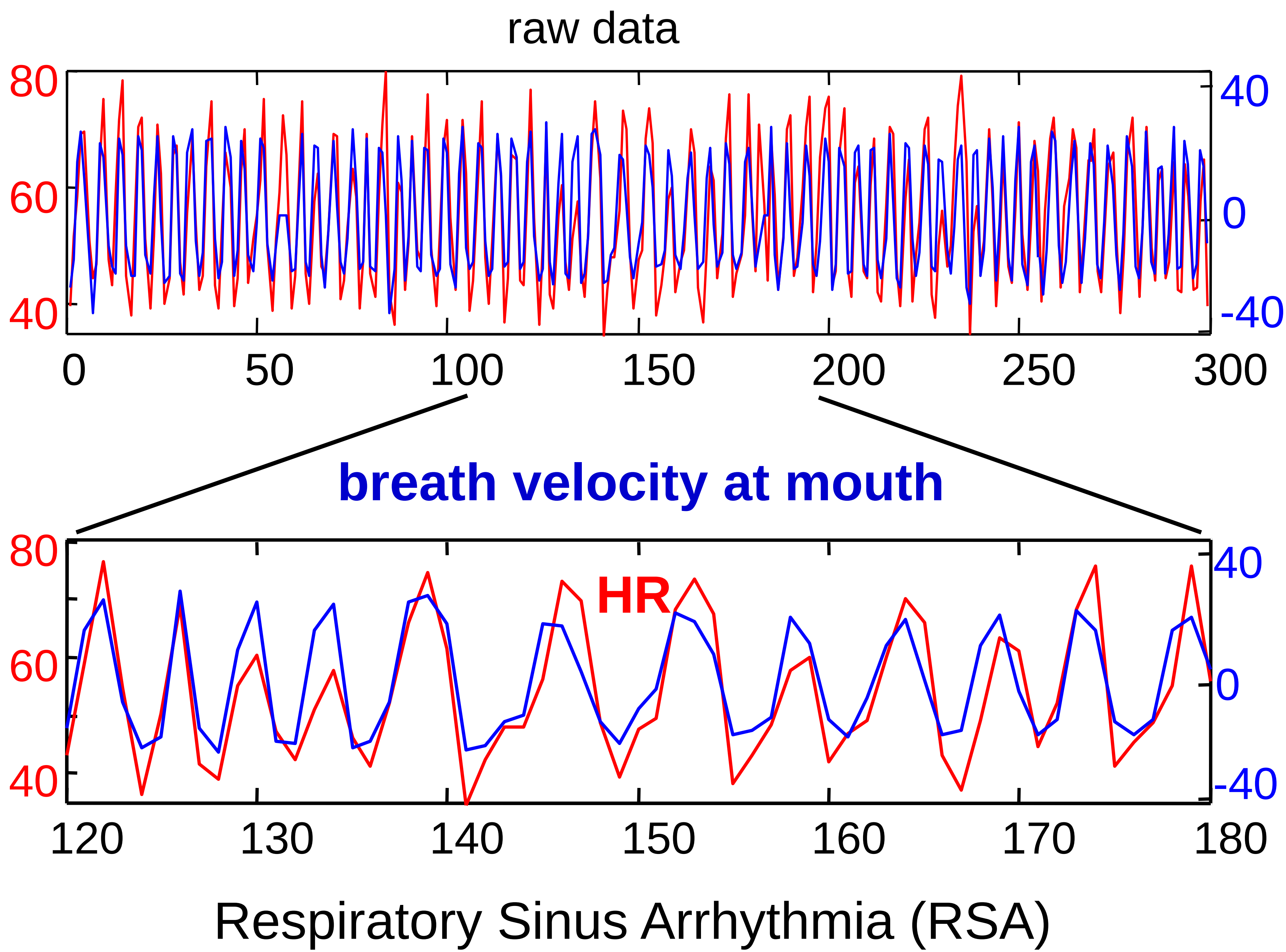


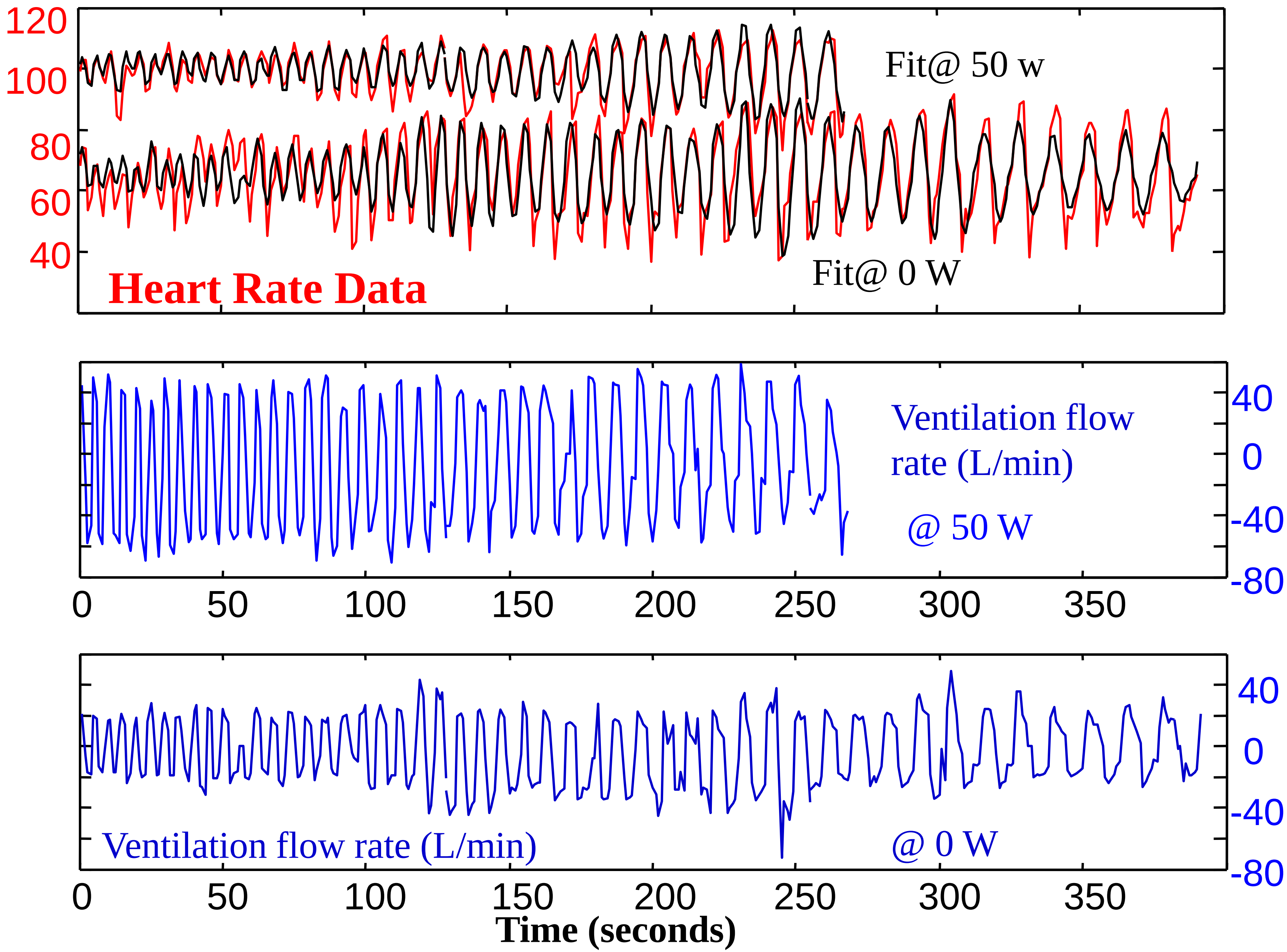
CBF
Controls:
H low
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
V_E
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$


CBF
$\dot{V}_E$
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low?
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$

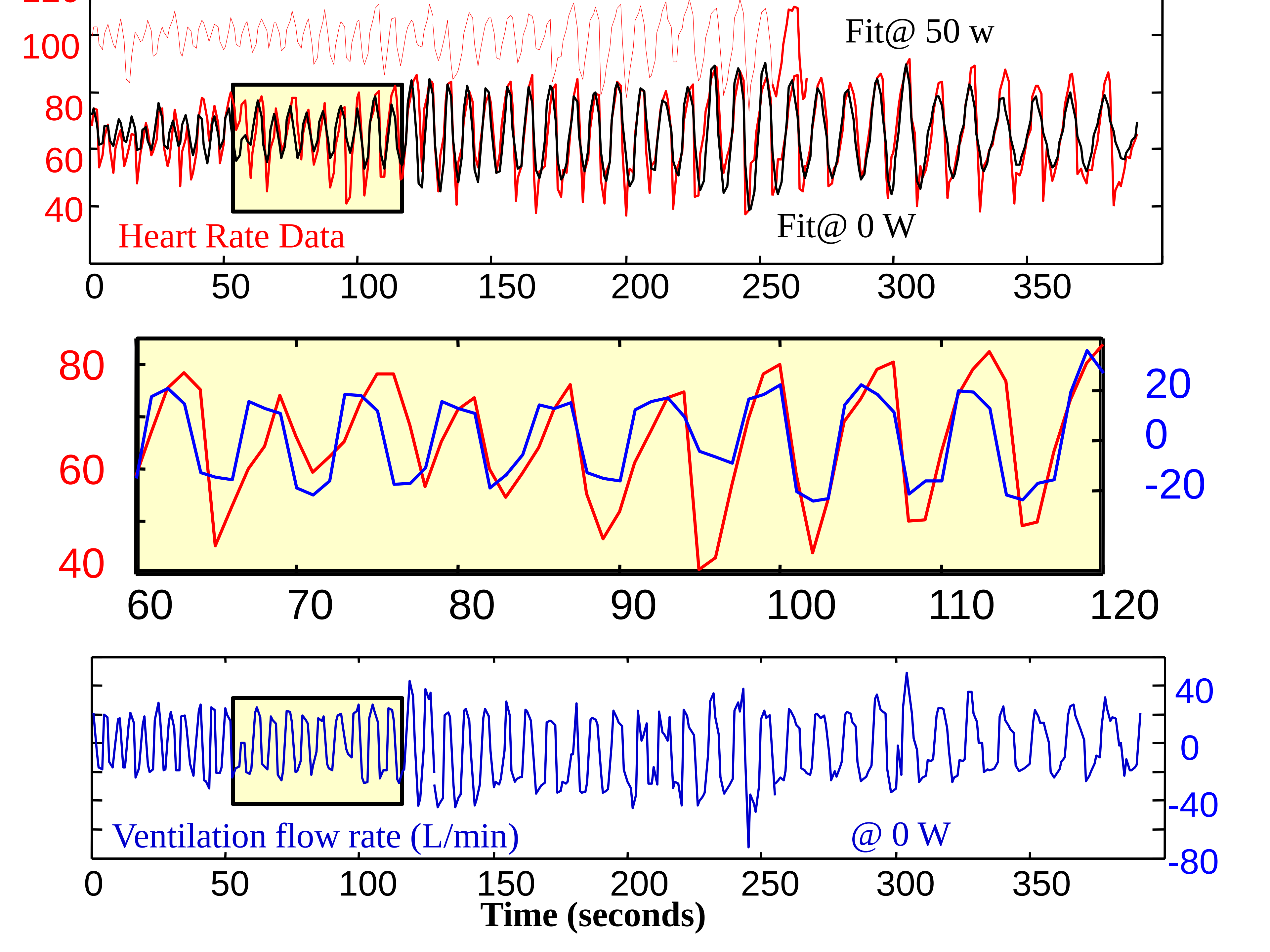


CBF
P_{as} ???
200
150
100
50
Cerebral Perfusion Pressure
$\approx P_{as}$
Normal Autoregulation
Danger
Max dilation
50
100
150
Cerebral Blood Flow (CBF)

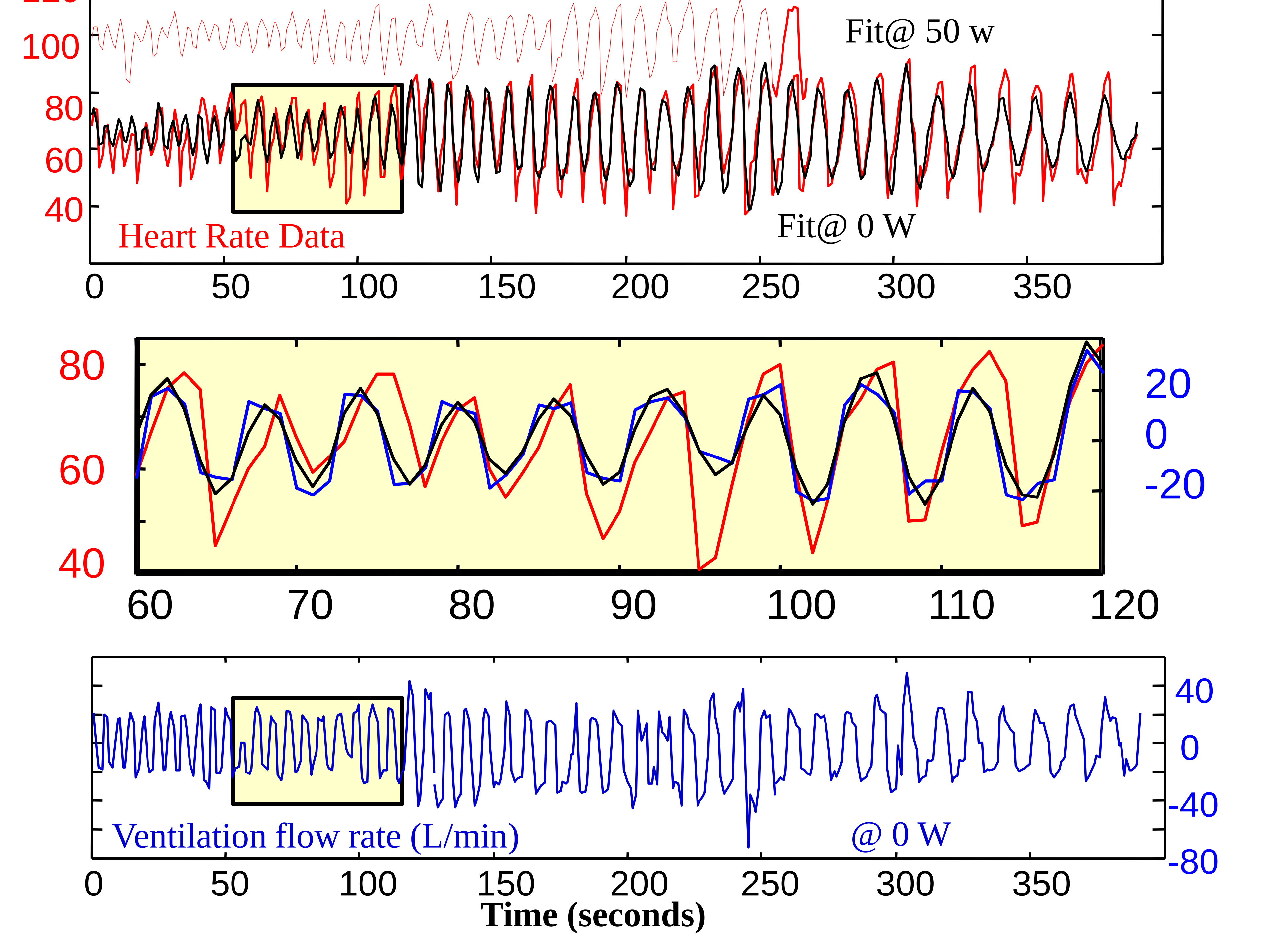

raw data
80
60
40
40
0
-40
0
50
100
150
200
250
300
breath velocity at mouth
HR
80
60
40
40
0
-40
120
130
140
150
160
170
180
Respiratory Sinus Arrhythmia (RSA)



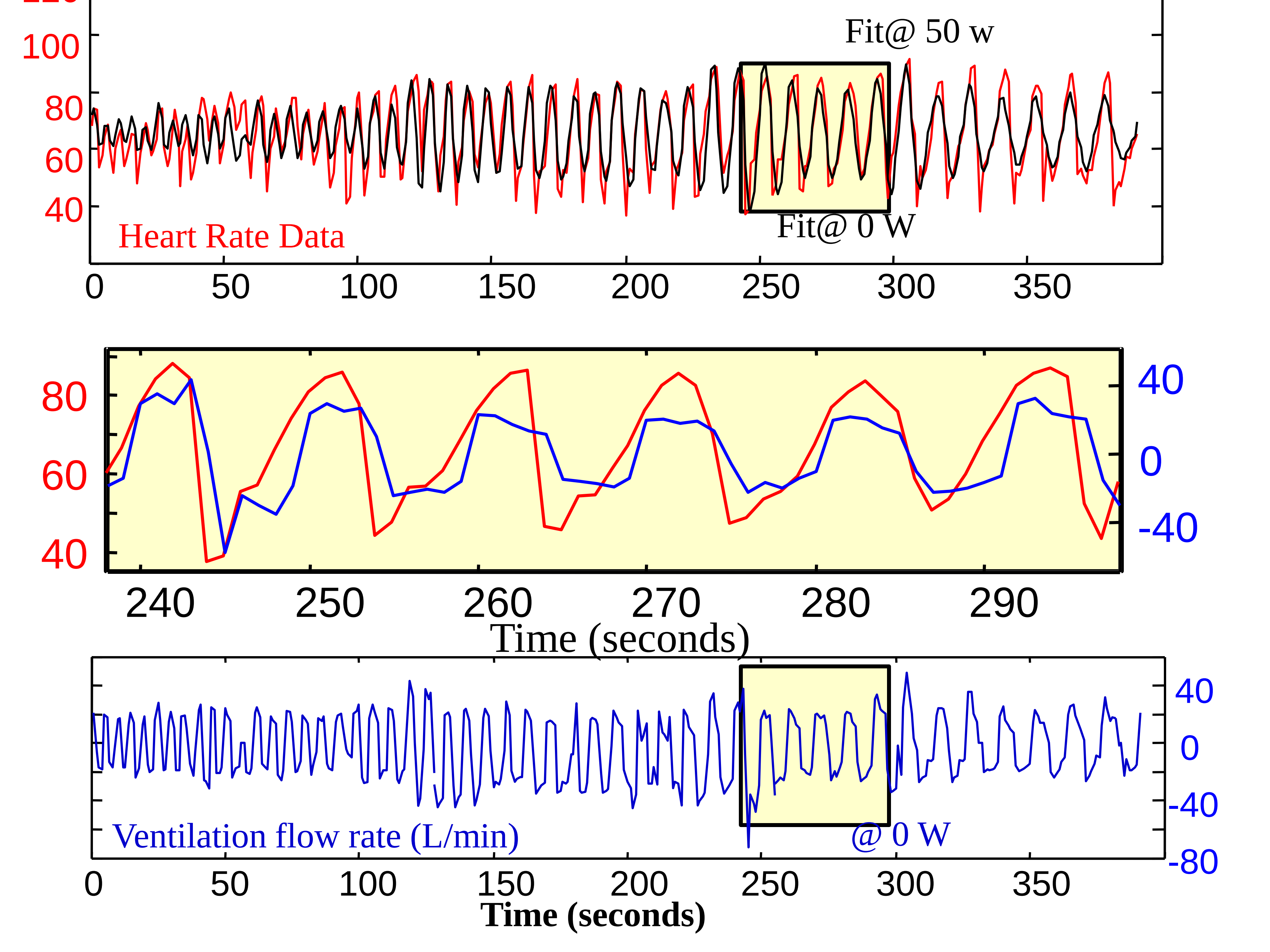
120
100
80
60
40
Fit@ 50 w
Fit@ 0 W
Heart Rate Data
Ventilation flow
rate (L/min)
@ 50 W
40
0
-40
-80
0
50
100
150
200
250
300
350
Ventilation flow rate (L/min)
@ 0 W
40
0
-40
-80
0
50
100
150
200
250
300
350
Time (seconds)



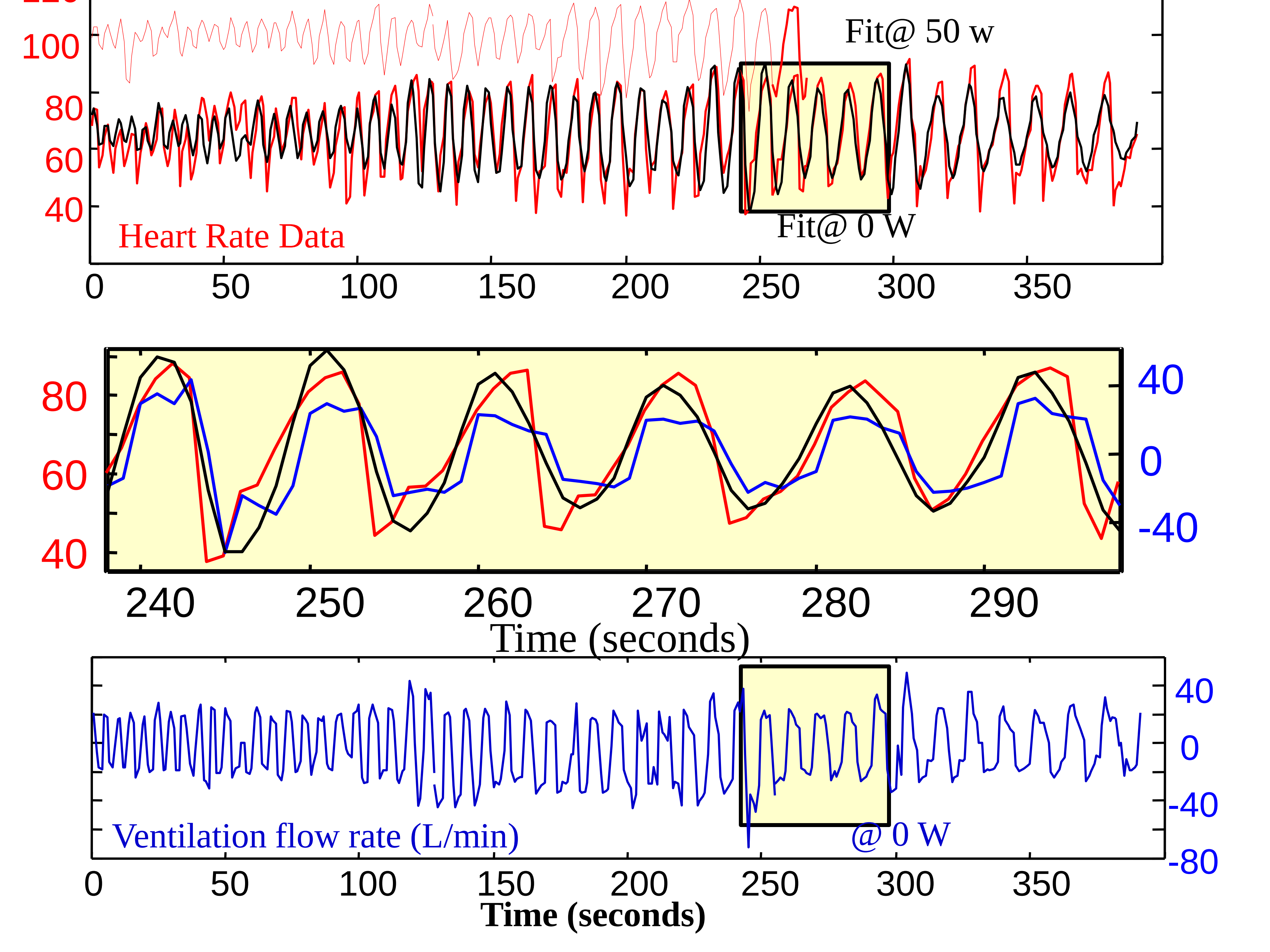
100
80
60
40
Fit@ 50 w
Fit@ 0 W
Heart Rate Data
0
50
100
150
200
250
300
350
80
60
40
20
0
-20
60
70
80
90
100
110
120
40
0
-40
-80
Ventilation flow rate (L/min)
@ 0 W
0
50
100
150
200
250
300
350
Time (seconds)



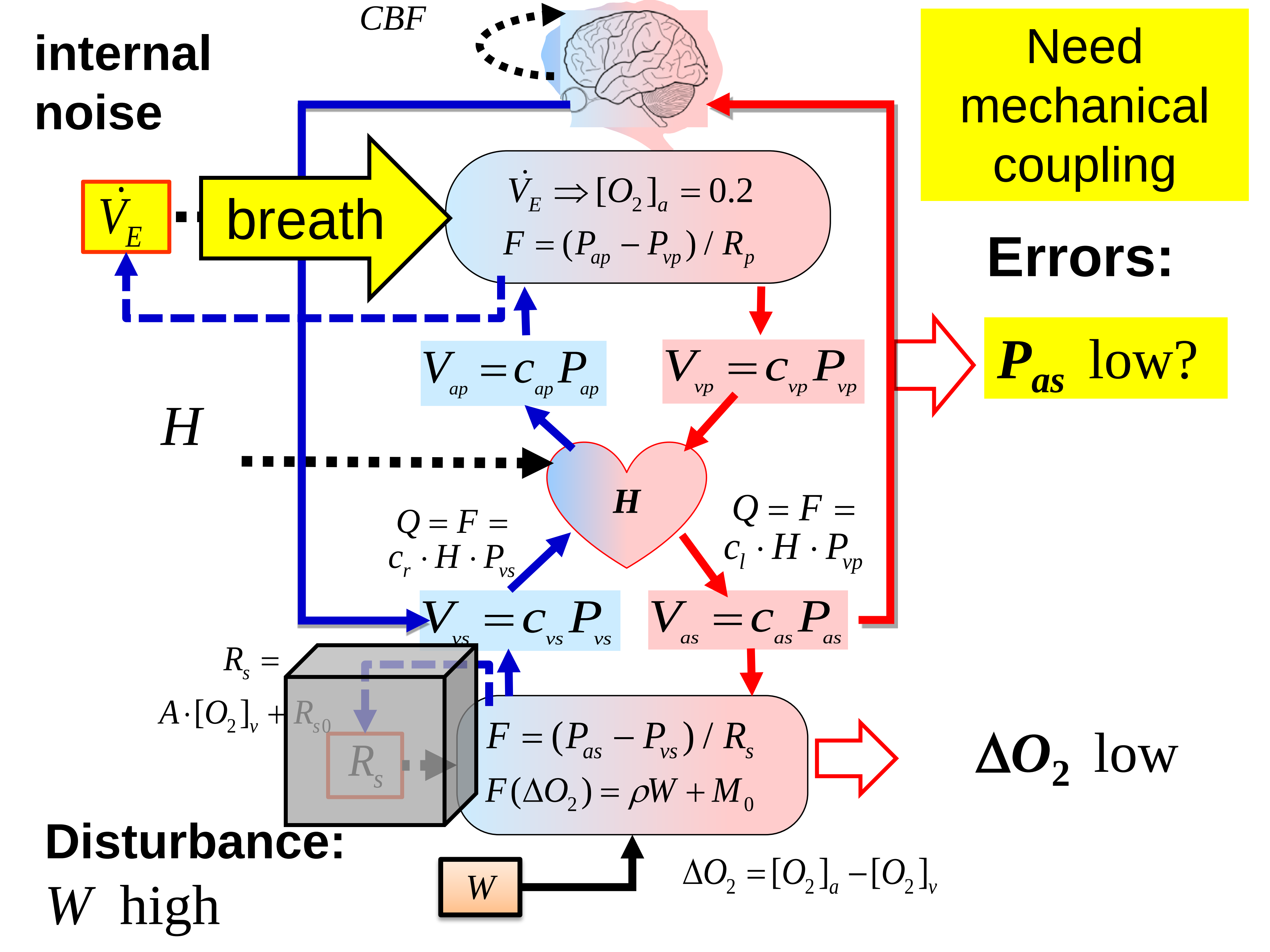
100
80
60
40
Fit@ 50 w
Fit@ 0 W
Heart Rate Data
0
50
100
150
200
250
300
350
80
60
40
20
0
-20
60
70
80
90
100
110
120
40
0
-40
-80
Ventilation flow rate (L/min)
@ 0 W
0
50
100
150
200
250
300
350
Time (seconds)



Fit@ 50 w
Fit@ 0 W
Heart Rate Data
100
80
60
40
0
50
100
150
200
250
300
350
40
0
-40
240
250
260
270
280
290
Time (seconds)
Ventilation flow rate (L/min)
@ 0 W
-80
Time (seconds)



Fit@ 50 w
Fit@ 0 W
Heart Rate Data
100
80
60
40
0
50
100
150
200
250
300
350
80
60
40
40
0
-40
240
250
260
270
280
290
Time (seconds)
Ventilation flow rate (L/min)
@ 0 W
40
0
-40
-80
0
50
100
150
200
250
300
350
Time (seconds)



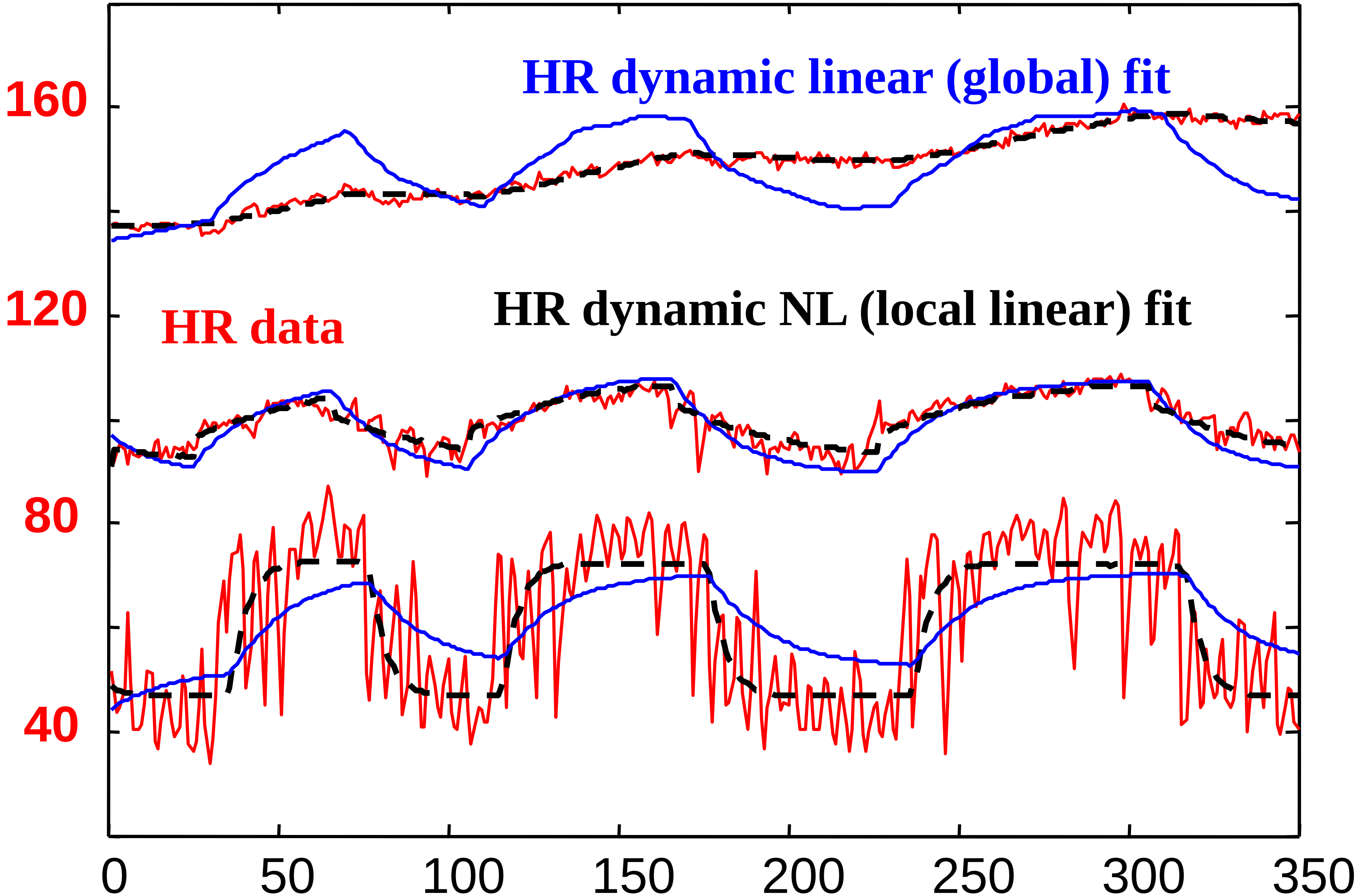
internal noise
CBF
Need mechanical coupling
$\dot{V}_E$
breath
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low?
H
H
$Q = F = c_r \cdot H \cdot P_{vs}$
$Q = F = c_l \cdot H \cdot P_{vp}$
$V_{vs} = c_{vs} P_{vs}$
$V_{as} = c_{as} P_{as}$
$R_s = A \cdot [O_2]_v + R_{s0}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$

Anaerobic and Aside on gas variables

- Gas exchange variables are also predictable with simple models
- VO2 is simplest and most predictable

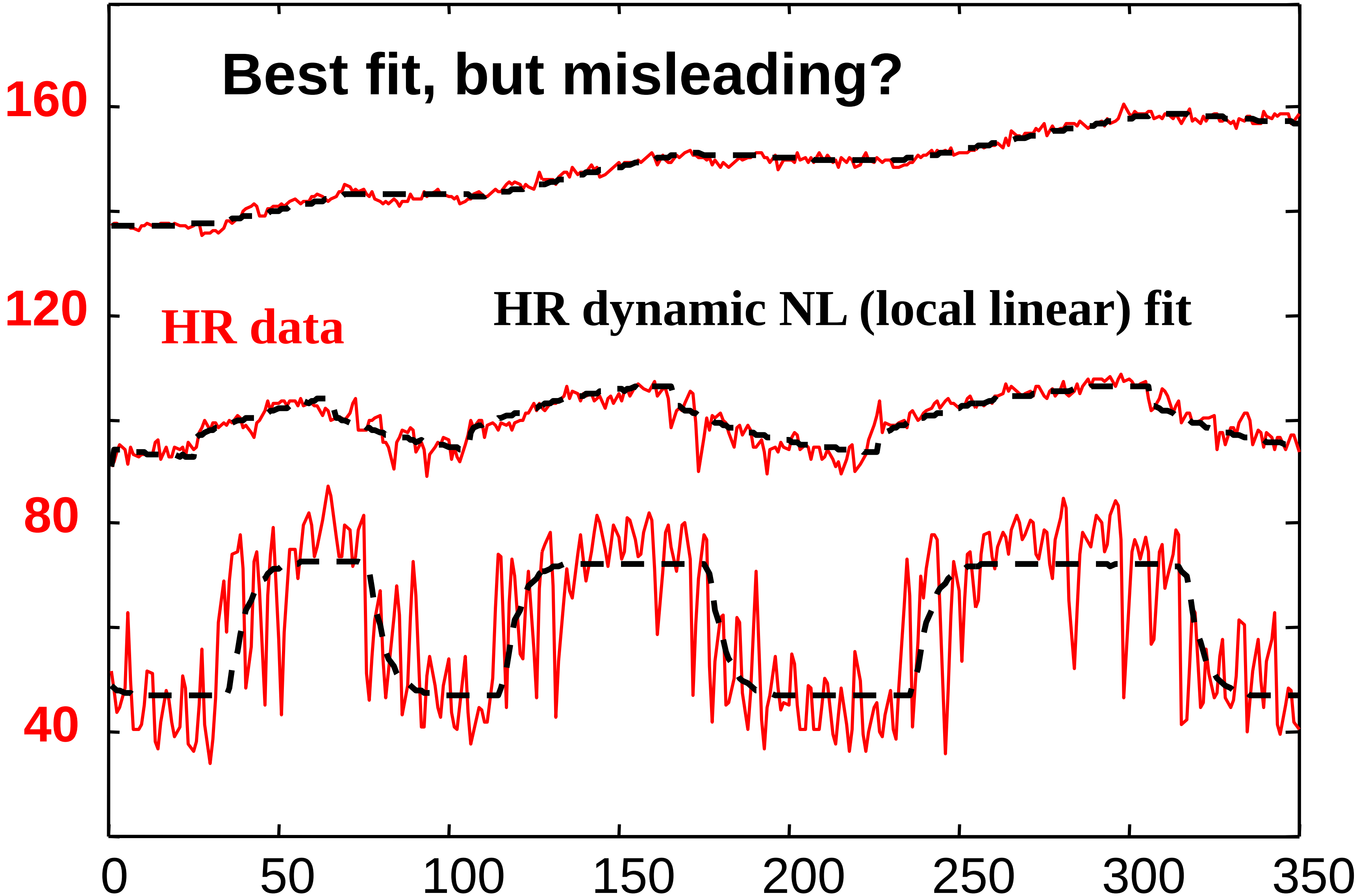
- VCO2-VO2 is most complex and we don't have first principles model
- Also HR model is bad at high watt levels

1st order linear model



$$\Delta h(t) = h(t+1) - h(t) = ah(t) + bw(t) + c$$

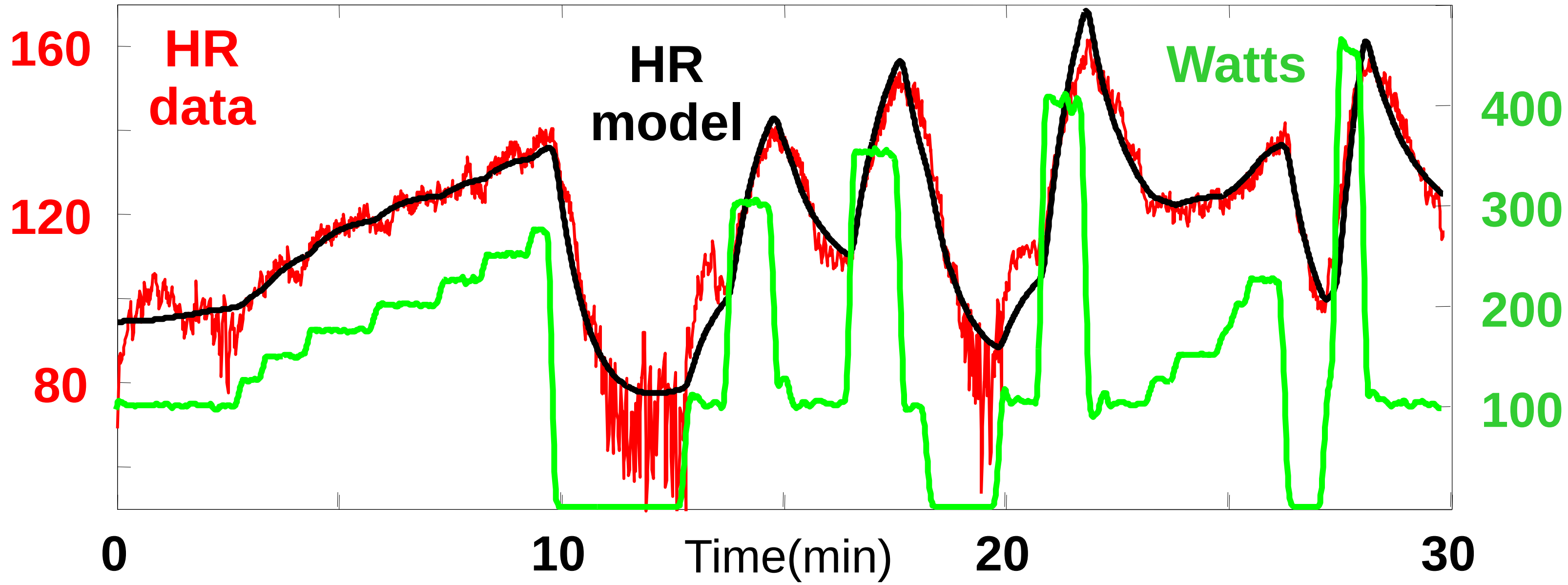
1^{st} order linear model

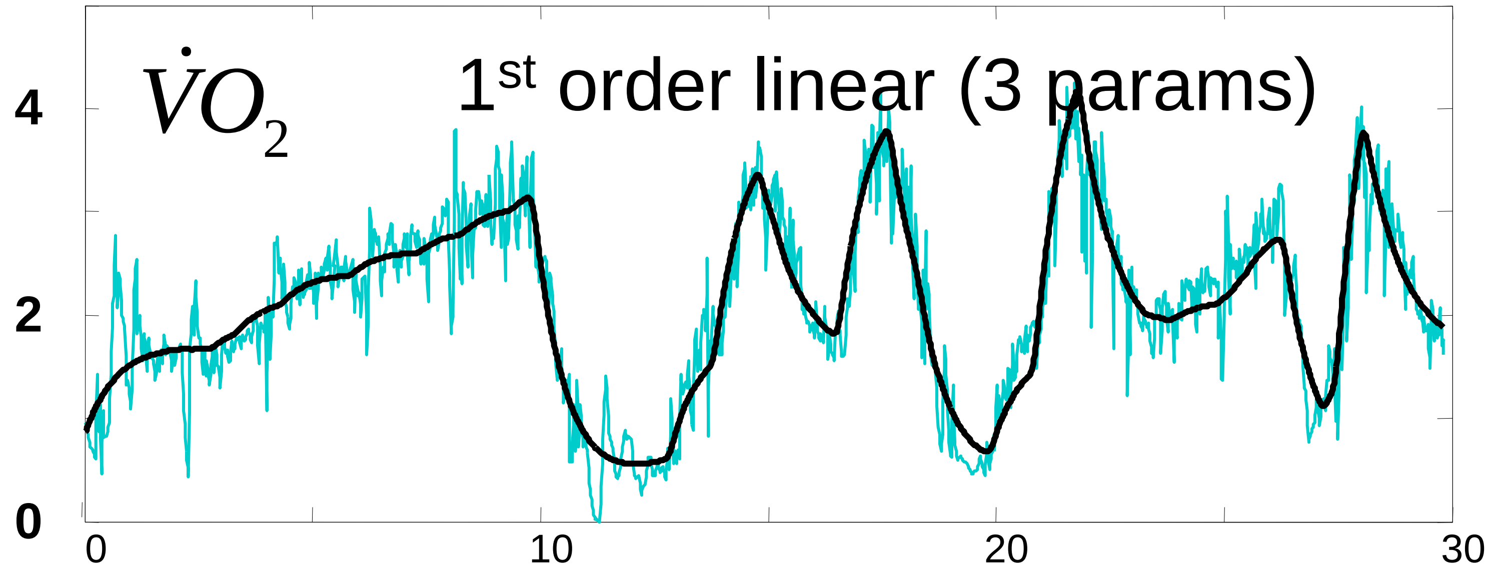


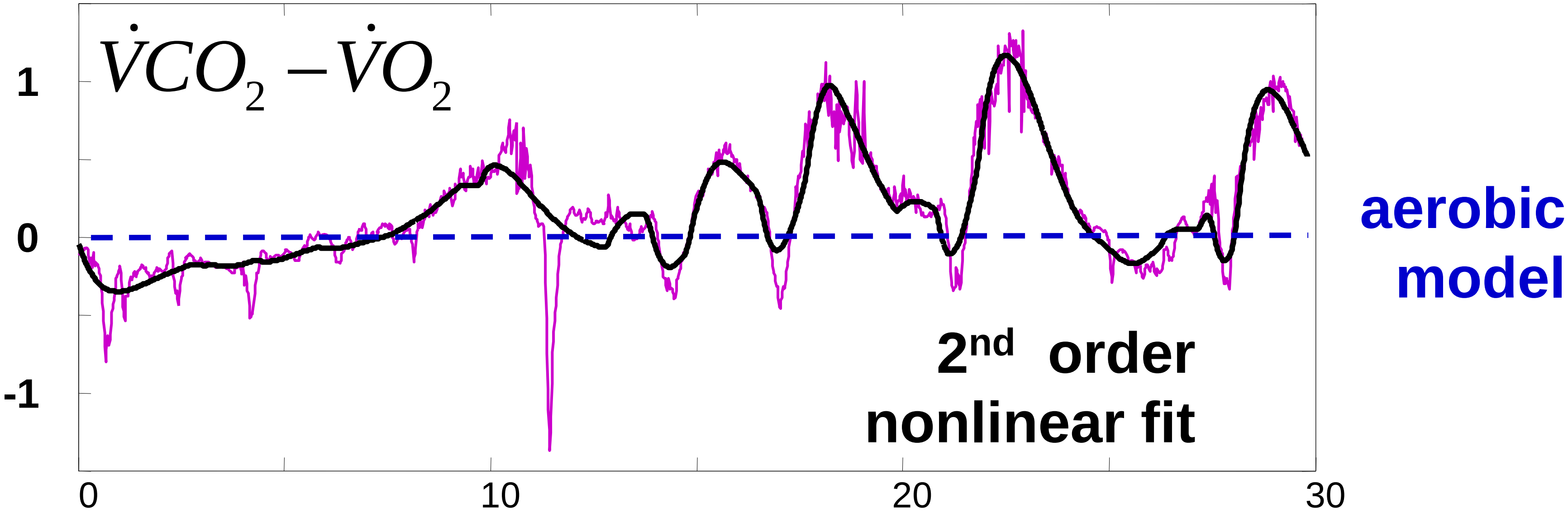
$$\Delta h(t) = h(t+1) - h(t) = ah(t) + bw(t) + c$$

JP data

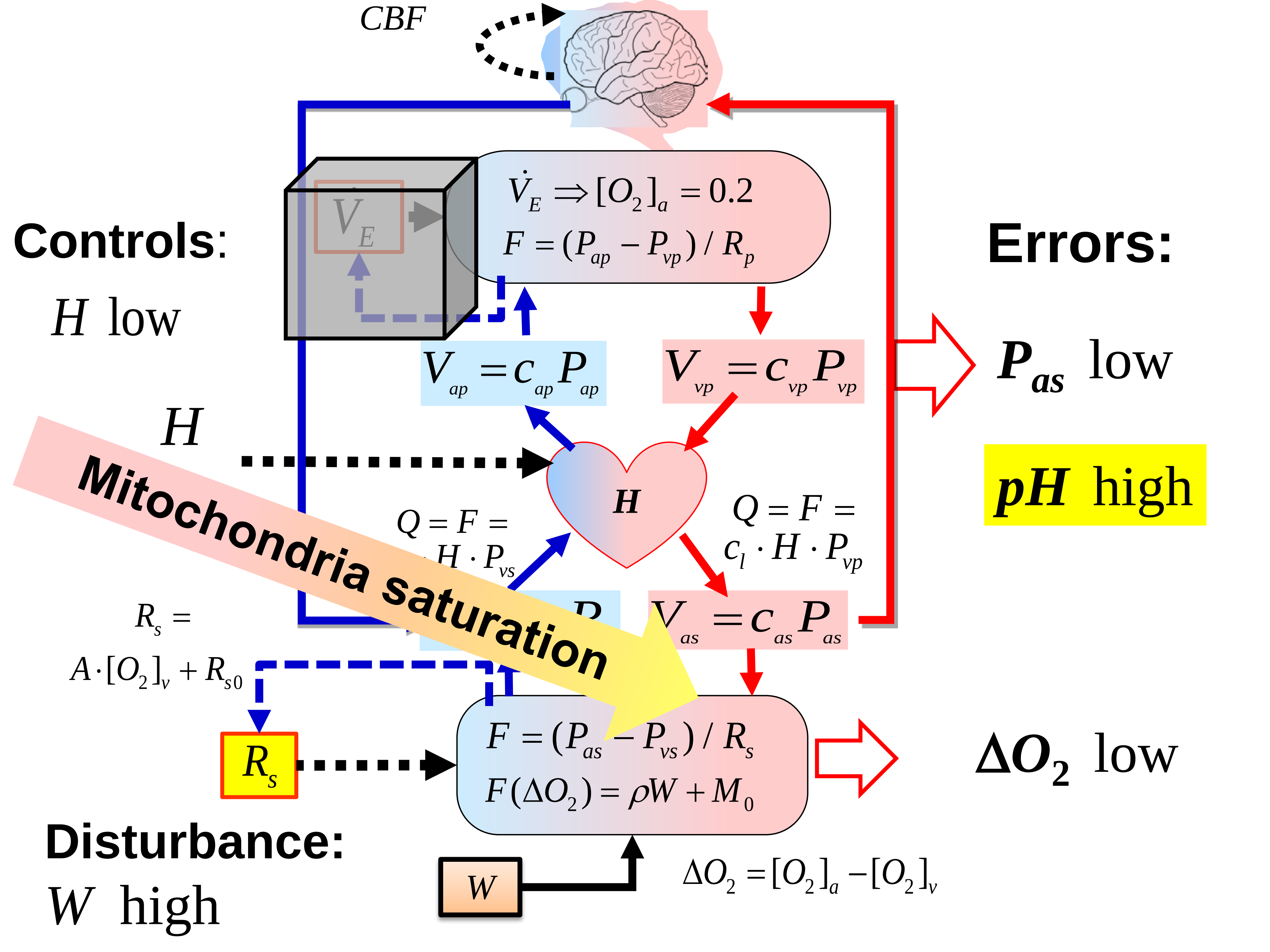
2^{nd} order nonlinear (7 parameters)



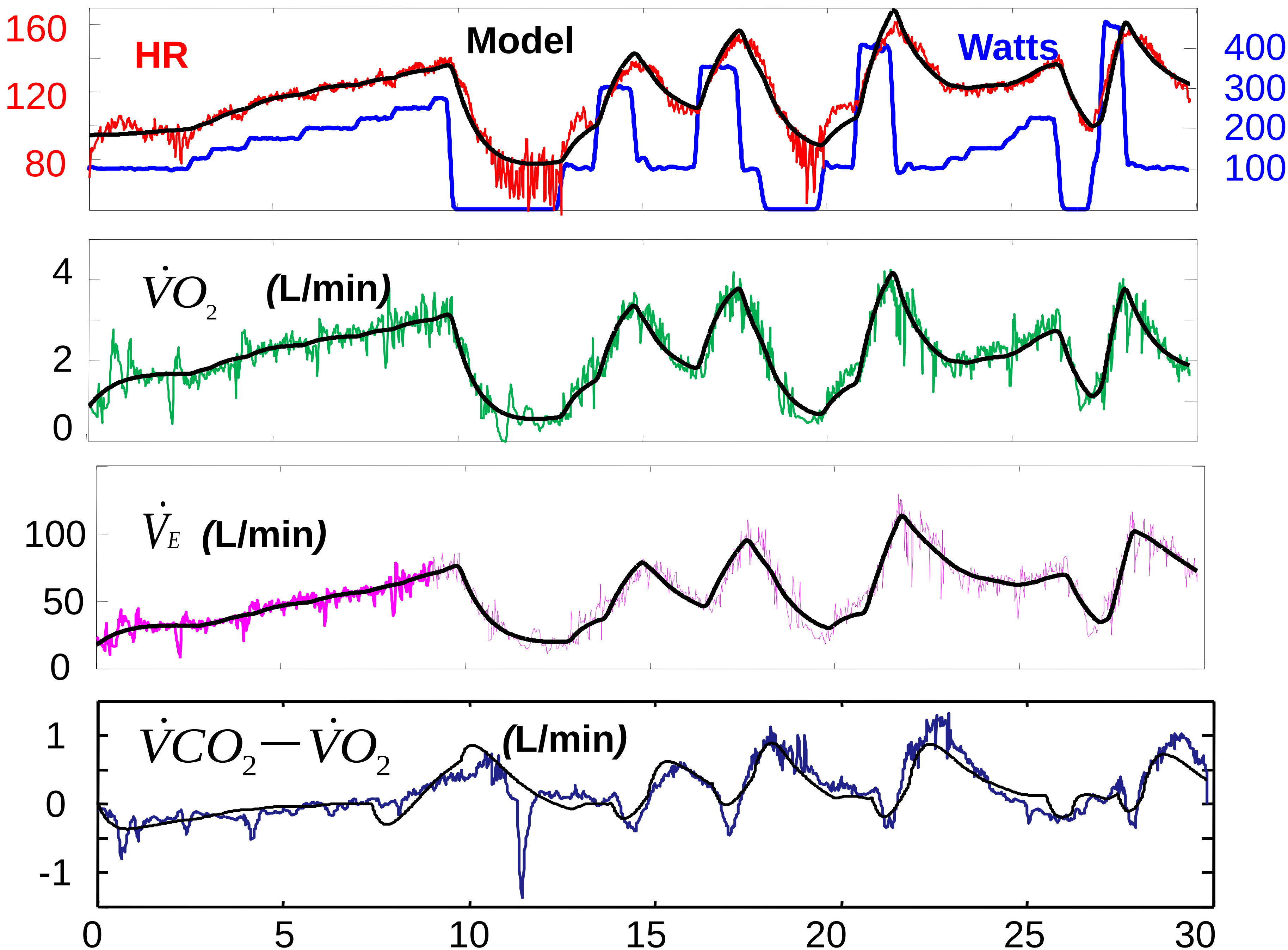




- Aerobic models can be way off at high watts
- (predict this signal should be constant)
- Can still fit with simple “black box” models, but…
- Need nonlinear dynamics
- Mechanistic models? (Redox ☹☠)
  - Need anaerobic mechanisms
  - Control of arterial pH is critical (and hard to model)

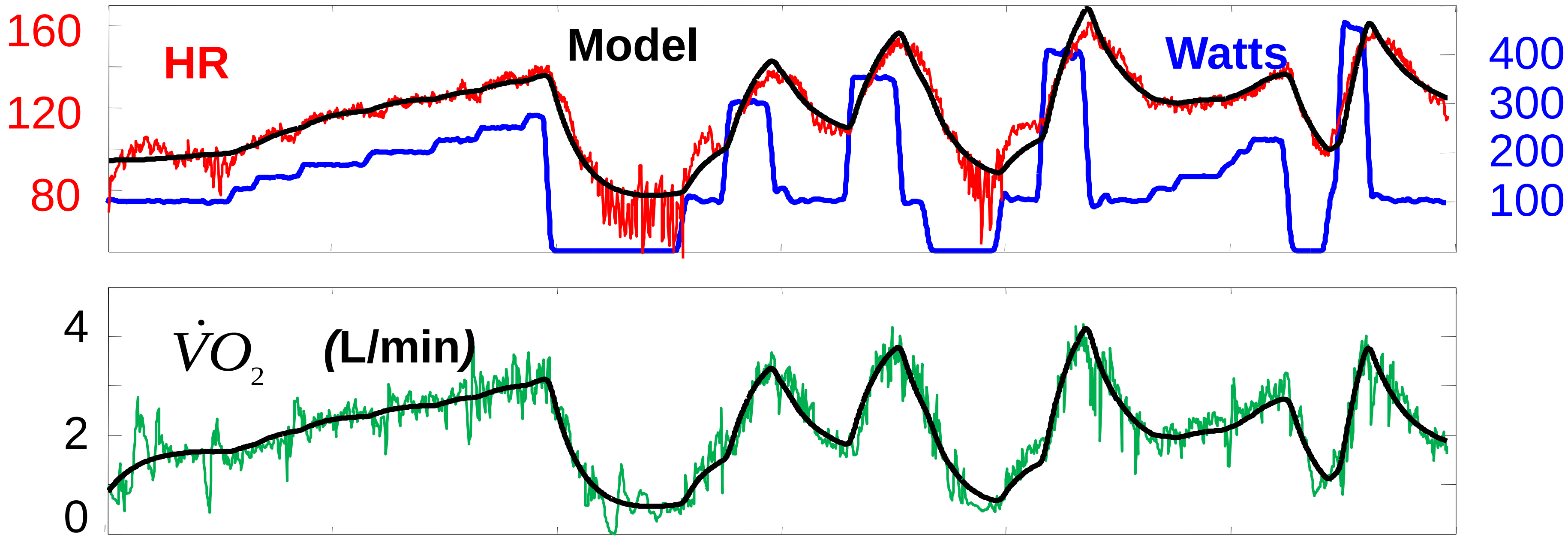


CBF
Controls:
H low
$\dot{V}_E \Rightarrow [O_2]_a = 0.2$
$F = (P_{ap} - P_{vp}) / R_p$
V_E
Errors:
$V_{ap} = c_{ap} P_{ap}$
$V_{vp} = c_{vp} P_{vp}$
P_{as} low
H
pH high
Mitochondria saturation
H
$Q = F =$
$H \cdot P_{vs}$
$Q = F =$
$c_l \cdot H \cdot P_{vp}$
$R_s =$
$A \cdot [O_2]_v + R_{s0}$
$V_{as} = c_{as} P_{as}$
R_s
$F = (P_{as} - P_{vs}) / R_s$
$F(\Delta O_2) = \rho W + M_0$
ΔO_2 low
Disturbance:
W high
W
$\Delta O_2 = [O_2]_a - [O_2]_v$

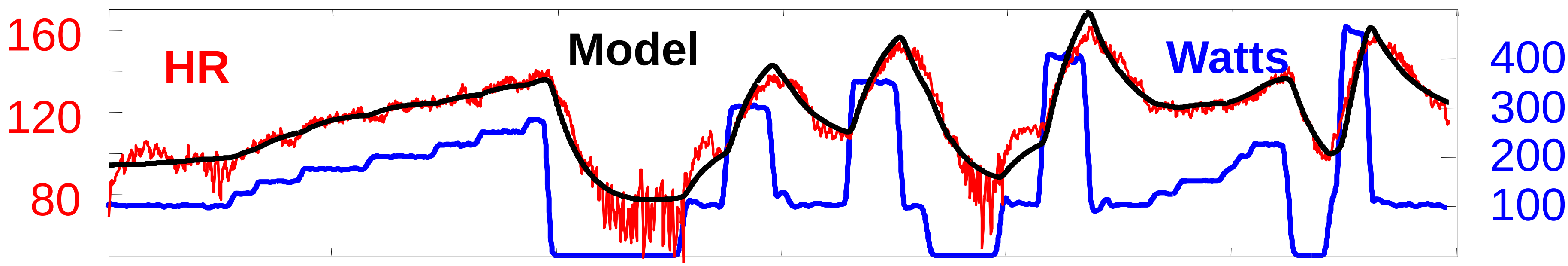


160
120
80
HR
Model
Watts
400
300
200
100
4
2
0
$\dot{V}O_2$ (L/min)
100
50
0
$\dot{V}_E$ (L/min)
1
0
-1
$\dot{V}CO_2 - \dot{V}O_2$ (L/min)
0
5
10
15
20
25
30

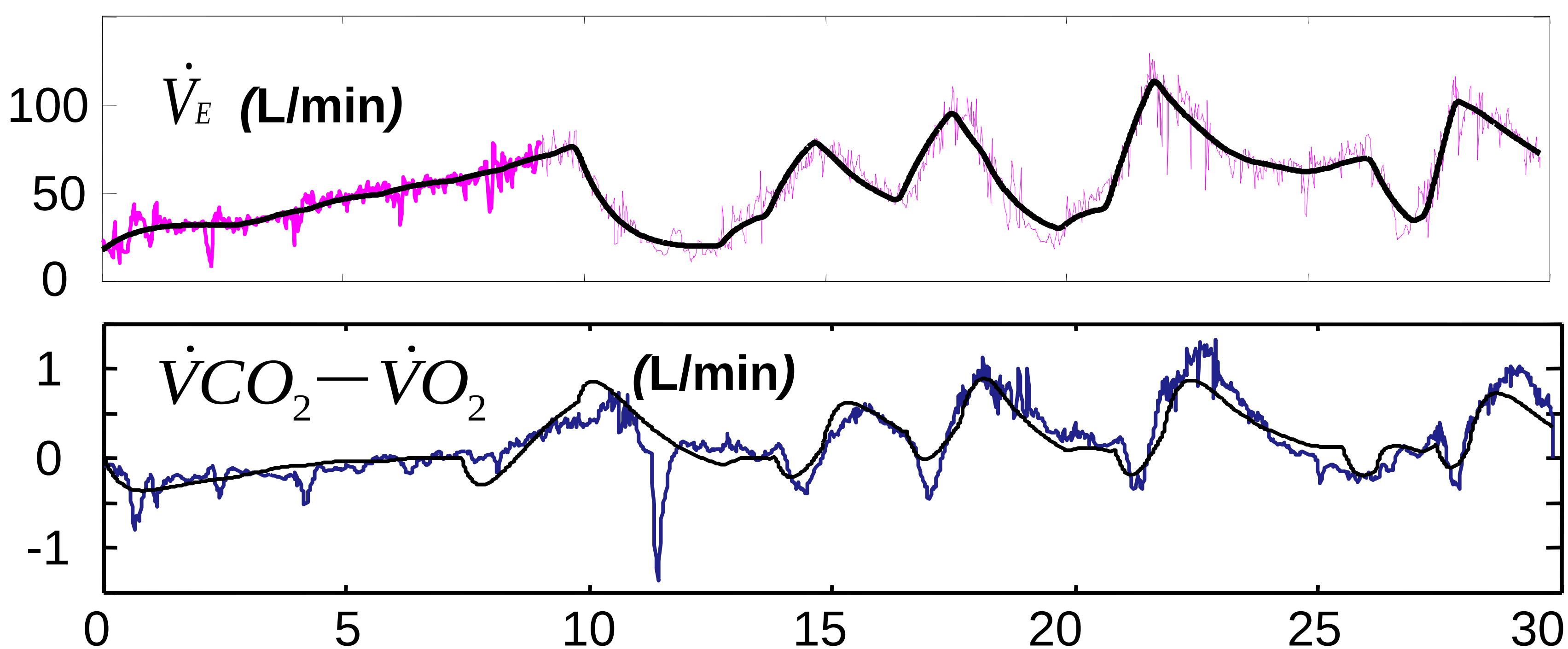
2^{nd} order nonlinear (7 parameters)

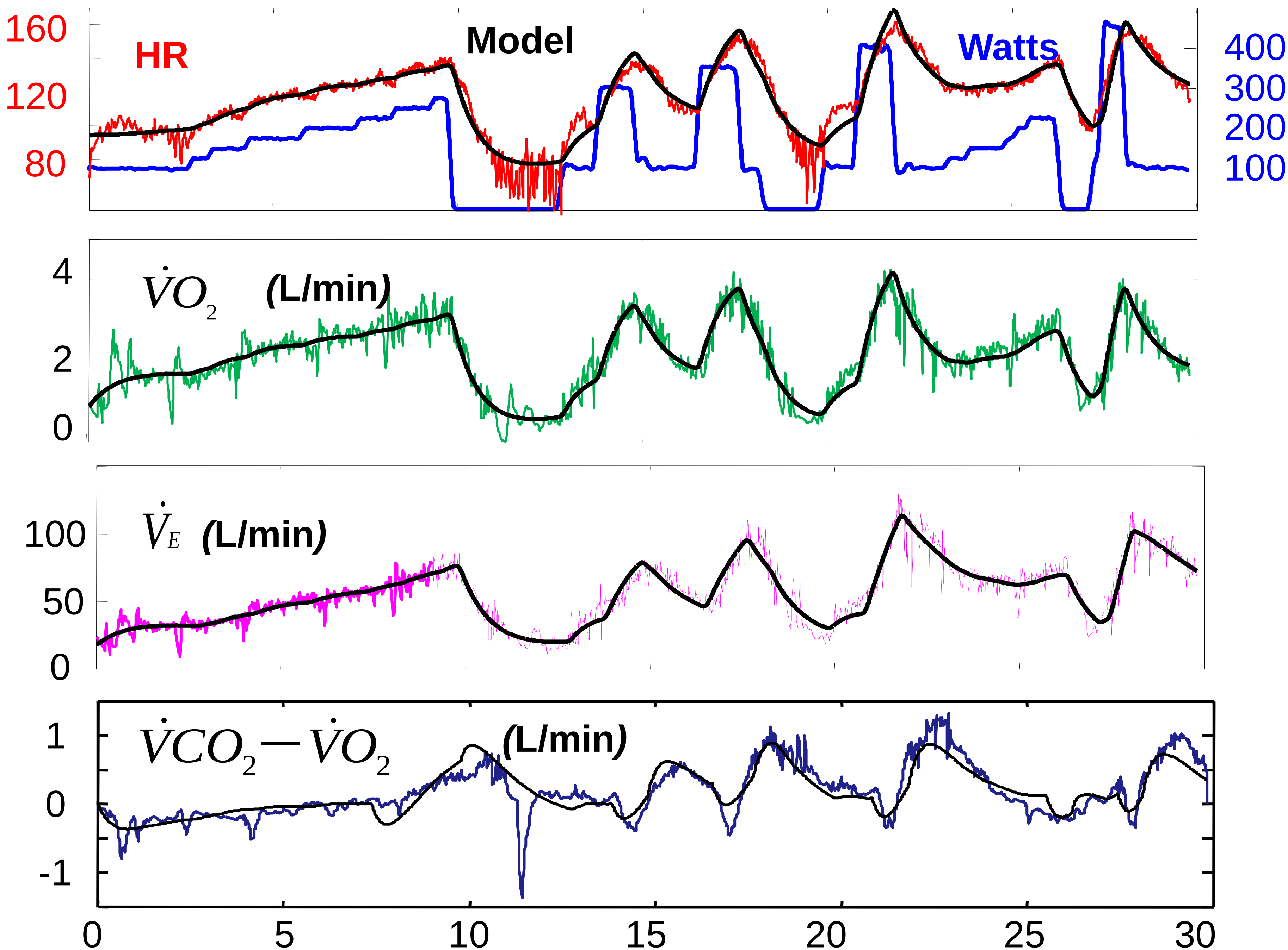


1^{st} order linear (3 params)

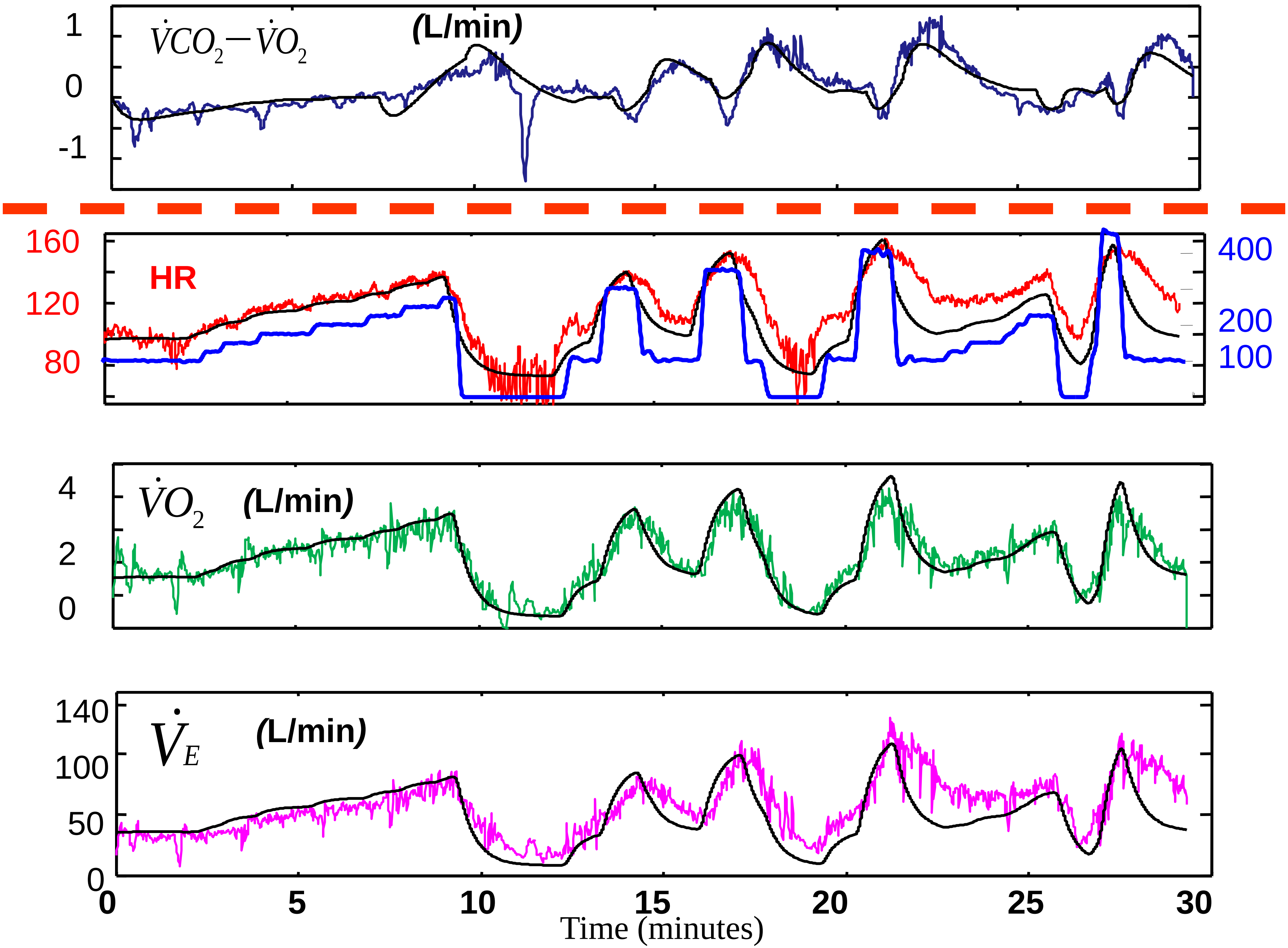


2[nd] order nonlinear (7 parameters)



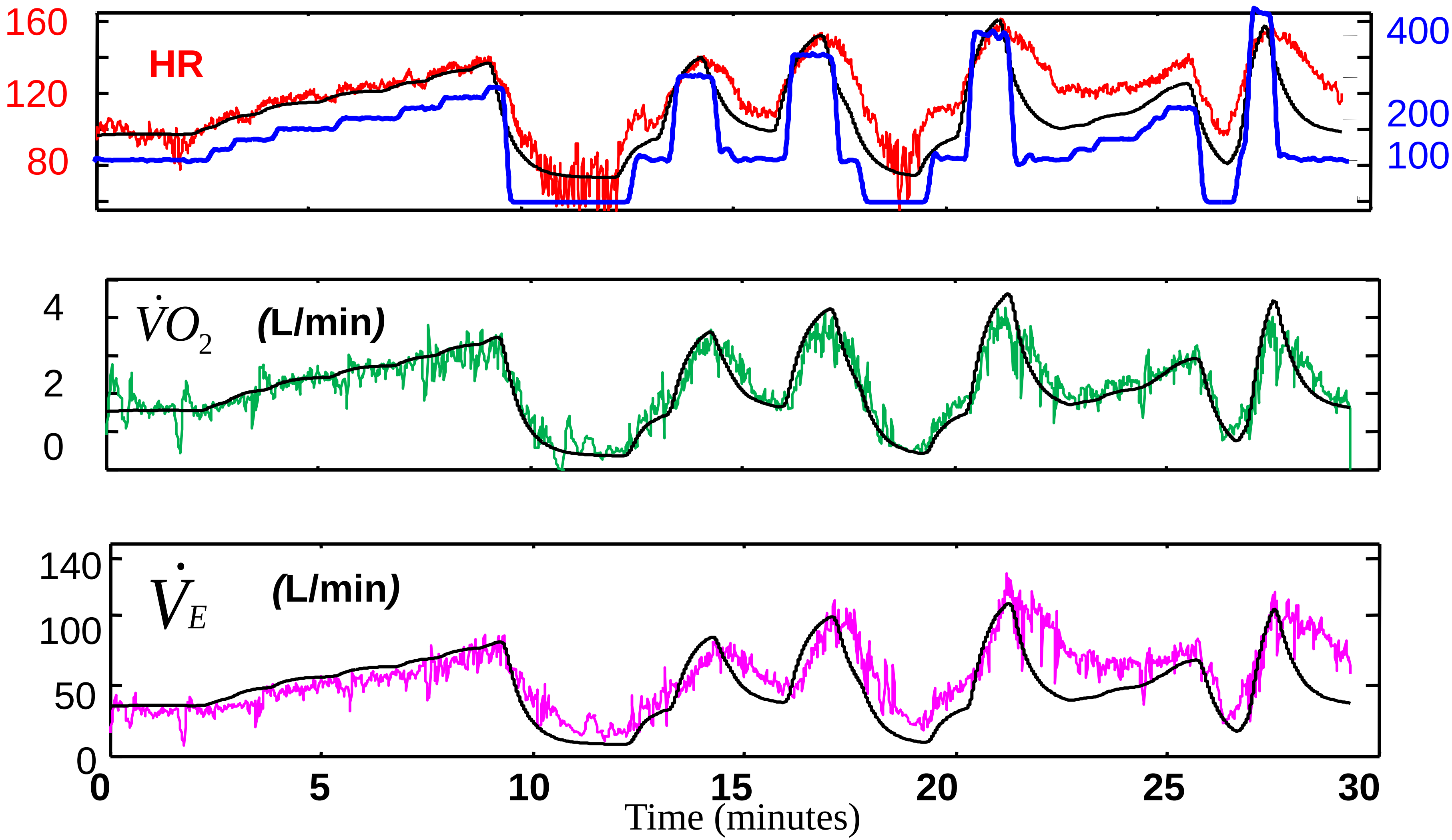


160
120
80
HR
Model
Watts
400
300
200
100
4
2
0
$\dot{V}O_2$ (L/min)
100
50
0
$\dot{V}_E$ (L/min)
1
0
-1
$\dot{V}CO_2 - \dot{V}O_2$ (L/min)
0
5
10
15
20
25
30

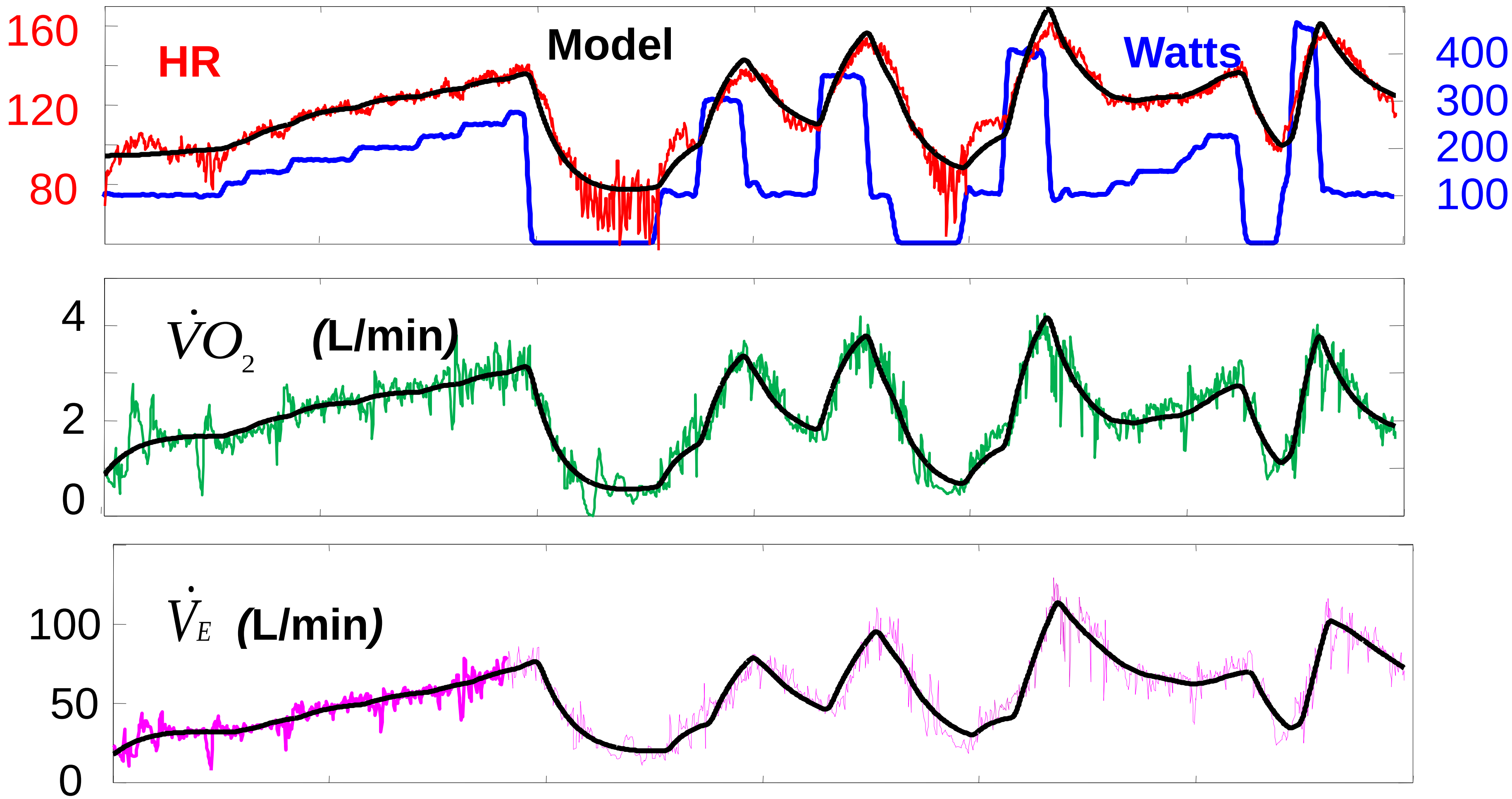


$\dot{V}CO_2 - \dot{V}O_2$ (L/min)
1
0
-1
HR
160
120
80
400
200
100
$\dot{V}O_2$ (L/min)
4
2
0
$\dot{V}_E$ (L/min)
140
100
50
0
0
5
10
15
20
25
30
Time (minutes)

First principles ***aerobic*** model

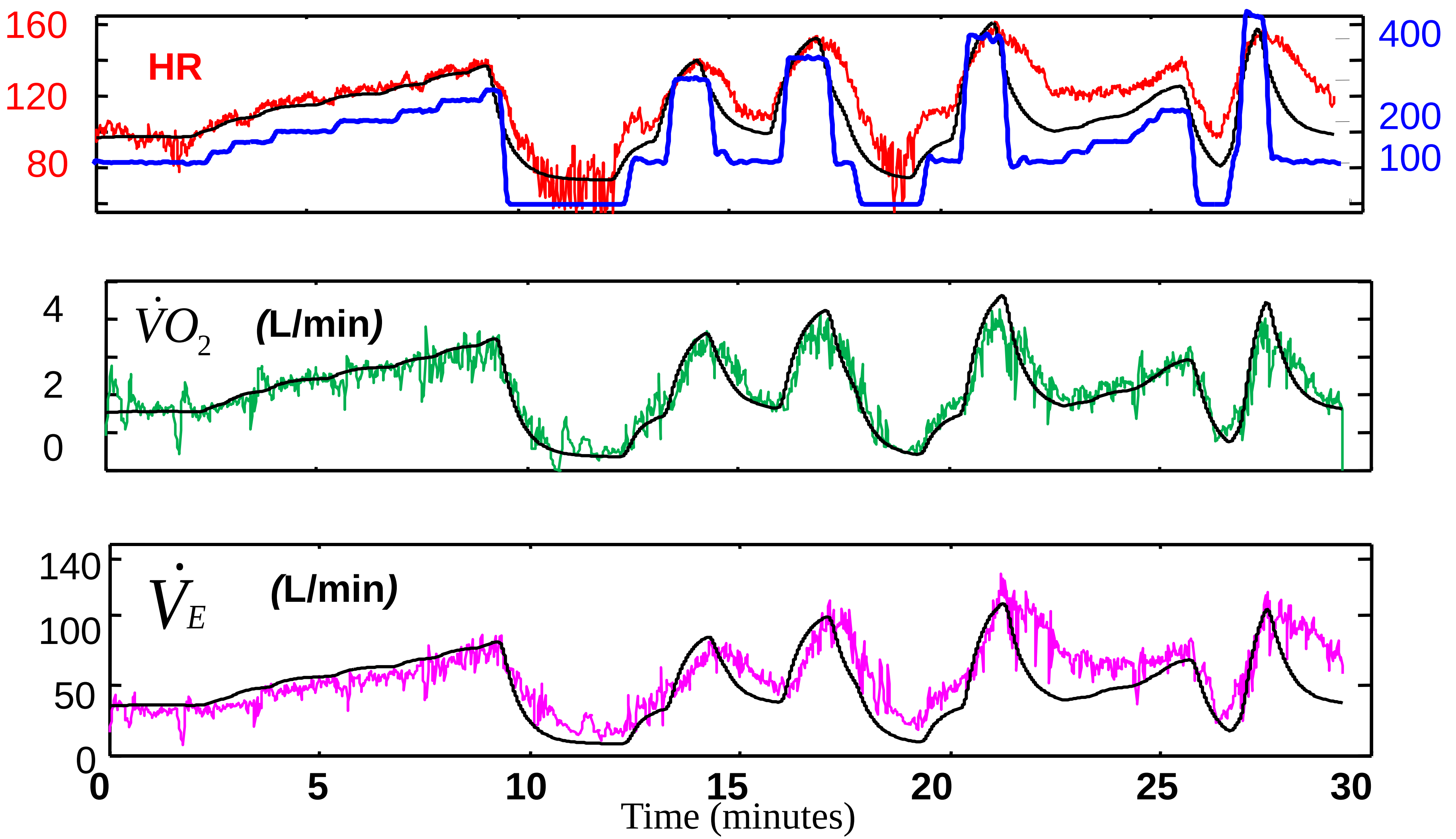


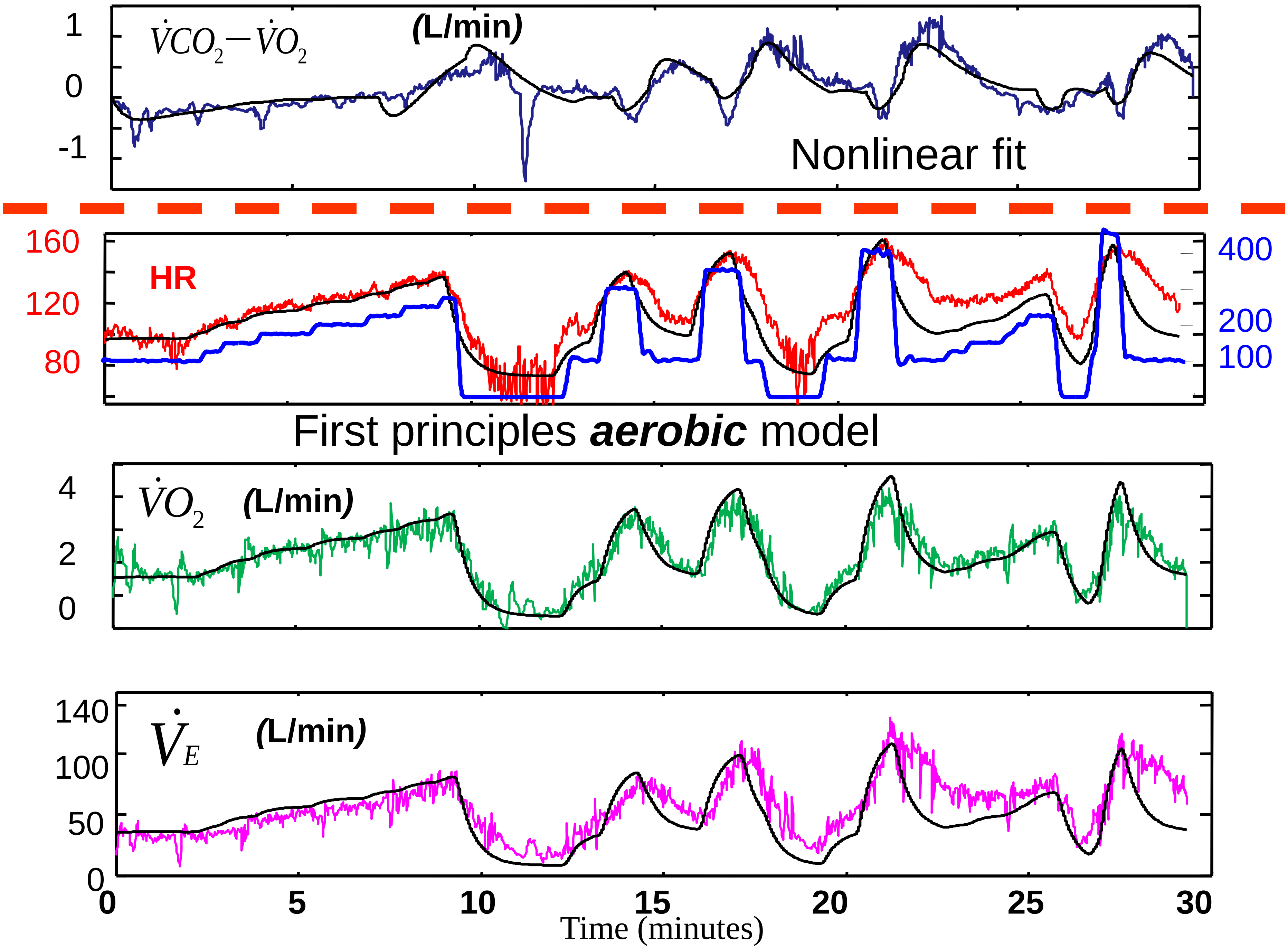
Fits



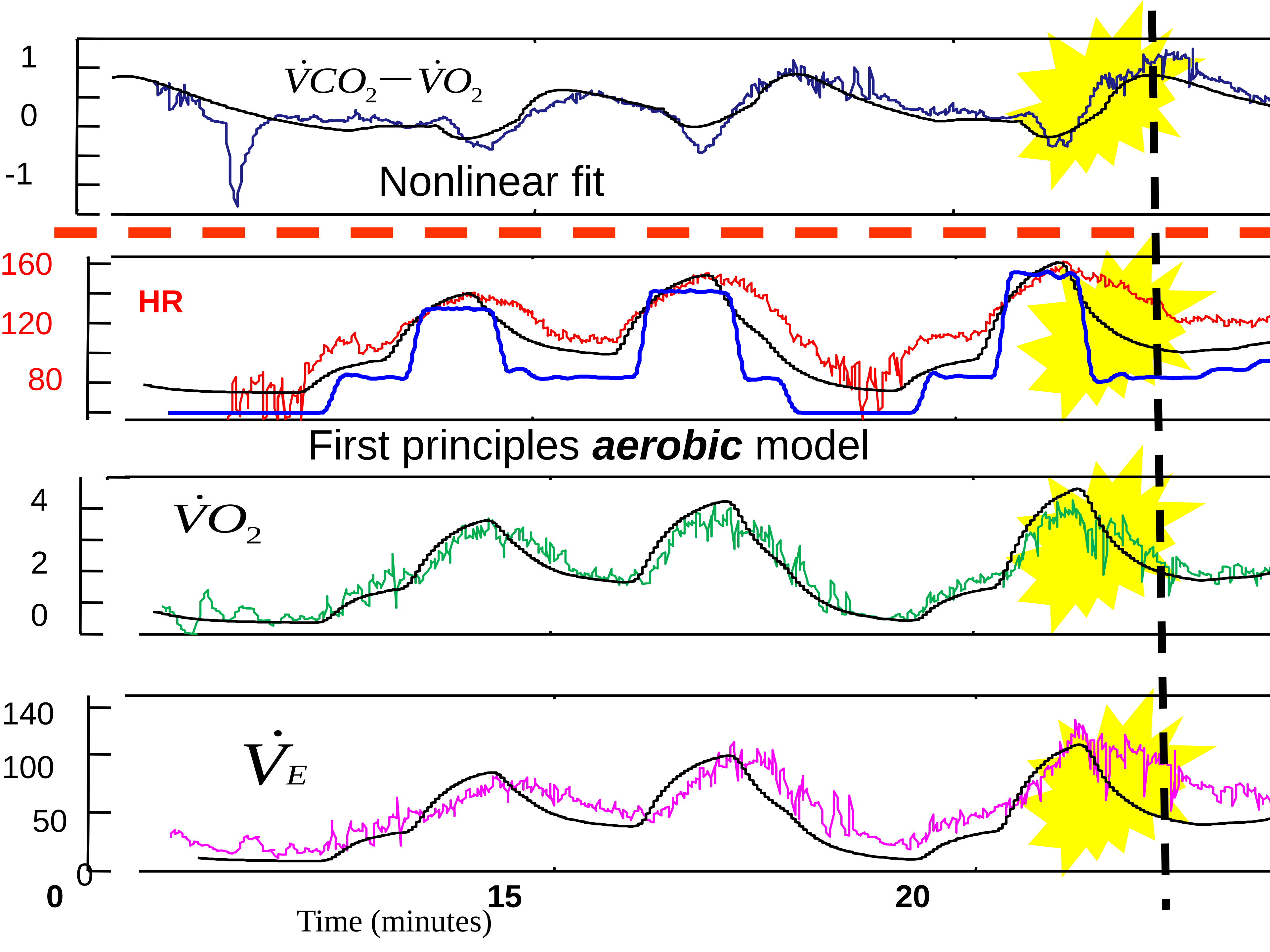
160
120
80
HR
Model
Watts
400
300
200
100
4
2
0
$\dot{V}O_2$ (L/min)
100
50
0
$\dot{V}_E$ (L/min)

First principles ***aerobic*** model





$\dot{V}CO_2 - \dot{V}O_2$
(L/min)
1
0
-1
Nonlinear fit
160
120
80
HR
400
200
100
First principles ***aerobic*** model
$\dot{V}O_2$
(L/min)
4
2
0
$\dot{V}_E$
(L/min)
140
100
50
0
0
5
10
15
20
25
30
Time (minutes)



$\dot{V}CO_2 - \dot{V}O_2$
1
0
-1
Nonlinear fit
160
120
80
HR
First principles ***aerobic*** model
4
2
0
$\dot{V}O_2$
140
100
50
0
$\dot{V}_E$
0
15
20
Time (minutes)

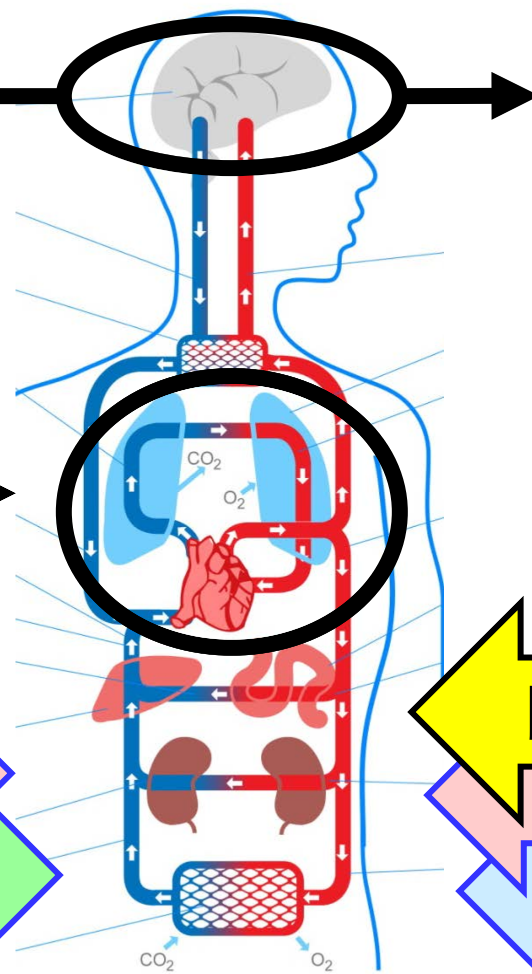
Homeostasis

controls

heart rate
ventilation
vasodilation
coagulation
inflammation
digestion
storage
…

errors

O2
BP
pH
Glucose
Energy store
Blood volume
…



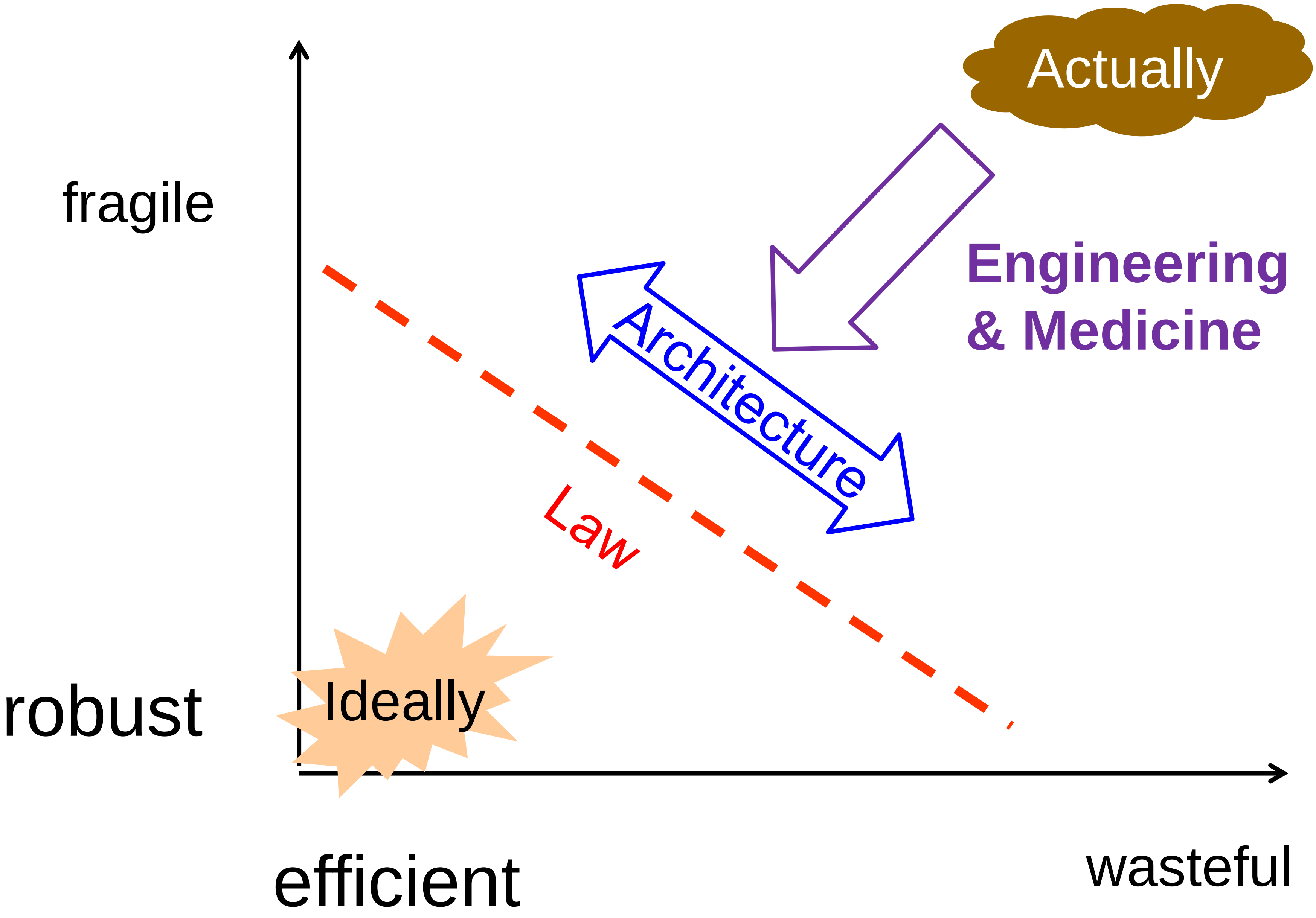
energy
trauma
infection

breath
heart beat
sensor

external disturbances

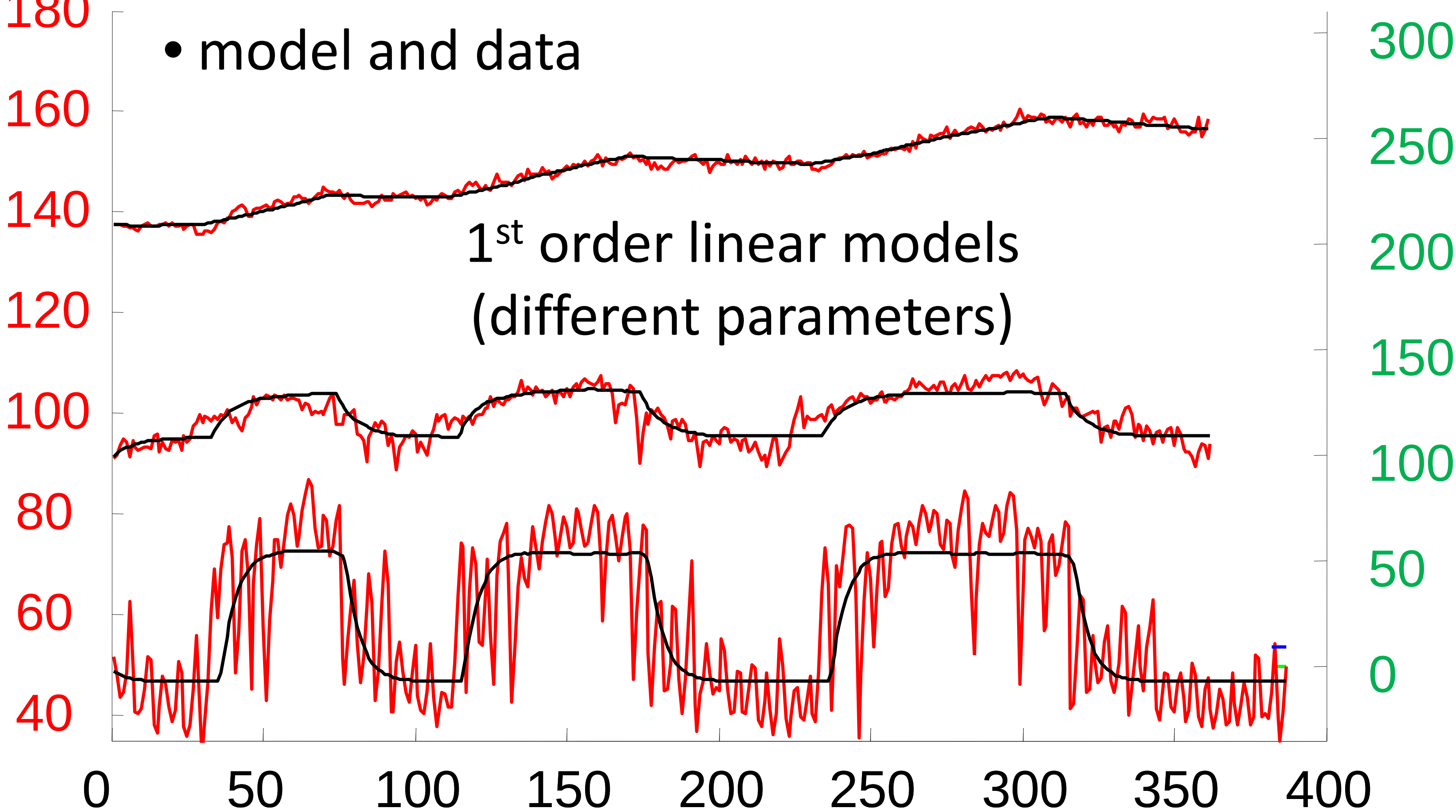
internal noise

Laws and Architecture



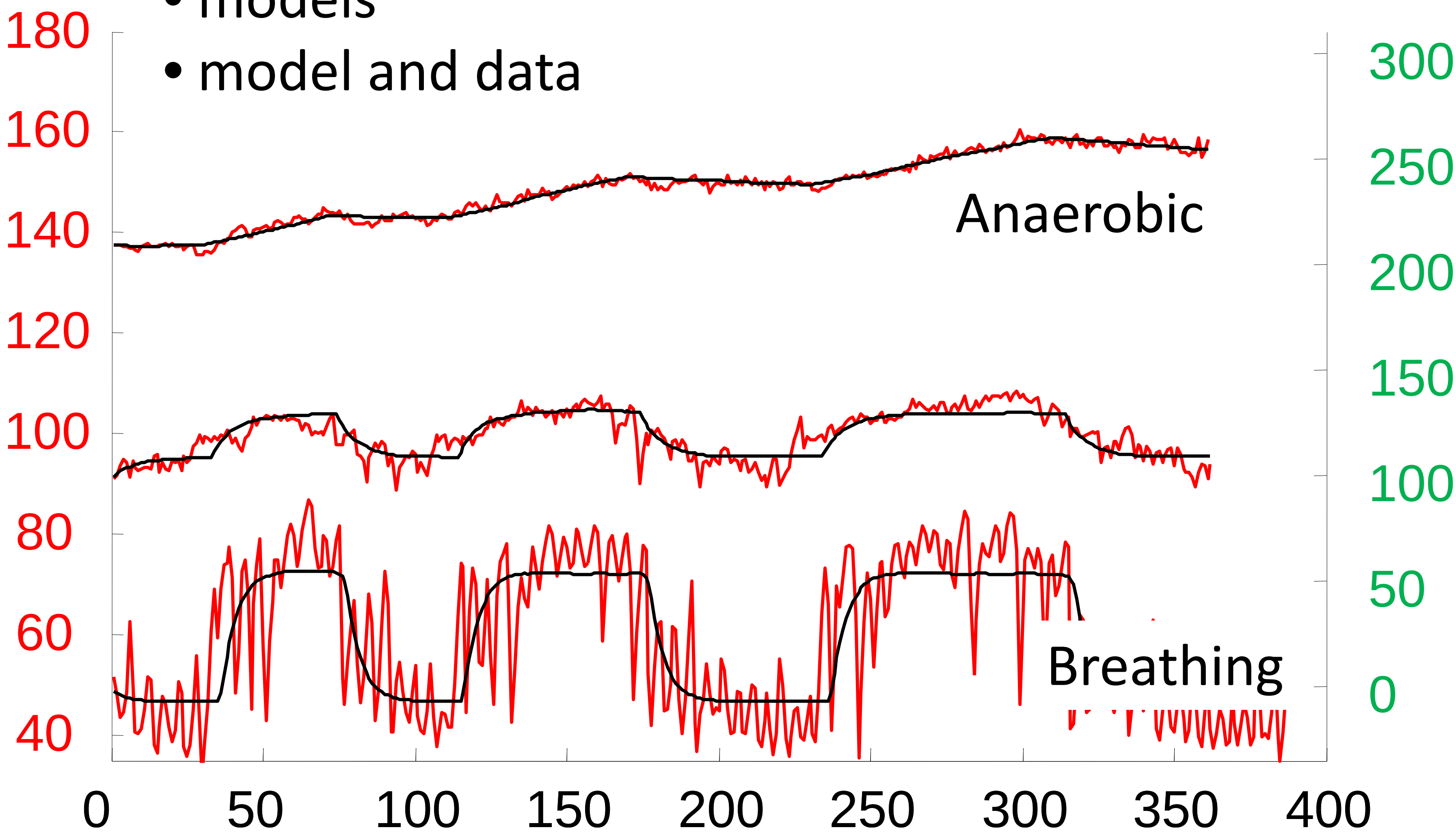
Explain differences between

- models
- model and data



Explain differences between

- models
- model and data



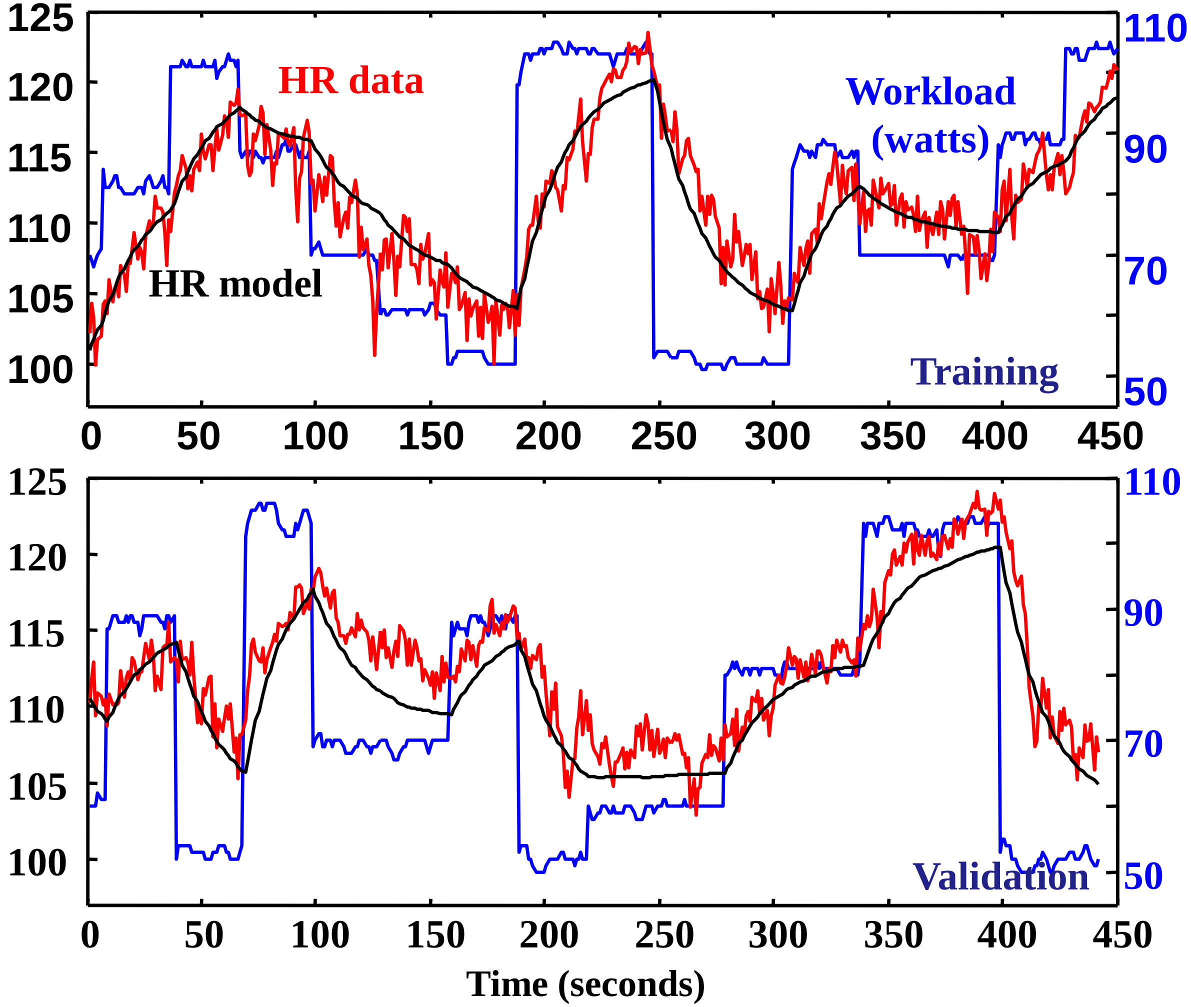
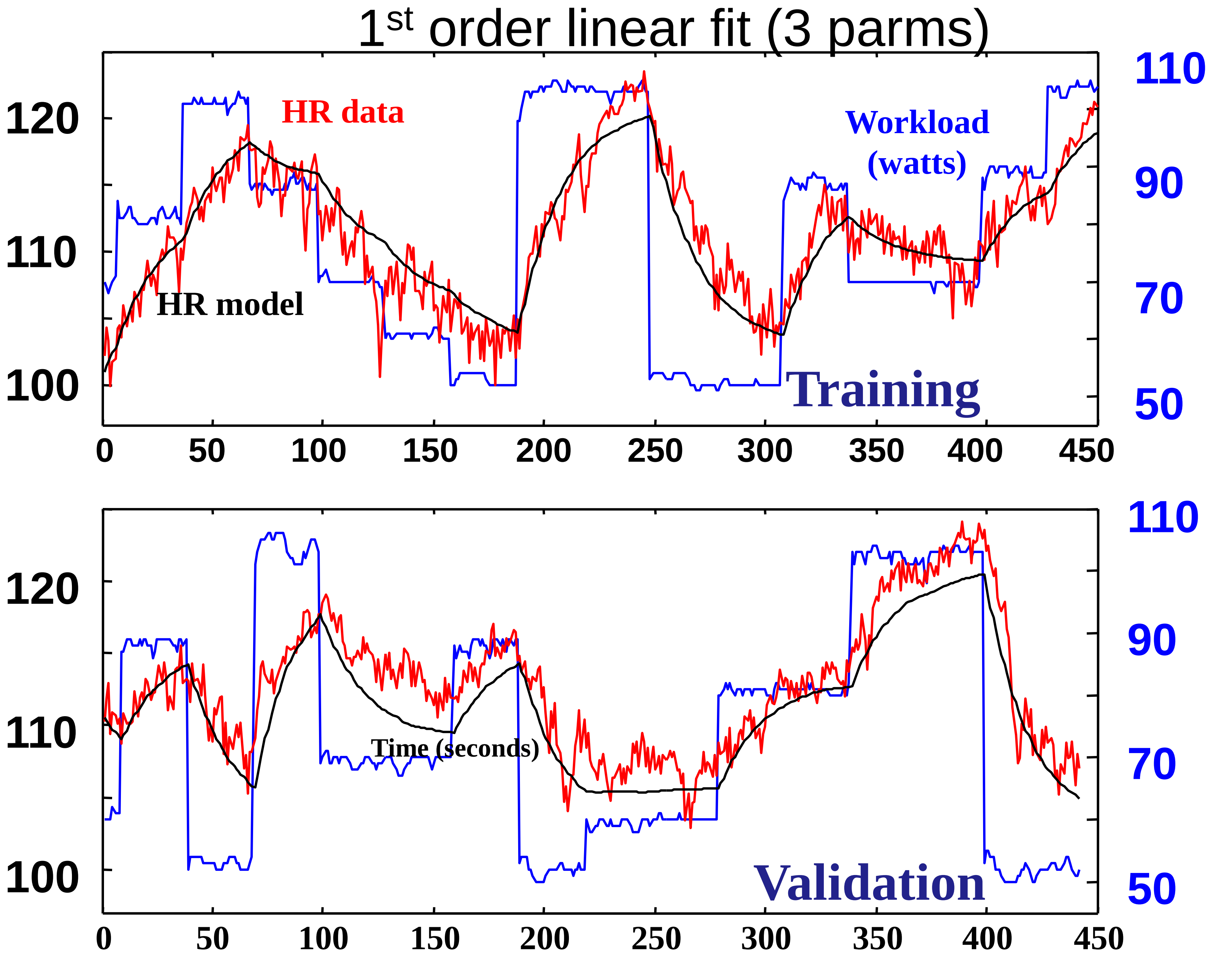
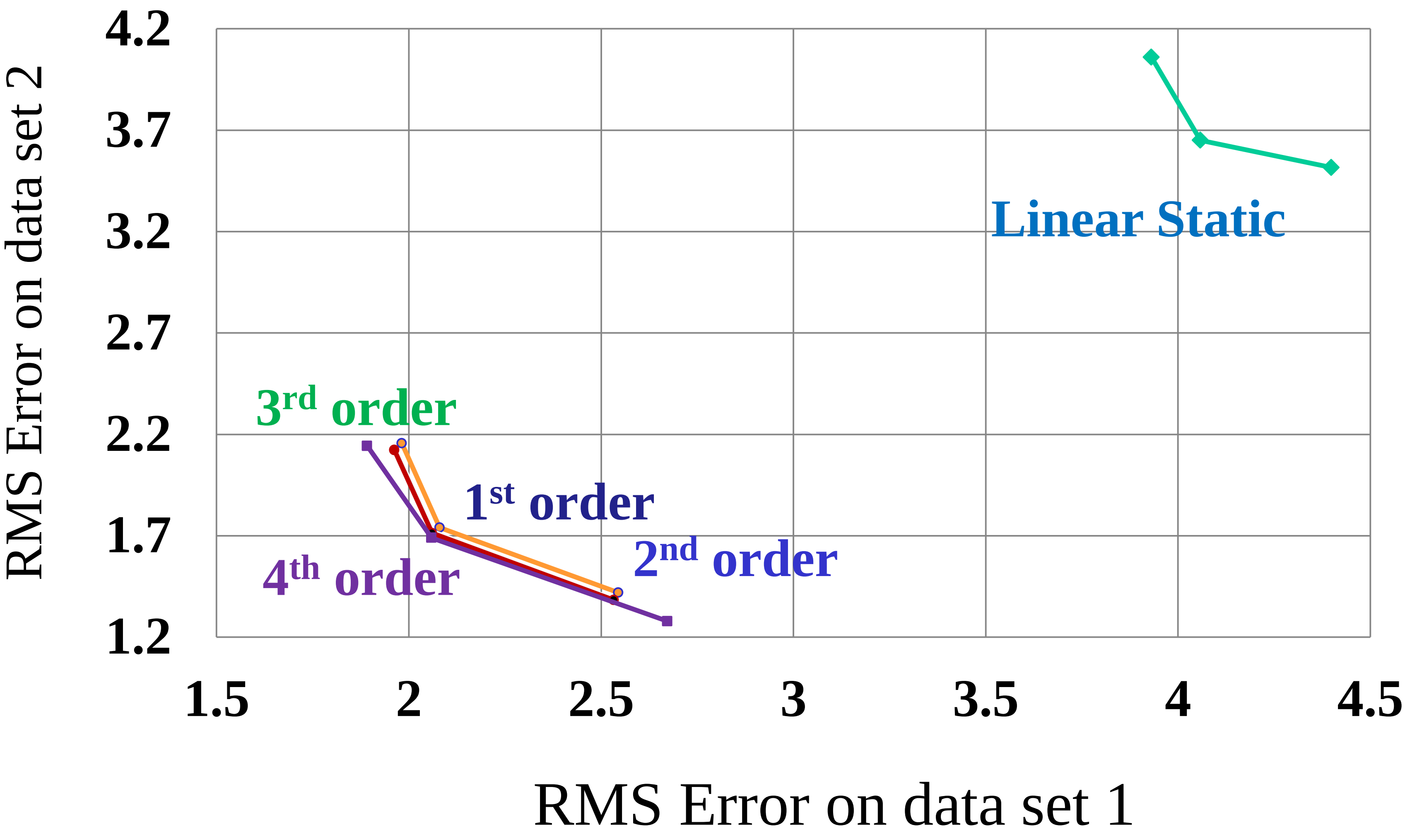


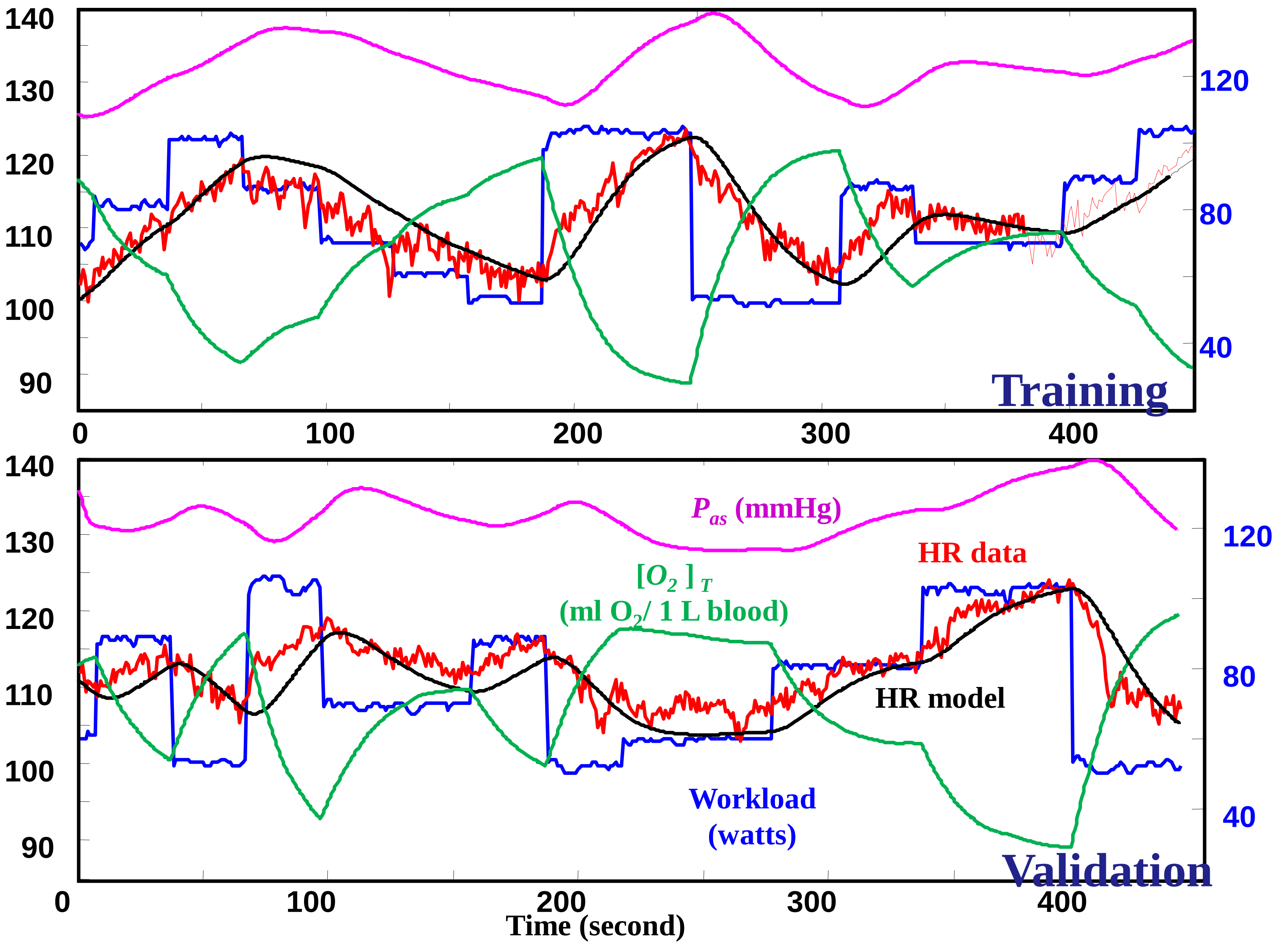
Figure S22: Subject #2 performed two separate experiments of less than 8 minutes each on a cycle ergometer including exercise levels between 50 watts and 100 watts. HR (left axis, red) is plotted for two different workload demands (right axis, blue). A 1st order linear dynamic ("black box") model (i.e., $\Delta h = ah + bW + c$) with 3 parameters (a,b,c) was fit using the upper exercise data with workload input and HR output. Simulations of this model with the 2 workload inputs are in black.

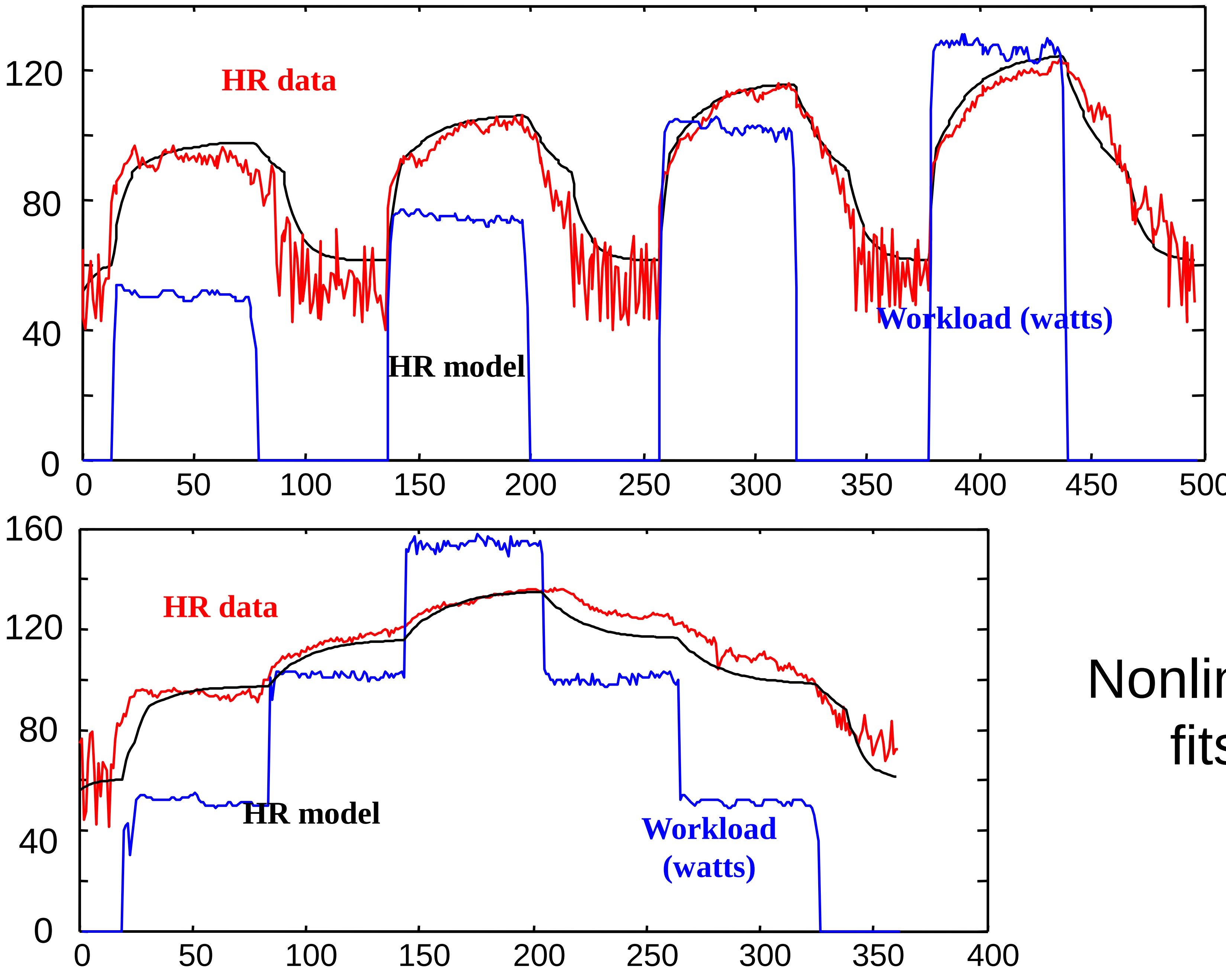

1st order linear fit (3 parms)
HR data
Workload
(watts)
HR model
Training
120
110
100
110
90
70
50
0
50
100
150
200
250
300
350
400
450
Time (seconds)
Validation
120
110
100
110
90
70
50
0
50
100
150
200
250
300
350
400
450



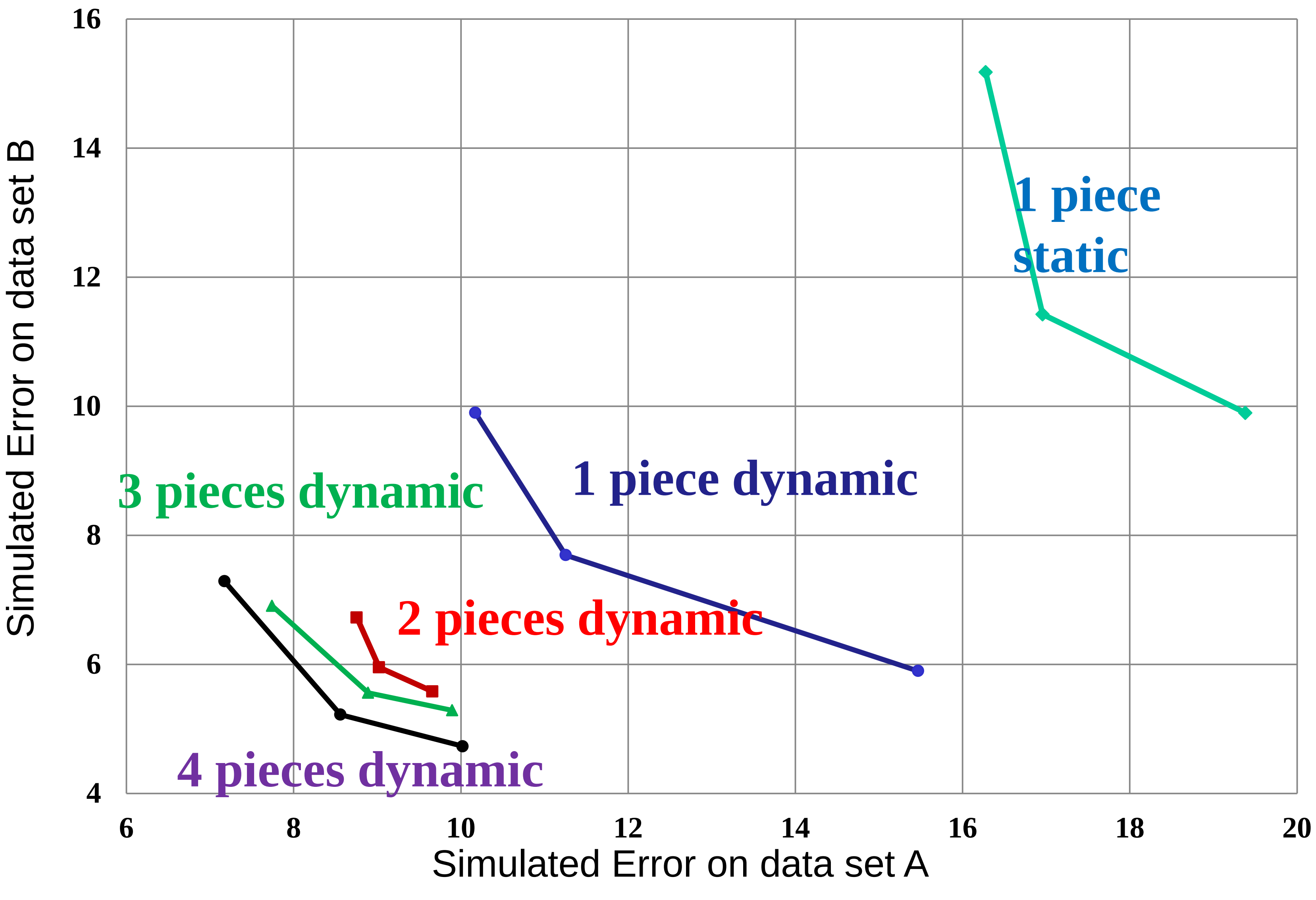
Linear models

First principles model





Nonlinear fits



Simulated Error on data set B
16
14
12
10
8
6
4
6
8
10
12
14
16
18
20
Simulated Error on data set A
1 piece static
1 piece dynamic
3 pieces dynamic
2 pieces dynamic
4 pieces dynamic