*Some open problems in obesity modeling

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Energy flux

Rate of storage = intake rate - expenditure rate

$$\frac{d(\rho_M M)}{dt} = I - E$$

M = body mass

Energy flux

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Energy flux

Rate of storage = intake rate - expenditure rate

$$\frac{d(\rho_M M)}{dt} = I - E$$

M = body mass

$$\rho_M M = \rho_F F + \rho_L L$$

Body composition model

$$\begin{aligned}\rho_F \frac{dF}{dt} &= I_F - fE \\ \rho_L \frac{dL}{dt} &= I_L - (1-f)E\end{aligned}$$

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f is fraction of energy use that is fat

Body composition model

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\end{aligned}
$$

f is fraction of energy use that is fat

E and f contains the physiology

Body composition model

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Completely General!

Steady state

$$\left.\begin{aligned} \rho_F \frac{dF}{dt} &= I_F - fE \quad = 0 \\[2em] \rho_L \frac{dL}{dt} &= I_L - (1-f)E = 0 \end{aligned}\right\} \text{Nullclines}$$

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$$E(F,L) = I_F + I_L \equiv I \qquad \text{energy balance}$$

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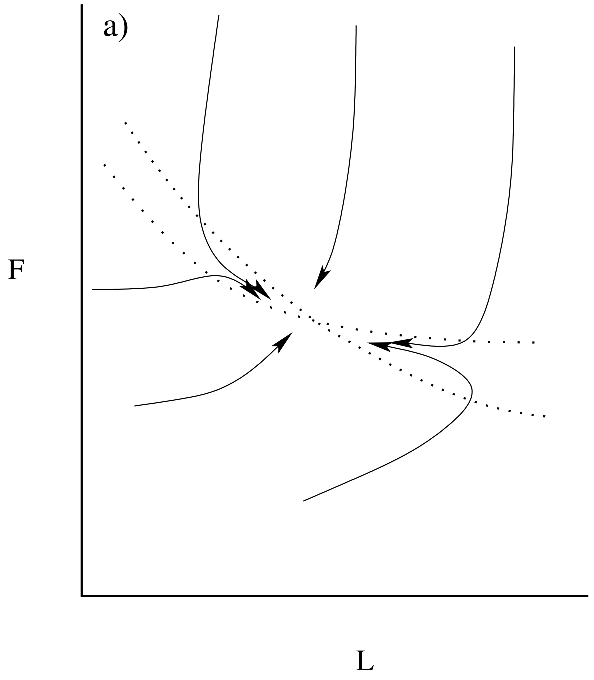
$$E(F, L) = I_F + I_L \equiv I$$

energy balance

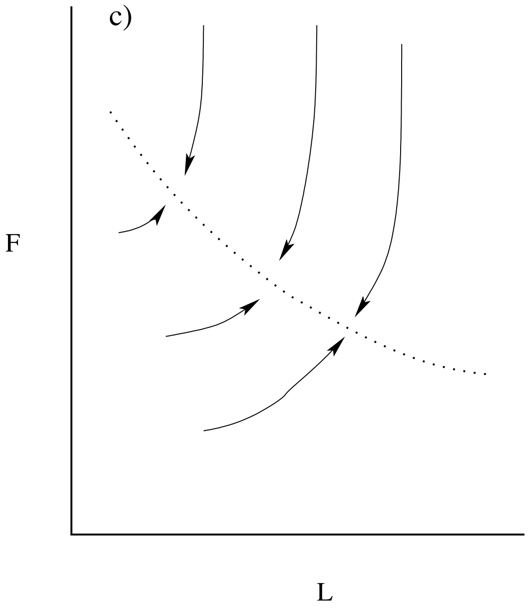
$$f(F, L) = \frac{I_F}{I}$$

macronutrient balance

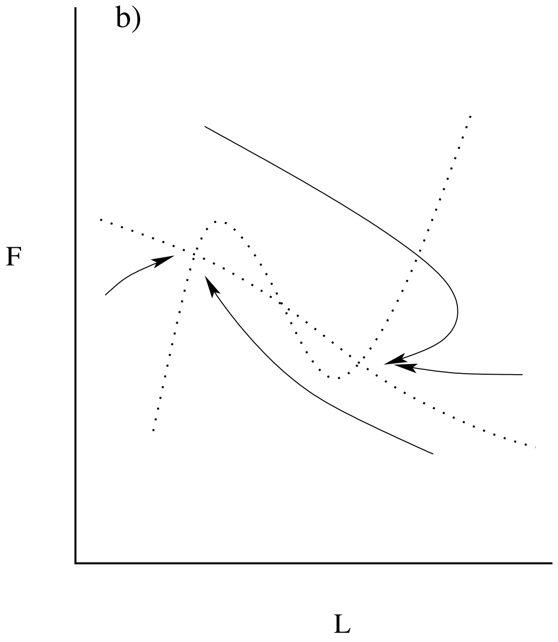
Asymptotic attractors



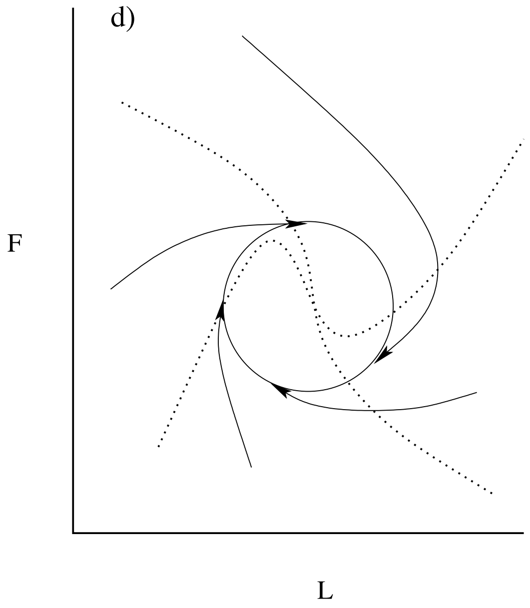
Fixed point



Invariant manifold



Multiple fixed points



Limit cycle

Chow and Hall, PLoS Comp Bio,4: e1000045, 2008

Energy expenditure rate E

Energy expenditure rate E

$E =$

Energy expenditure rate E

$E =$

Basal metabolic rate (BMR)

Energy expenditure rate E

$E =$

$+$

Basal metabolic rate (BMR)

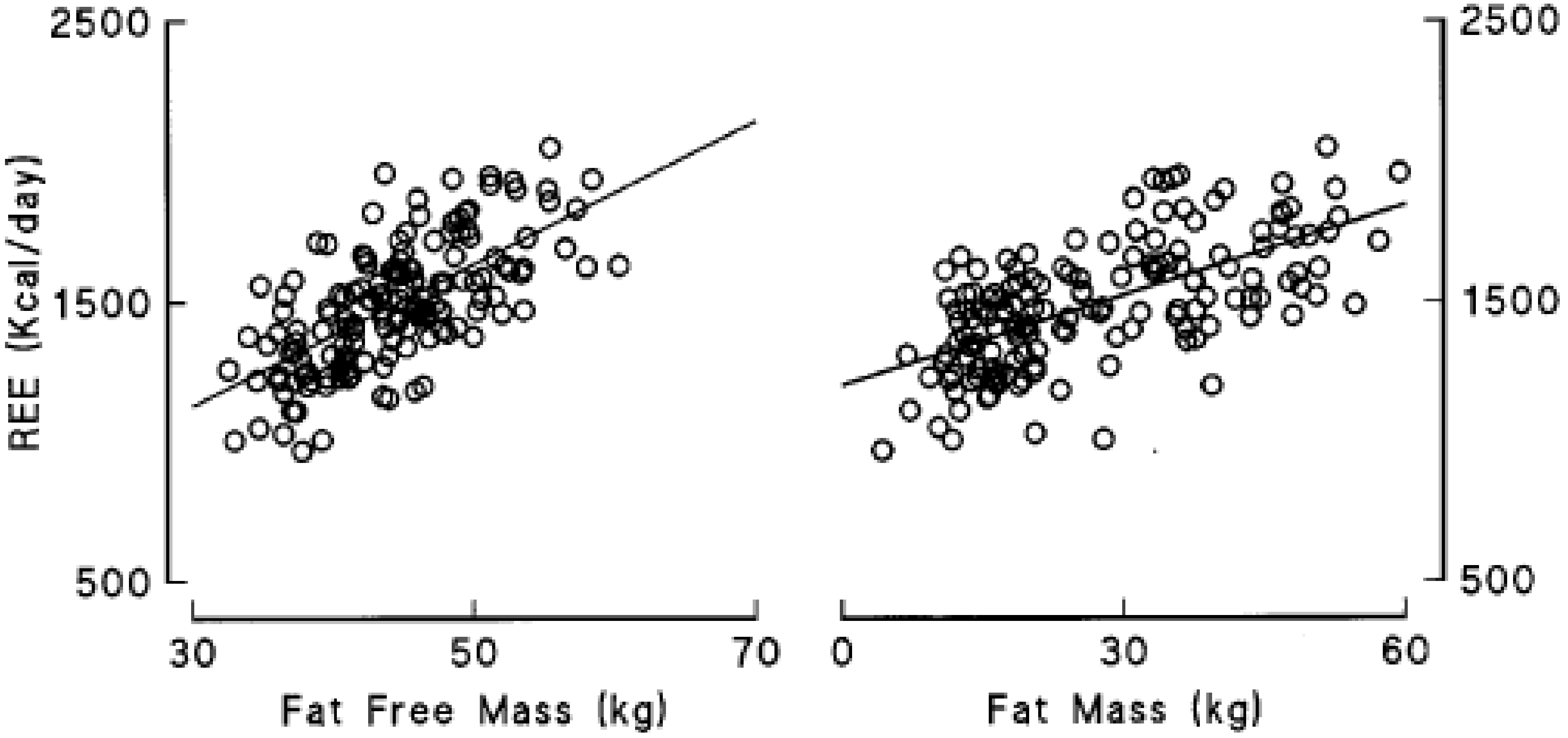
Energy expenditure rate E

E =

+

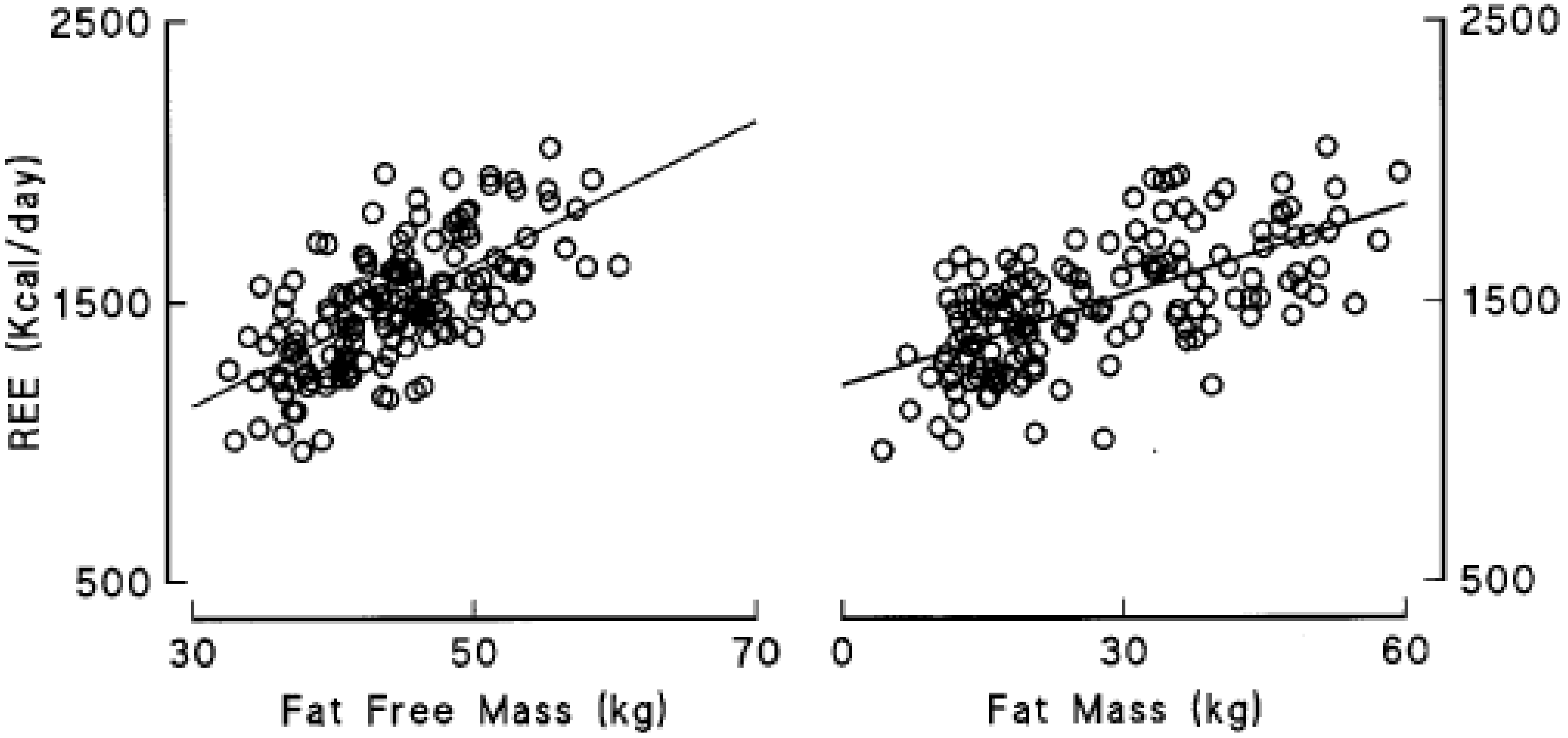
Basal metabolic rate (BMR)   Physical activity

Basal metabolic rate



Nielson, 2000

Basal metabolic rate



Nielson, 2000

e.g. $BMR\ (MJ/day) = 0.9\ L\ (kg) + 0.01\ F\ (kg) + 1.1$

Physical activity

Energy due to PA ∝ Mass

$$E_{PA} = aM = a(L + F)$$

a ranges from *0* to *0.1 MJ/kg/day*

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E is linear in F and L

The problem with measuring f

In energy balance, f reflects diet

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In energy balance, f reflects diet $f(F,L) = \frac{I_F}{I}$

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Need dynamical (i.e. longitudinal) data

$$\begin{aligned} \rho_F \frac{dF}{dt} &= I_F - fE \\ \rho_L \frac{dL}{dt} &= I_L - (1-f)E \end{aligned}$$

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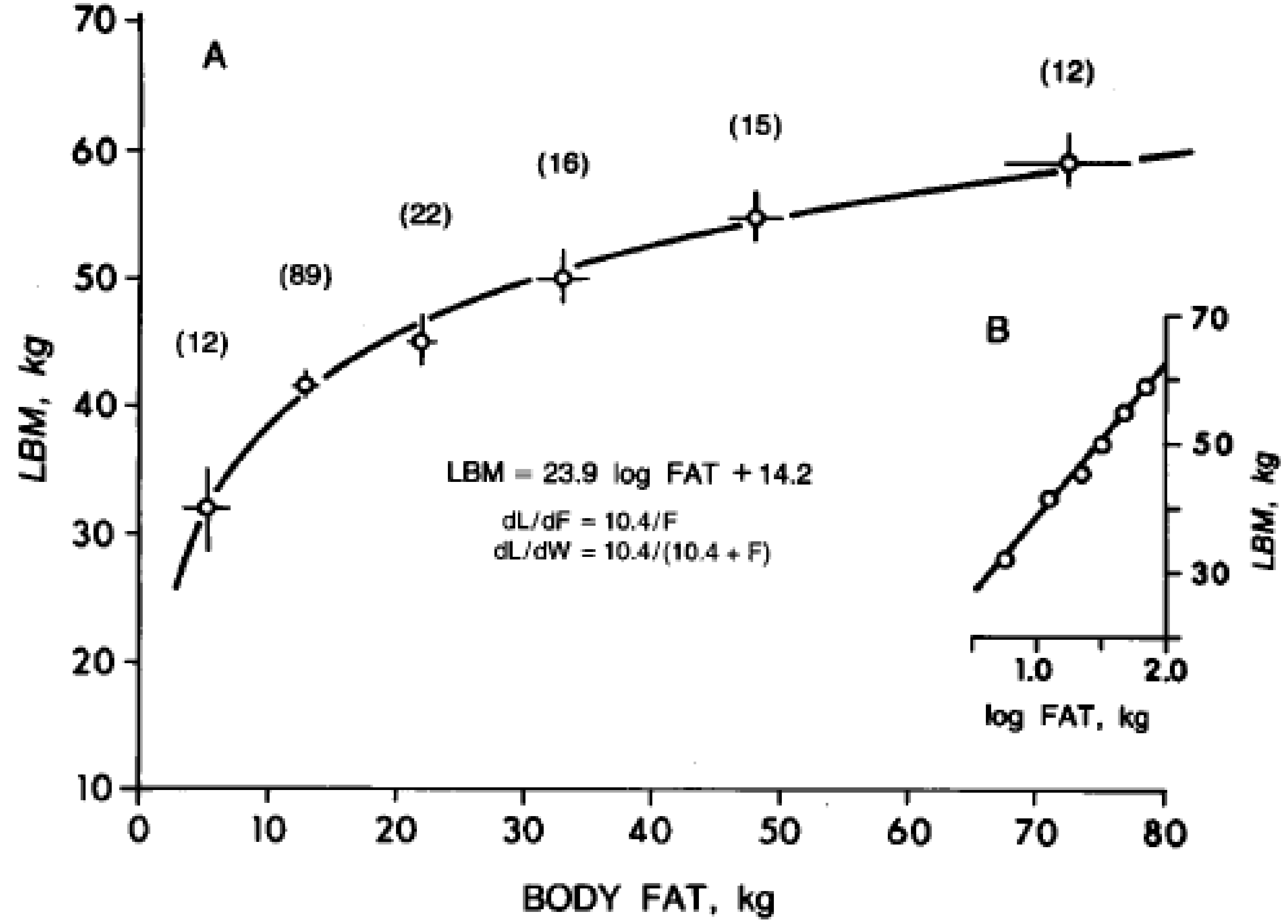
Cross-sectional = longitudinal assumption

Forbes Law



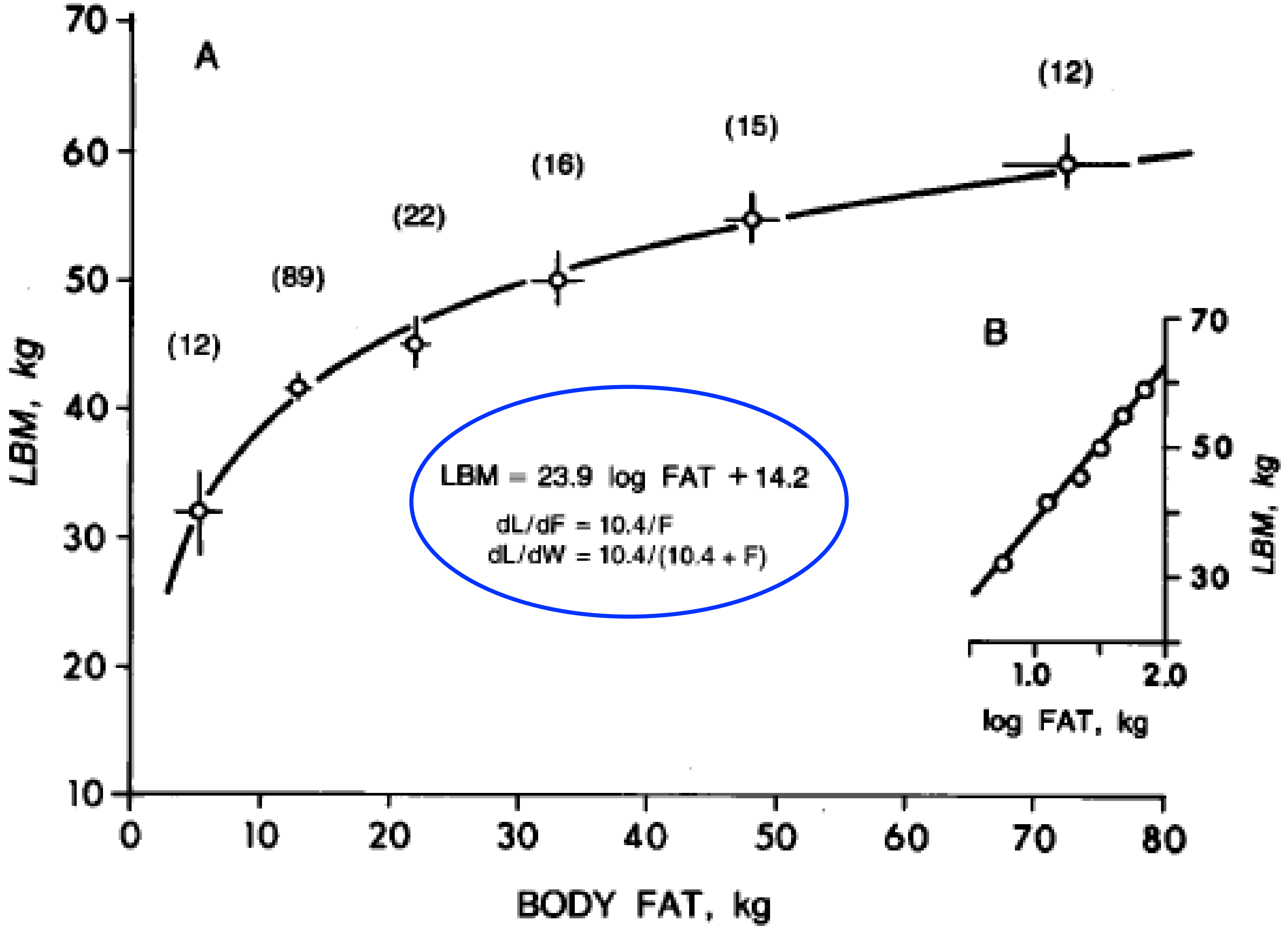
L

F

Forbes, 1987

Forbes Law

L



F

Forbes, 1987

Impose Forbes law

$$\frac{dF}{dL} = \frac{F}{10.4}$$

$$\rho_F \, \frac{dF}{dt} = \, (I_F - fE)$$

$$\rho_L \, \frac{dL}{dt} = \, (I_L - (1 - f)E)$$

Impose Forbes law

$$\frac{dF}{dL} = \frac{F}{10.4}$$

$$\frac{dF}{dL} = \frac{(I_F - fE)\,\rho_L}{(I_L - (1-f)E)\rho_F}$$

Impose Forbes law

$$\frac{(I_F - fE)\,\rho_L}{(I_L - (1-f)E)\rho_F} = \frac{F}{10.4}$$

Impose Forbes law

$$\frac{(I_F - fE)\,\rho_L}{(I_L - (1-f)E)^{\rho_F}} = \frac{F}{10.4}$$

$$f = \frac{I_F - (1-p)(I-E)}{E} \qquad p = \frac{1}{1 + \frac{\rho_F}{\rho_L}\frac{F}{10.4}}$$

Impose Forbes law

$$\frac{(I_F - fE)\,\rho_L}{(I_L - (1-f)E)^{\rho_F}} = \frac{F}{10.4}$$

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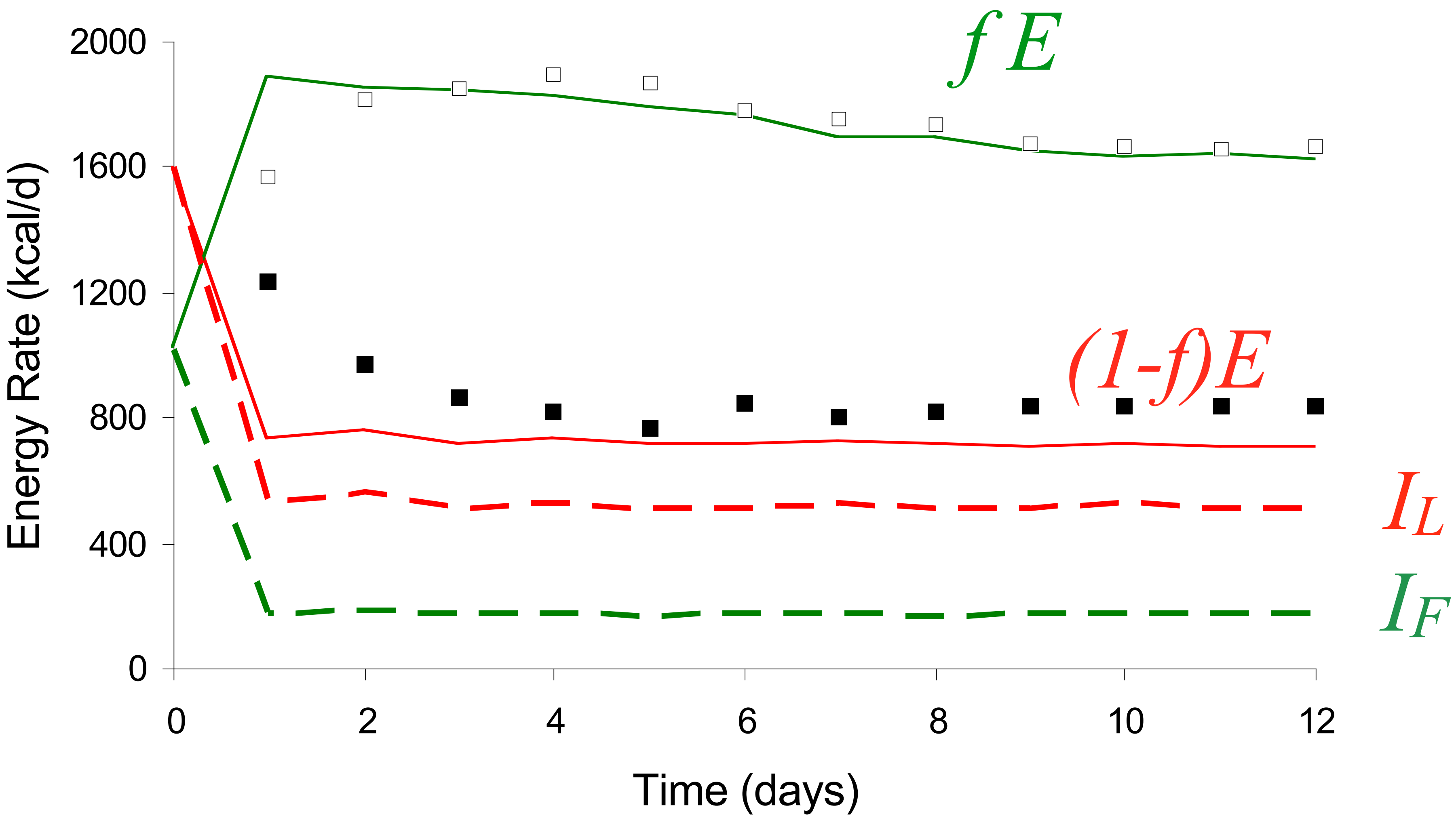
Matches data



Hall, Bain, and Chow, Int J. Obesity, (2007)

Energy partition model

$$\rho_F \frac{dF}{dt} = I_F - fE$$

$$f = \frac{I_F - (1-p)(I-E)}{E}$$

$$\rho_L \frac{dL}{dt} = I_L - (1-f)E$$

Energy partition model

$$\rho_F \frac{dF}{dt} = I_F - I_F + (1-p)(I-E)$$

$$\rho_L \frac{dL}{dt} = I_L - (1-f)E$$

Energy partition model

$$\rho_F \frac{dF}{dt} = (1-p)(I-E)$$

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Energy partition model

$$\rho_F \frac{dF}{dt} = (1-p)(I-E)$$

$$\rho_L \frac{dL}{dt} = p(I-E)$$

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Energy partition model

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Most previous models use energy partition

-difference is choice of p

Energy partition model

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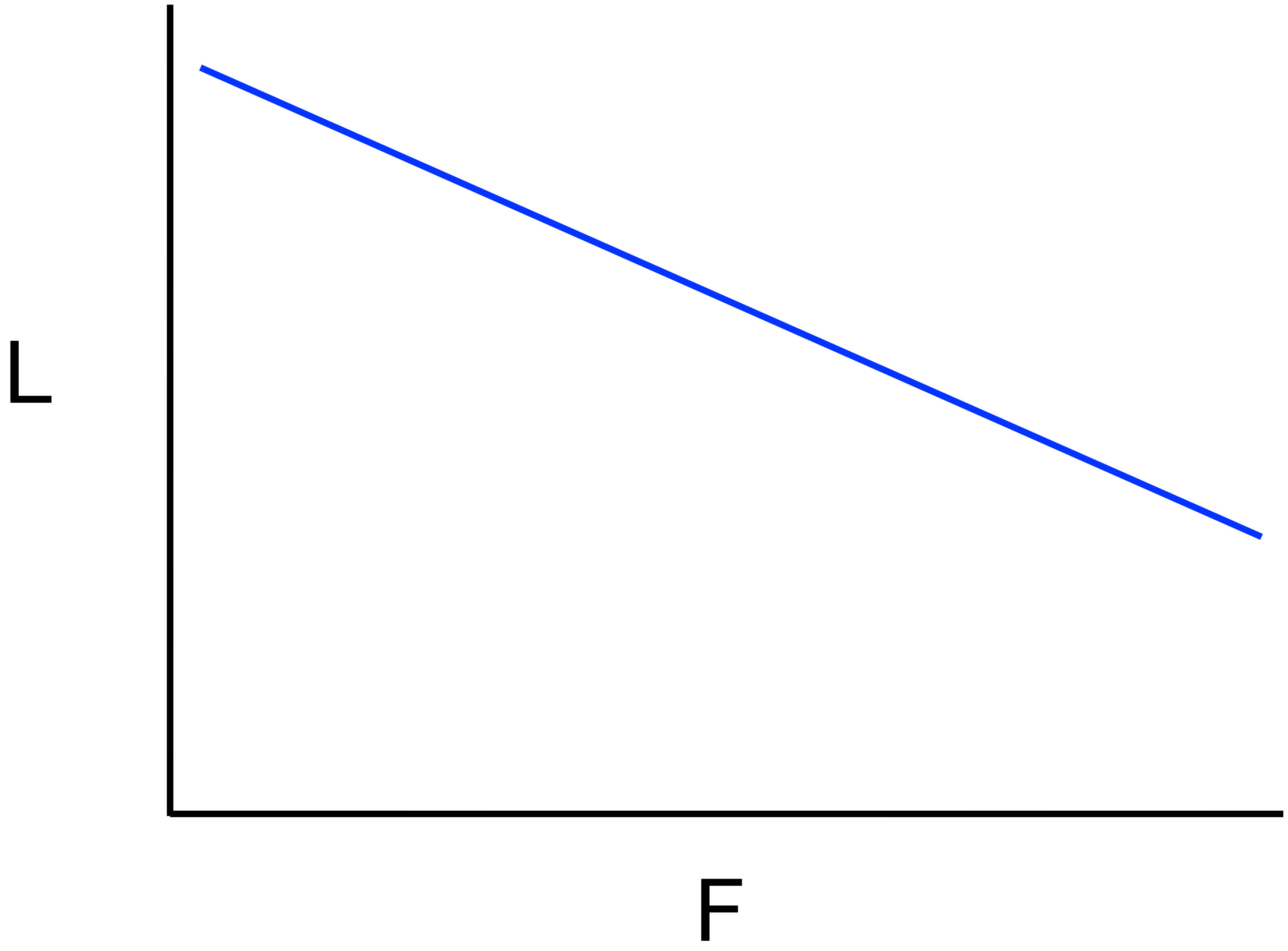
Most previous models use energy partition
-difference is choice of p

Steady state is line attractor $E(F,L) = I$

Consequences of line attractor

$E(F,L)=I$



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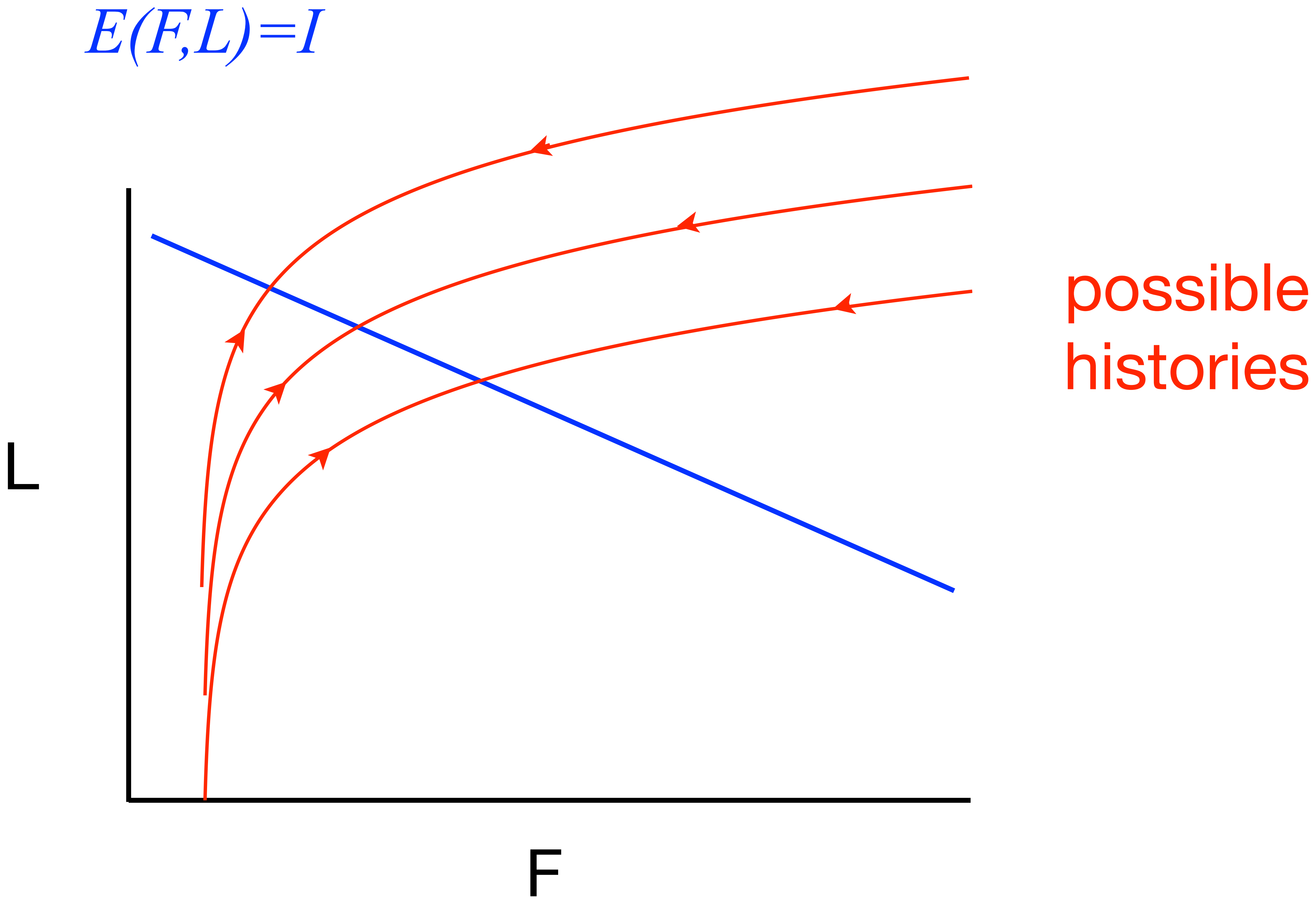

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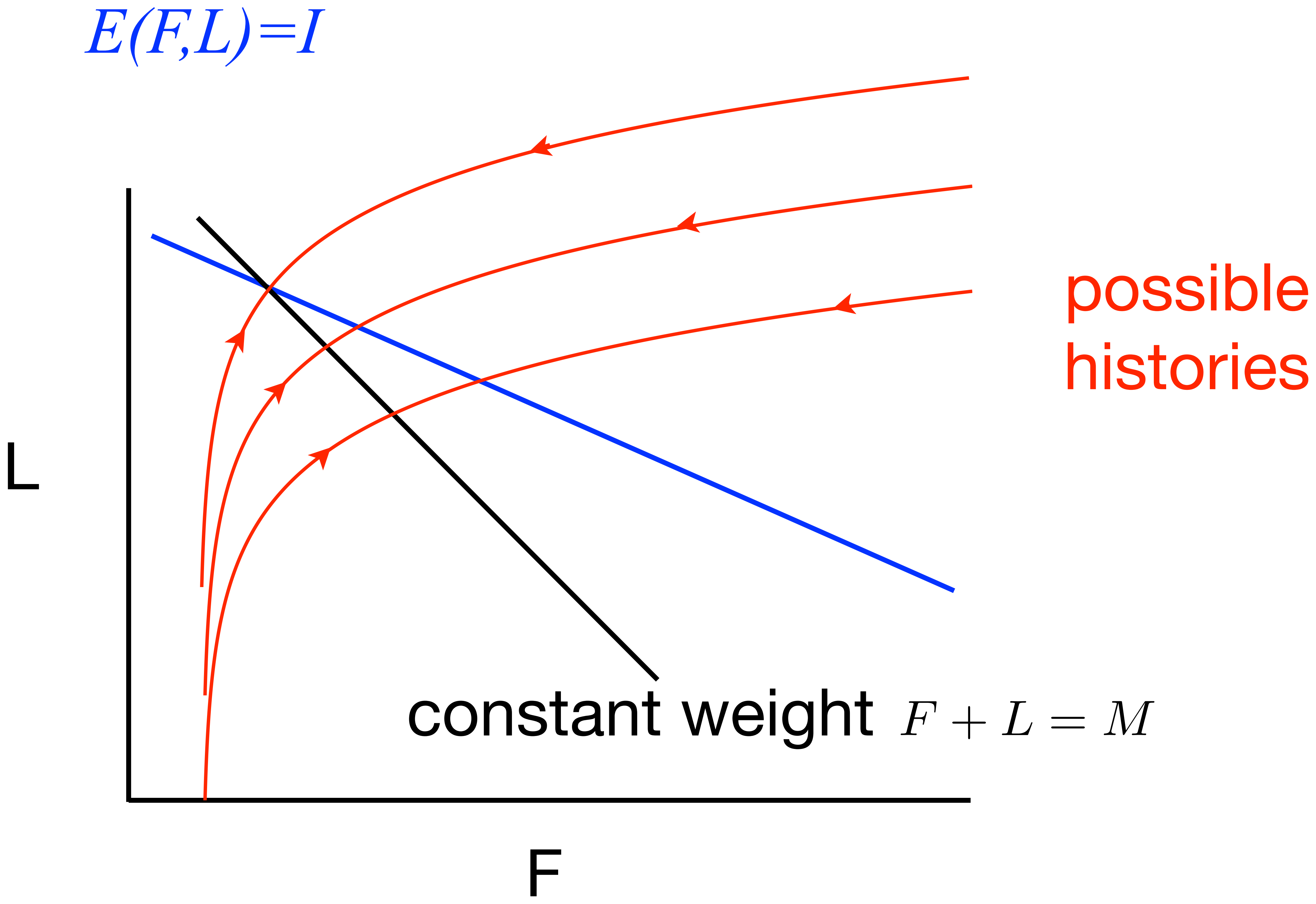

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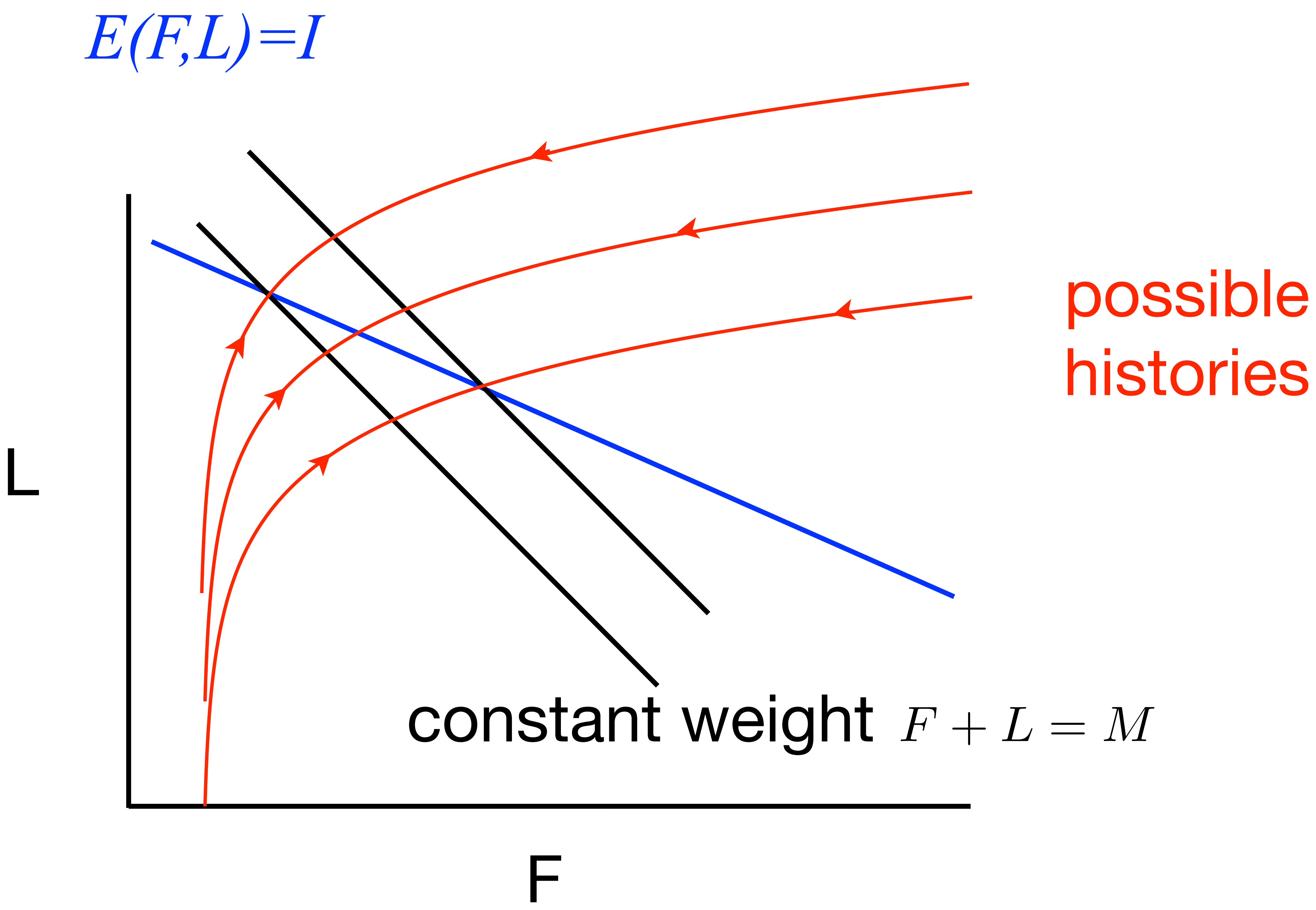
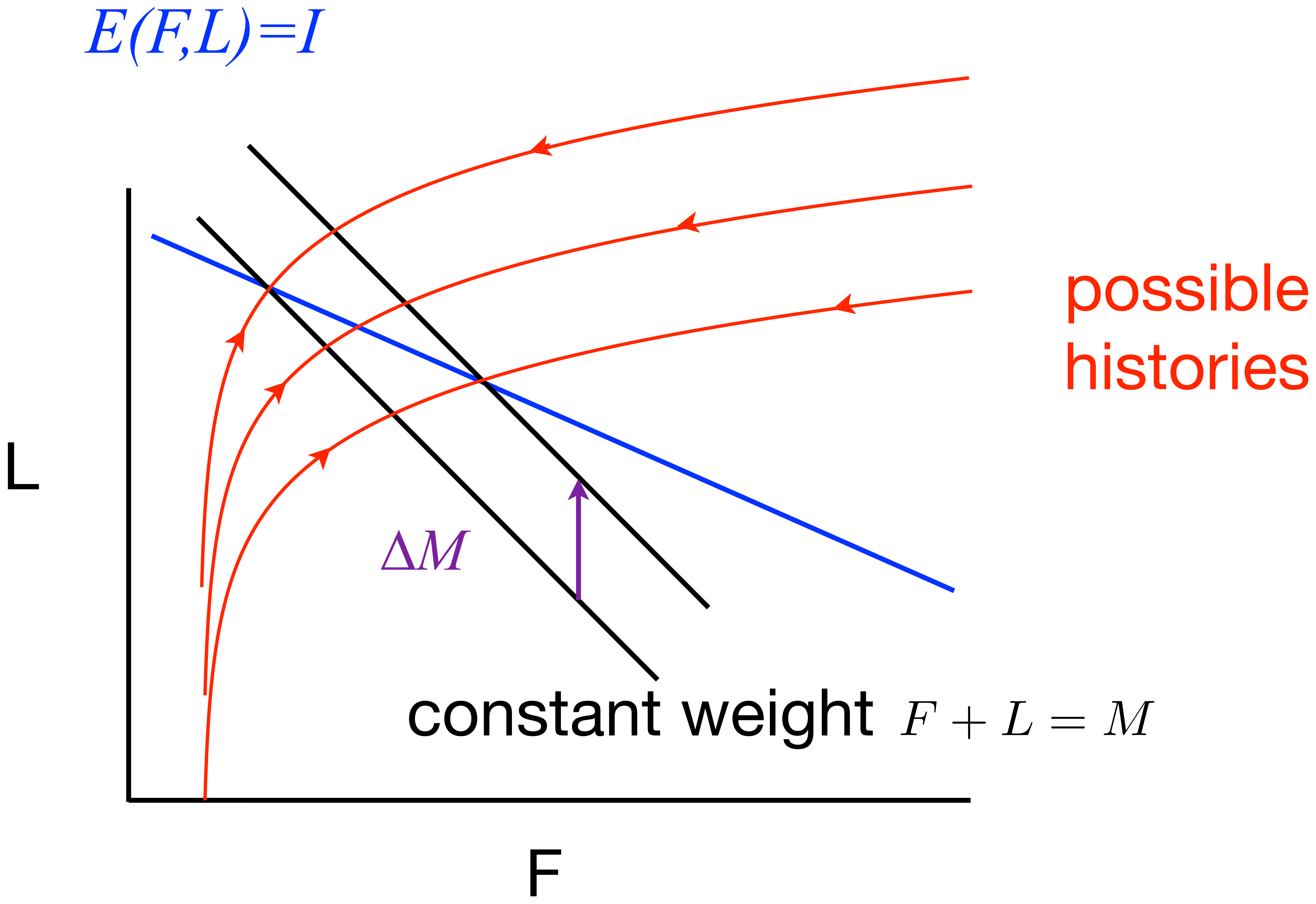
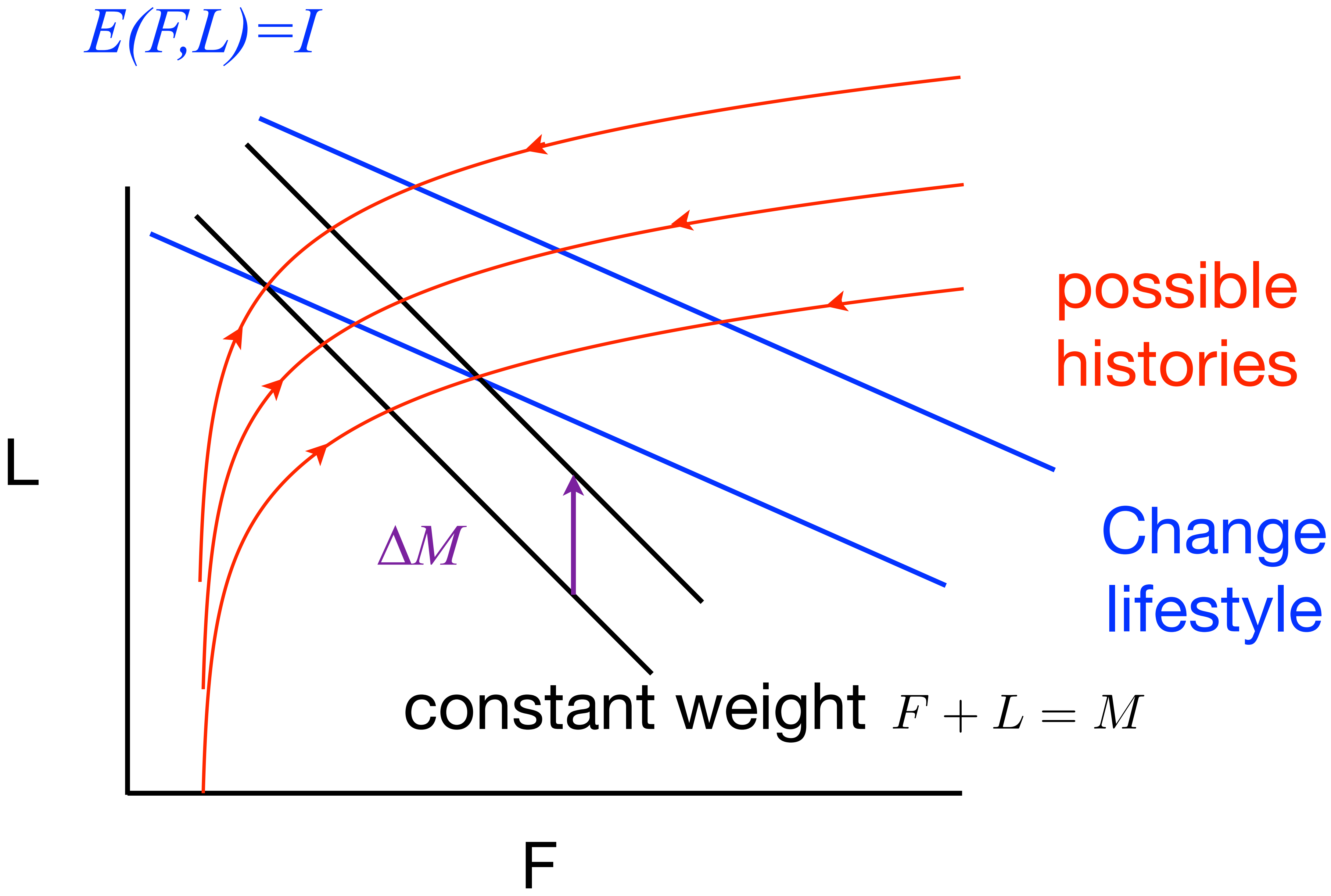


Consequences of line attractor



Tuesday, July 12, 2011

Consequences of line attractor



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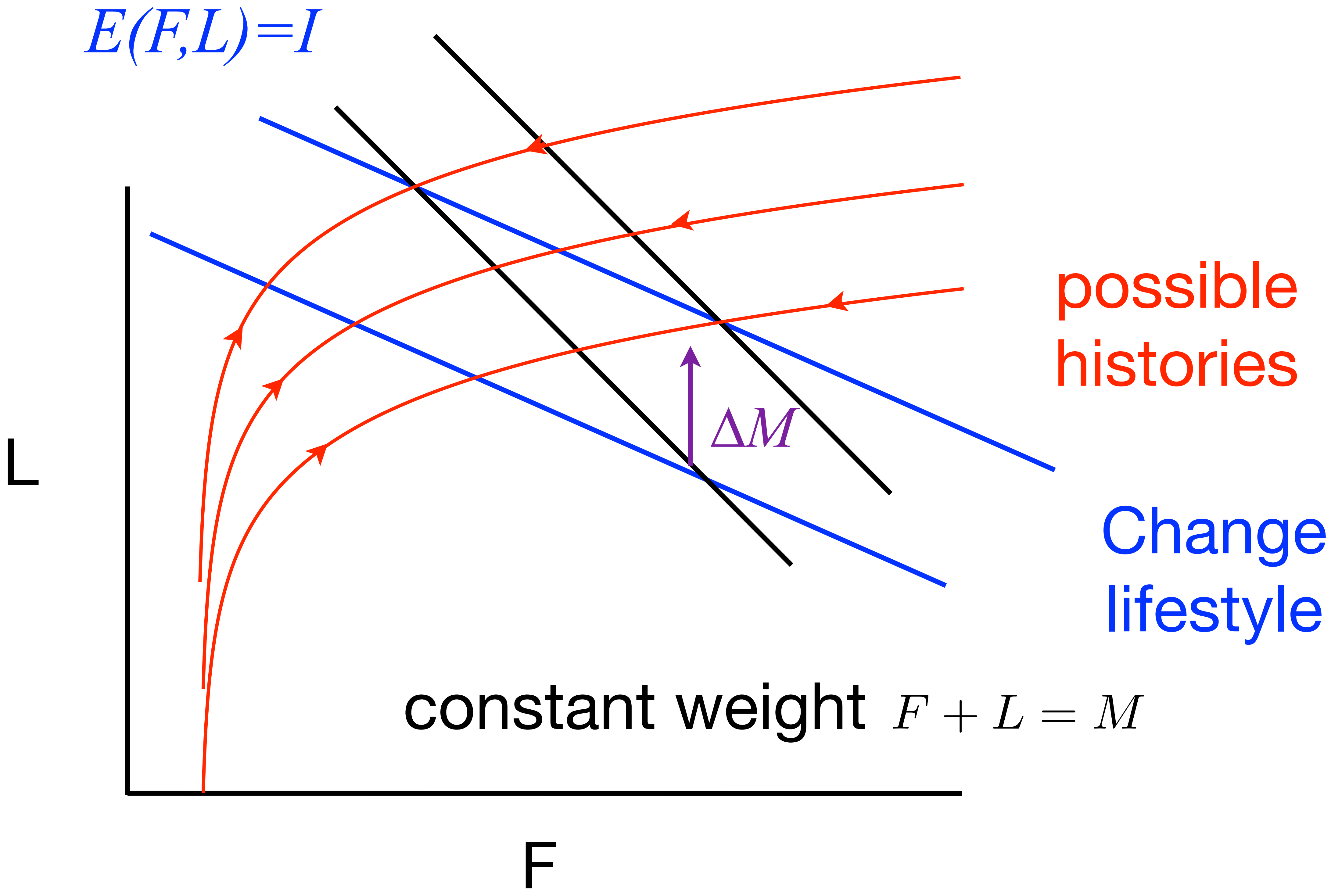
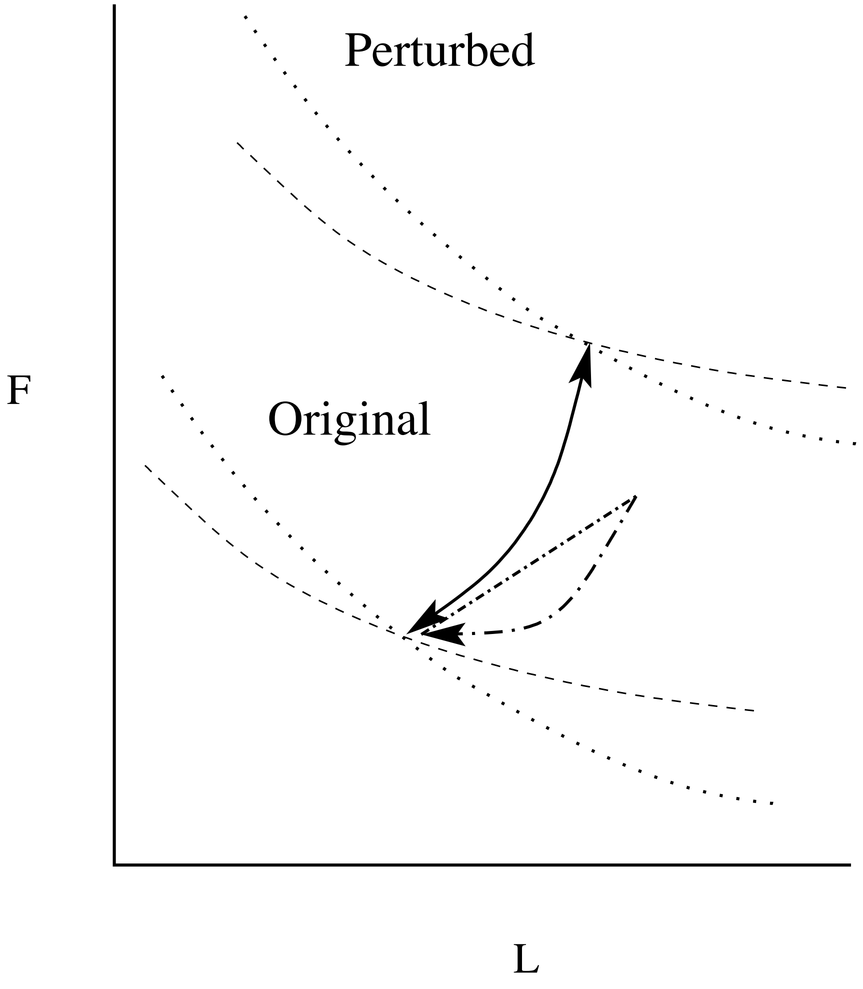


possible histories

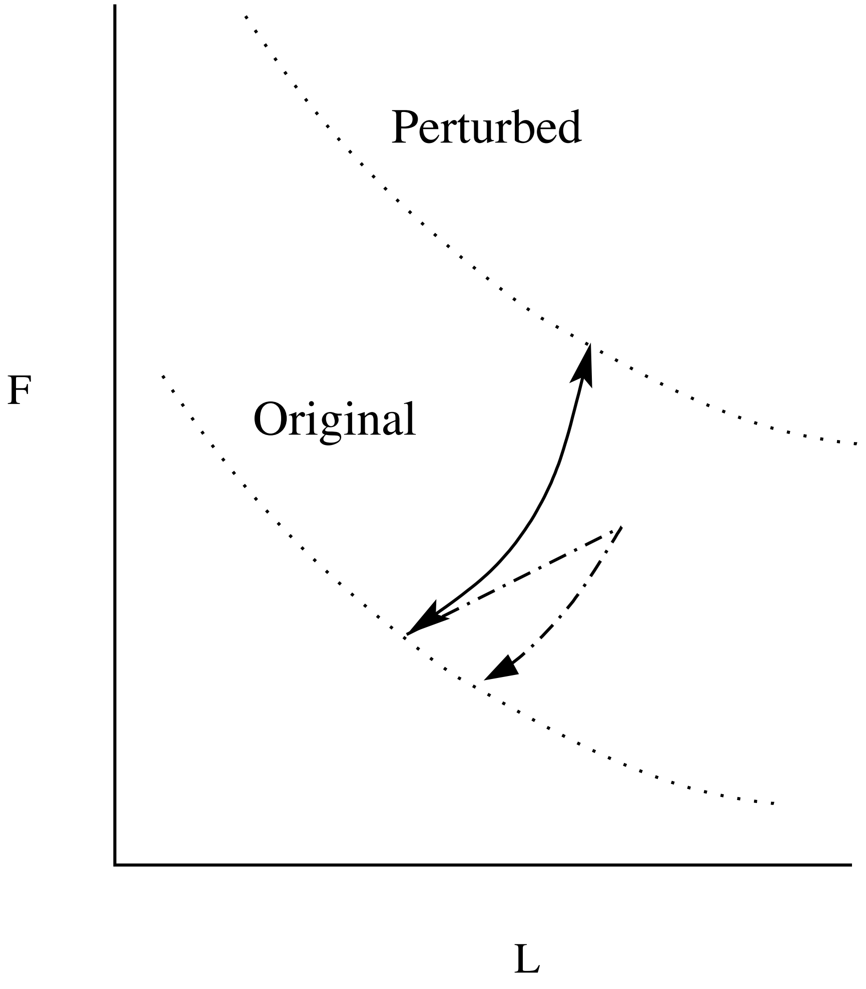
Change lifestyle

constant weight $F + L = M$

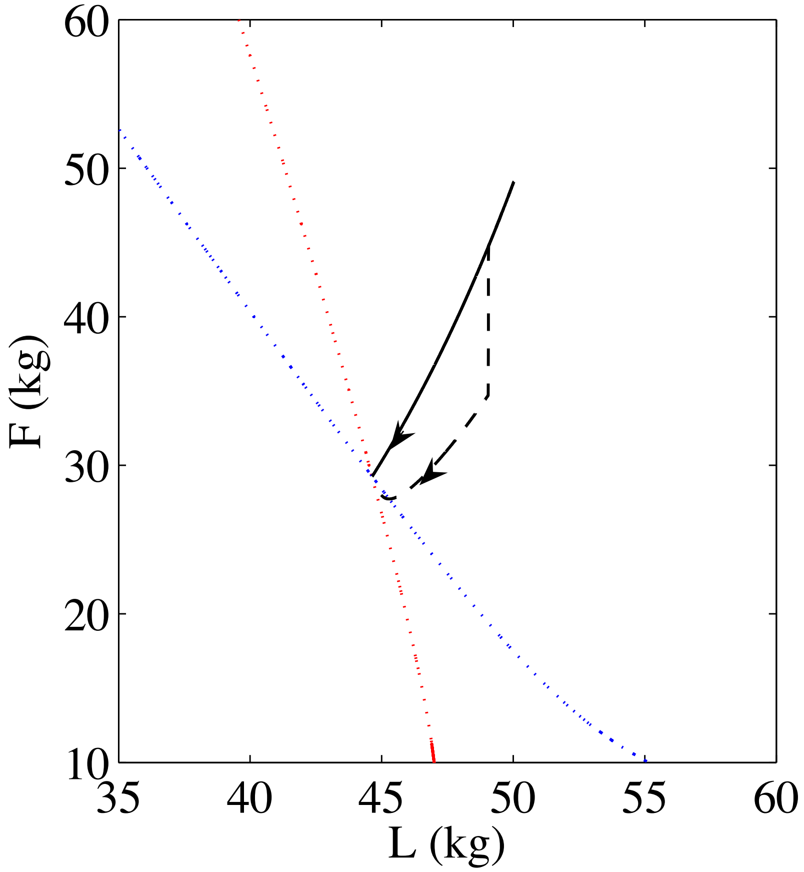
Effect of perturbations



fixed point



line attractor



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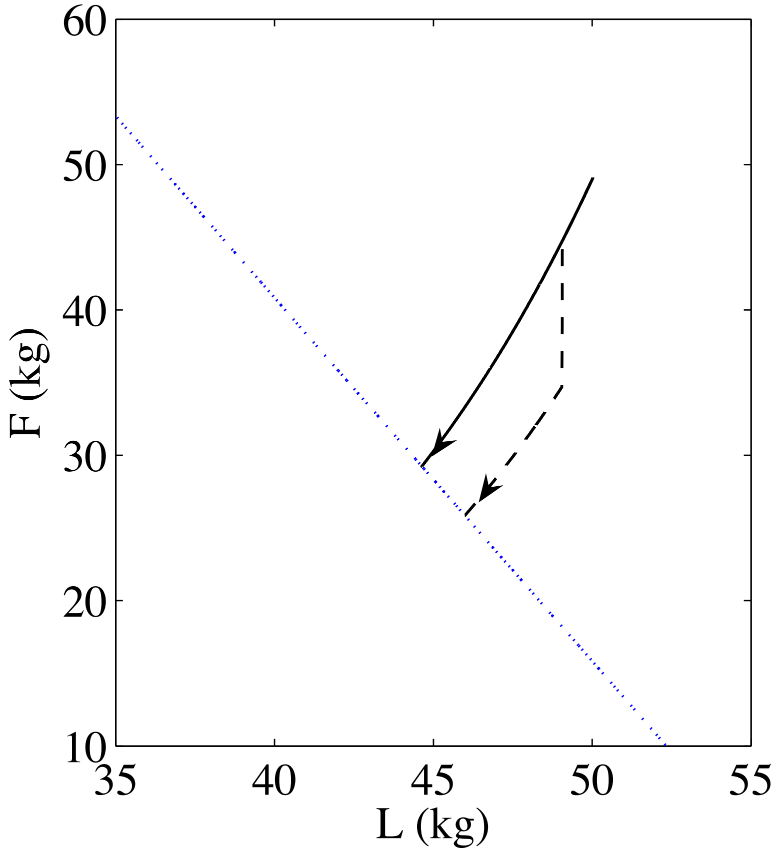
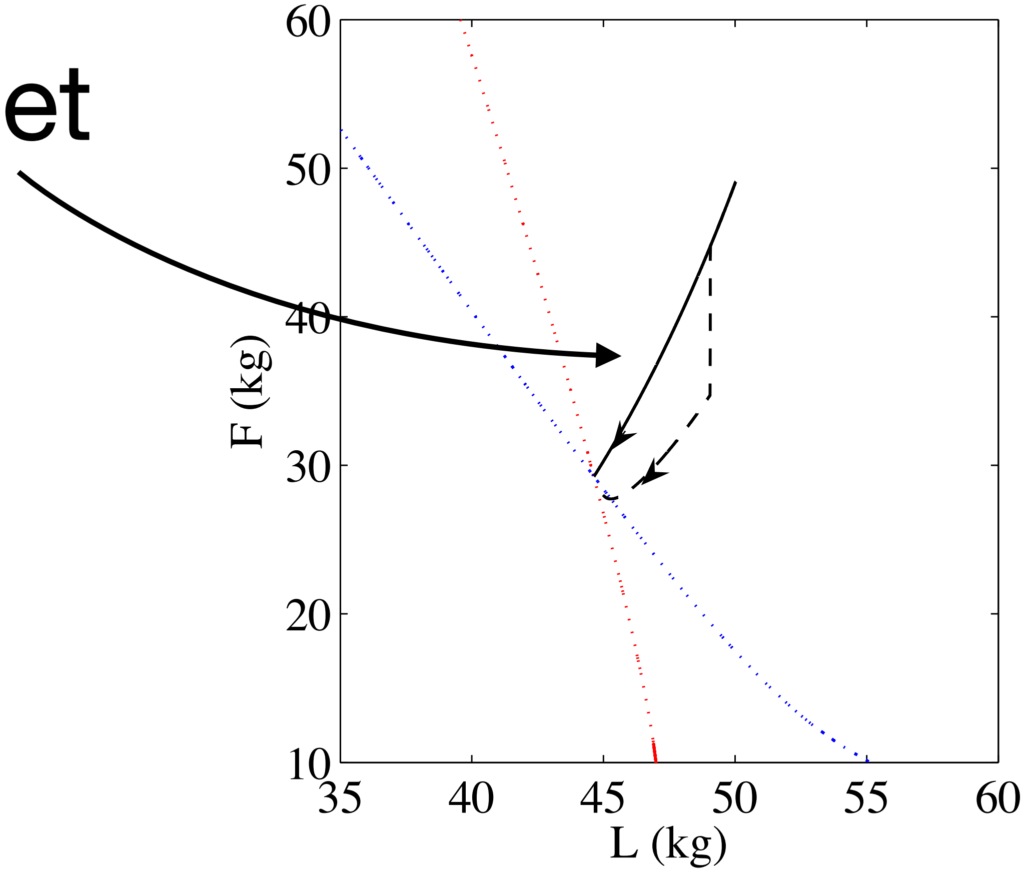
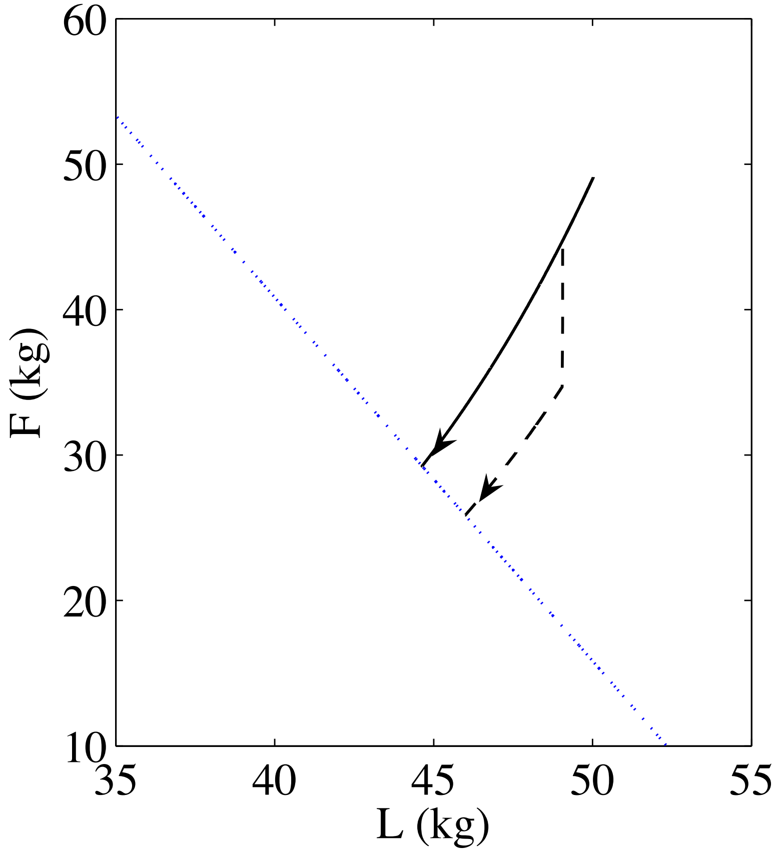


line attractor



Diet

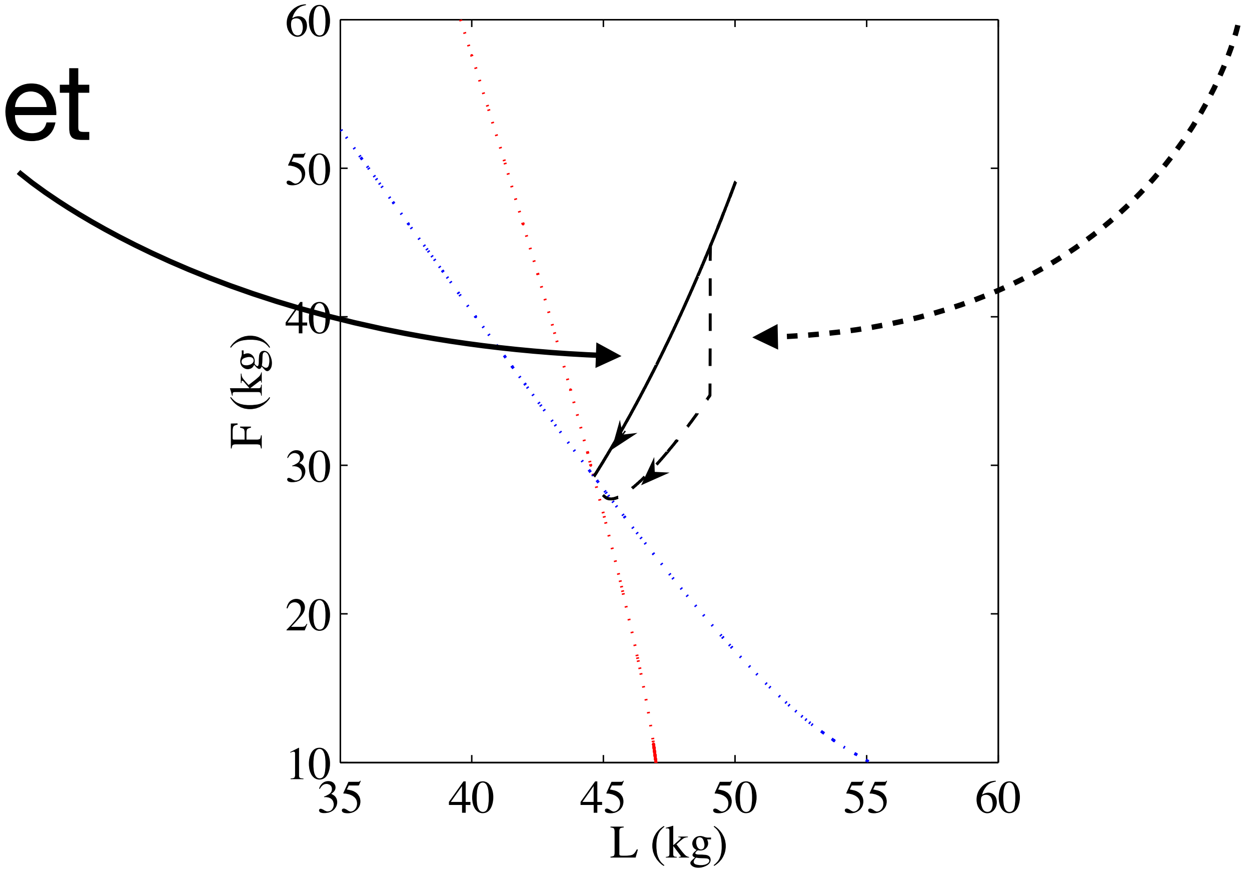
fixed point



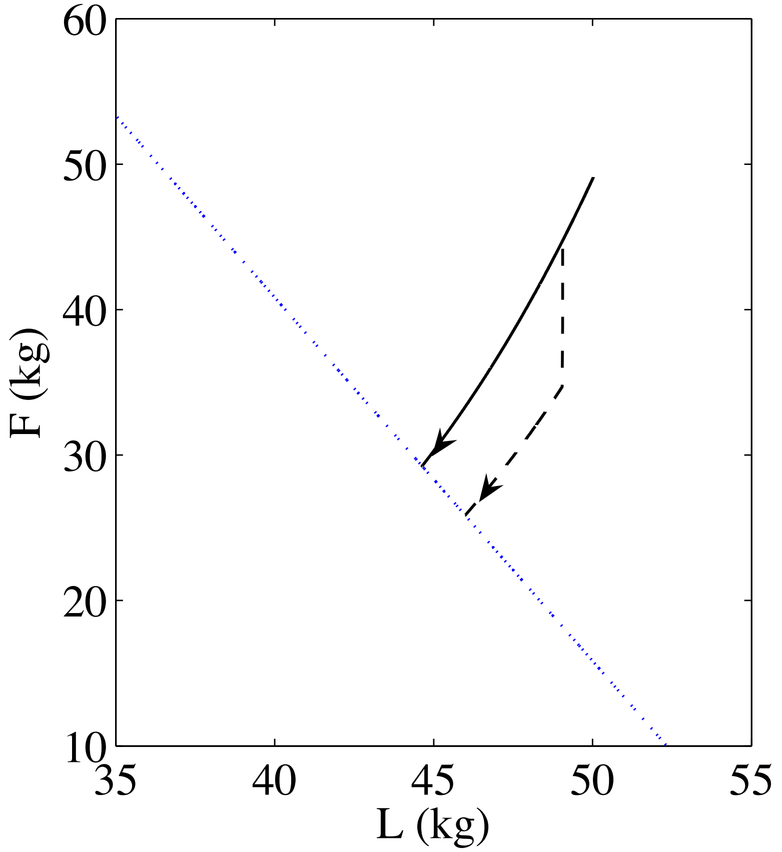
line attractor

Remove fat

Diet



fixed point



line attractor

Remove fat

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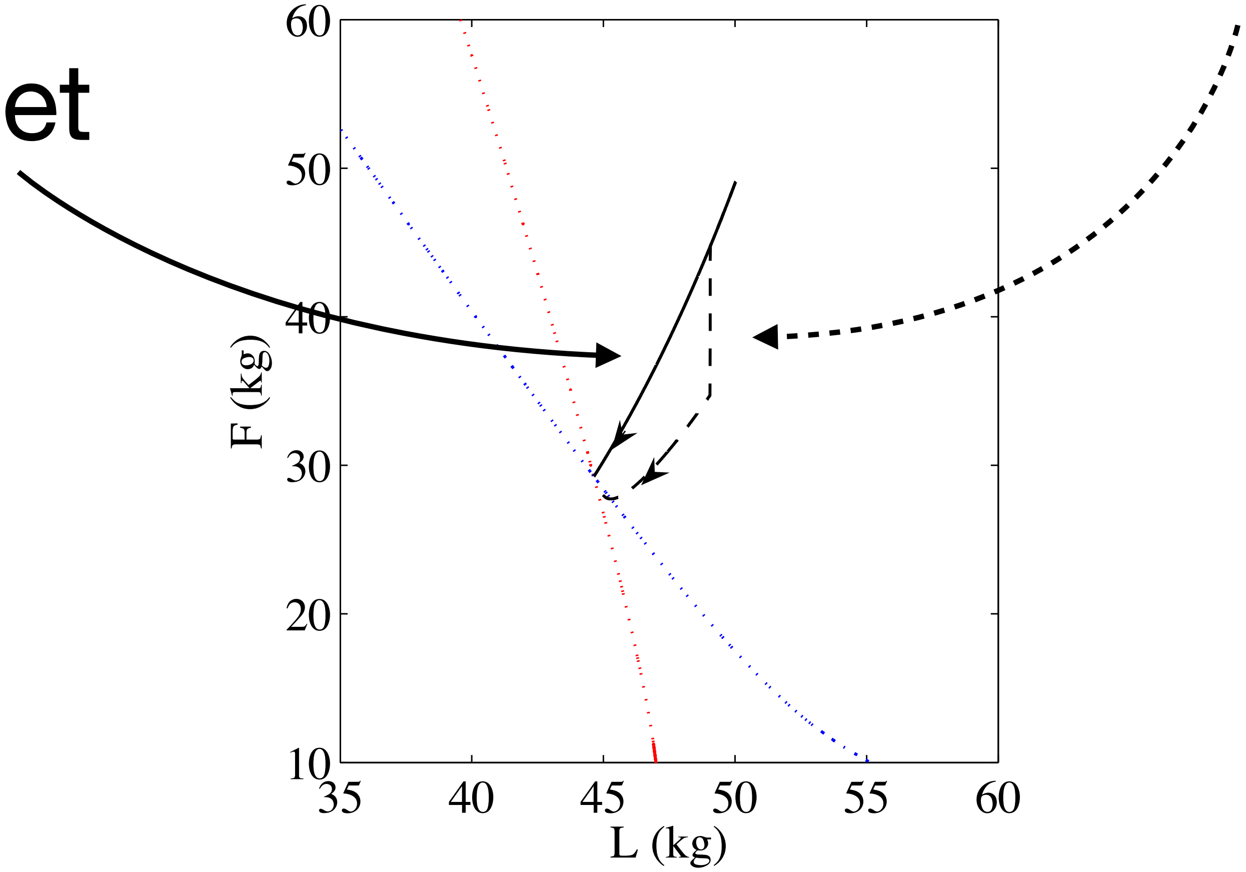

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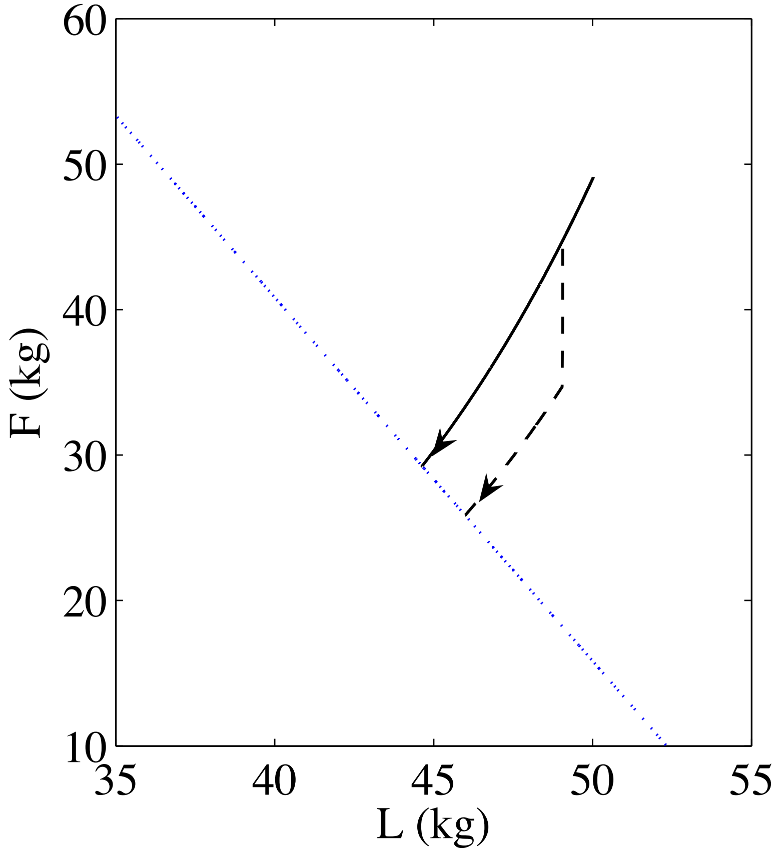
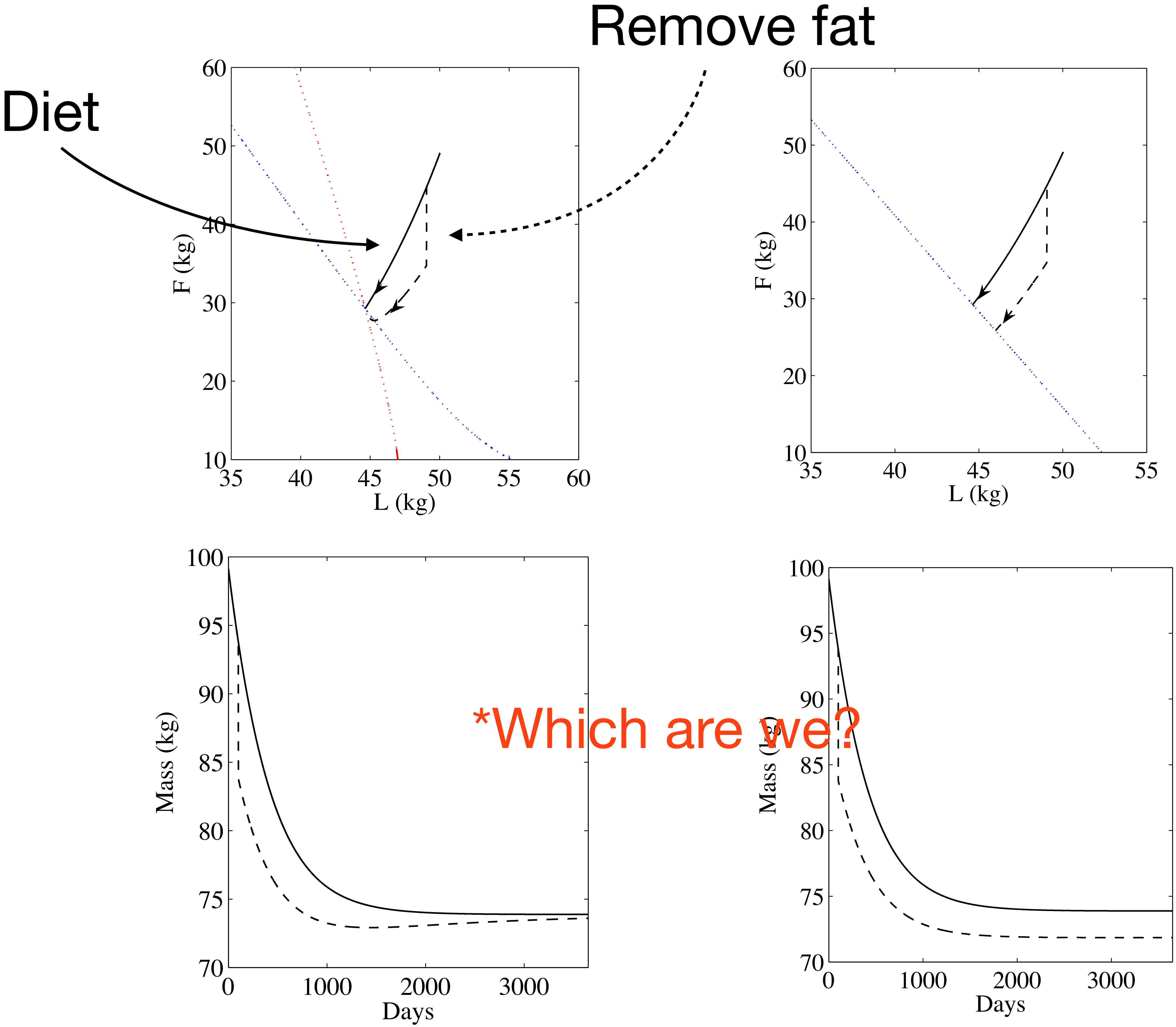


line attractor

*Which are we?



Diet

Remove fat

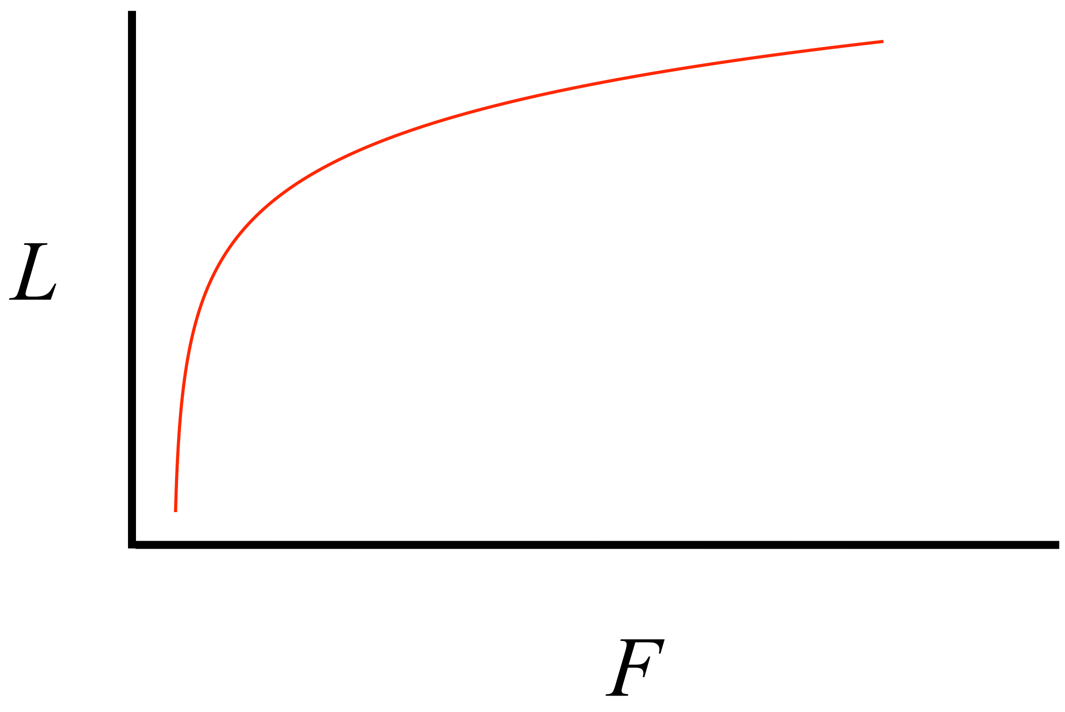
*Which are we?

Living on the Forbes curve

$$\rho_F \frac{dF}{dt} = (1-p)(I-E)$$

$$\rho_L \frac{dL}{dt} = p(I-E)$$

$$L = 10.4 \ln F + D$$



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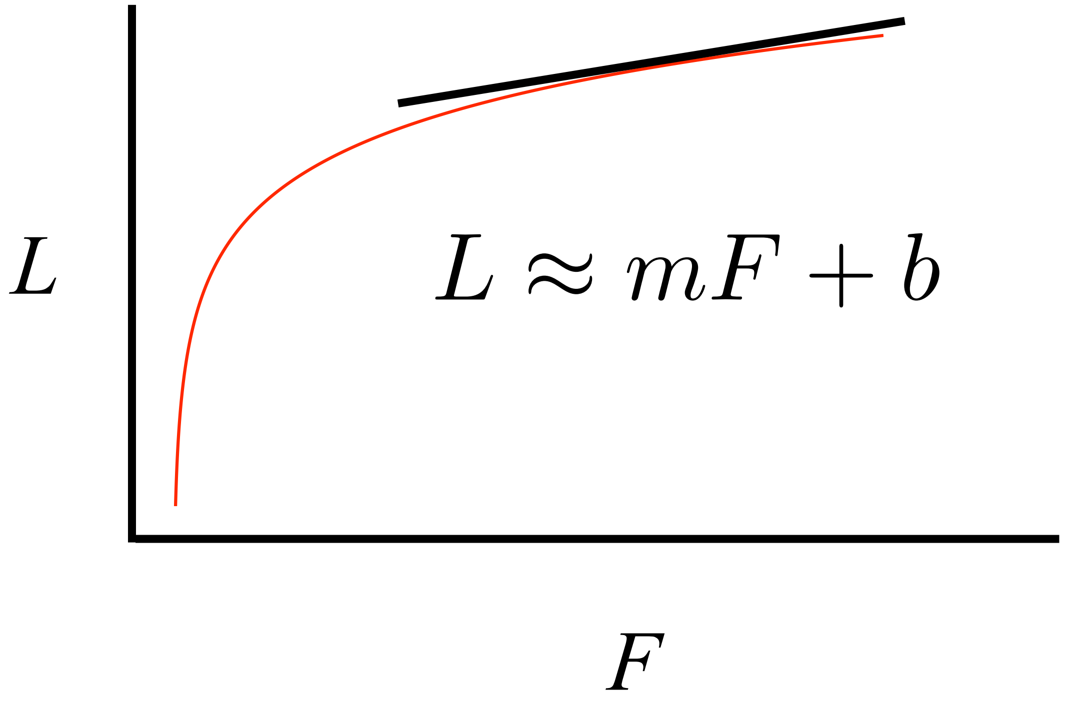

Living on the Forbes curve

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E$$

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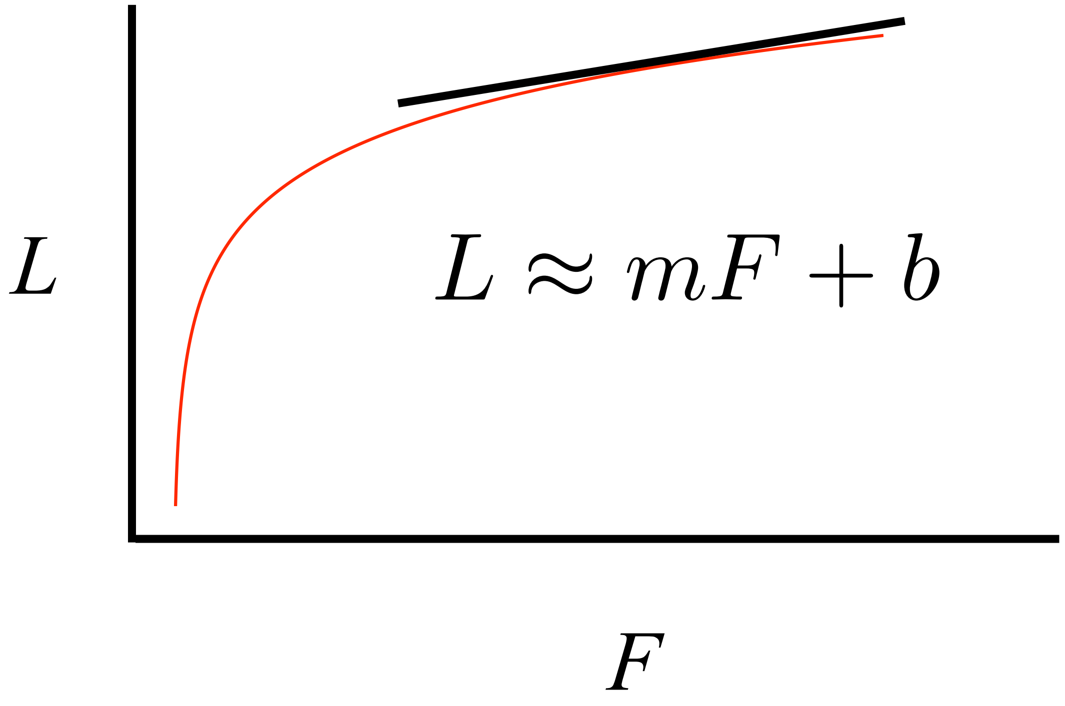

One dimensional model

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E$$

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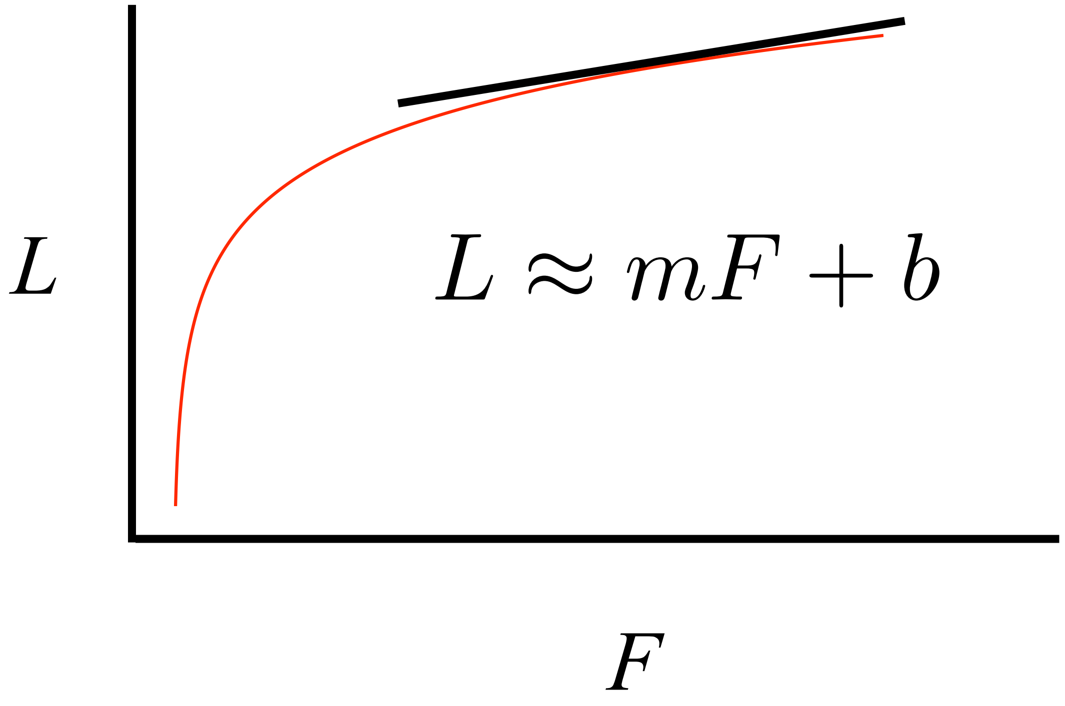


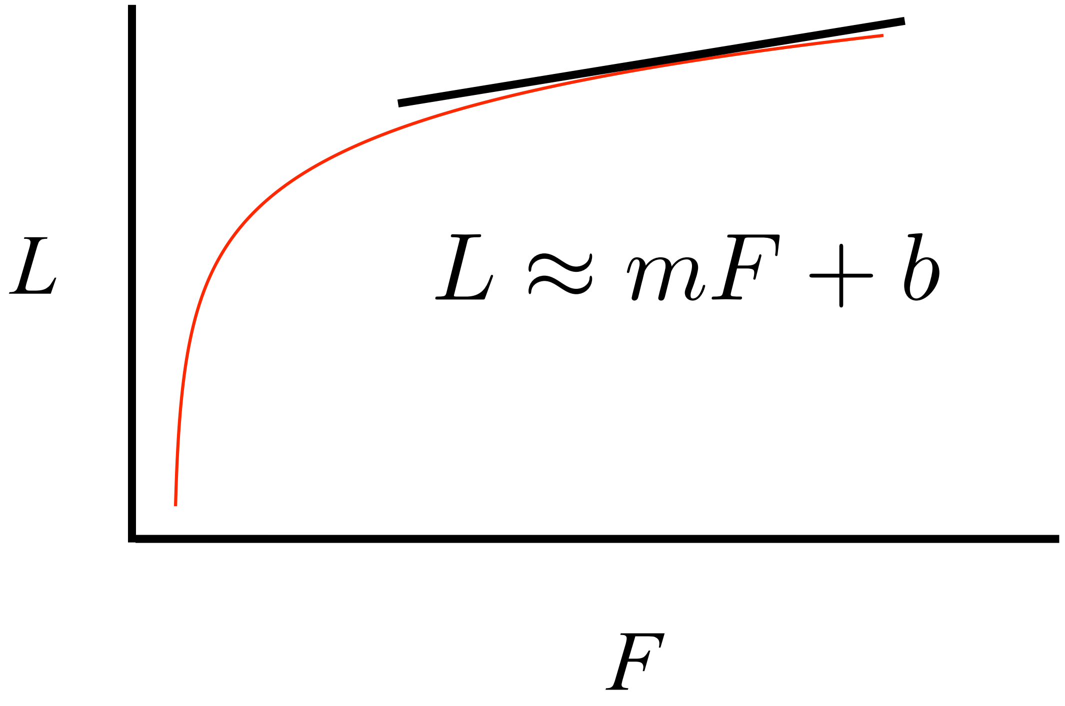
$$L \approx mF + b$$

One dimensional model

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E$$

$$M = F + L$$

$$L = 10.4 \ln F + D$$



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One dimensional model

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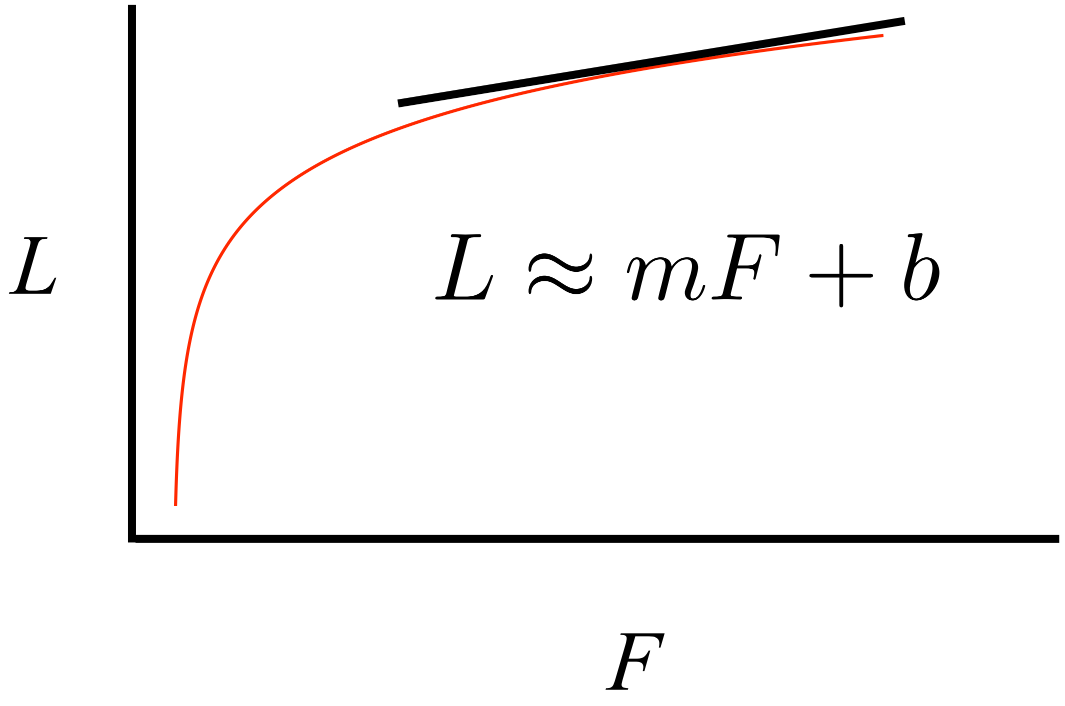
$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

$$L = 10.4 \ln F + D$$



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Steady state

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$$\Delta M \sim \frac{1}{\epsilon} \Delta I$$

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ϵ ~ 0.1 MJ/kg/day

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~ 22 kcal/kg/day

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10 Calories a day = 1 pound

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ϵ ~ 0.1 MJ/kg/day

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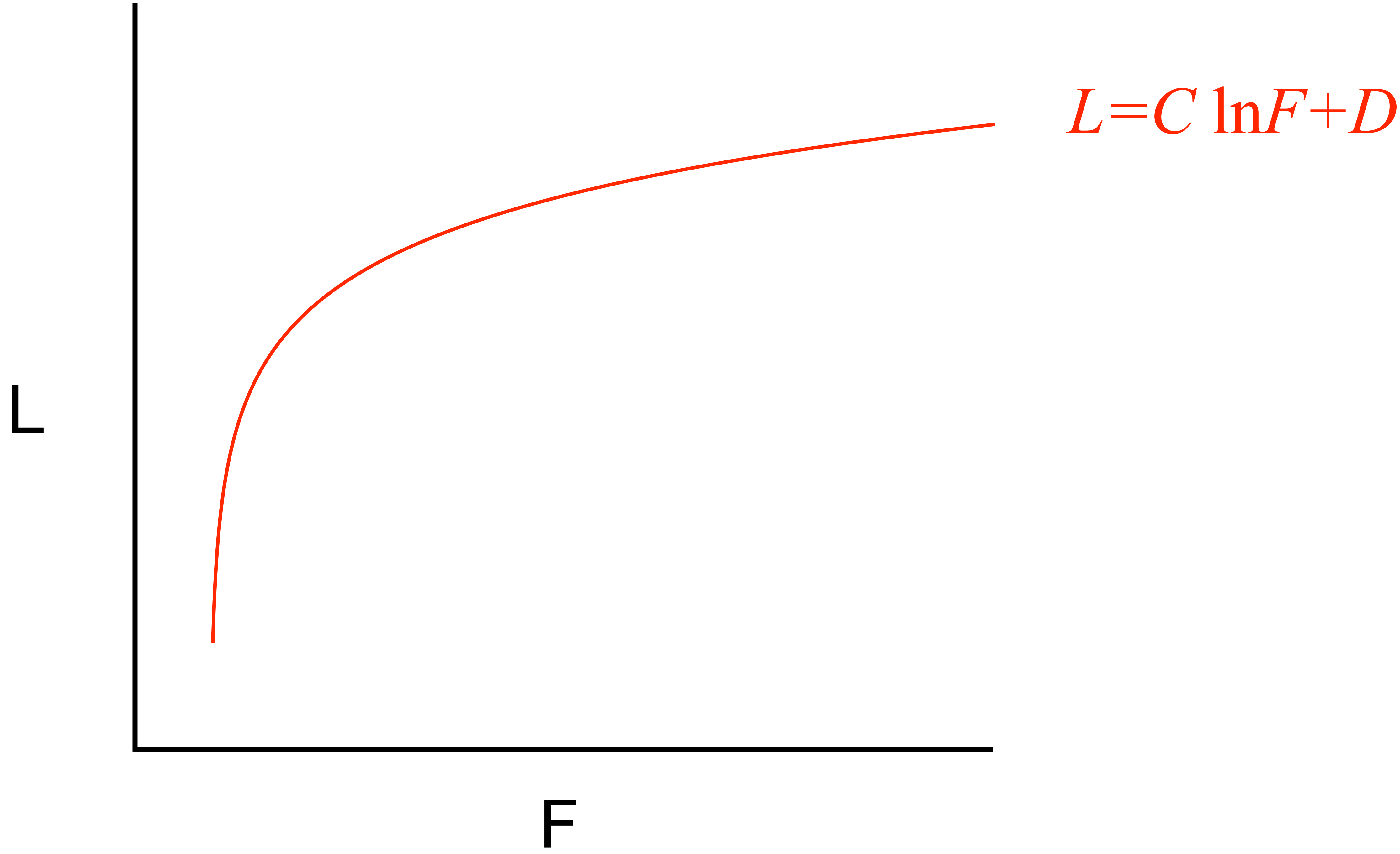
*Need catchy name for ϵ

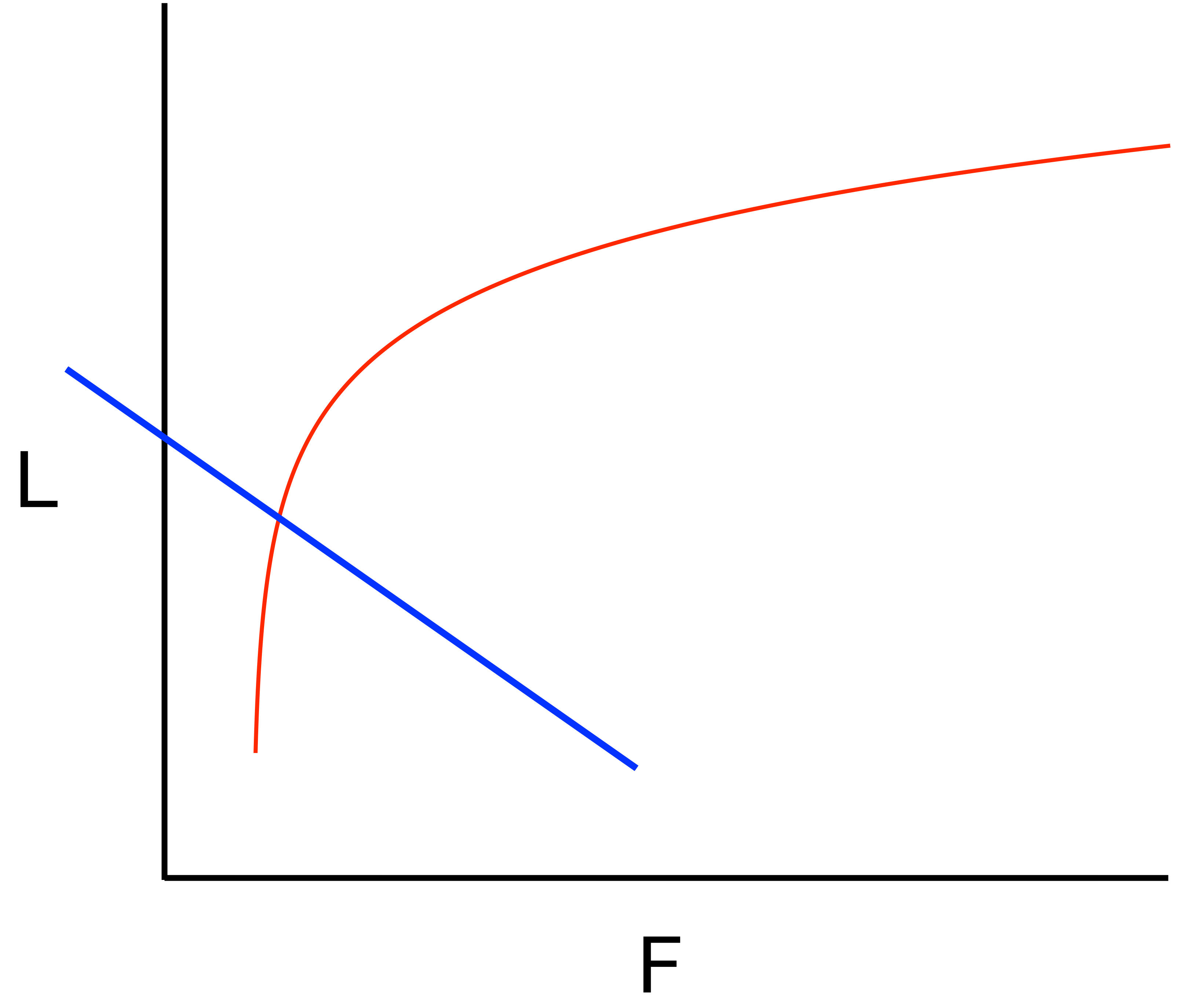
10 Calories a day = 1 pound

Weight gain increases with weight



Weight gain increases with weight

$E(F,L)=I$



$L=C\ \ln F+D$

Weight gain increases with weight

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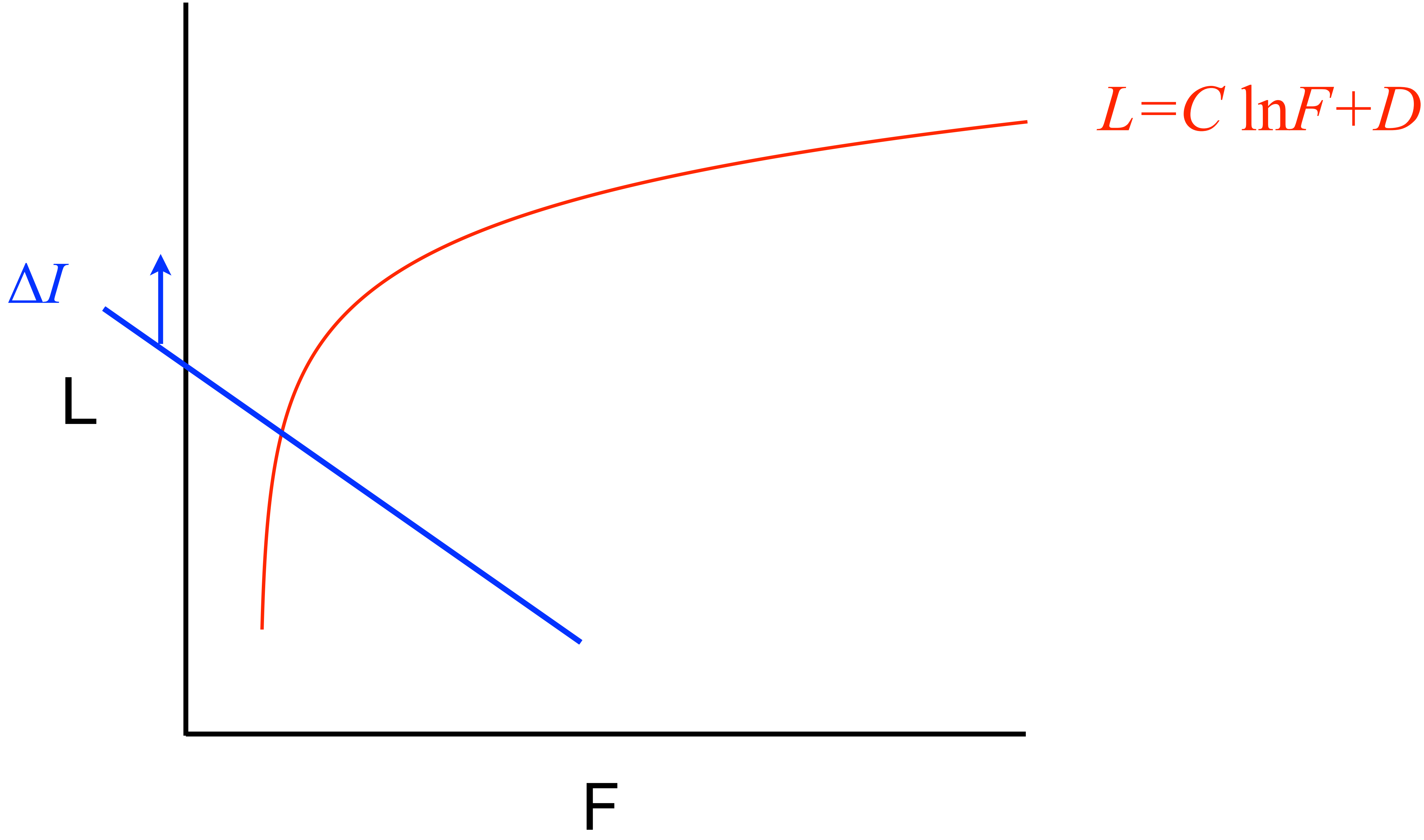

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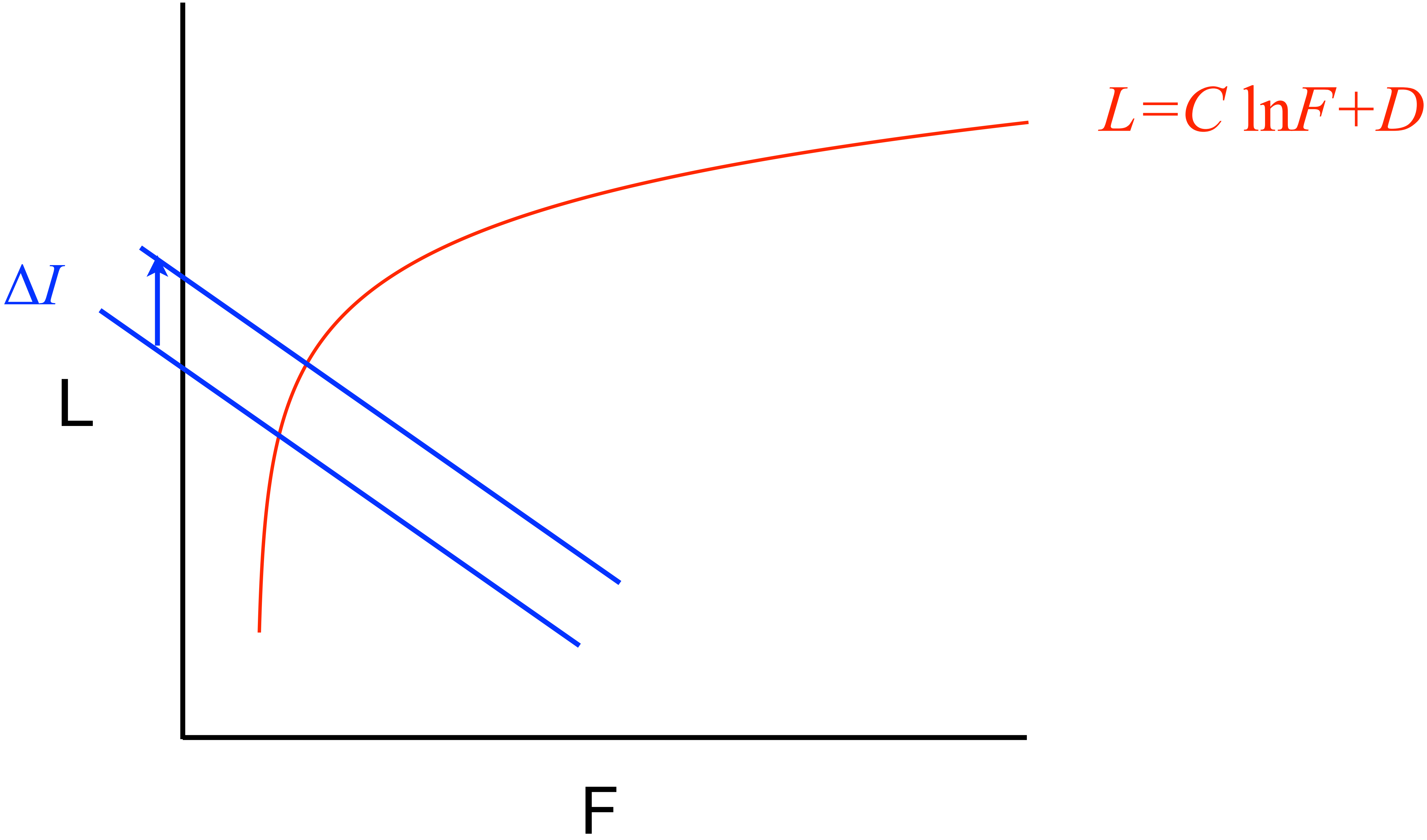

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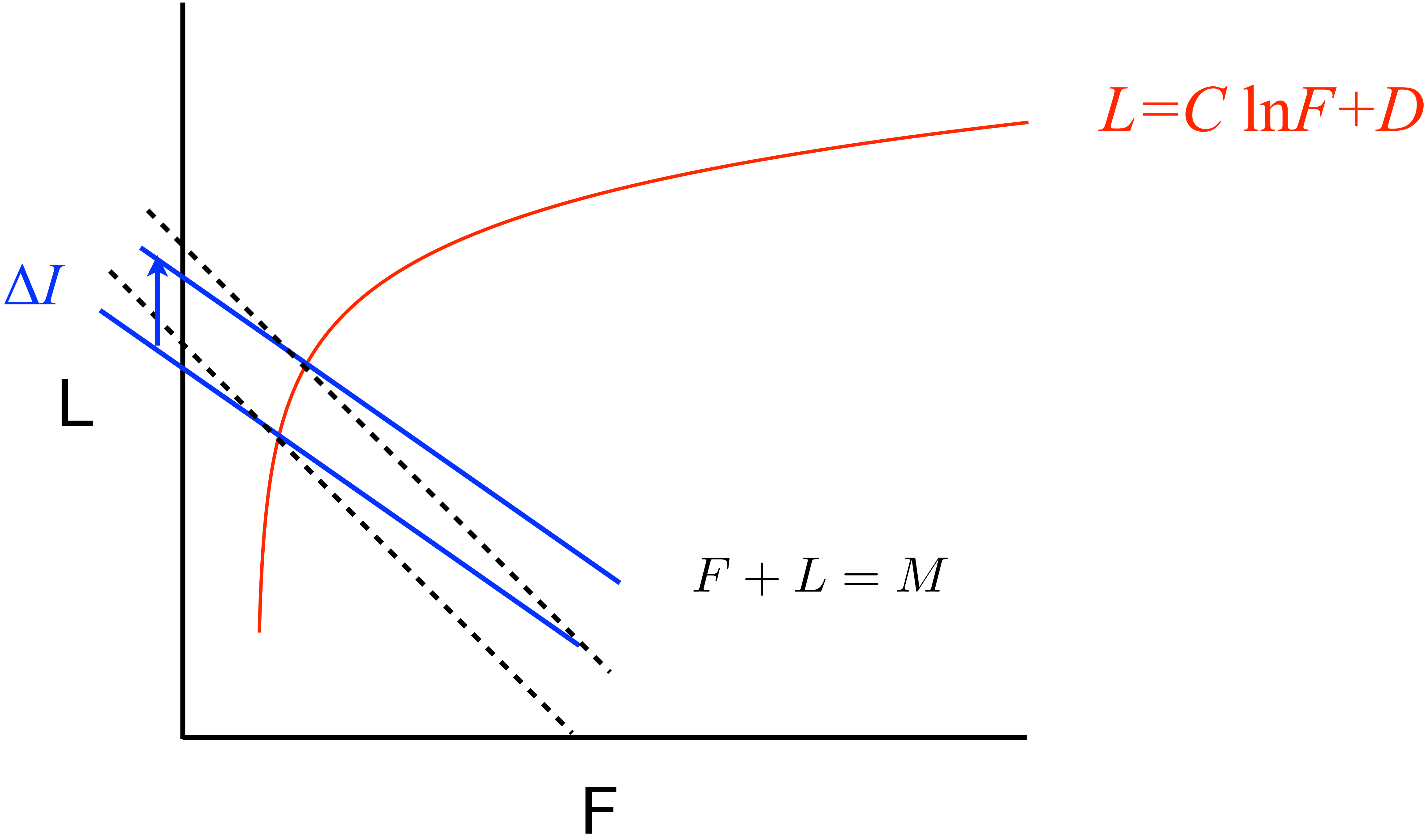

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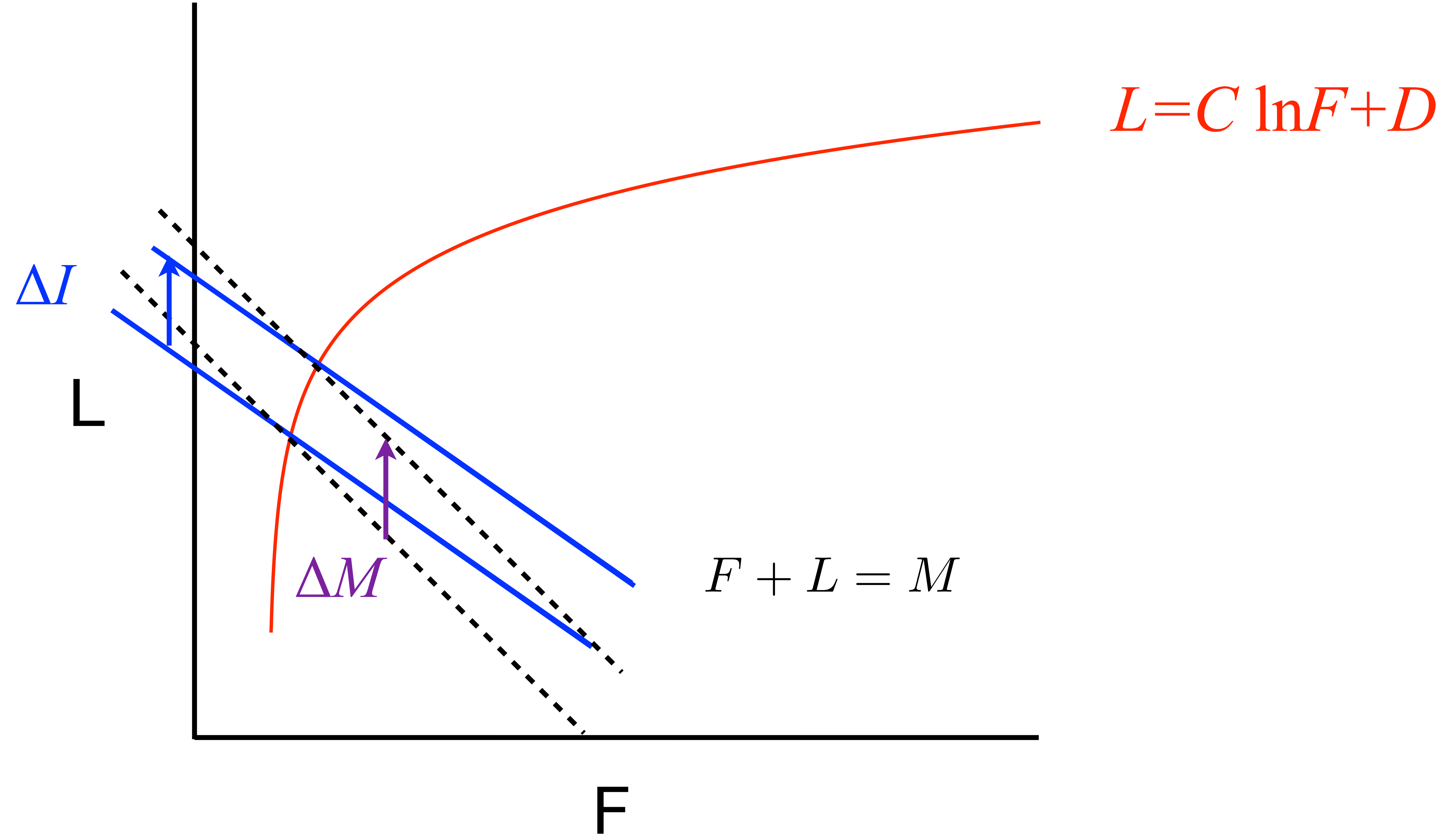

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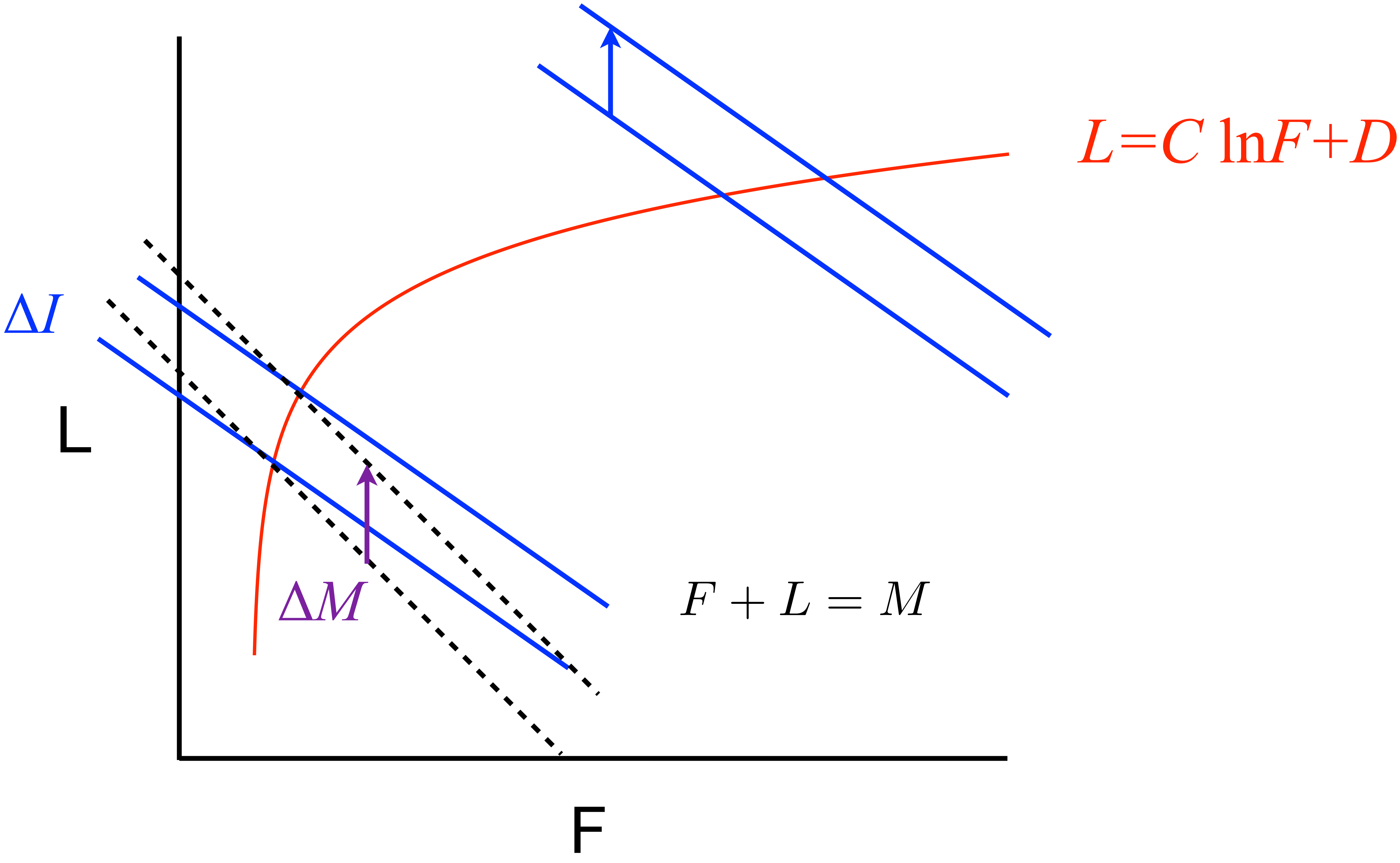

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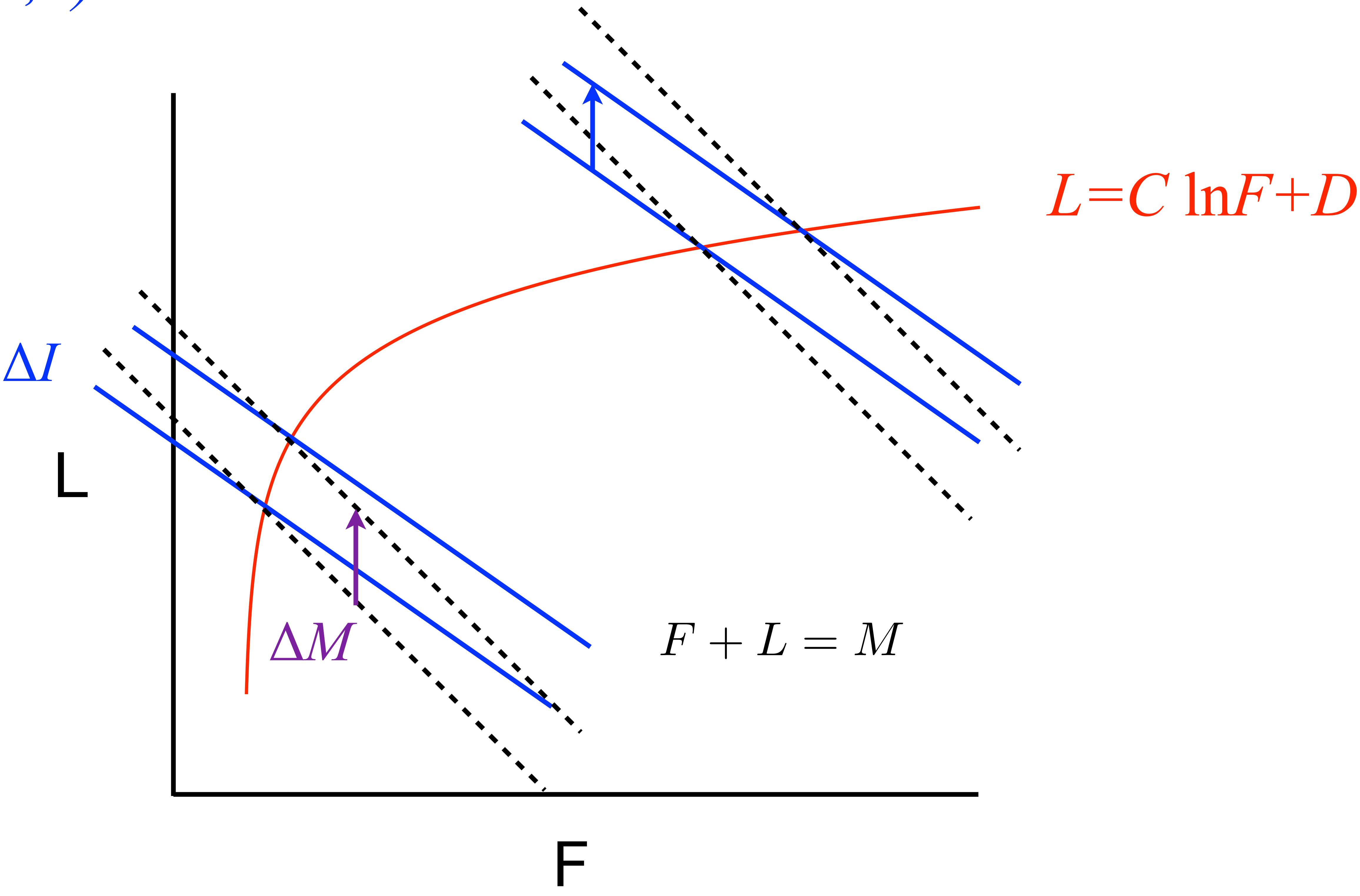

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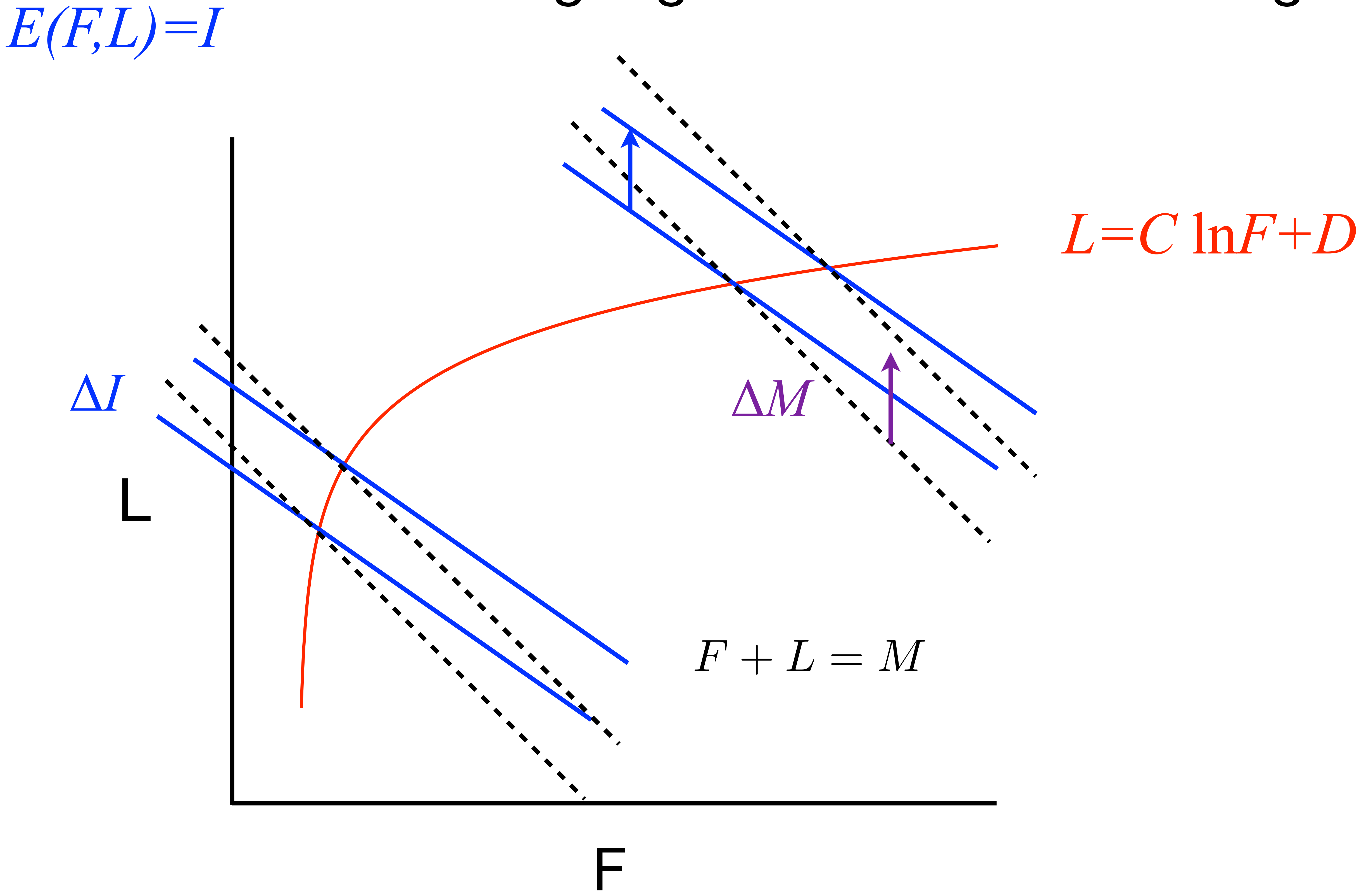

Time Constant

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

Time Constant

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$$\tau = \rho / \epsilon$$

Time Constant

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

$$\tau = \rho / \epsilon$$

ρ ~ 7700 kcal/kg, ϵ ~ 22 kcal/day ⇒ τ ~1 year

Time Constant

$$\rho\frac{dM}{dt} = I - \epsilon M - b$$

$$\tau = \rho/\epsilon$$

ρ ~ 7700 kcal/kg, ϵ ~ 22 kcal/day ⇒ τ ~1 year

Time Constant

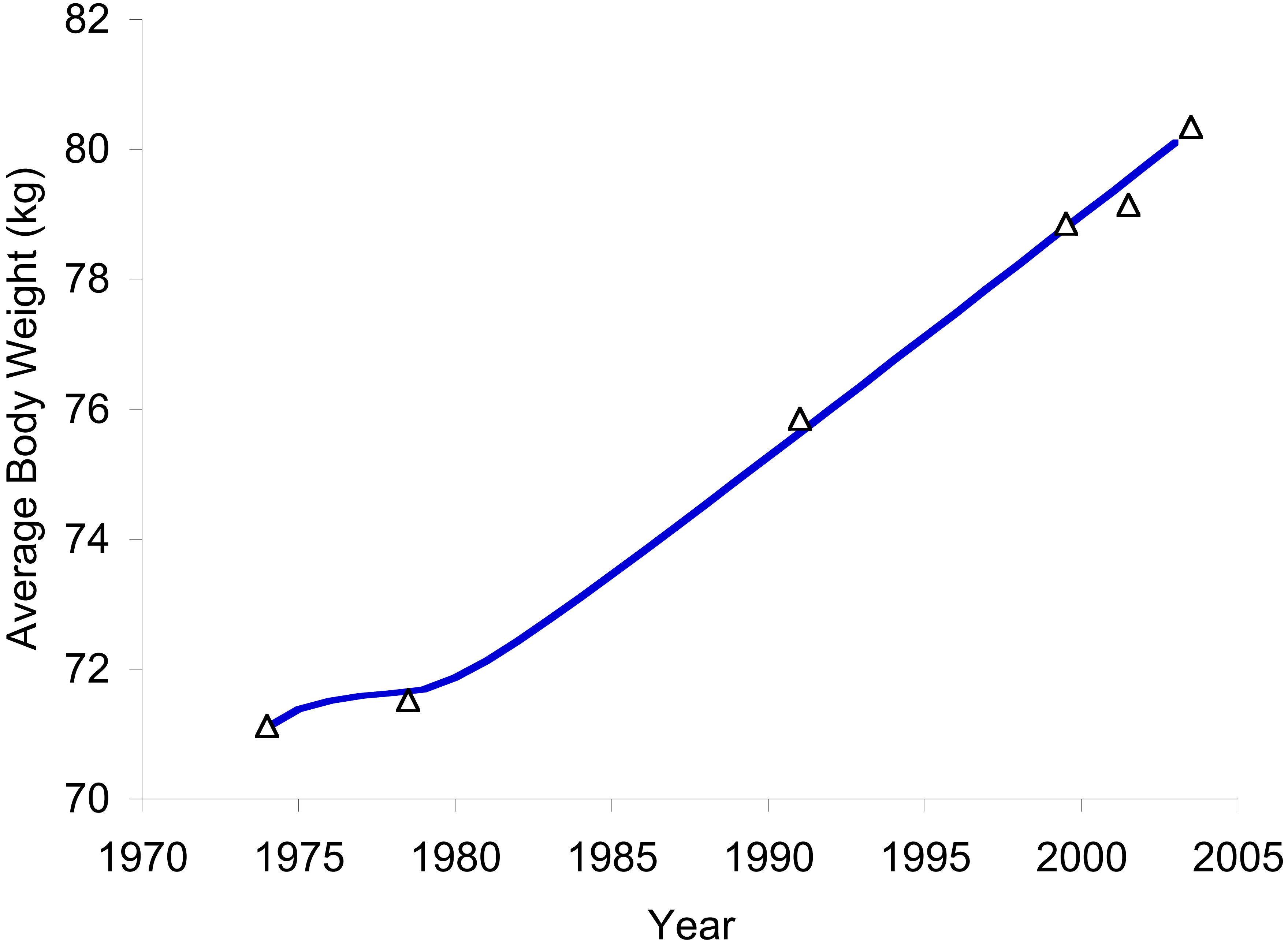
$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

$$\tau = \rho / \epsilon$$

ρ ~ 7700 kcal/kg, ϵ ~ 22 kcal/day ⇒ τ ~1 year

τ increases with weight, decreases with activity

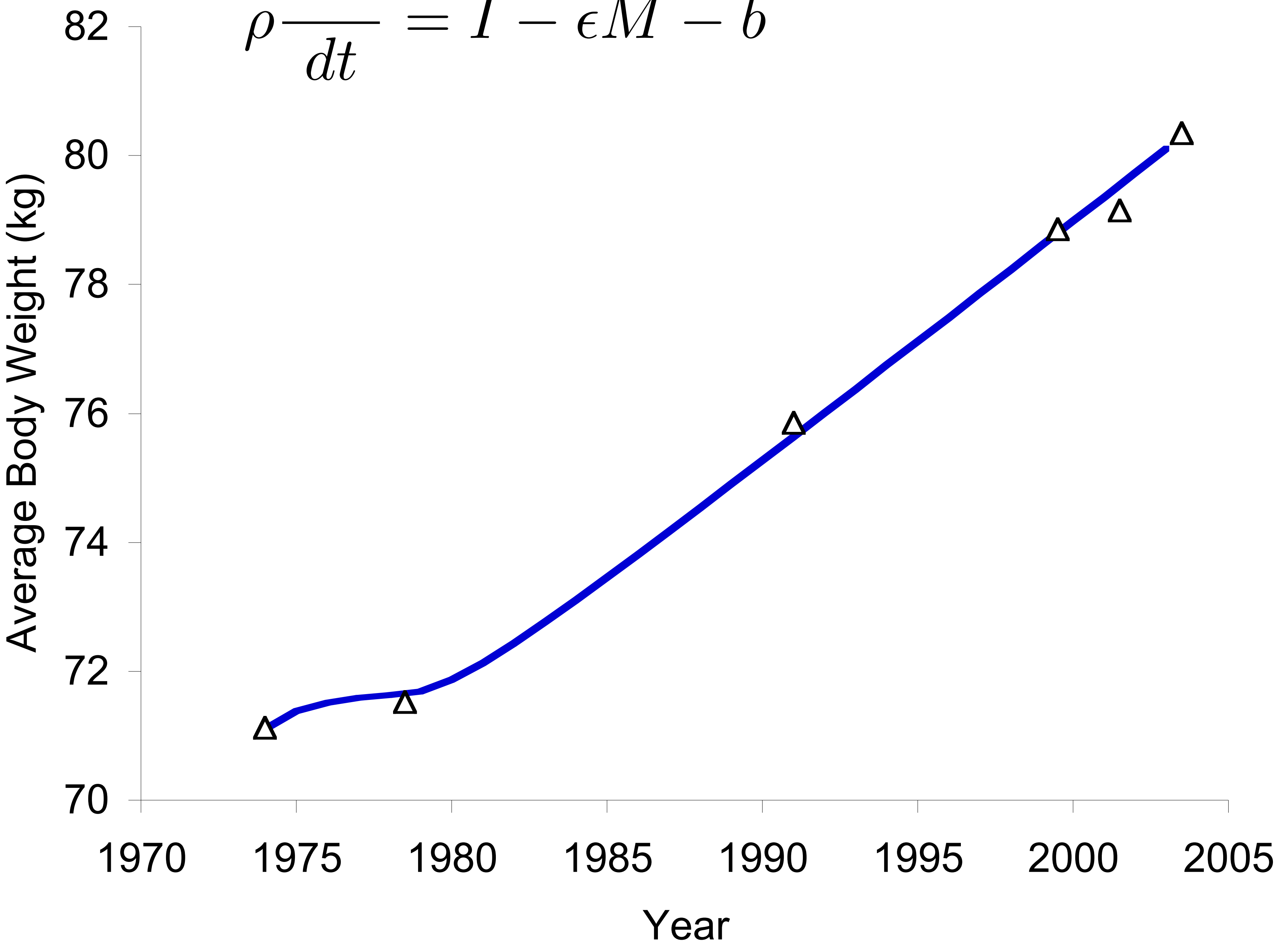
Mean US body weight



Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight

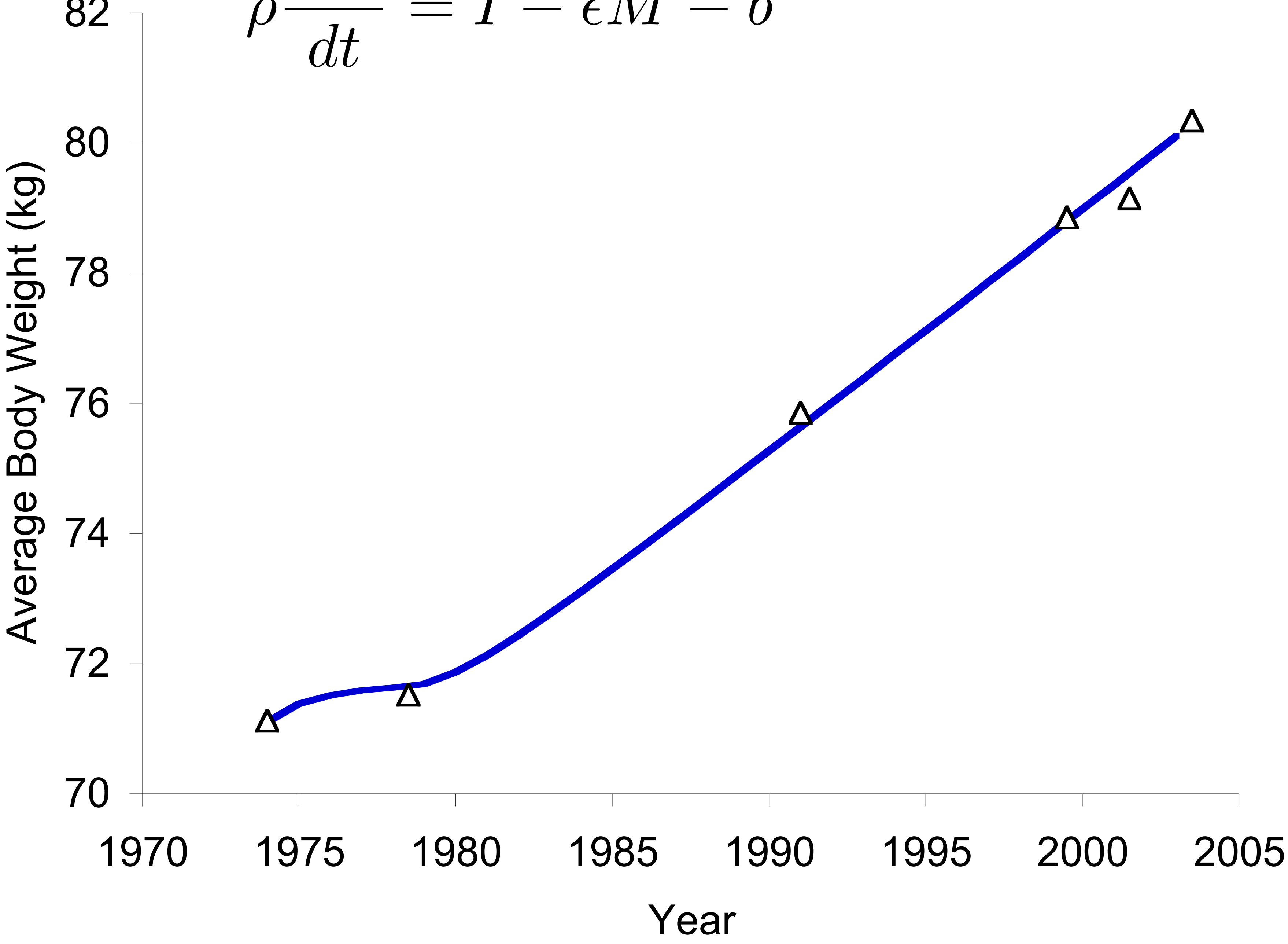
$$\rho \frac{dM}{dt} = I - \epsilon M - b$$



Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight

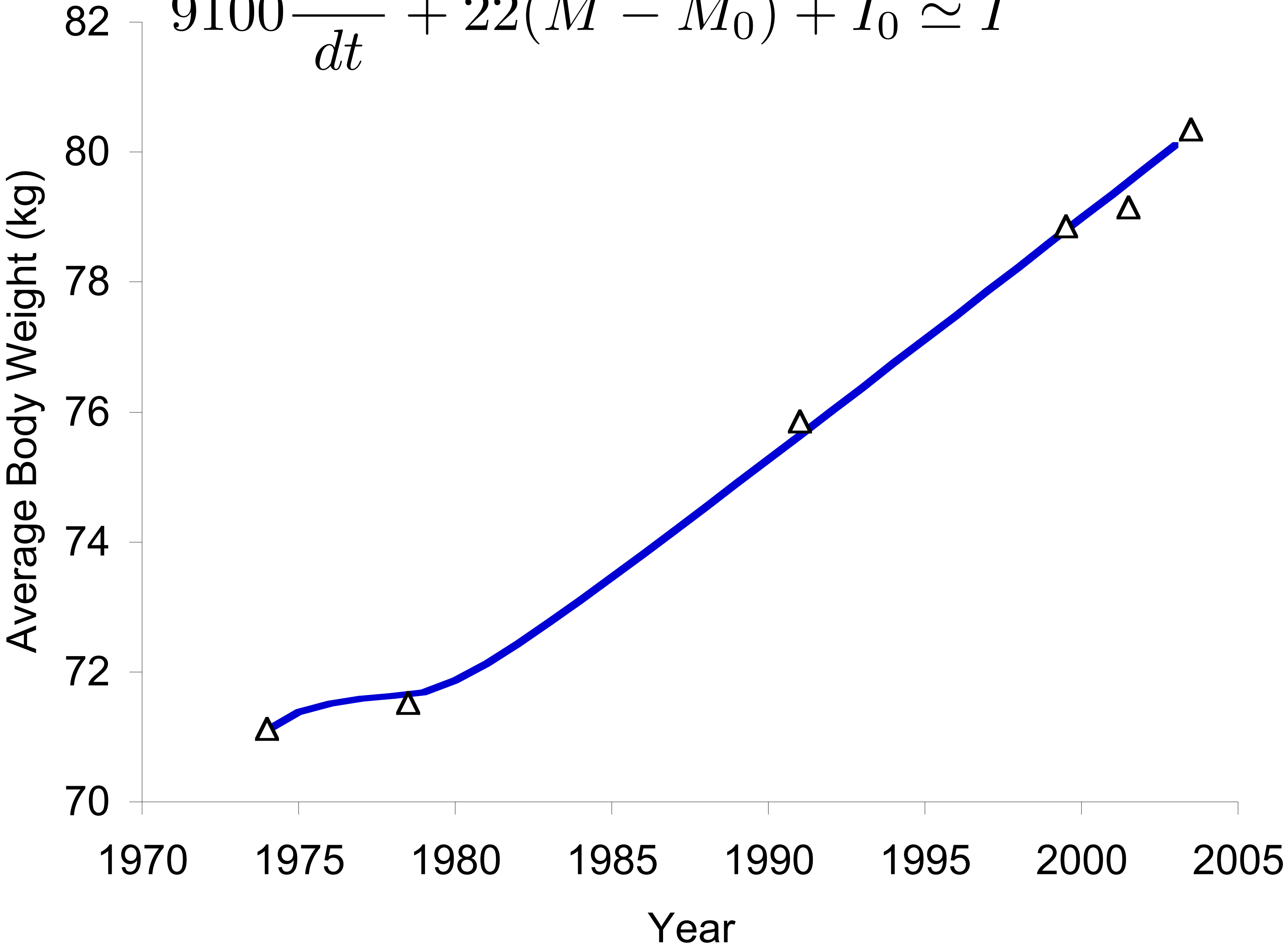
$$\overline{\rho \frac{dM}{dt}} = \overline{I} - \overline{\epsilon M} - b$$



Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight

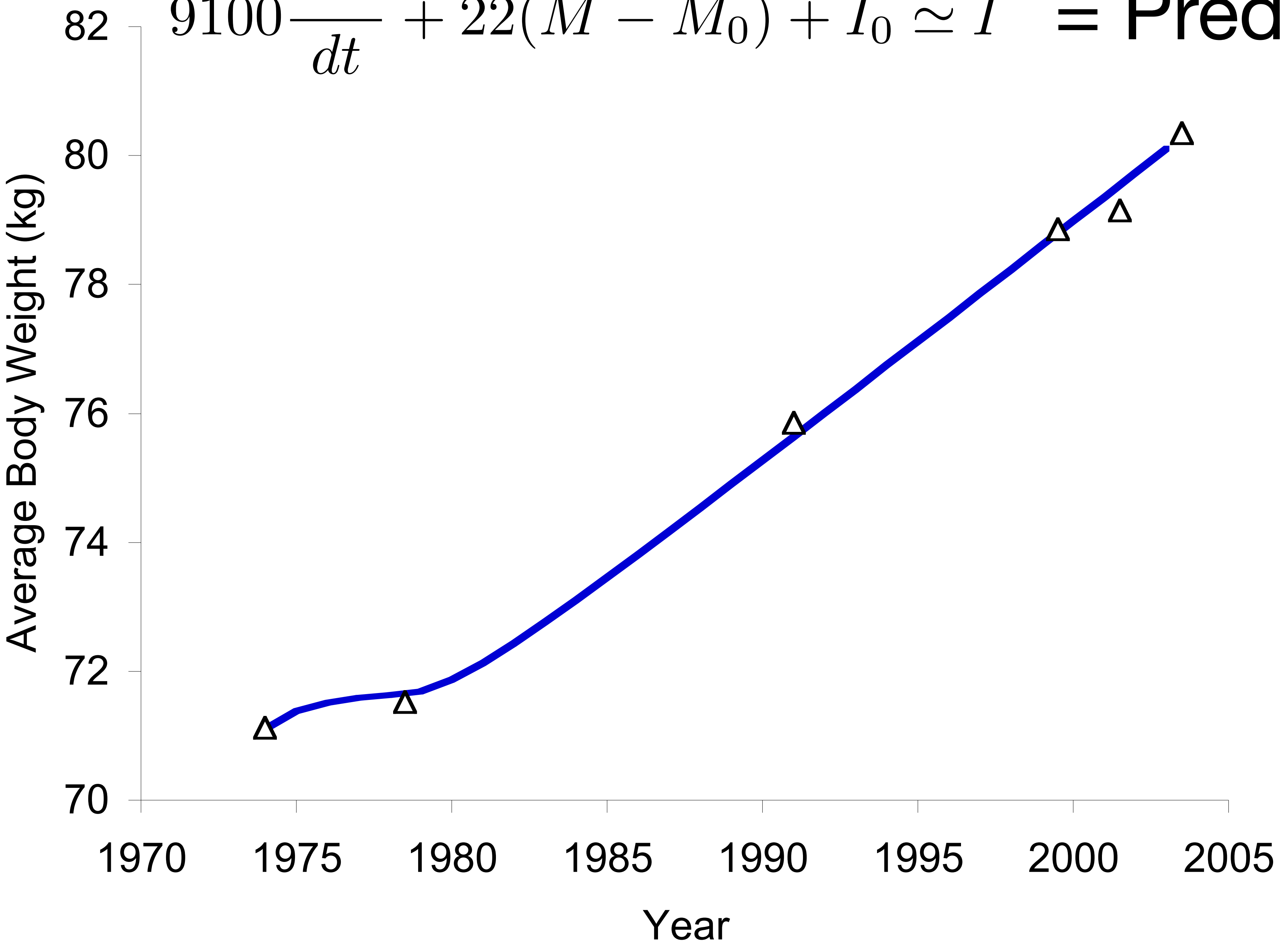
$$9100\frac{d\overline{M}}{dt} + 22(\overline{M} - M_0) + I_0 \simeq \overline{I}$$



Data from National Health and Nutrition Examination Survey (NHANES)

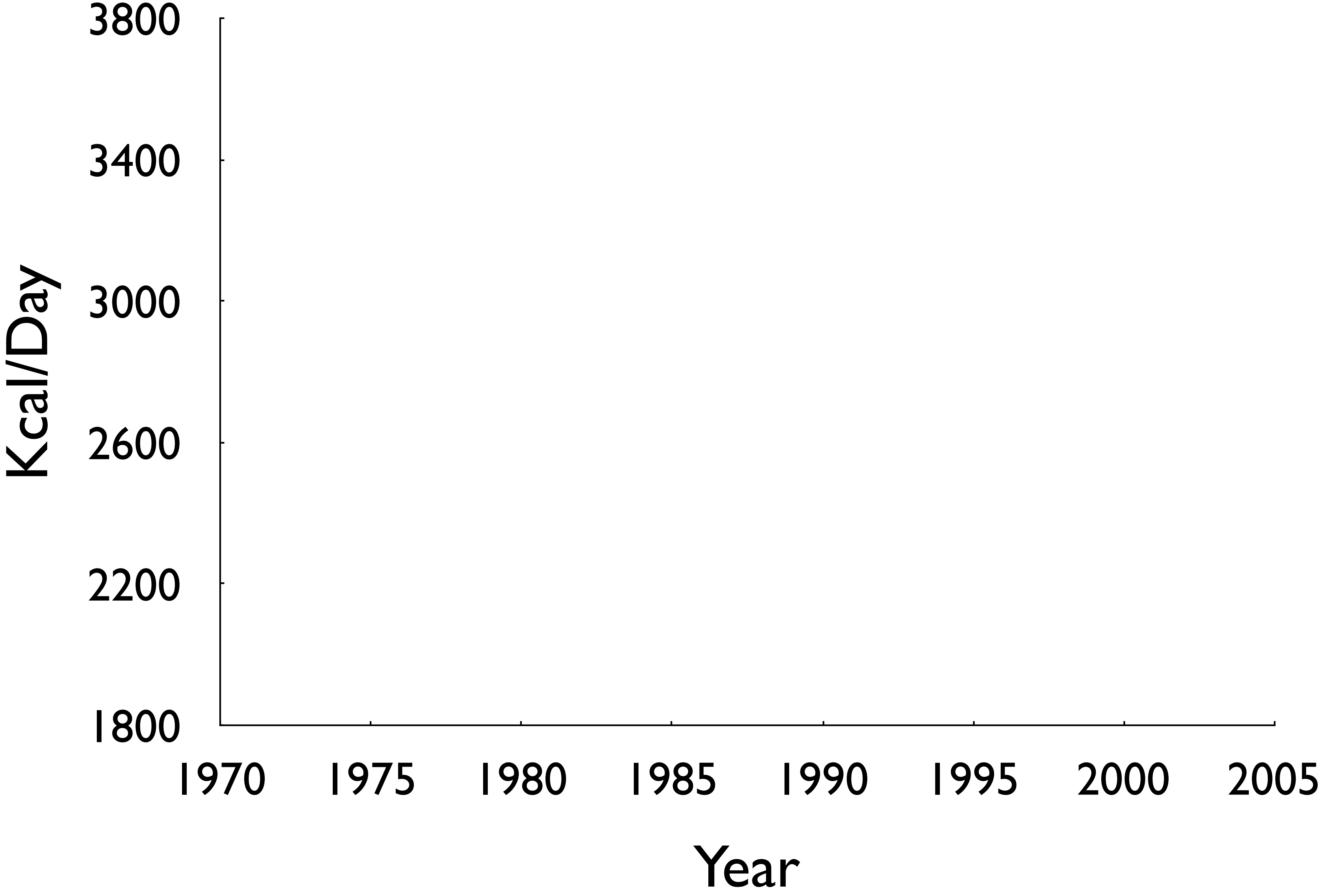
Mean US body weight

$$9100\frac{d\overline{M}}{dt} + 22(\overline{M} - M_0) + I_0 \simeq \overline{I}$$ = Predicted intake



Data from National Health and Nutrition Examination Survey (NHANES)

Hall, Guo, Dore, Chow. *PLoS One* (2009)



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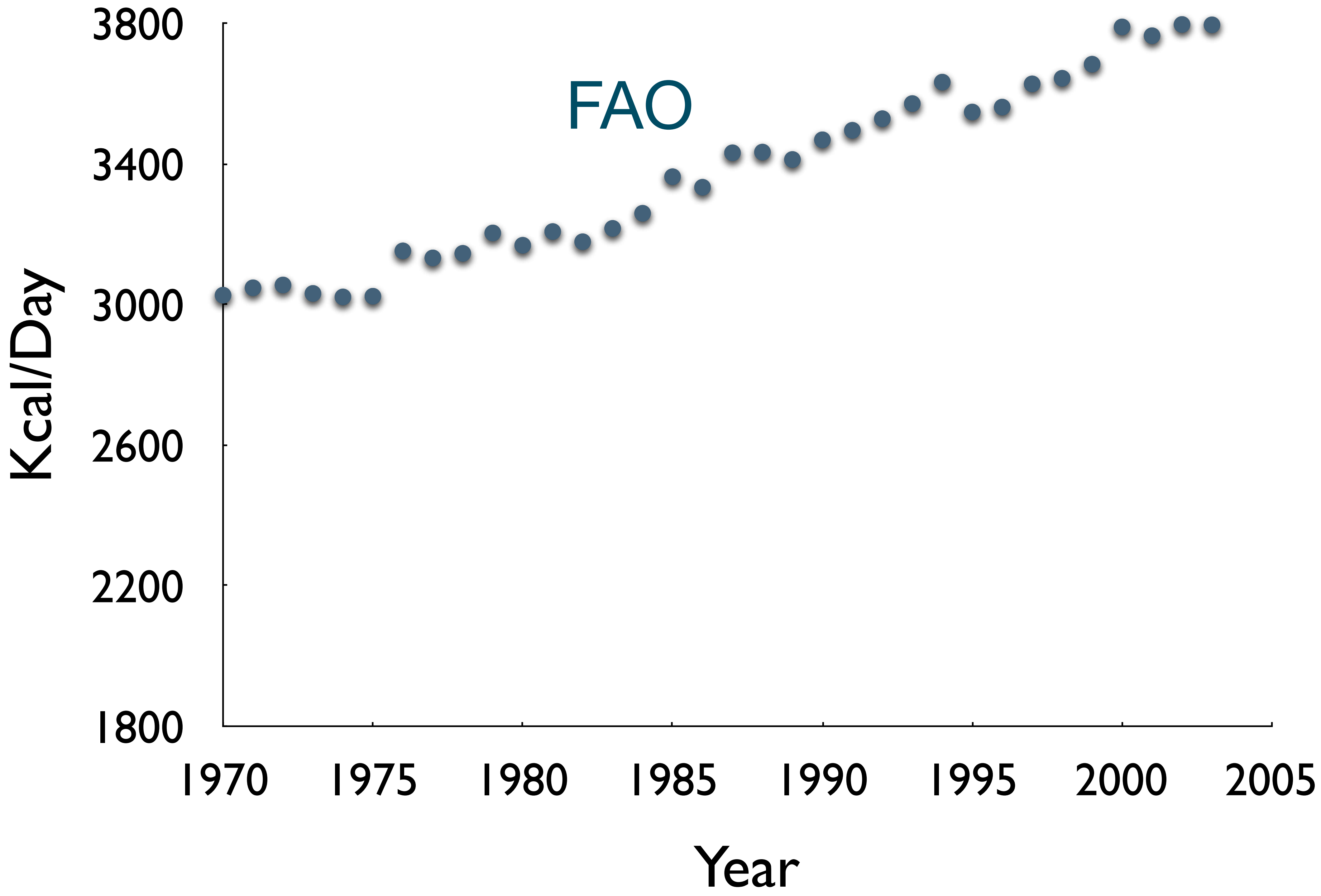

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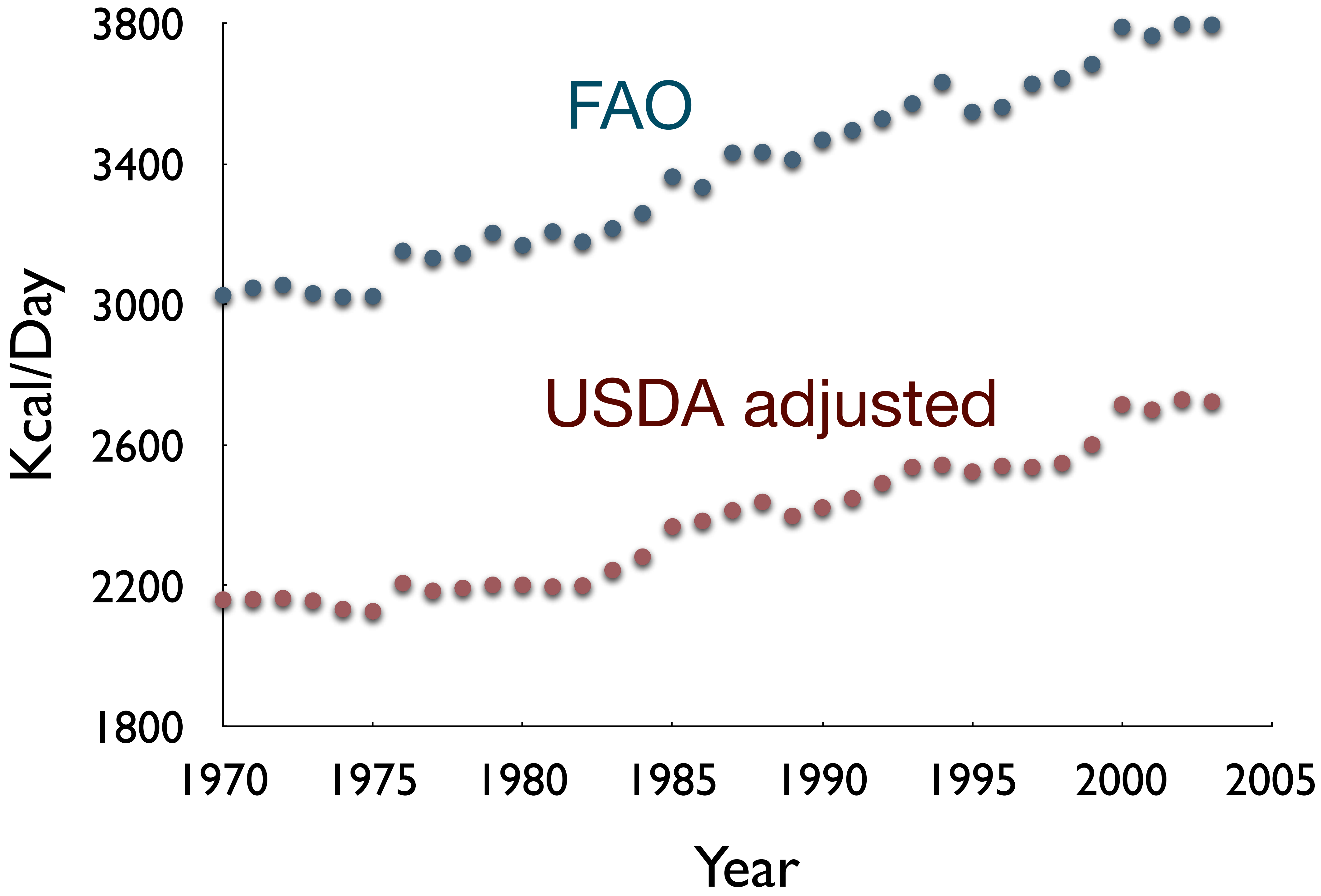

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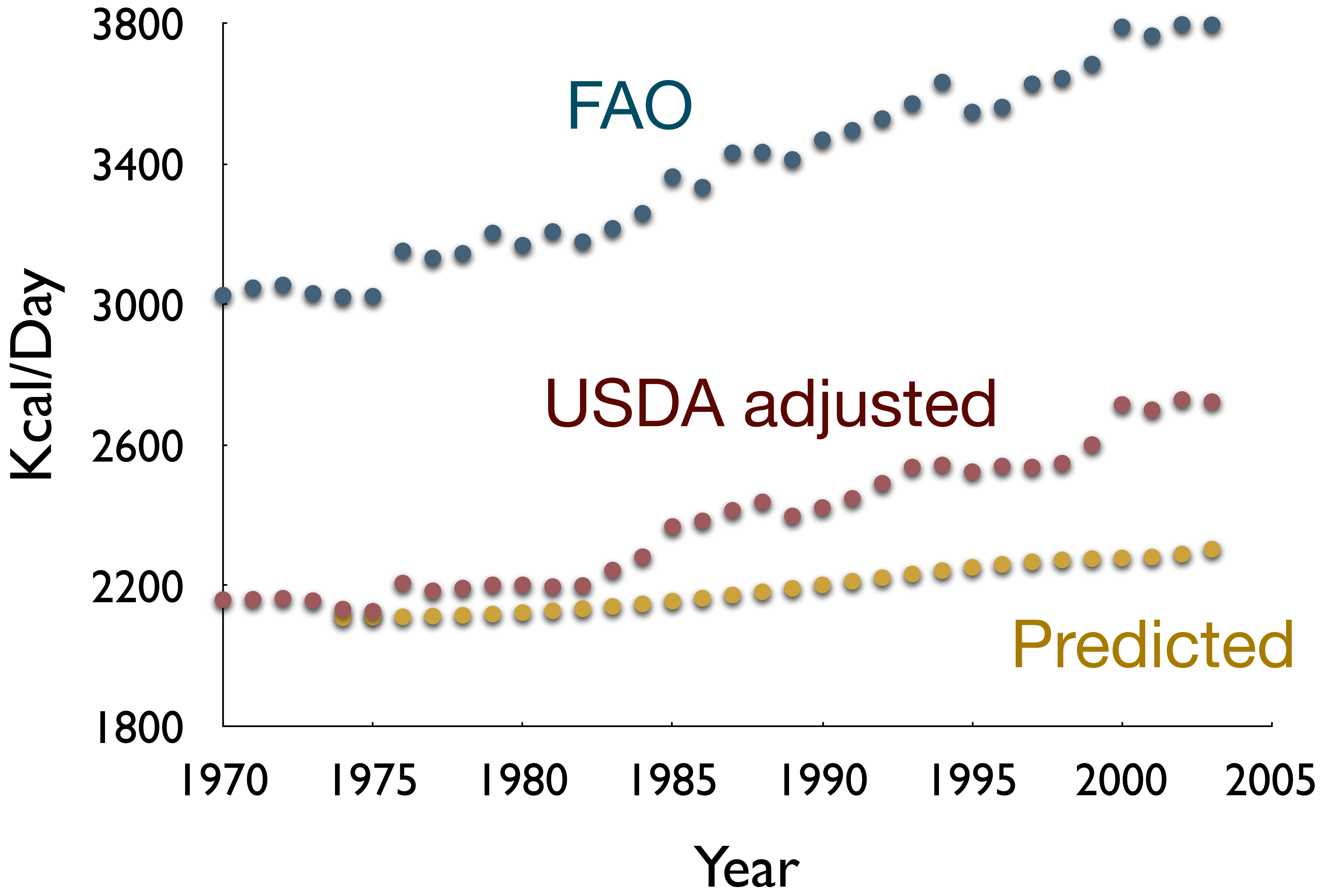

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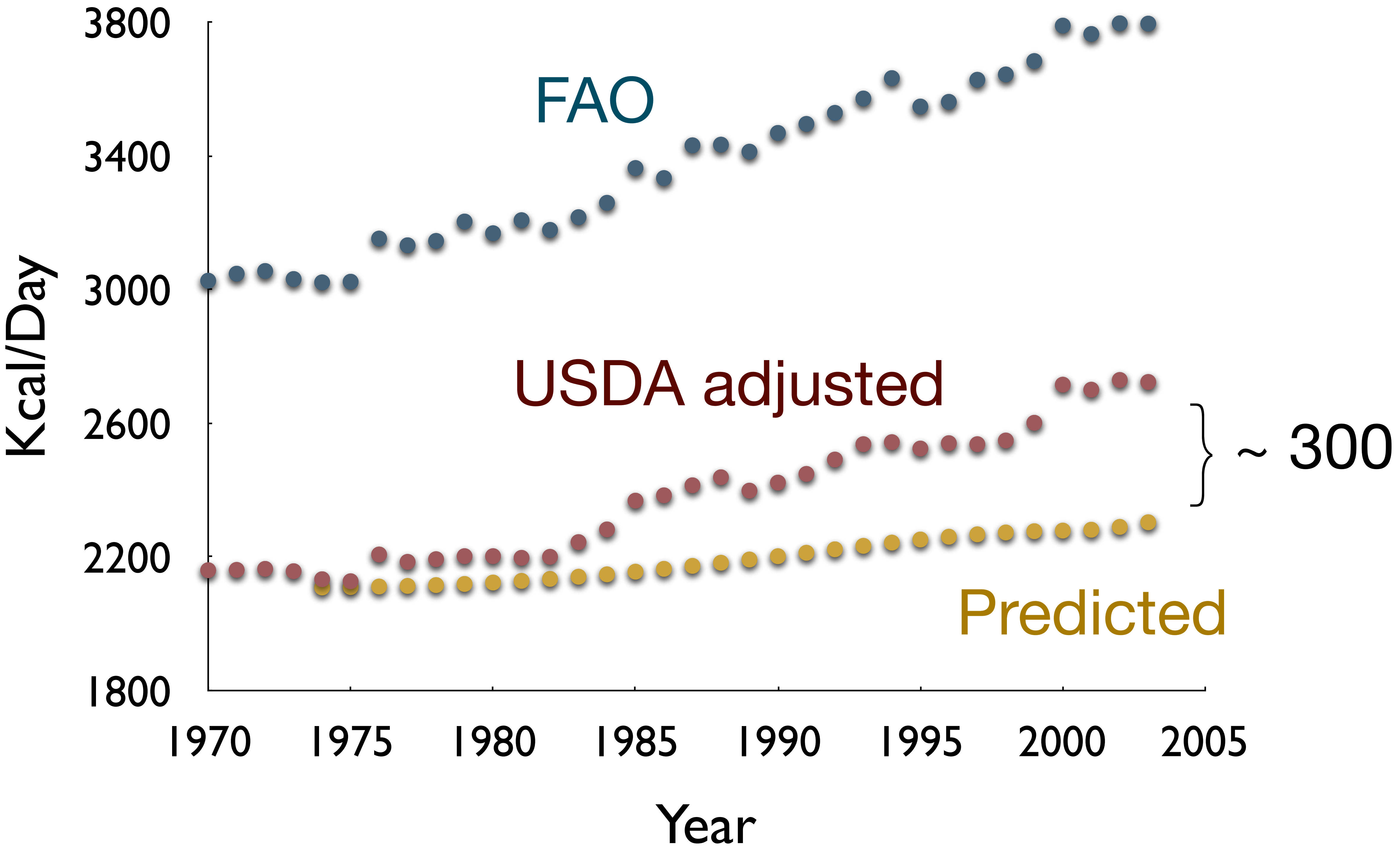

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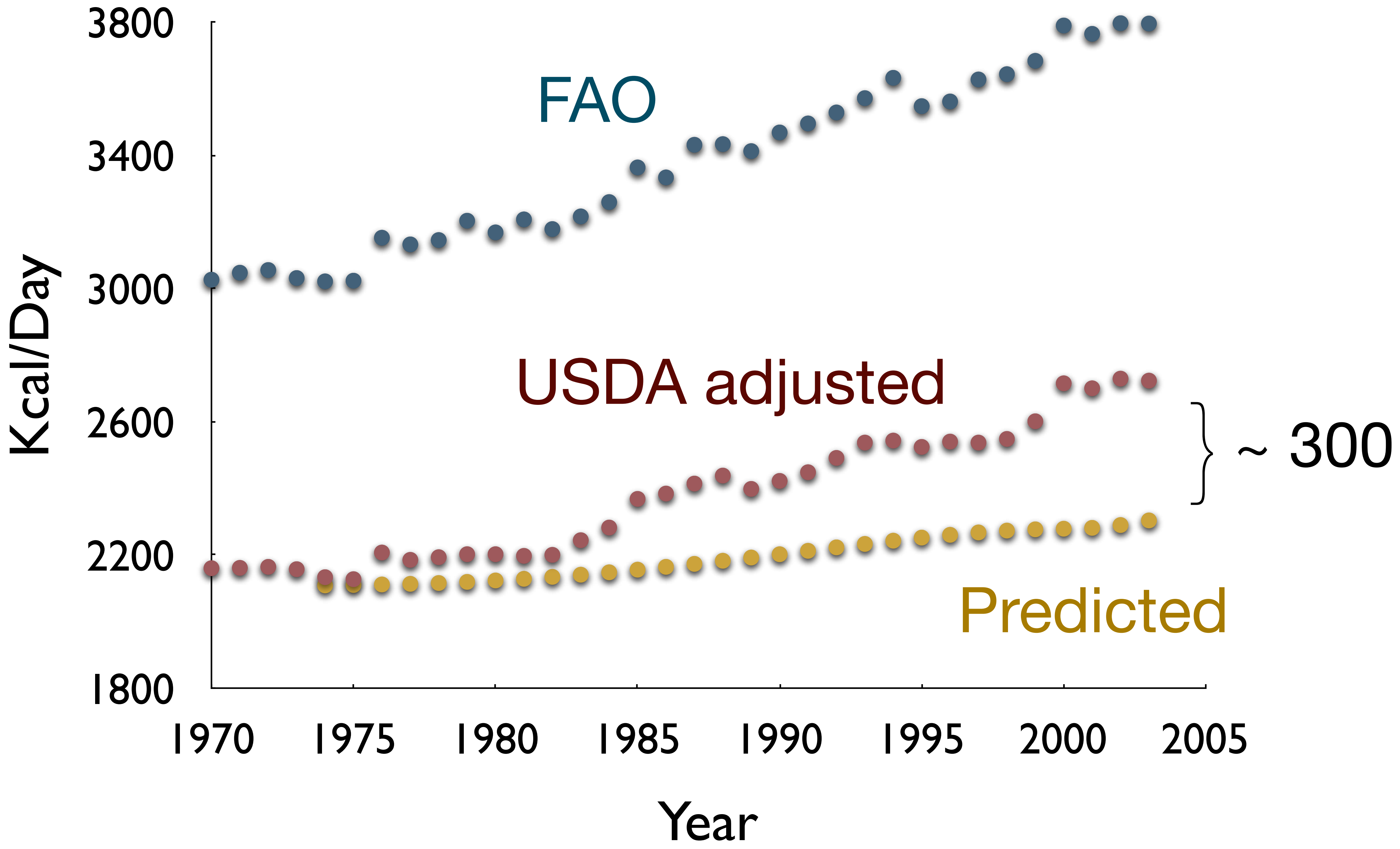
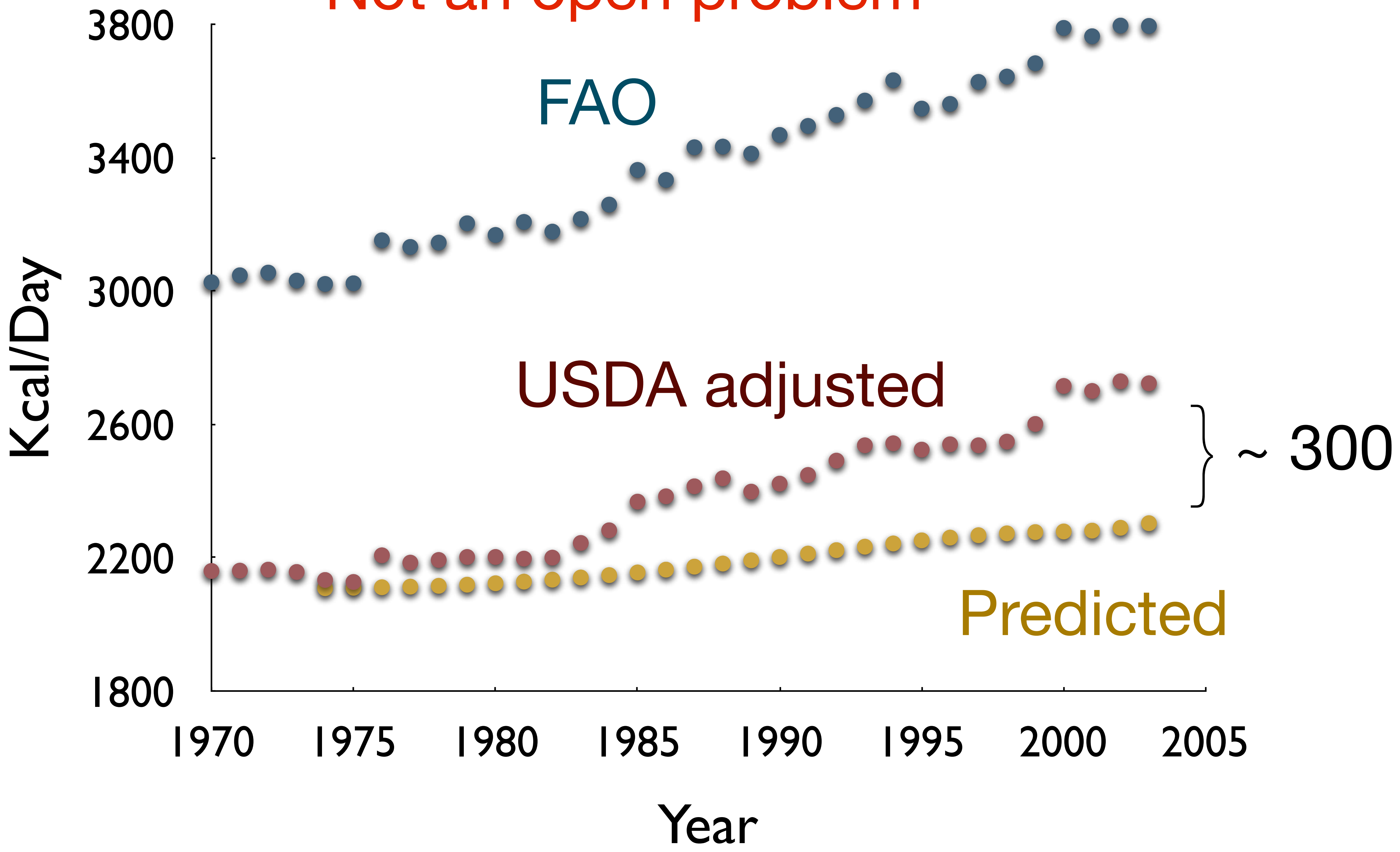
Excess food more than explains obesity epidemic



Hall, Guo, Dore, Chow. *PLoS One* (2009)

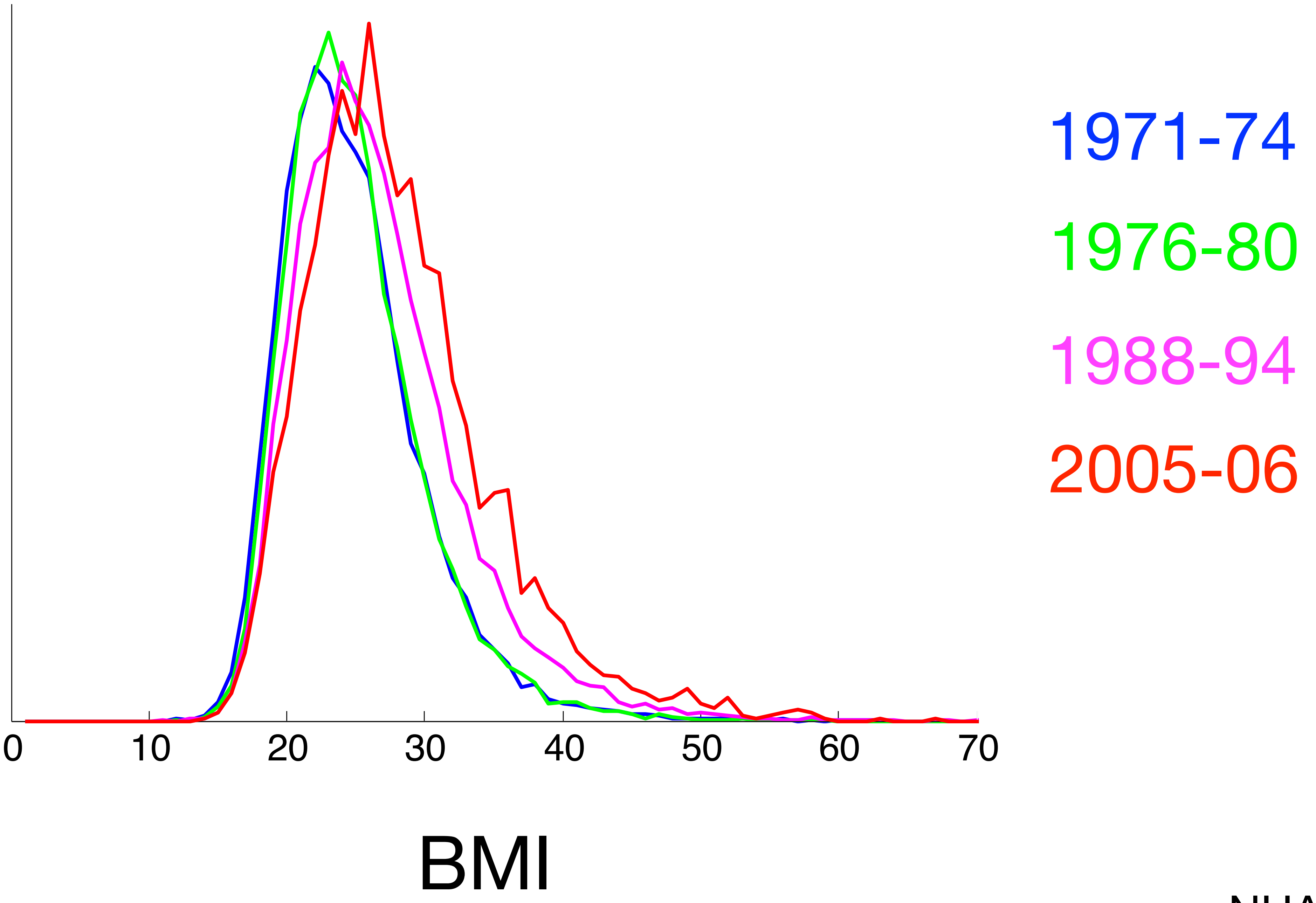
Excess food more than explains obesity epidemic

*Not an open problem



Hall, Guo, Dore, Chow. *PLoS One* (2009)

*But what explains BMI distribution?



NHANES data

Predicting intake in individuals

$$\rho \frac{dM}{dt} = I \ - \ \epsilon(M - M_0)$$

Hall and Chow, 2011

Predicting intake in individuals

$$\epsilon(M - M_0) \quad + \quad \rho\frac{dM}{dt} = I$$

Hall and Chow, 2011

Predicting intake in individuals

use linear regression

$$\epsilon(M - M_0) \quad + \quad \rho\frac{dM}{dt} = I$$

Hall and Chow, 2011

Predicting intake in individuals

use linear regression

$$\epsilon(M - M_0) \quad + \quad \rho\frac{dM}{dt} = I$$

$$\text{var}(I) = \left(2\epsilon^2 + \frac{12\rho^2}{n(n^2-1)T^2} + \frac{12\epsilon\rho}{(n+1)T^2}\right)\text{var}(M)$$

Hall and Chow, 2011

Predicting intake in individuals

use linear regression

$$\epsilon(M - M_0) \quad + \quad \rho\frac{dM}{dt} = I$$

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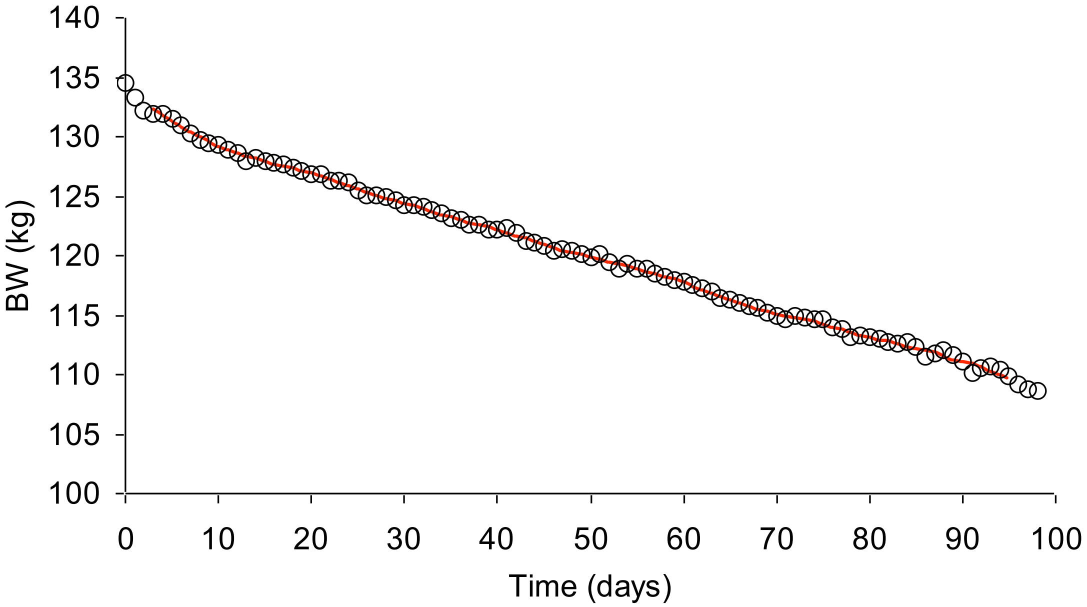

Hall and Chow, 2011

Predicting intake in individuals

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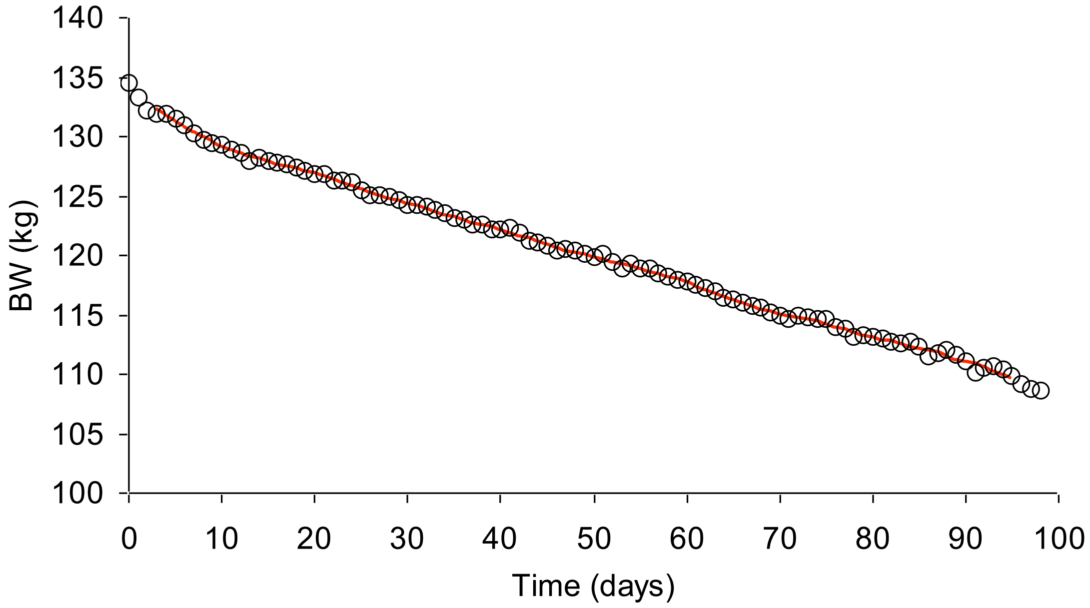
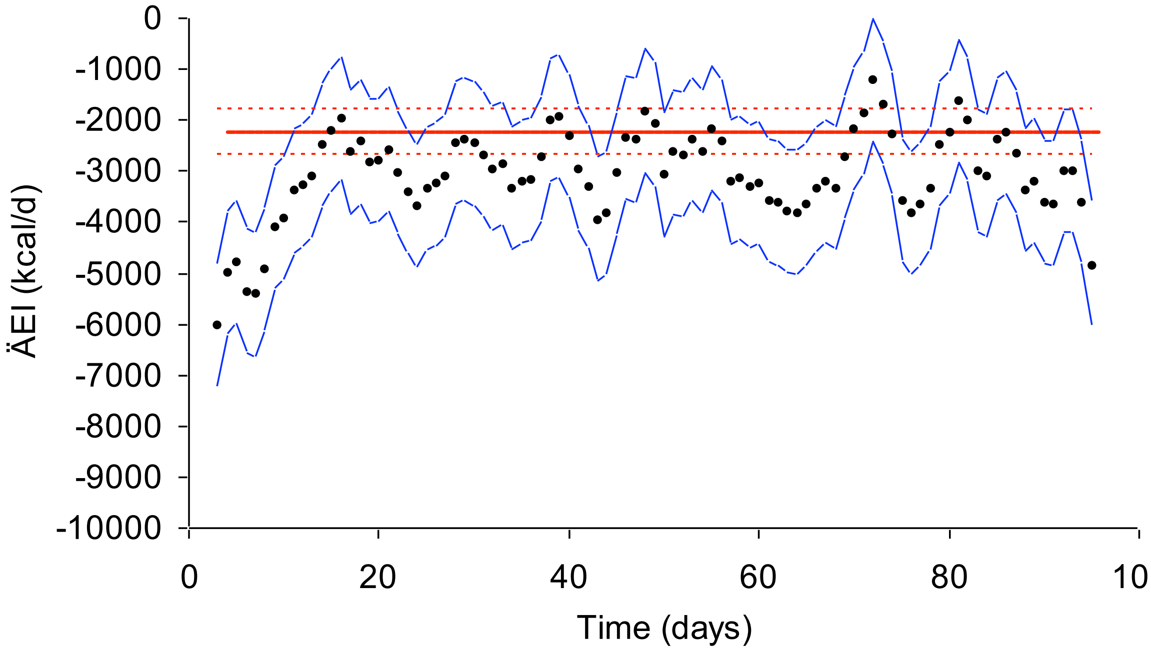




Hall and Chow, 2011

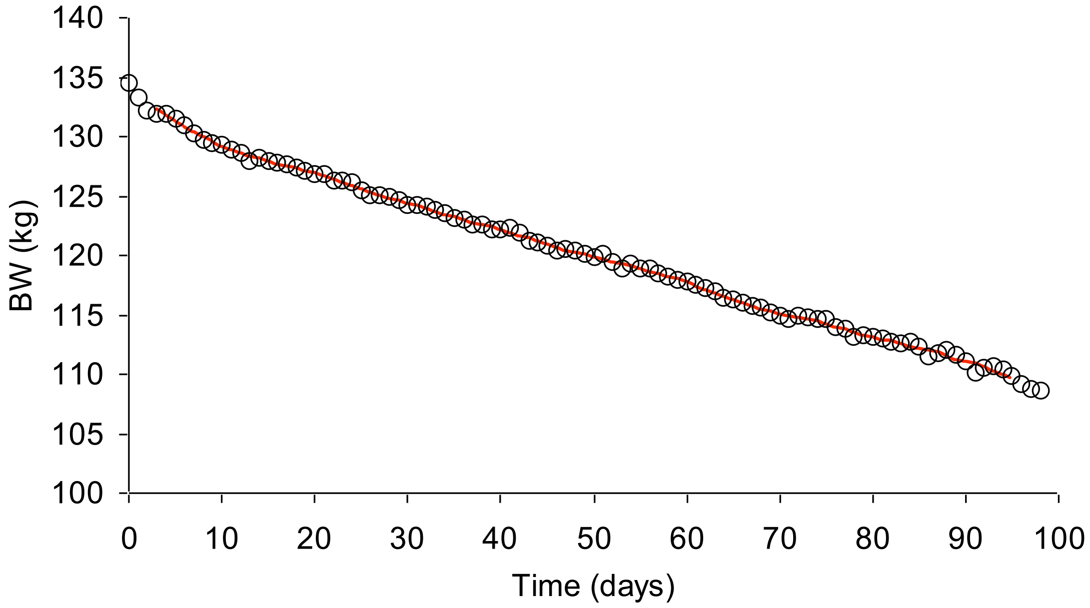
Predicting intake in individuals

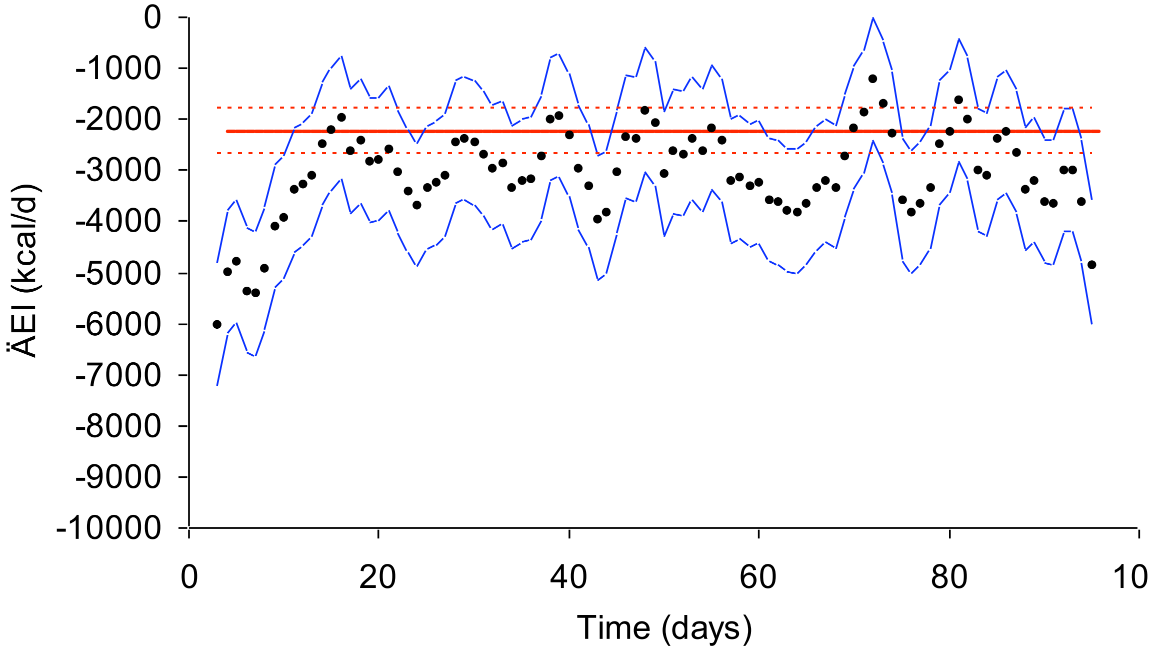
use linear regression

$$\epsilon(M - M_0) \quad + \quad \rho\frac{dM}{dt} = I$$

*Need to estimate initial intake

$$\mathrm{var}(I) = \left(2\epsilon^2 + \frac{12\rho^2}{n(n^2-1)T^2} + \frac{12\epsilon\rho}{(n+1)T^2}\right)\mathrm{var}(M)$$





Hall and Chow, 2011

*How do we model children?

*How do we model children?

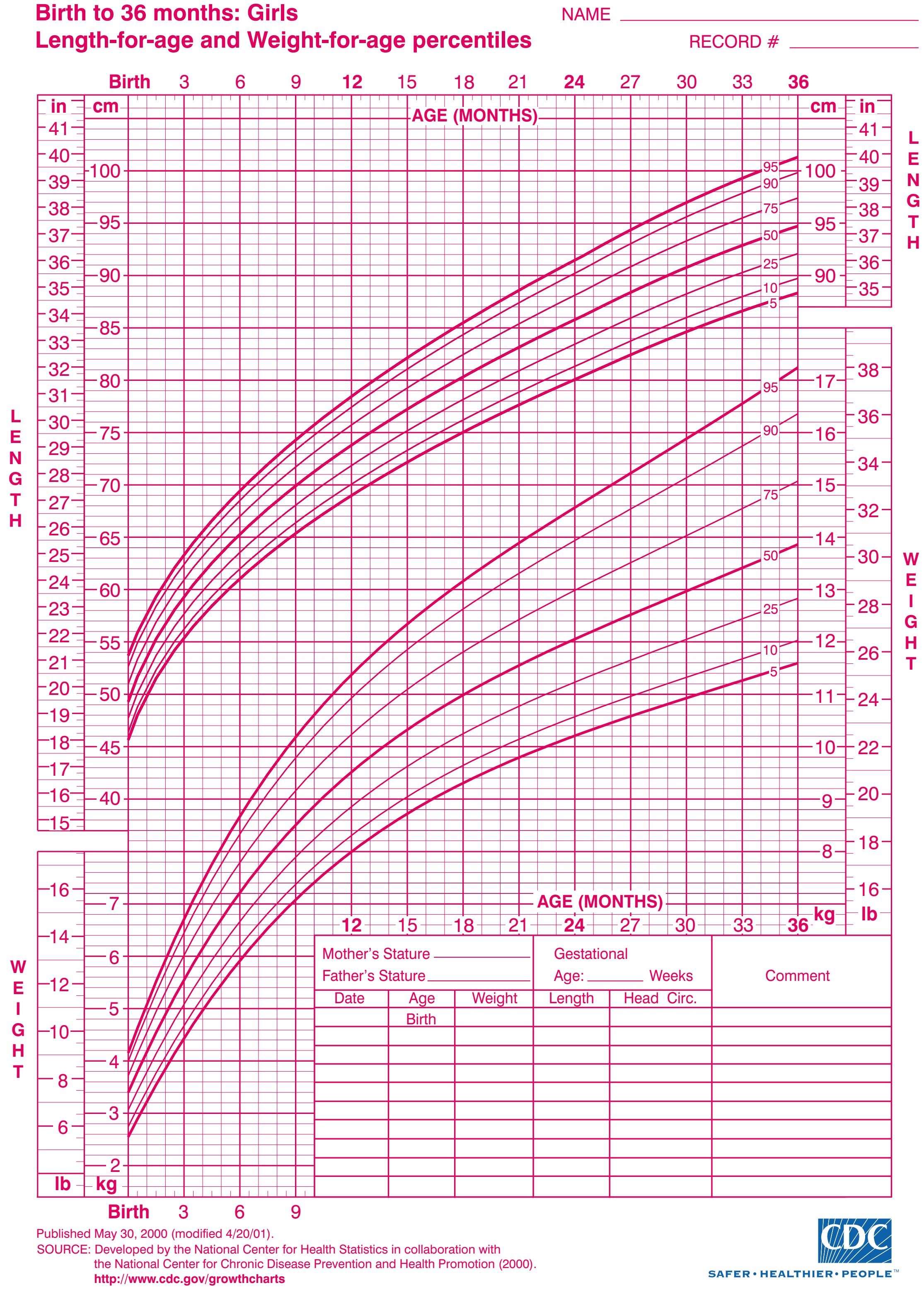
$$\rho \frac{dM}{dt} = I - \epsilon M - b$$?

*How do we model children?

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$?

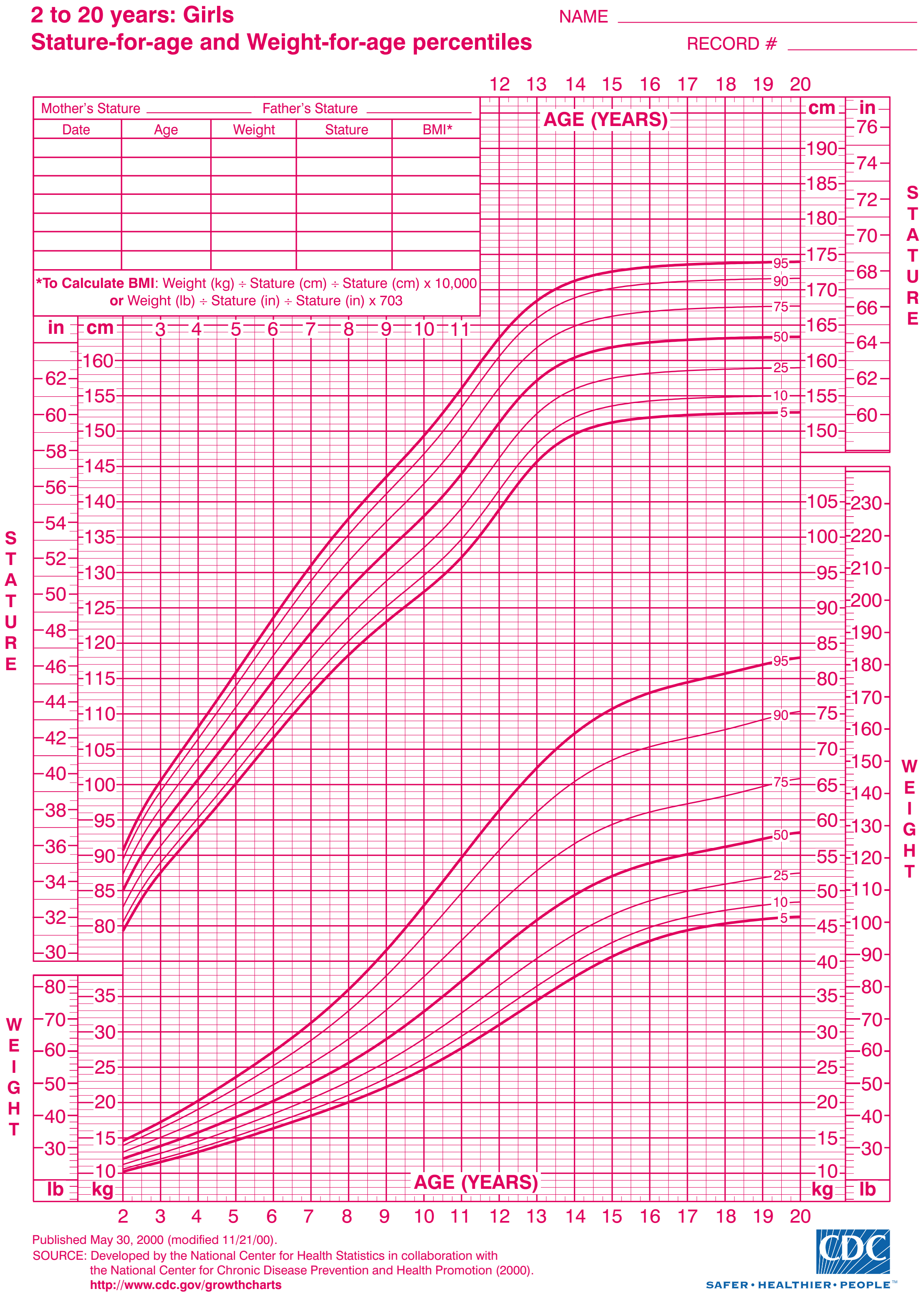
Hard because children grow

Growth is nonlinear



Birth to 36 months: Girls
Length-for-age and Weight-for-age percentiles

Published May 30, 2000 (modified 4/20/01).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts



2 to 20 years: Girls
Stature-for-age and Weight-for-age percentiles

Published May 30, 2000 (modified 11/21/00).
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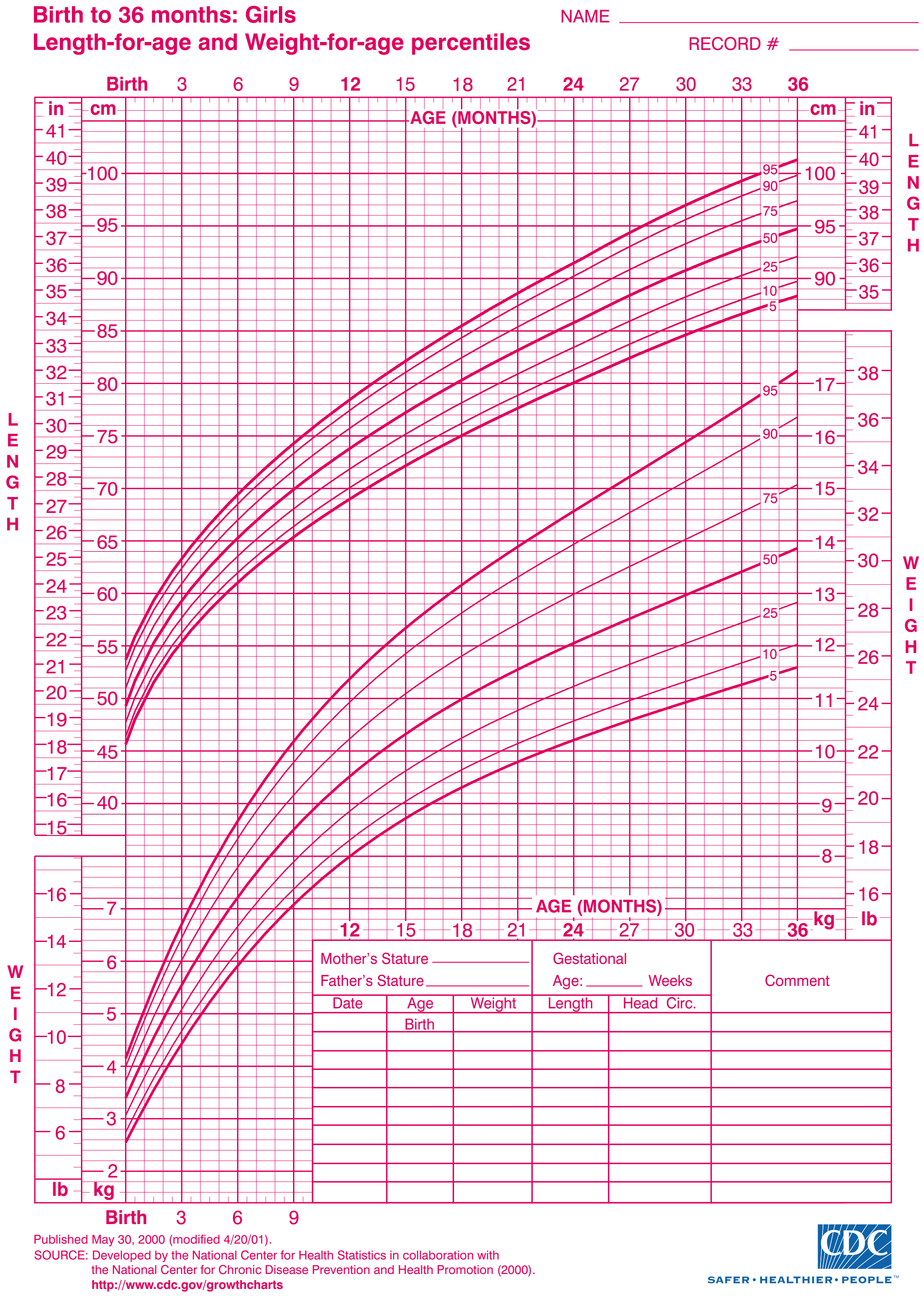
http://www.cdc.gov/growthcharts

Growth is nonlinear

moving target


Birth to 36 months: Girls
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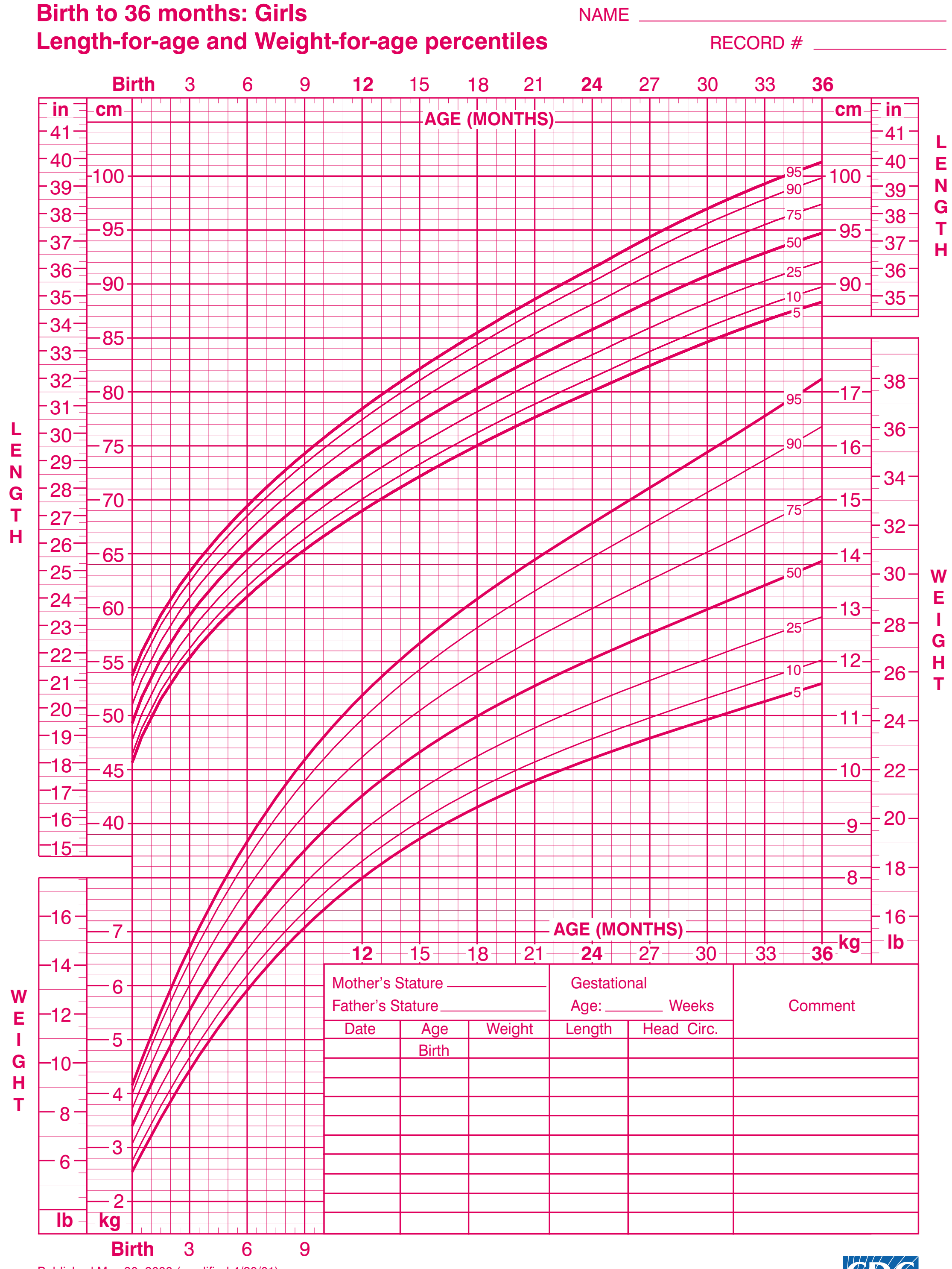

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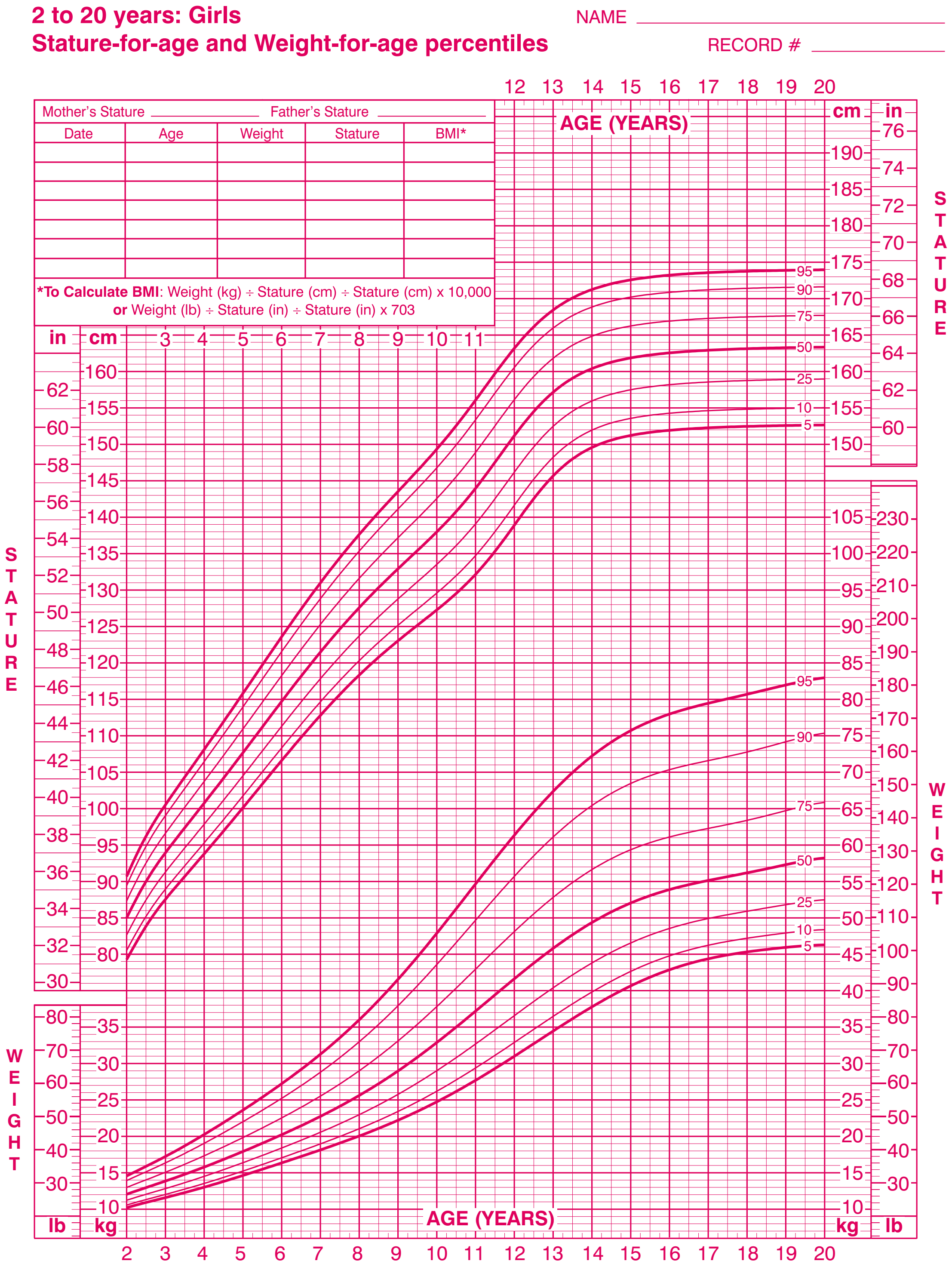
CDC
SAFER • HEALTHIER • PEOPLE™



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CDC
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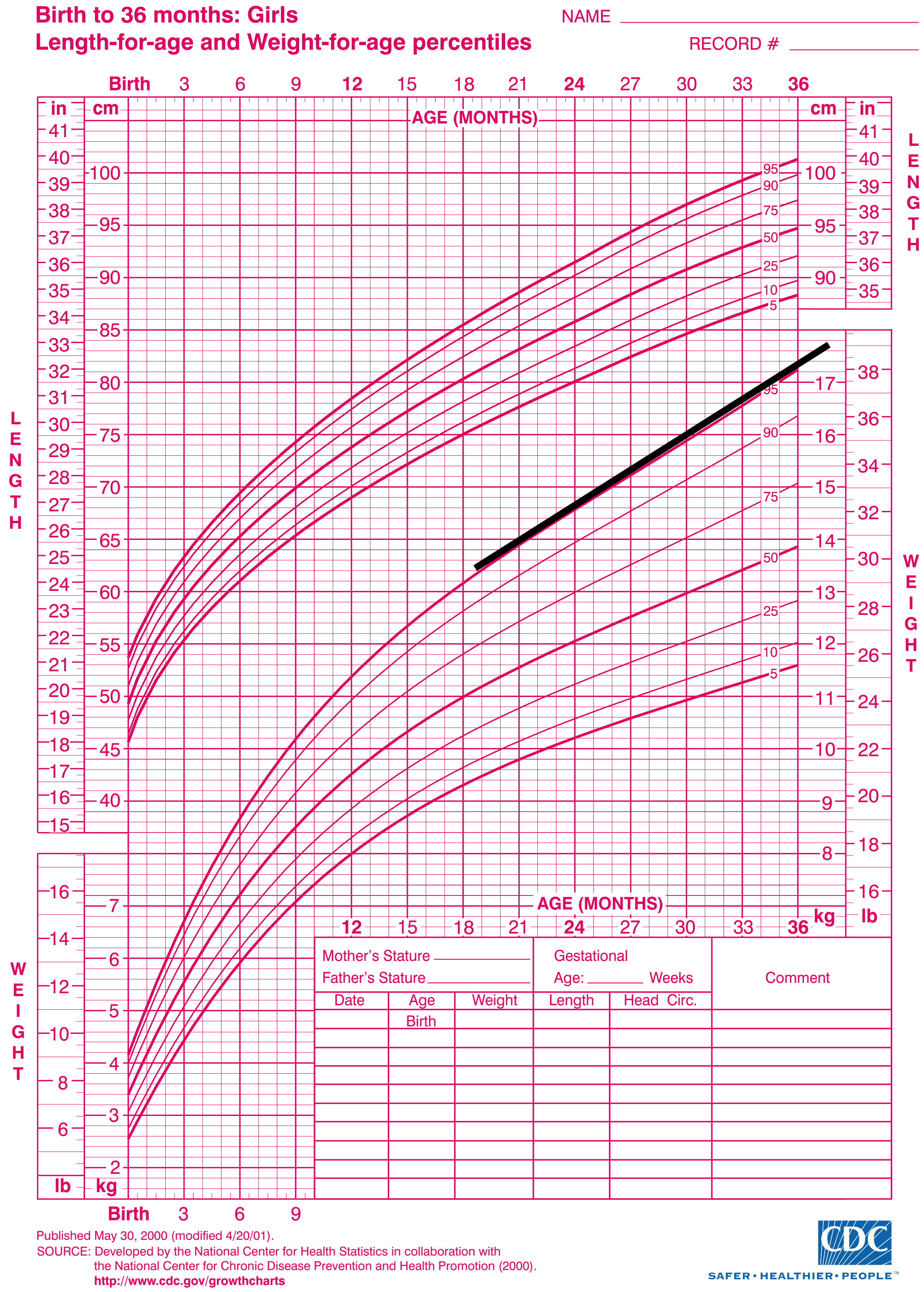
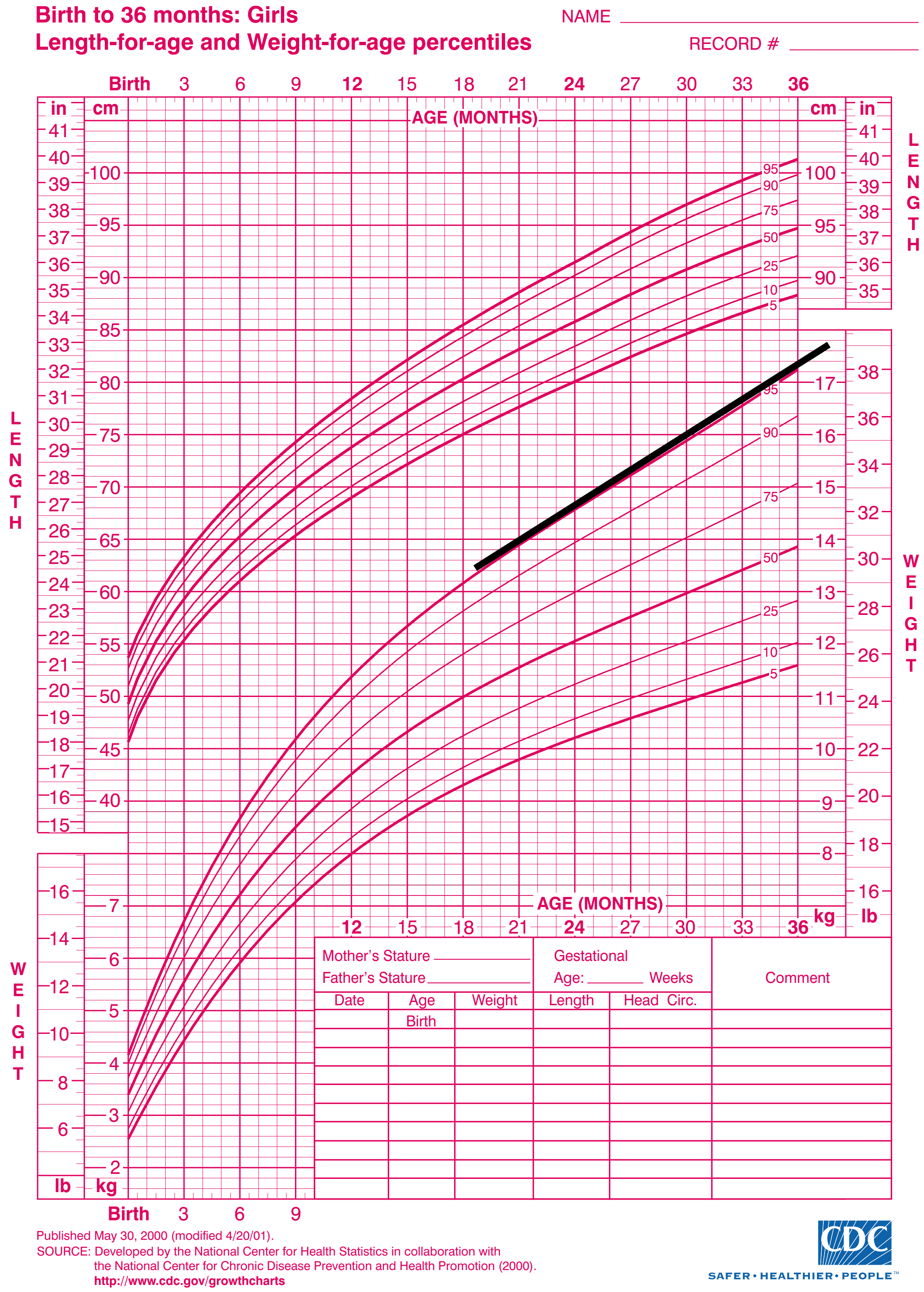
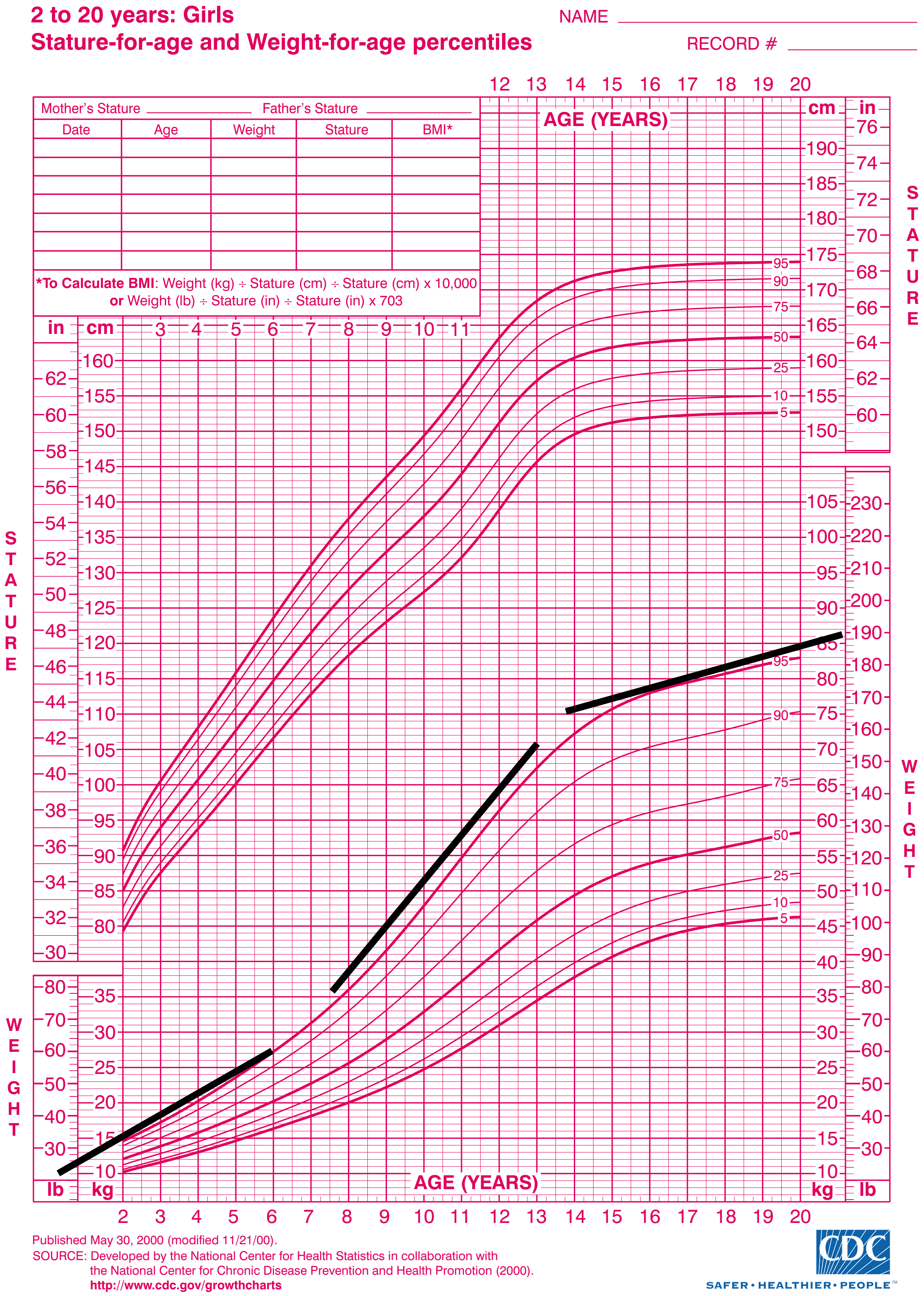
Growth is nonlinear



Growth is piecewise linear





Growth depends on history

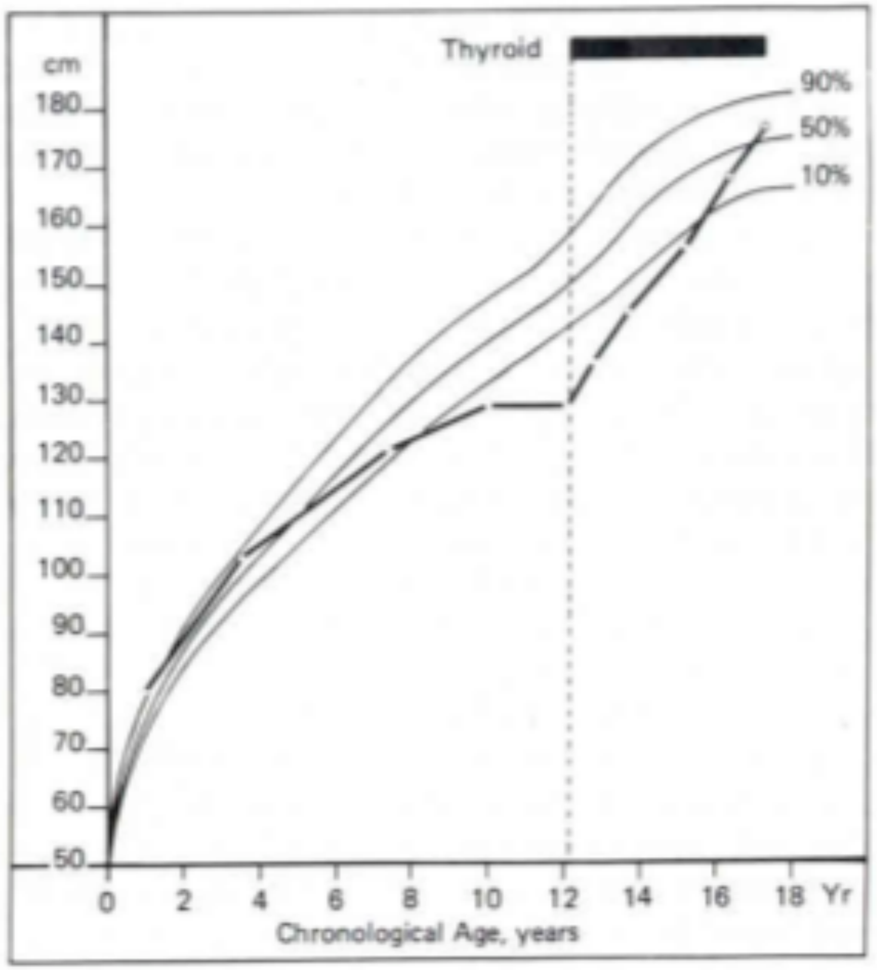


FIG. 2. Height (growth distance) chart of a boy with acquired hypothyroidism, diagnosed at the age of 12 years and followed for a period of 6 years under substitution therapy with thyroid extract (from Prader, A., Tanner, J.M. and von Harnack, C.A., Catch-up growth following illness or starvation. An example of developmental canalization in man. *Journal of Pediatrics*, **62**, 646 (1963) by permission of the publisher).

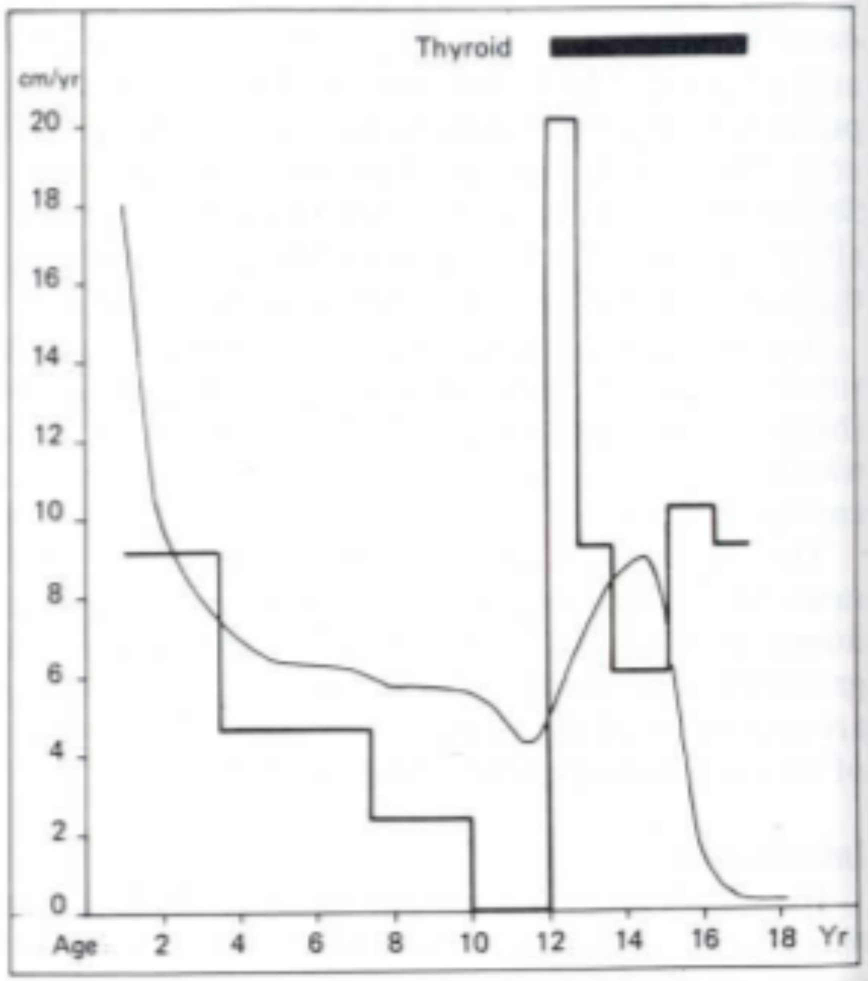
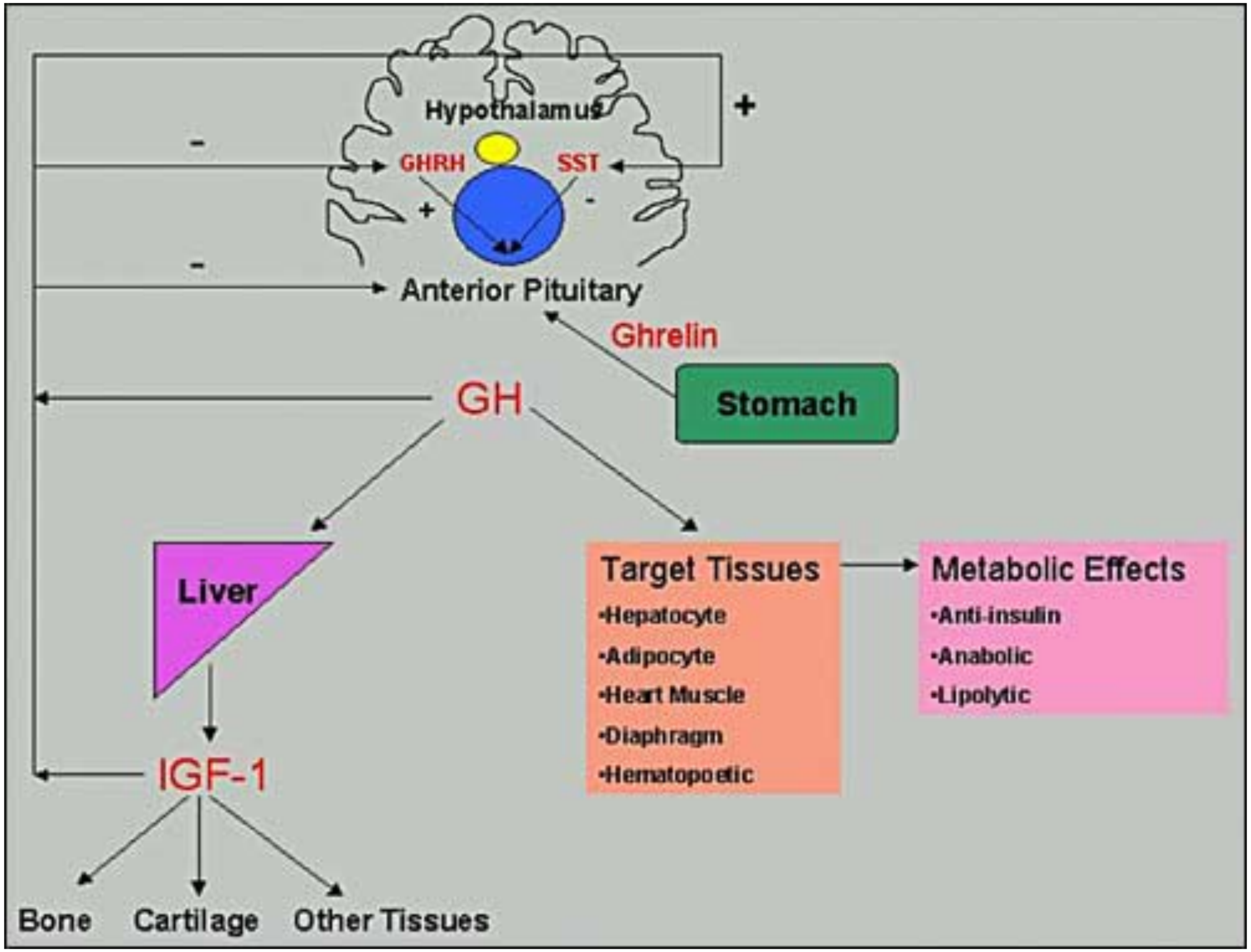


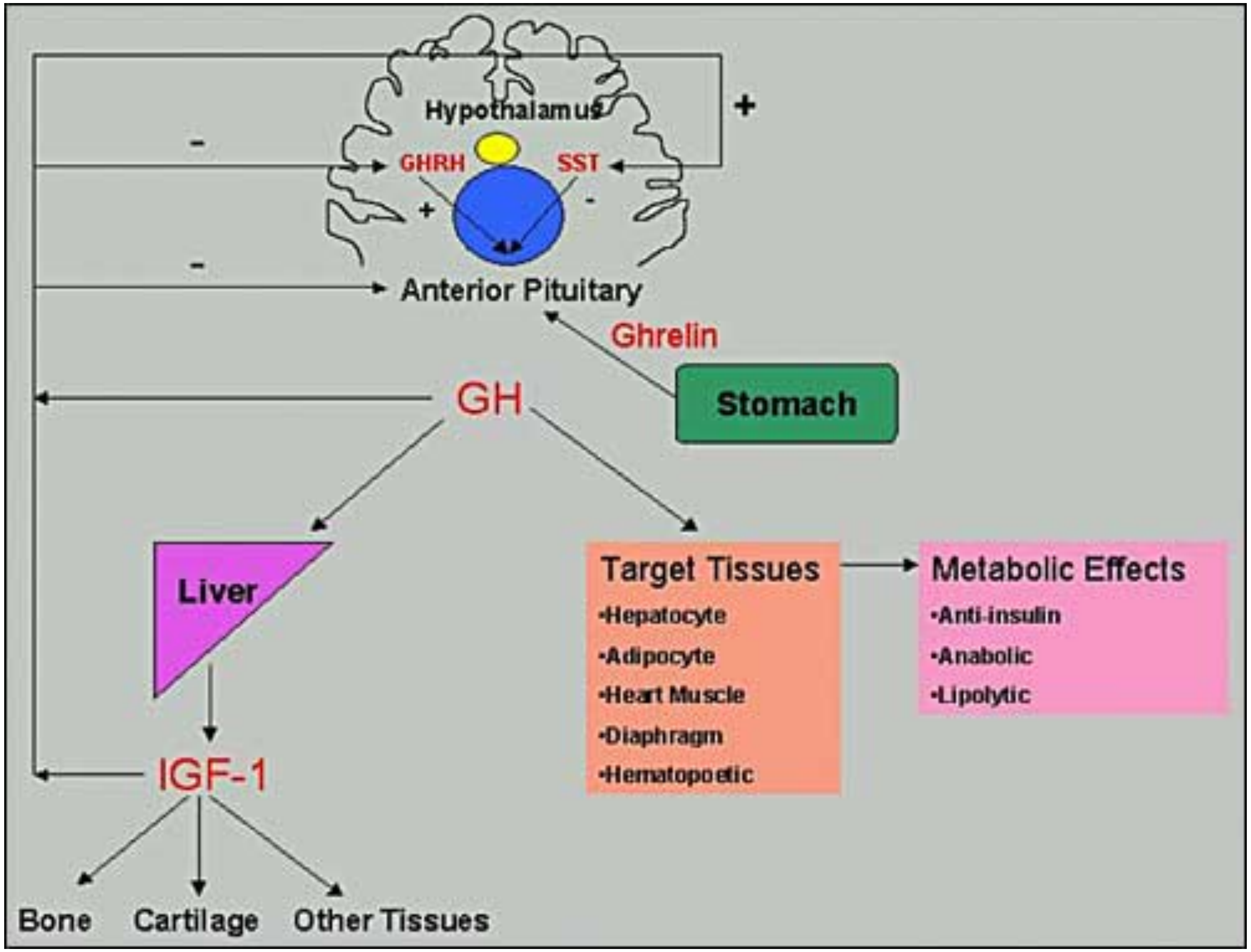
FIG. 4. Growth velocity chart of the same boy as in Figs 2 and 3, plotted in a stepwise fashion.

"Catch-up" growth

Can we model growth?

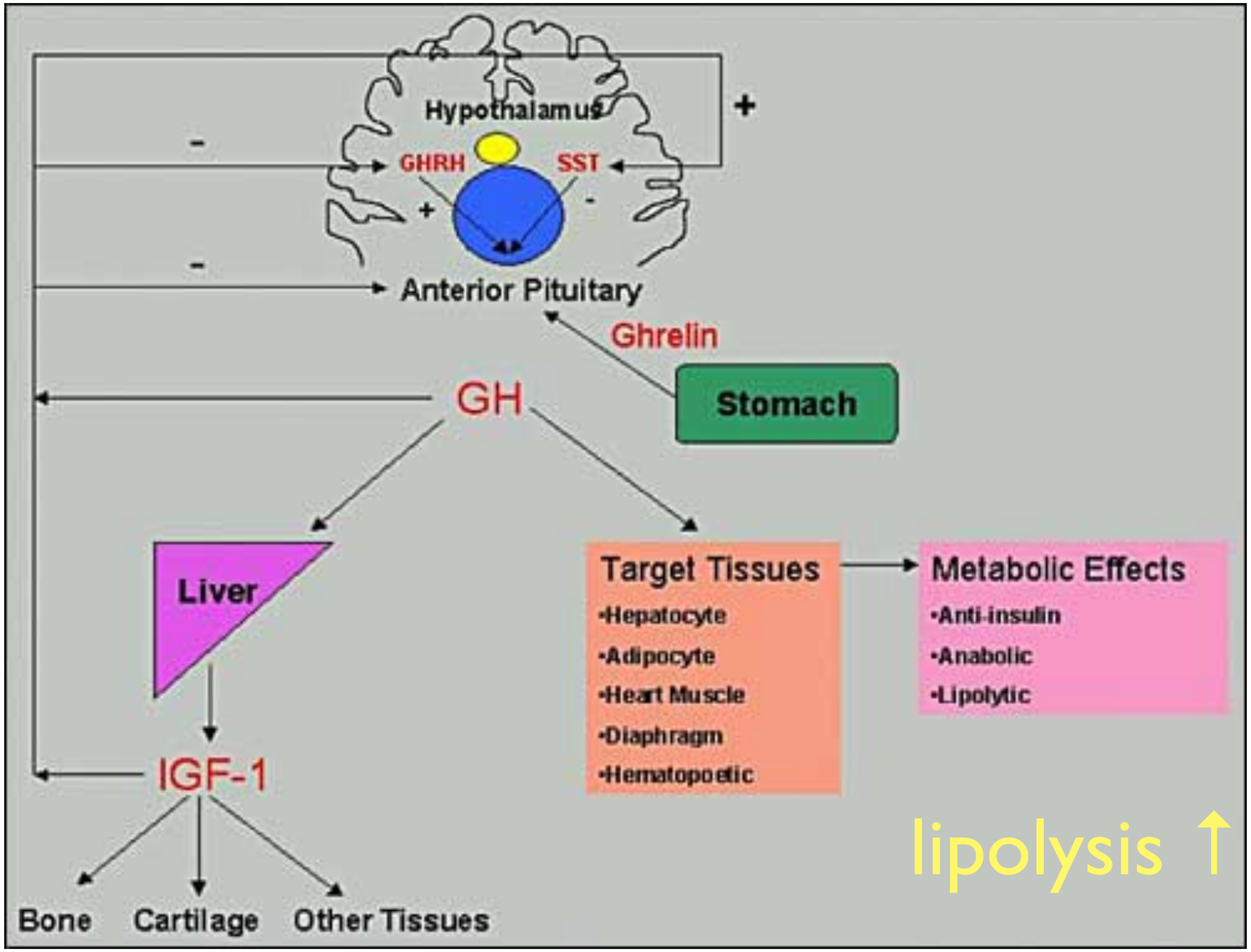


Can we model growth?



Growth hormones ↑

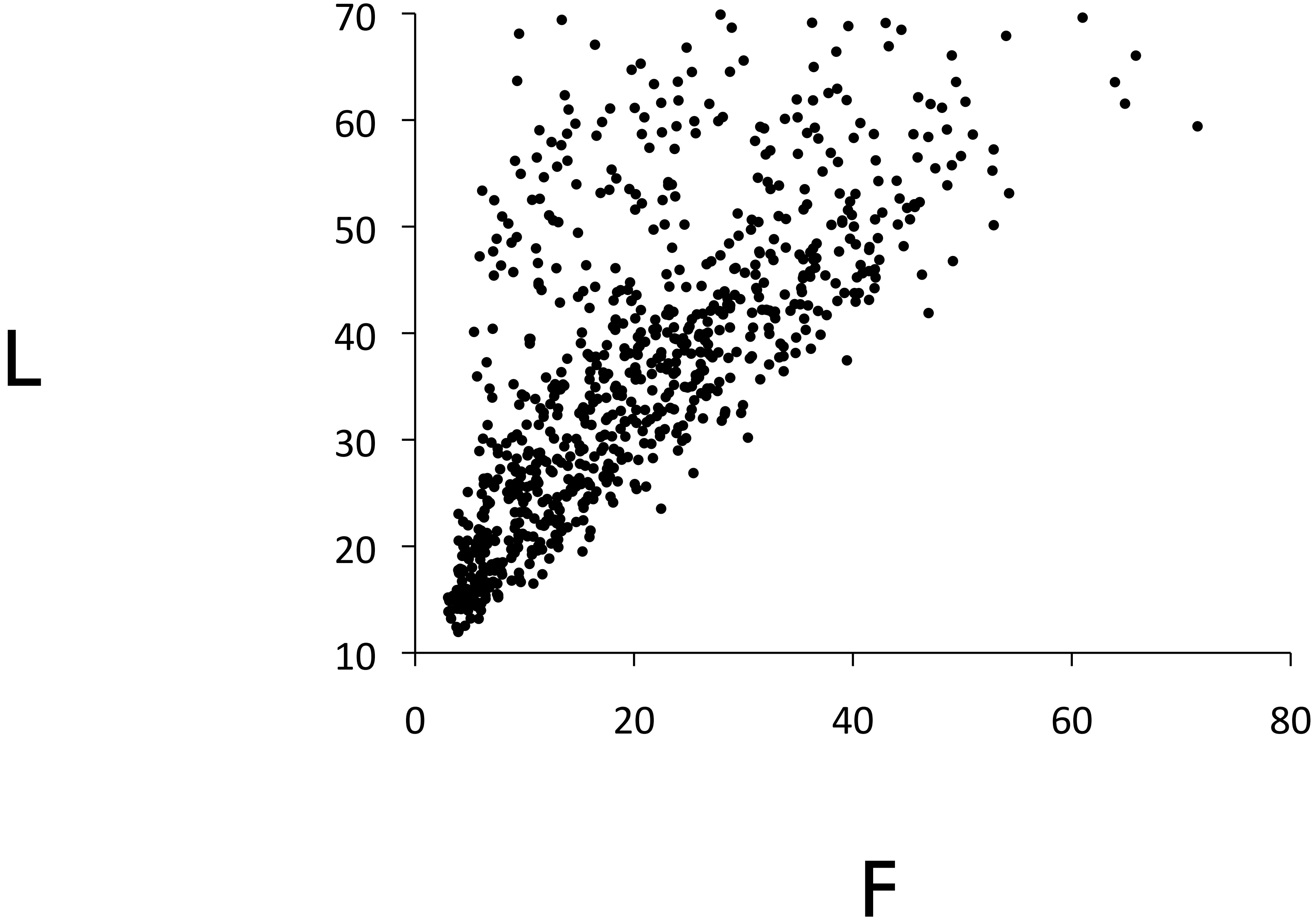
Can we model growth?



lipolysis ↑ growth ↑

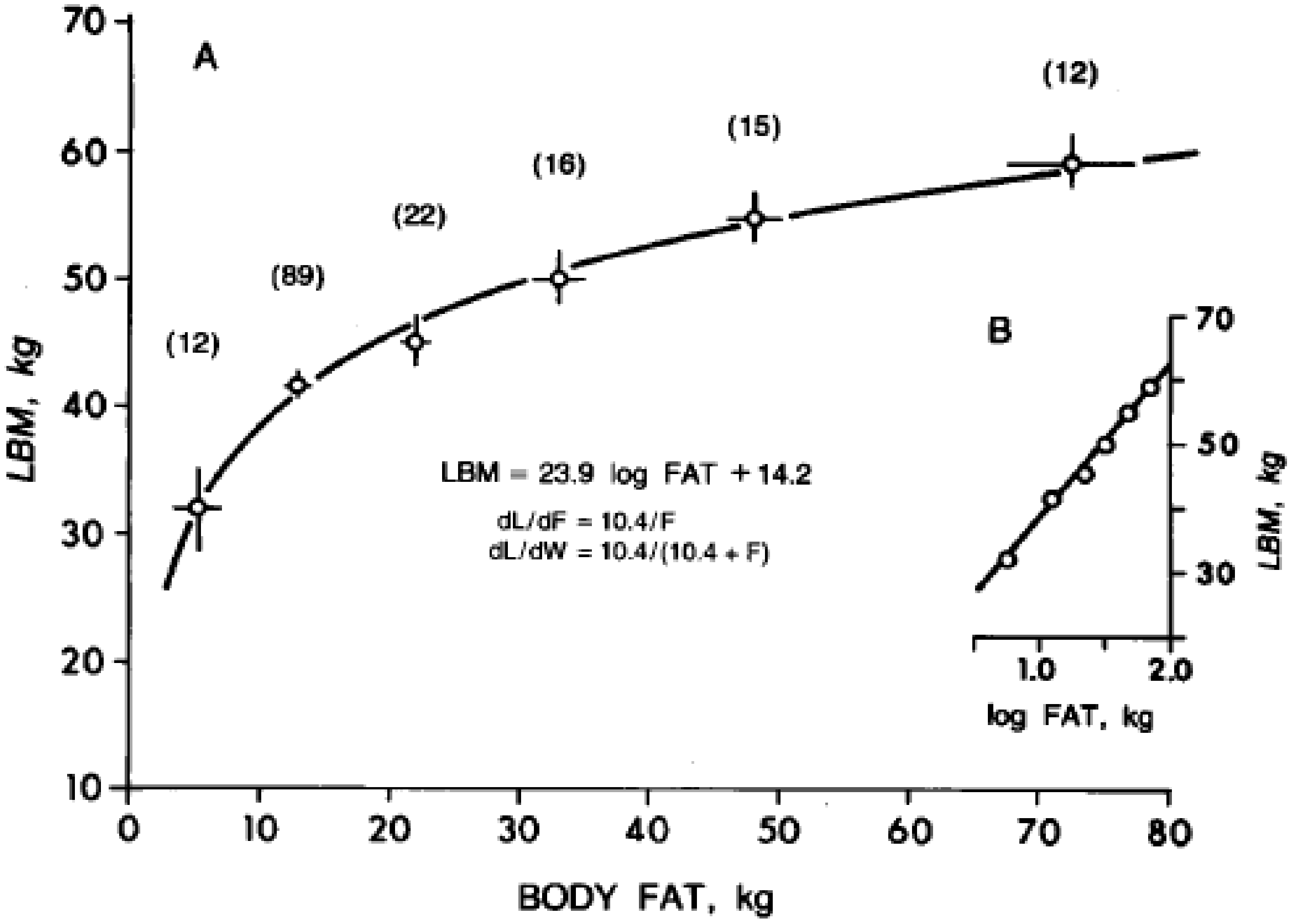
Growth hormones ↑

Viva data (N. Butte)



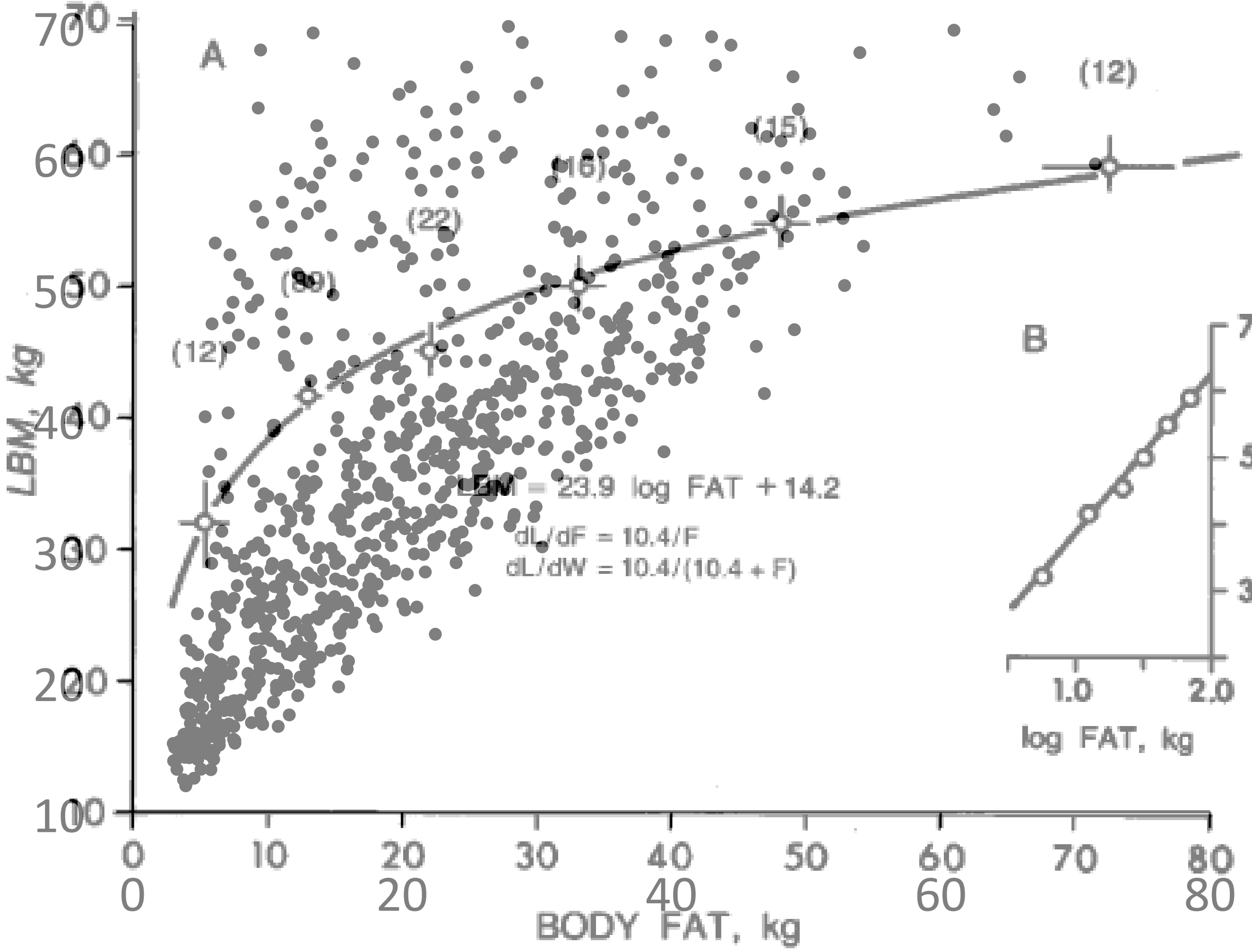
Viva data (N. Butte)

L



F

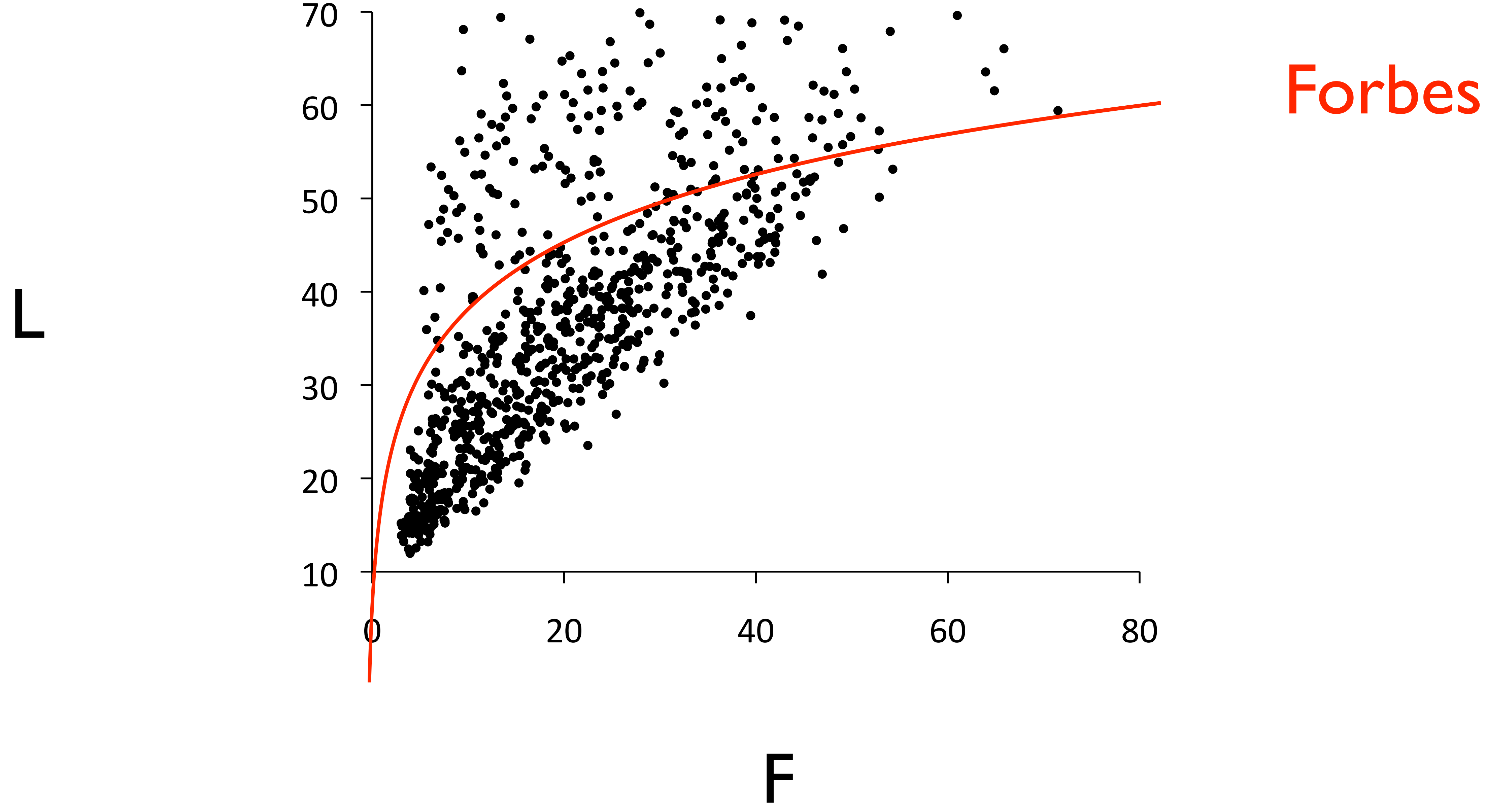
Viva data (N. Butte)



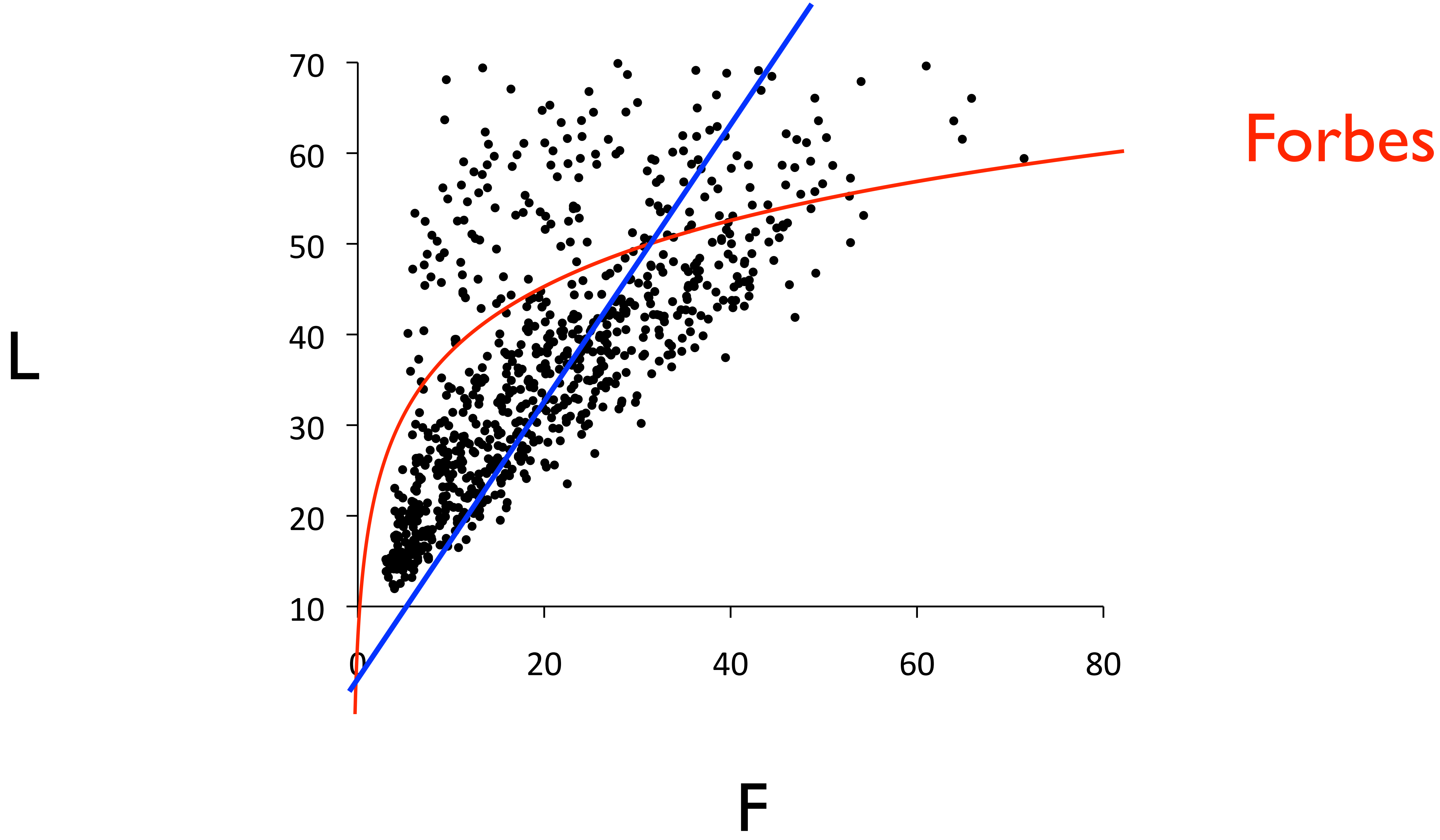
L

F

Viva data (N. Butte)



Viva data (N. Butte)



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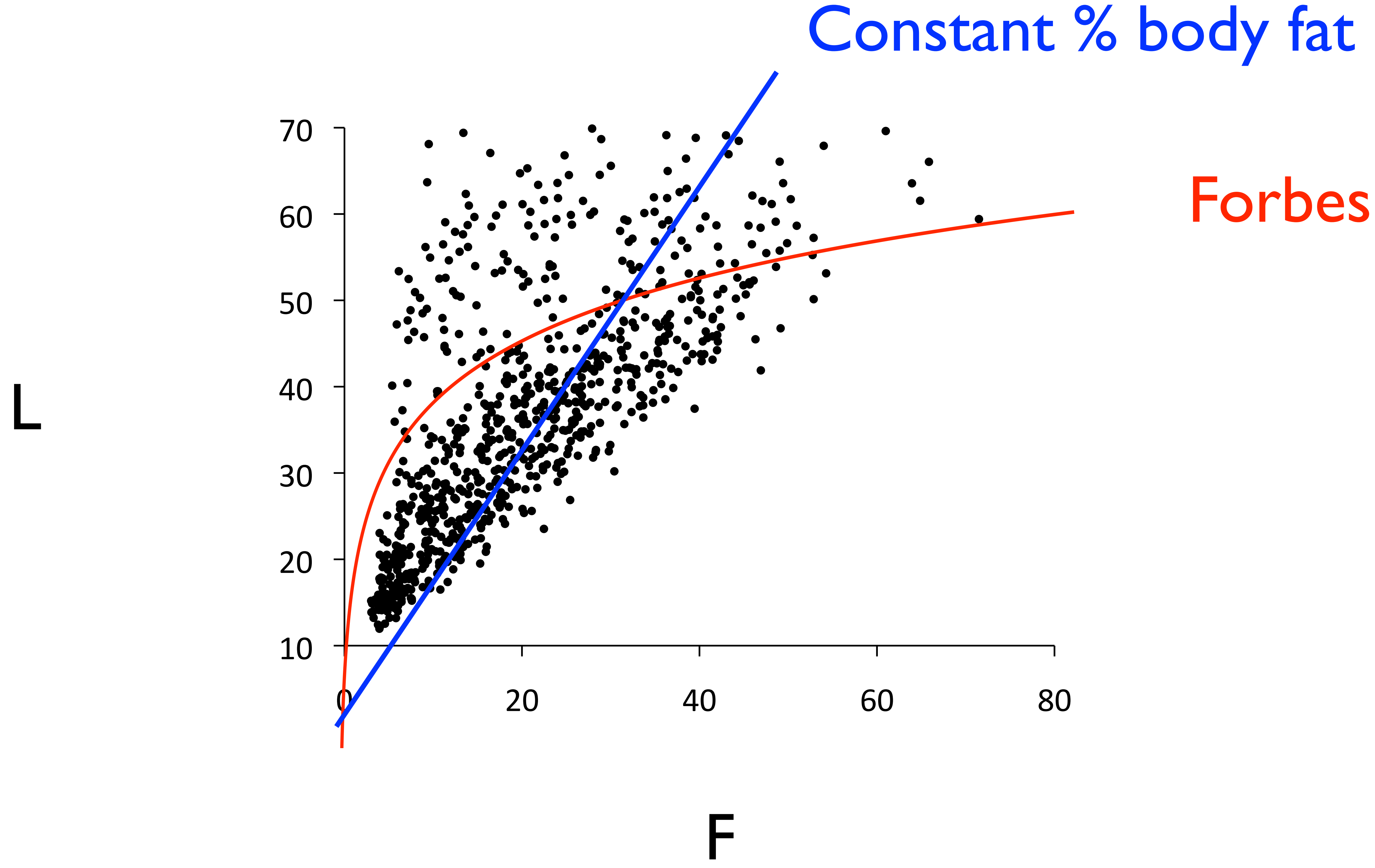
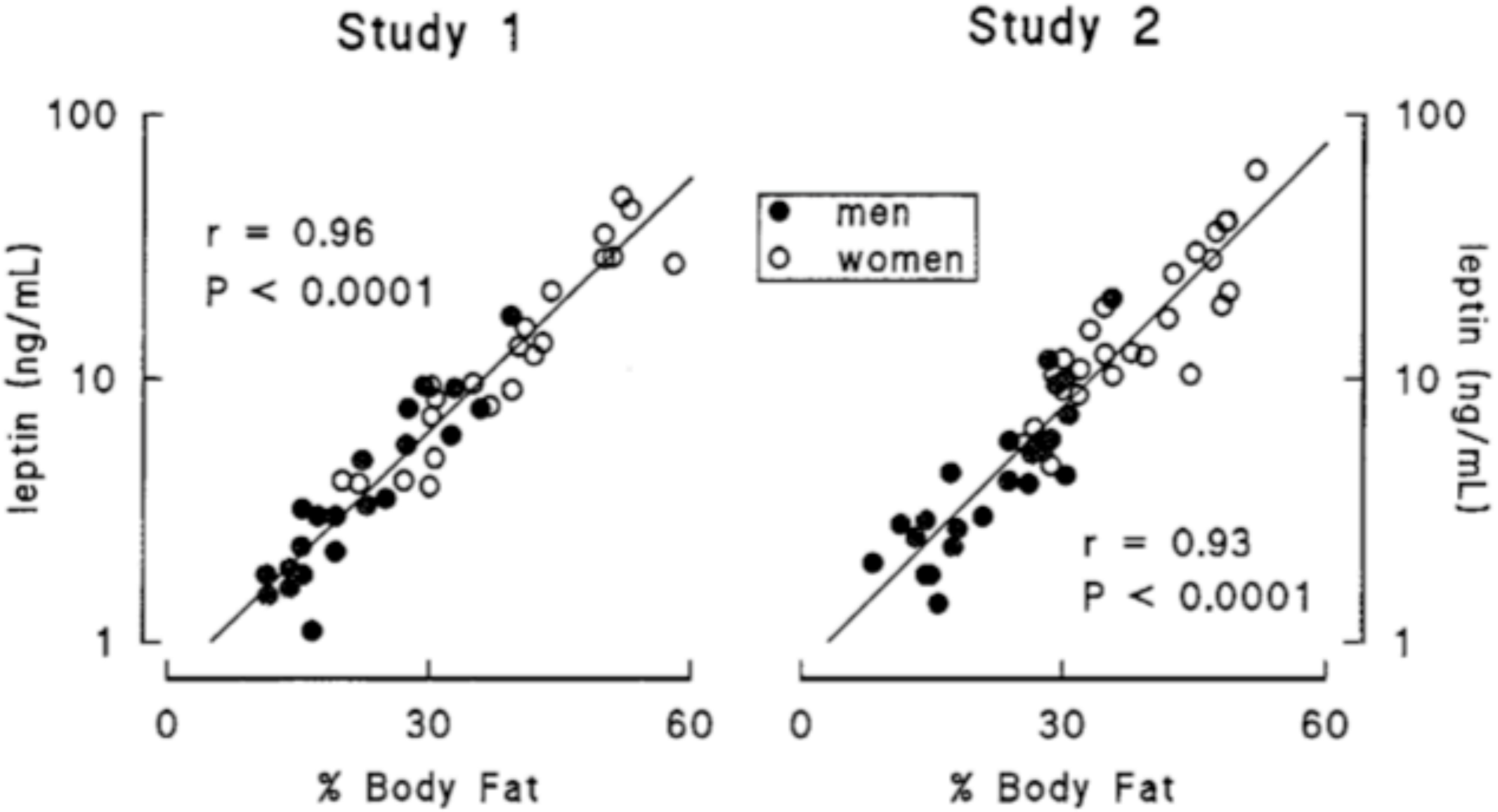


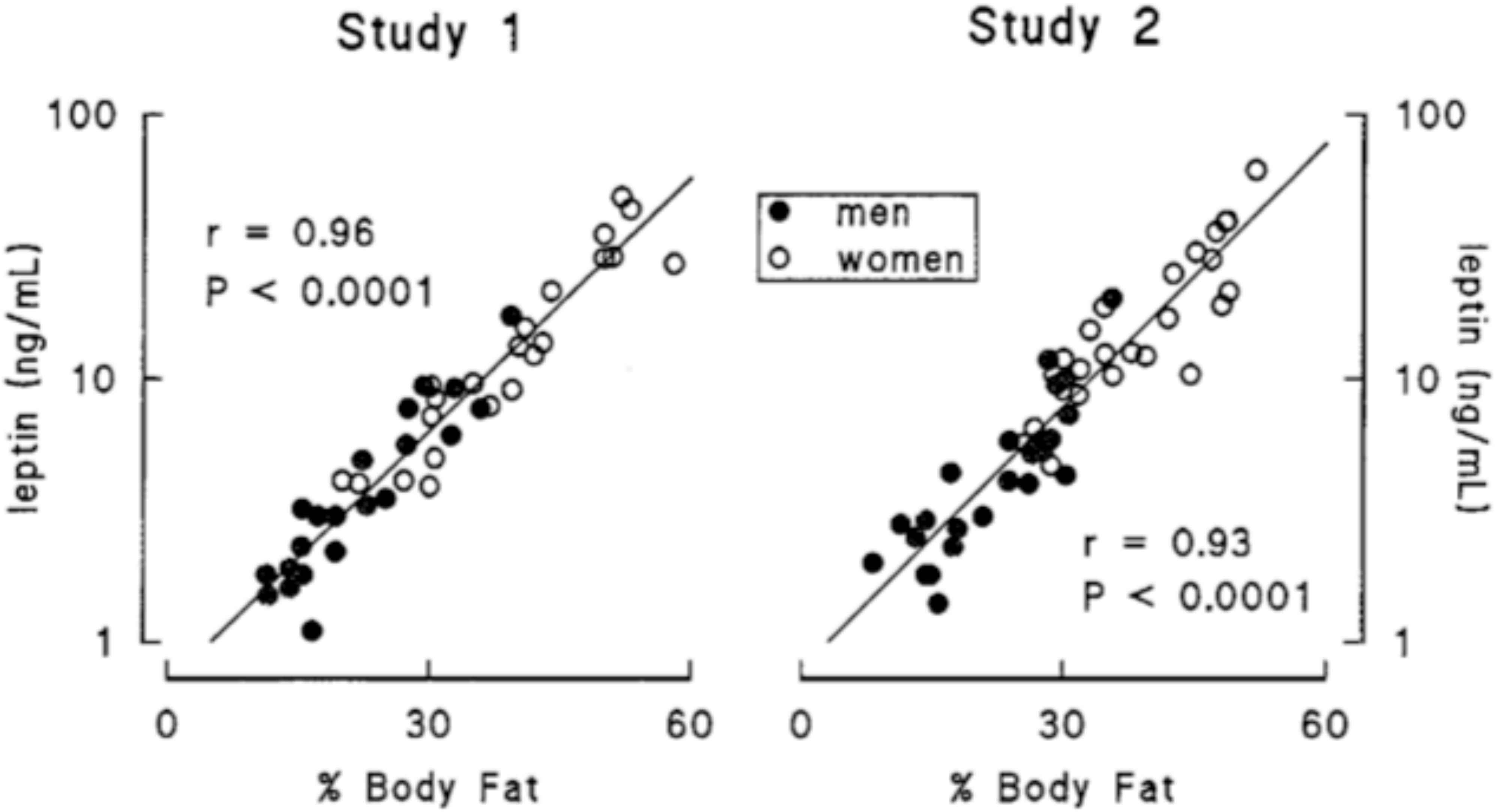
Tuesday, July 12, 2011

Leptin scales with body fat percentage



Jensen et al. Obesity Research (1999)

Leptin scales with body fat percentage



Jensen et al. Obesity Research (1999)

Low leptin - eat more, high leptin - eat less

Growth model

$$\begin{aligned}
\rho_F \dot{F} &= (1-p)(I-E) - g \\
\rho_L \dot{L} &= p(I-E) + g \\
\dot{I} &= h\left(\frac{F}{L}\right)
\end{aligned}$$

Growth model

$$\begin{aligned}
\rho_F \dot{F} &= (1-p)(I-E) - g \\
\rho_L \dot{L} &= p(I-E) + g \\
\dot{I} &= h\left(\frac{F}{L}\right)
\end{aligned}$$

growth hormones

Growth model

$$\begin{aligned} \rho_F \dot{F} &= (1-p)(I-E) - g \\ \rho_L \dot{L} &= p(I-E) + g \\ \dot{I} &= h\left(\frac{F}{L}\right) \end{aligned}$$

growth hormones

Leptin signal

Growth model

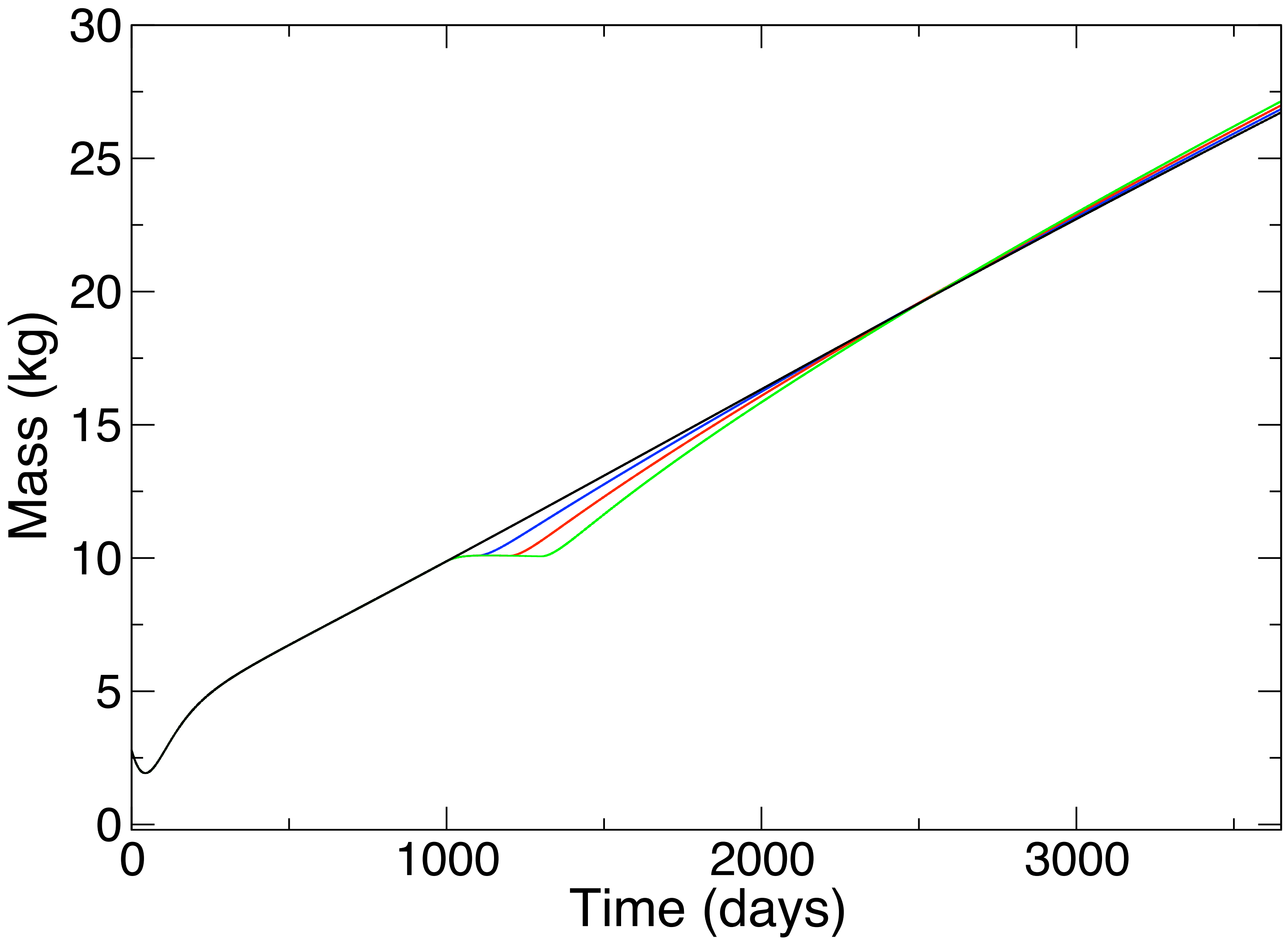
$$\begin{aligned} \rho_F \dot{F} &= (1-p)(I-E) - g \\ \rho_L \dot{L} &= p(I-E) + g \\ \dot{I} &= h\left(\frac{F}{L}\right) \end{aligned}$$

growth hormones

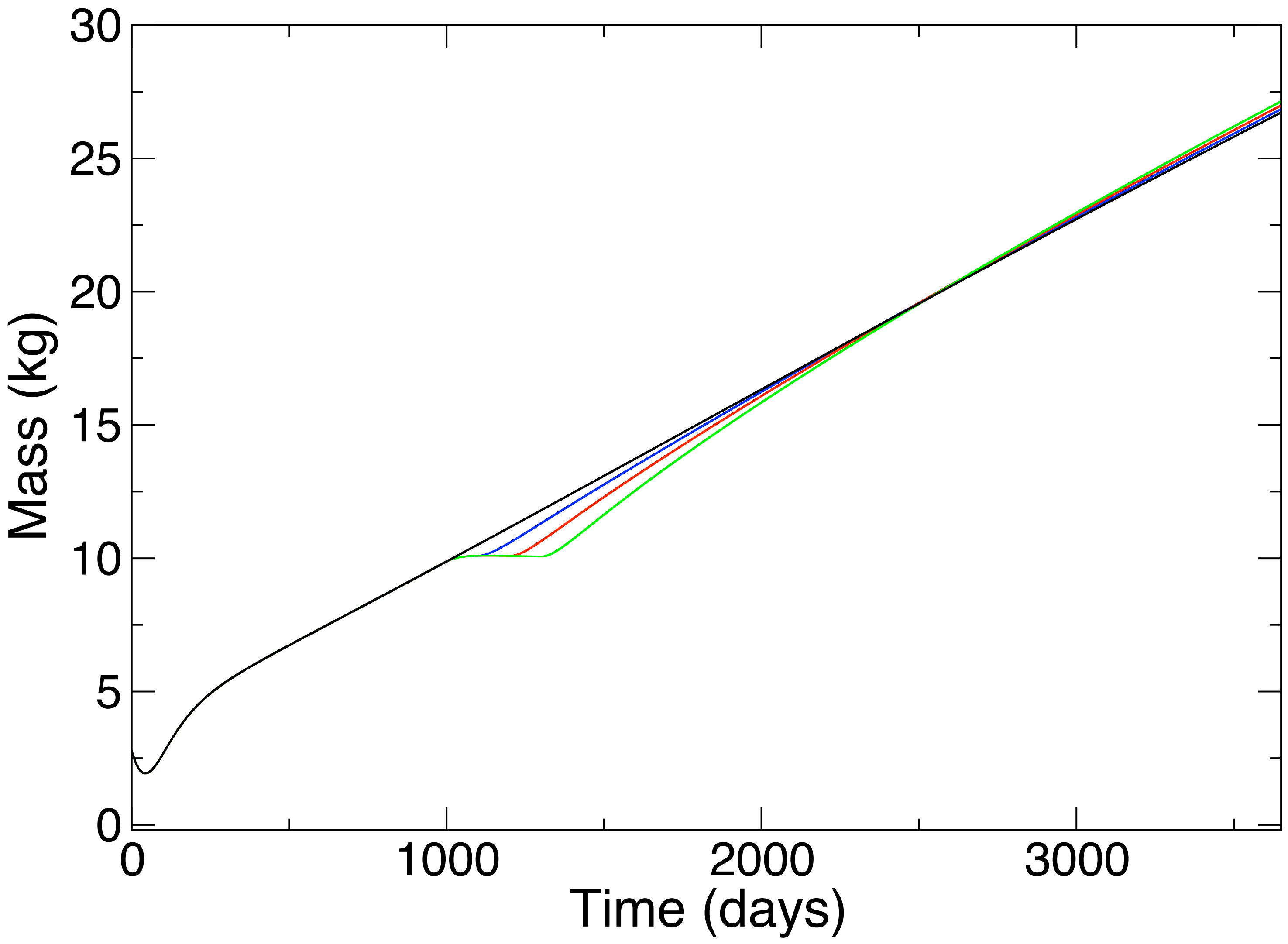
Leptin signal

Eat more when % body fat below threshold

Numerical simulation

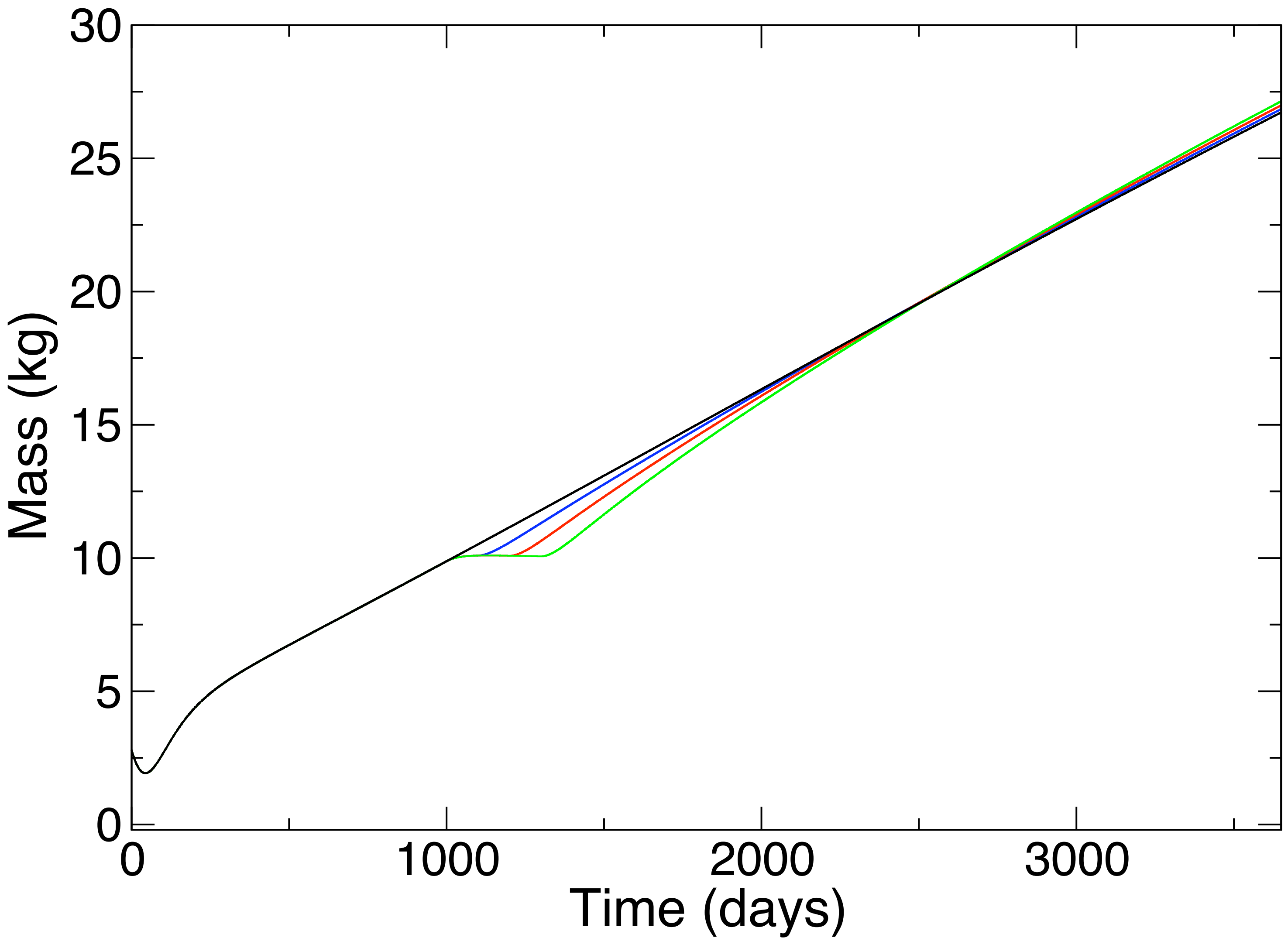


Numerical simulation



*Is growth model correct?

Numerical simulation



*Is growth model correct? *Will it ever be published?

Asymptotic solution

$$\begin{aligned} F &= \frac{\delta - g}{\rho_F} t - \frac{\delta}{\delta - g} \ln t + \phi_F(0) \\ L &= \frac{g}{\rho_L} t + \frac{\rho_F \delta}{\rho_L(\delta - g)} \ln t + \phi_L(0) \end{aligned}$$

$$I - E = \delta + \Delta(t)$$

Transients decay (i.e. catch up growth)

Linear growth model

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

Linear growth model

$$\rho\frac{dM}{dt} = I - \epsilon M - b$$

Cost of tissue deposition here

Linear growth model

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

Cost of tissue
deposition here

$$M = vt + M_0$$

Linear growth model

$$\rho \frac{dM}{dt} = I - \epsilon M - b$$

Cost of tissue deposition here

$$M = vt + M_0$$

Velocity

Linear growth model

$$\rho\frac{dM}{dt} = I - \epsilon M - b$$

Cost of tissue deposition here

$$M = vt + M_0$$

Velocity

$$I(t) = \epsilon vt + \rho v + \epsilon M_0 + b$$

Linear growth model

$$\rho\frac{dM}{dt} = I - \epsilon M - b$$

Cost of tissue deposition here

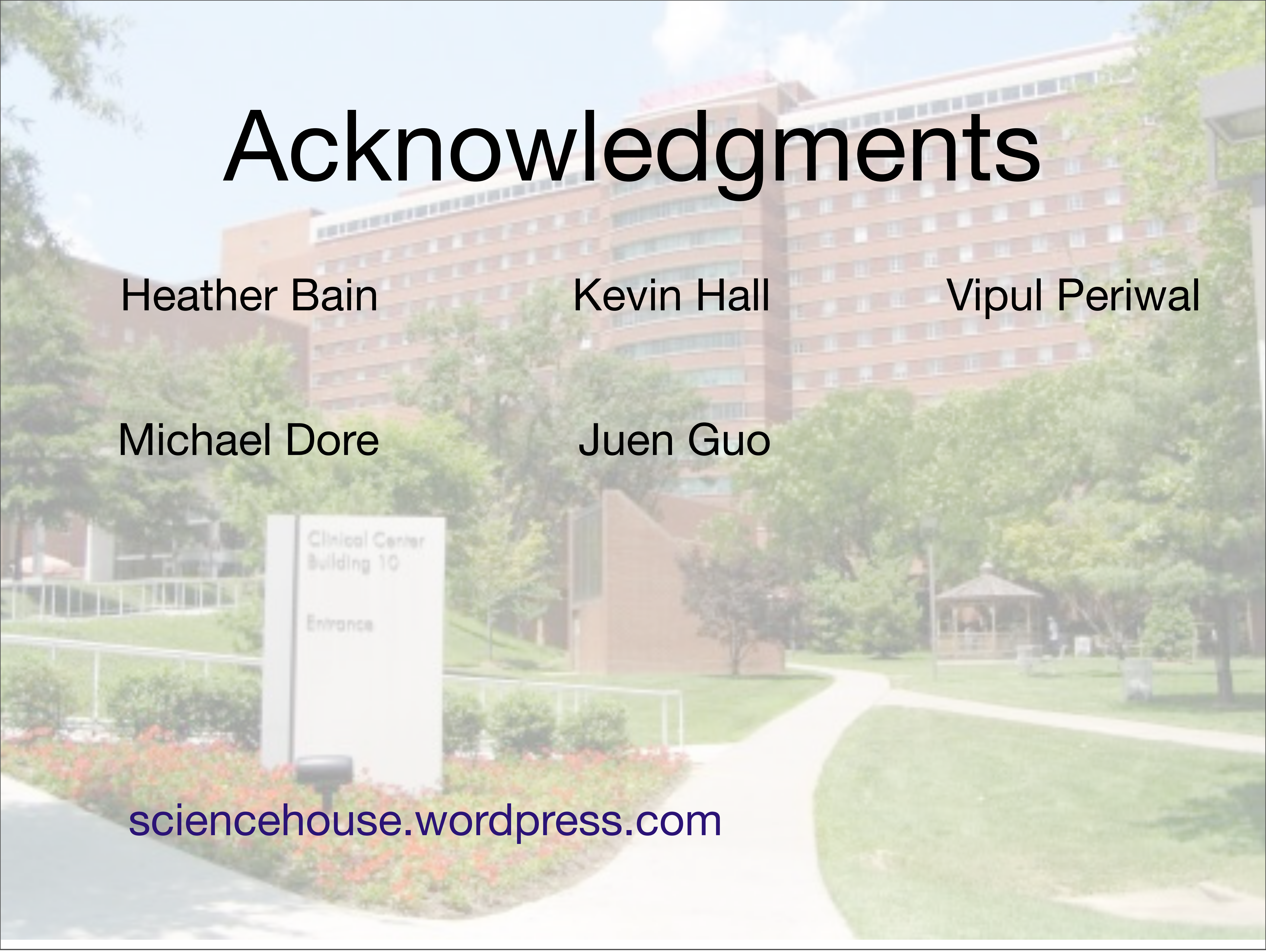
$$M = vt + M_0$$

Velocity

$$\boxed{I(t) = \epsilon vt + \rho v + \epsilon M_0 + b}$$

Predicted intake

Acknowledgments



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Michael Dore Juen Guo

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