

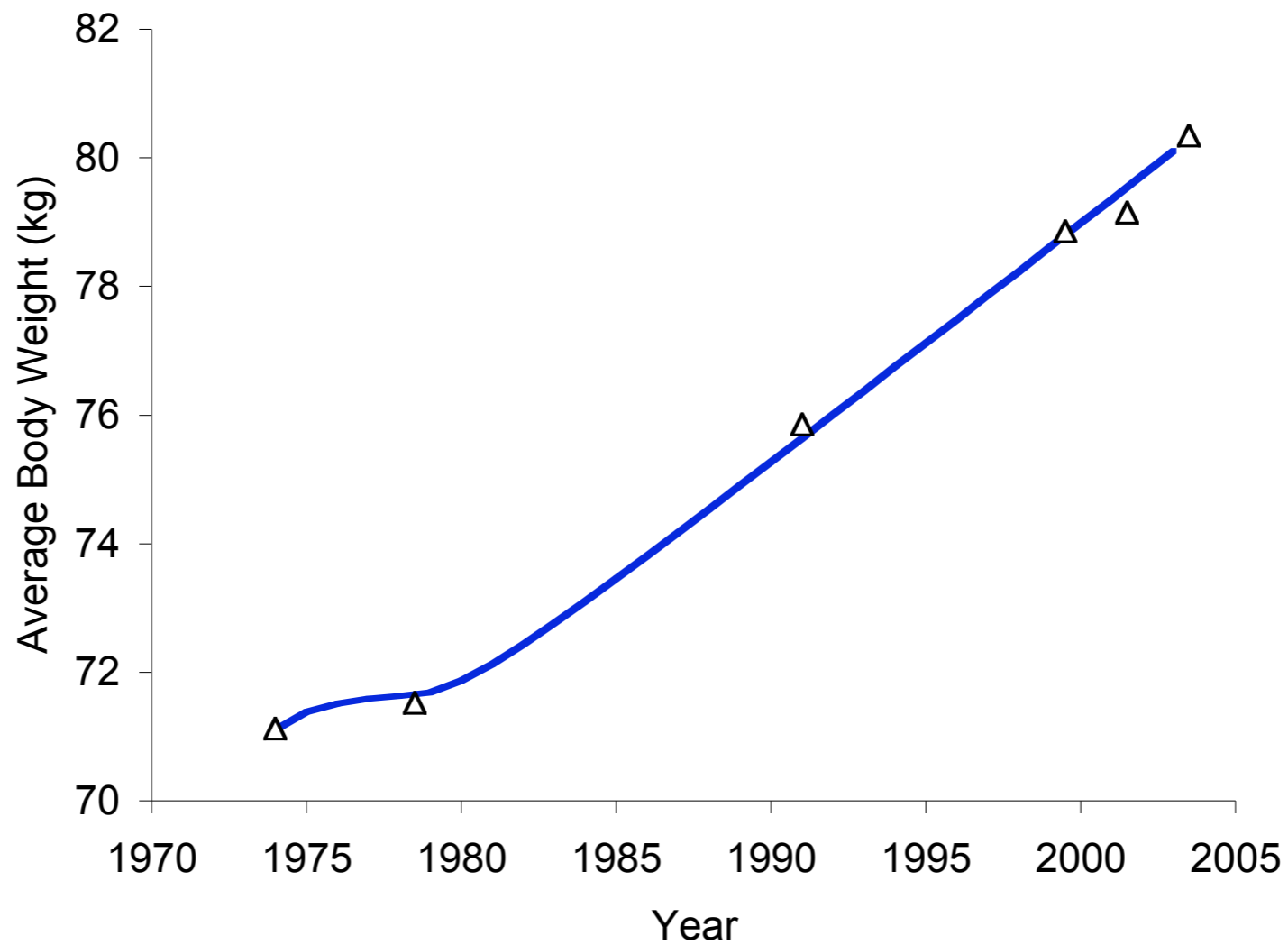
A photograph of a pear and an apple placed side-by-side on a white surface. The pear is on the left, green and pear-shaped. The apple is on the right, round and red with yellow streaks. The text "The physics of obesity" is overlaid in large black font across the center of the image.

The physics of obesity

Carson Chow
Laboratory of Biological Modeling, NIDDK, NIH

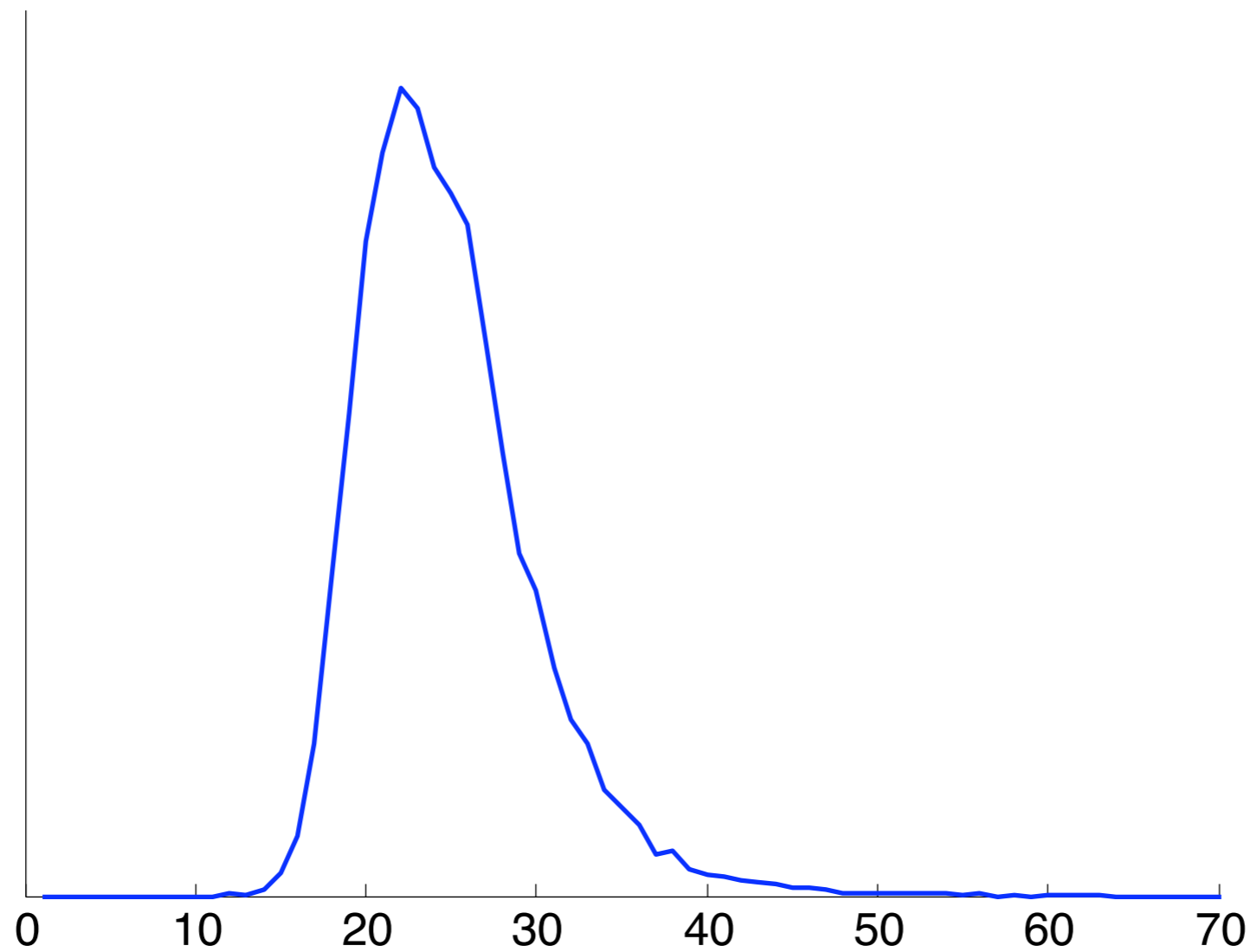


US obesity epidemic



Data from National Health and Nutrition Examination Survey (NHANES)

US obesity epidemic

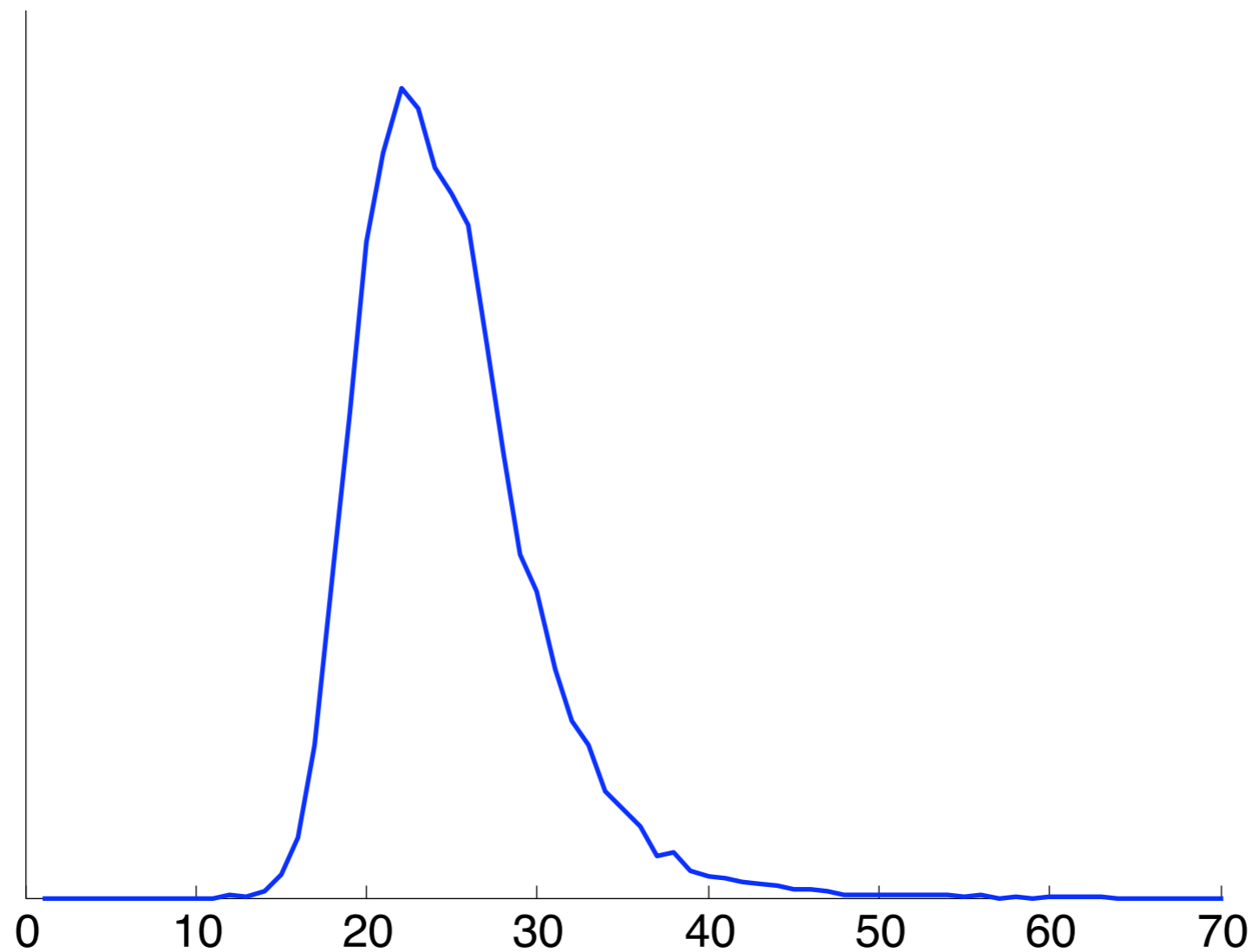


1971-74

BMI

NHANES data

US obesity epidemic

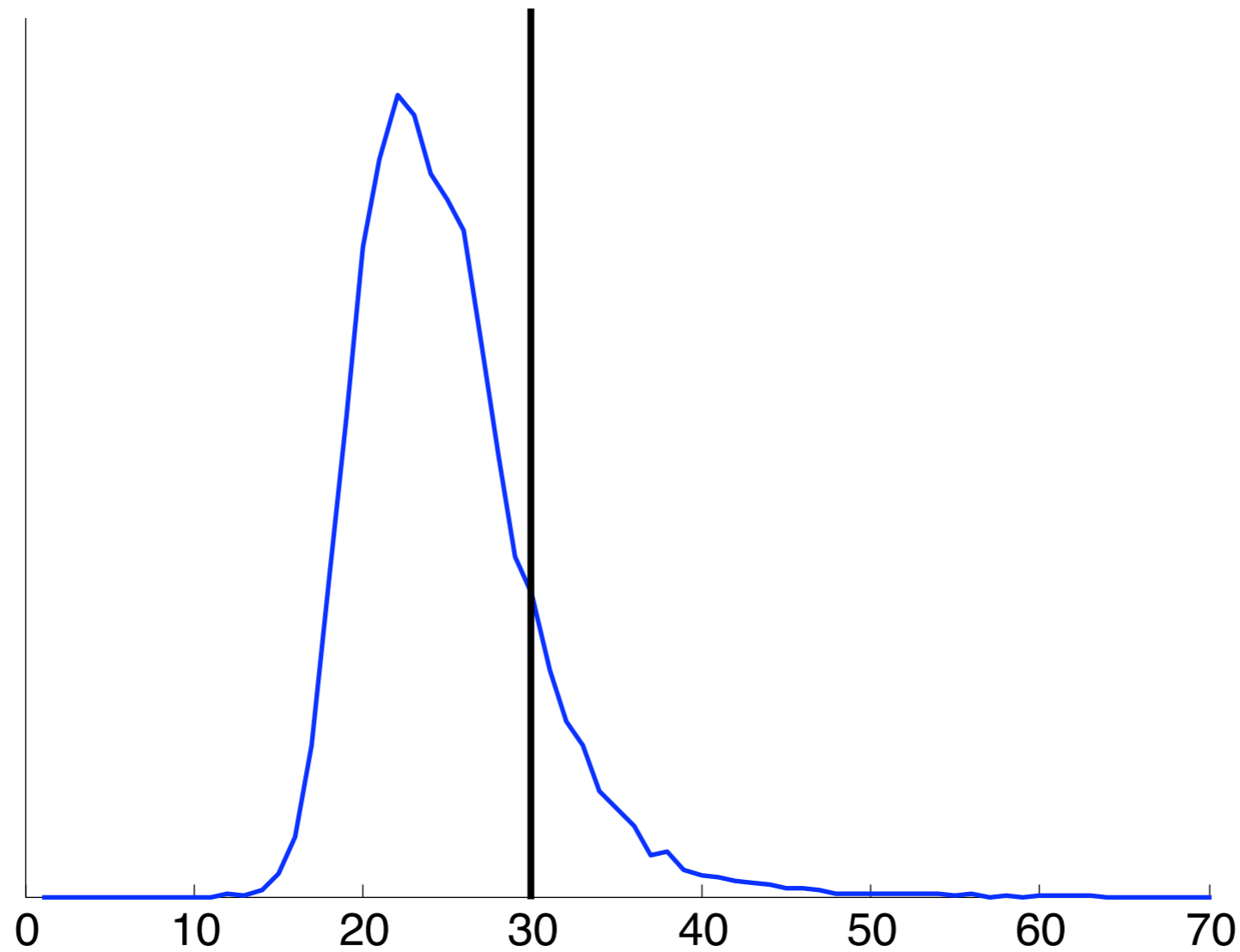


$$\text{BMI} = \text{weight} / \text{height}^2$$

NHANES data

US obesity epidemic

obese



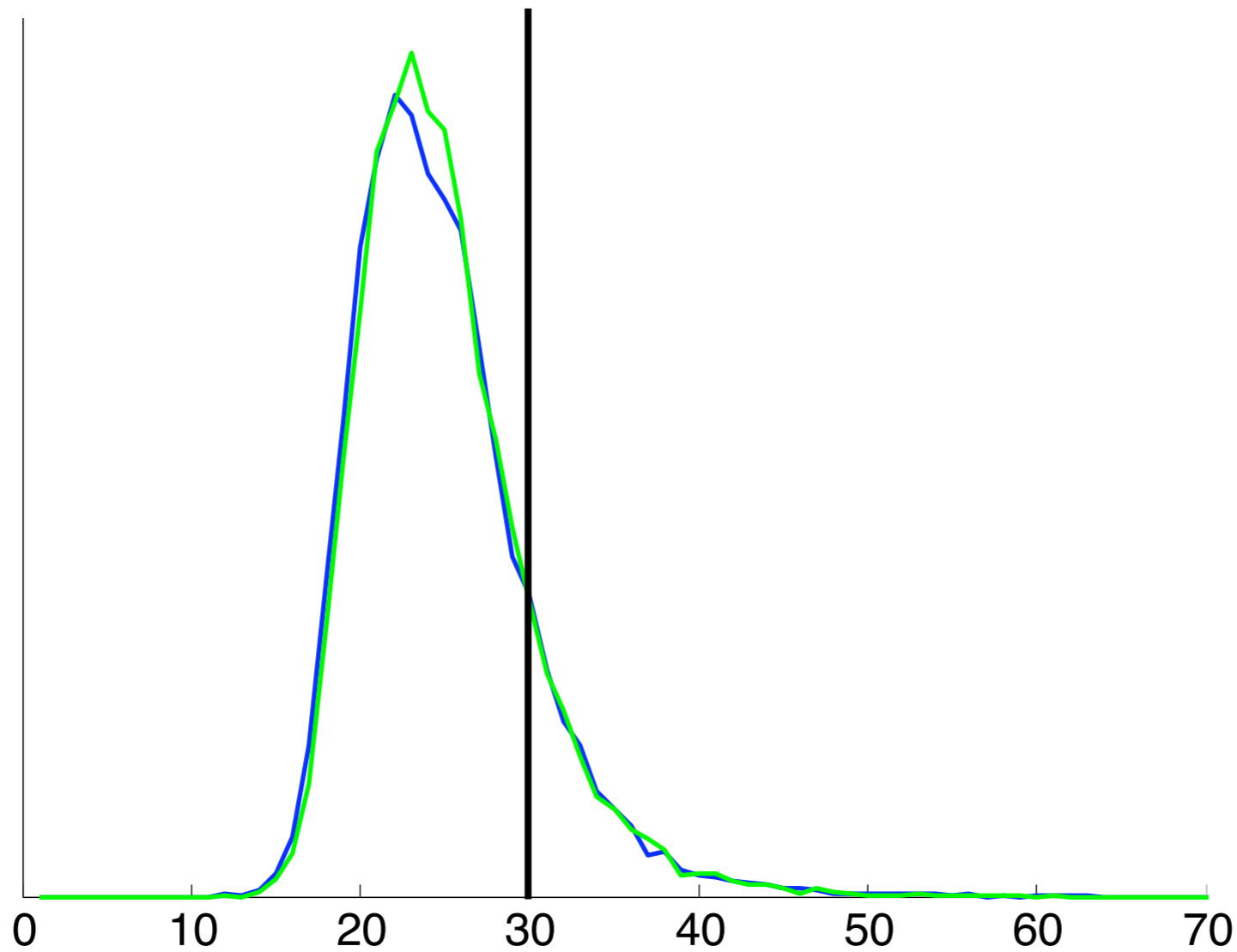
1971-74

$$\text{BMI} = \text{weight} / \text{height}^2$$

NHANES data

US obesity epidemic

obese



1971-74

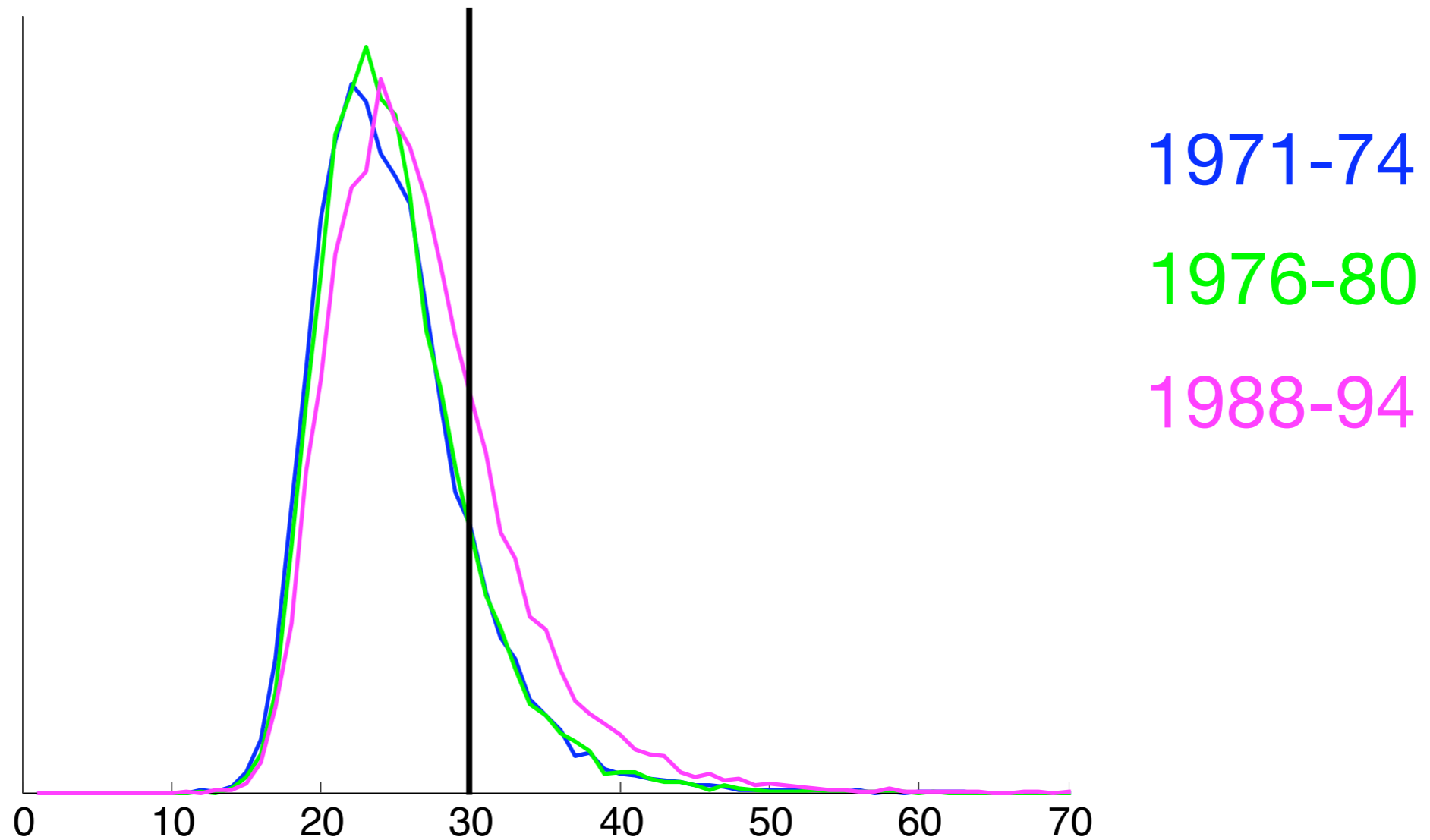
1976-80

$$\text{BMI} = \text{weight} / \text{height}^2$$

NHANES data

US obesity epidemic

obese

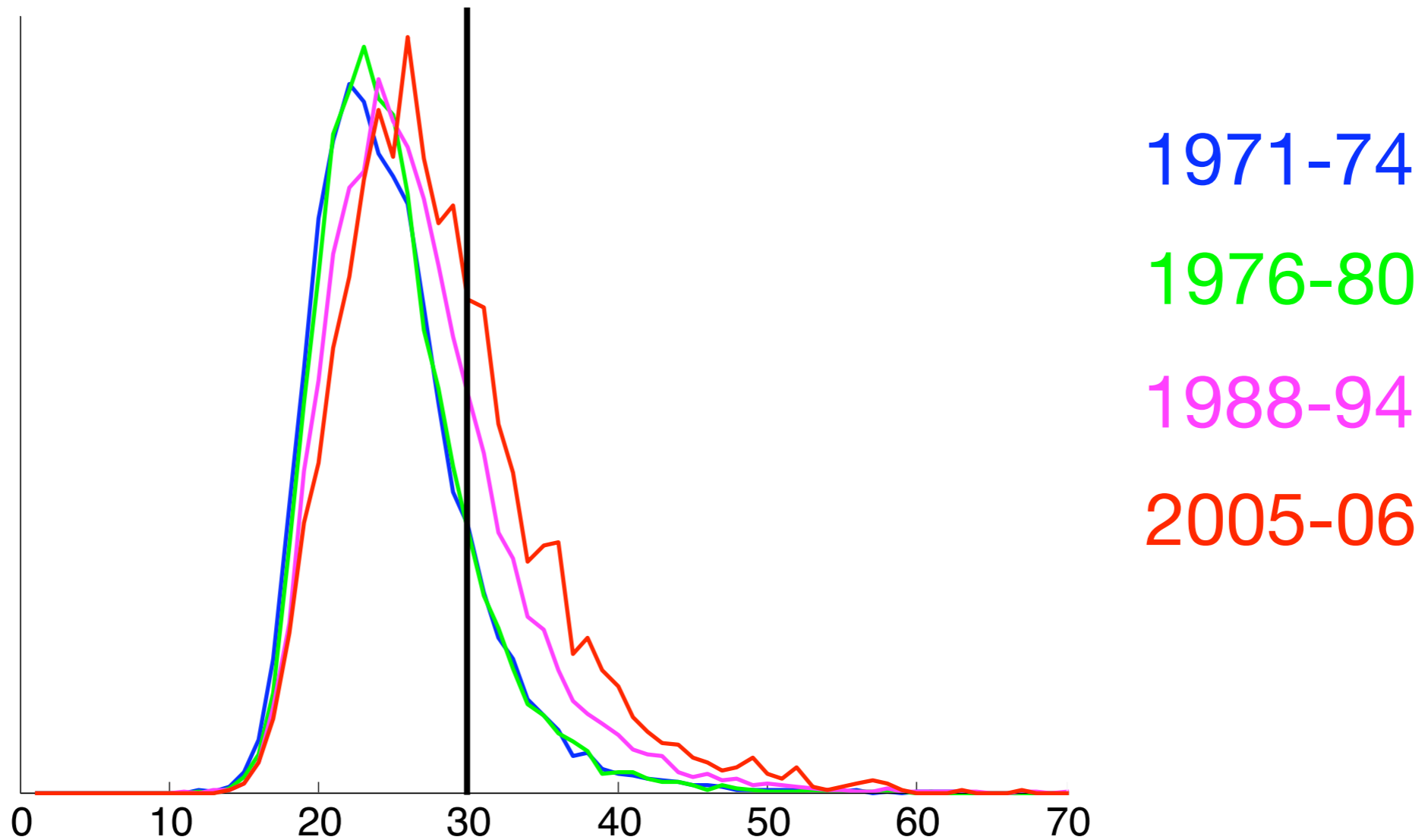


$$\text{BMI} = \text{weight} / \text{height}^2$$

NHANES data

US obesity epidemic

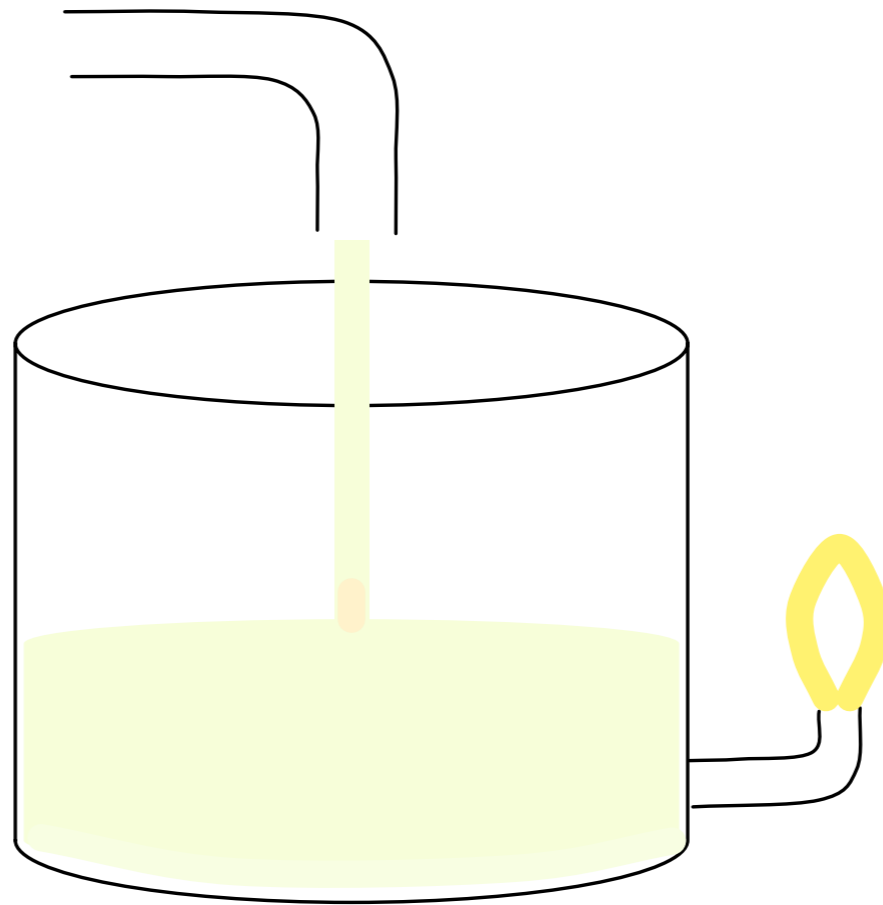
obese



$$\text{BMI} = \text{weight} / \text{height}^2$$

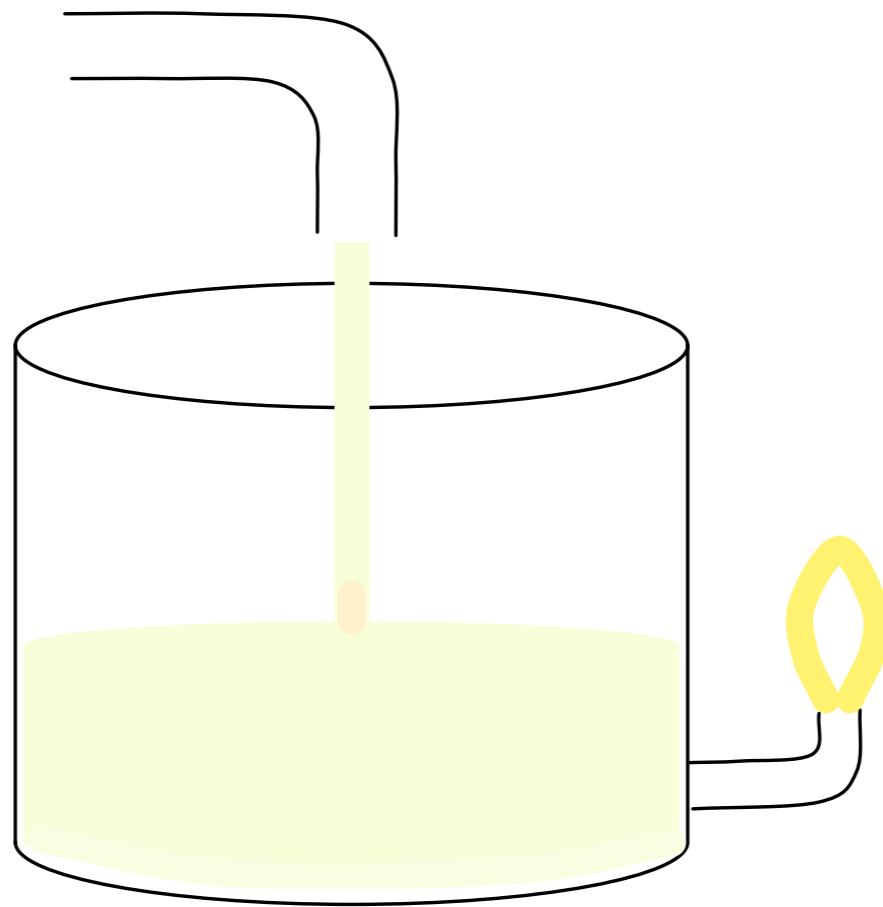
NHANES data

Conservation of energy



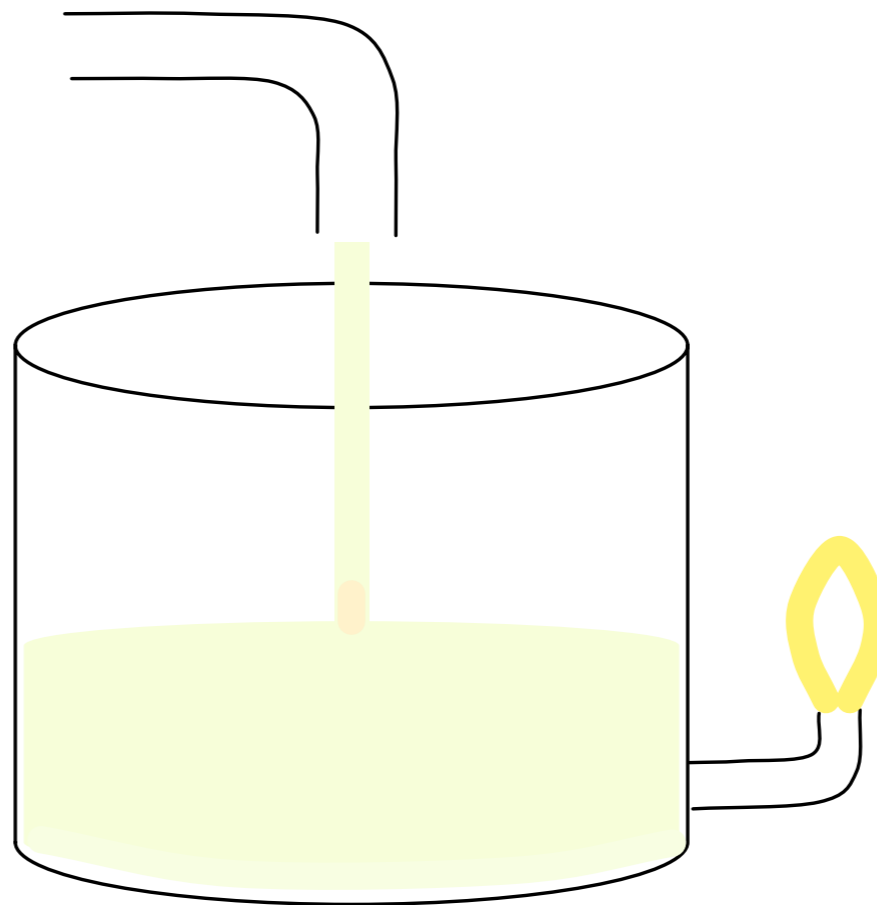
Conservation of energy

Food Intake



Conservation of energy

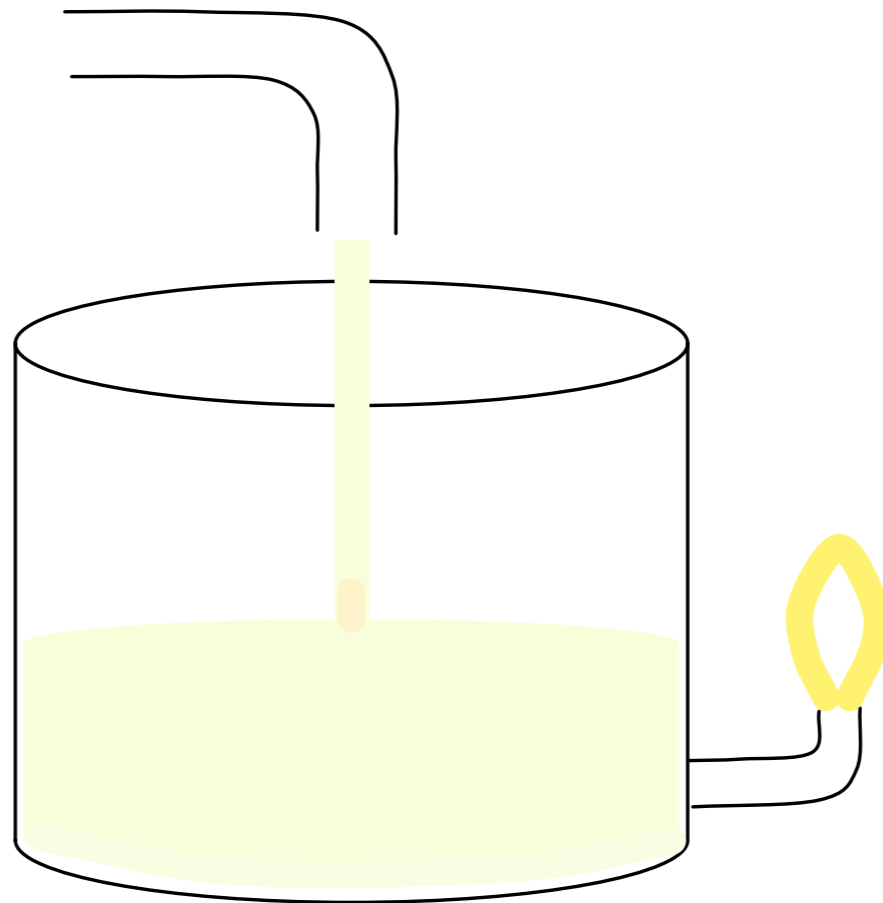
Food Intake



Energy
expenditure

Conservation of energy

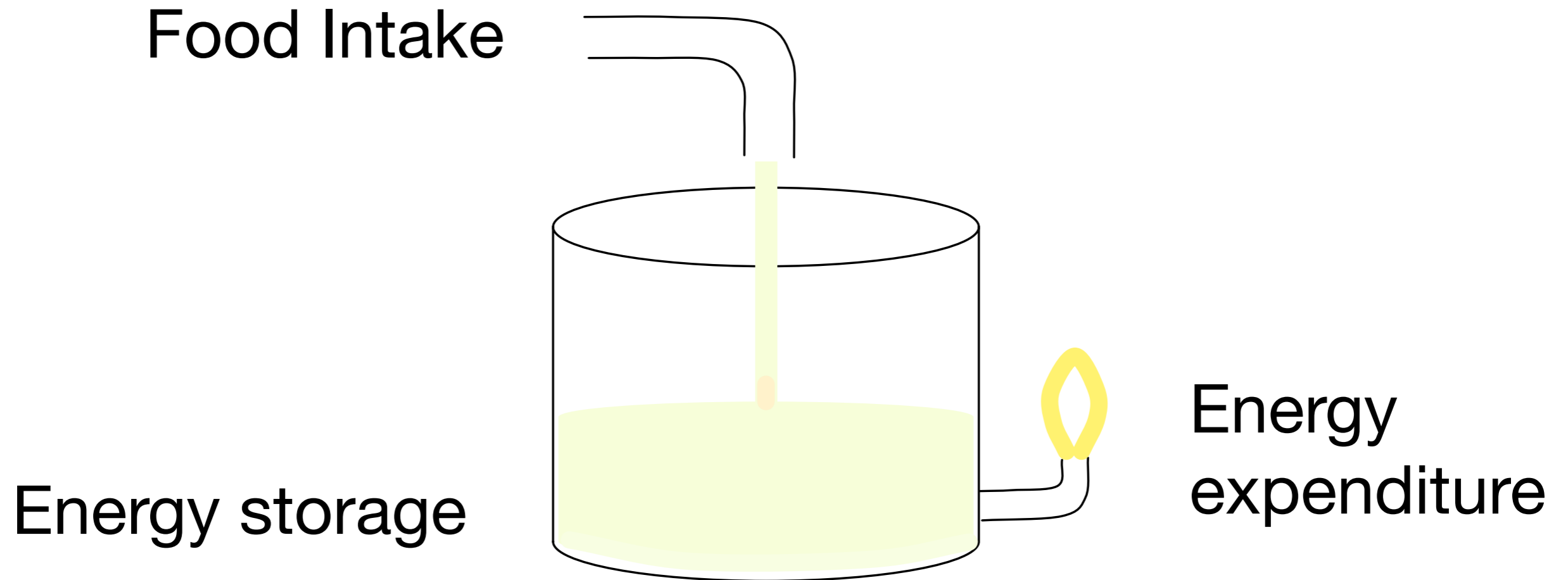
Food Intake



Energy storage

Energy expenditure

Conservation of energy



$$\Delta\text{Storage} = \text{Intake} - \text{Expenditure}$$

Energy flux

Rate of storage = intake rate - expenditure rate

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

M = body mass

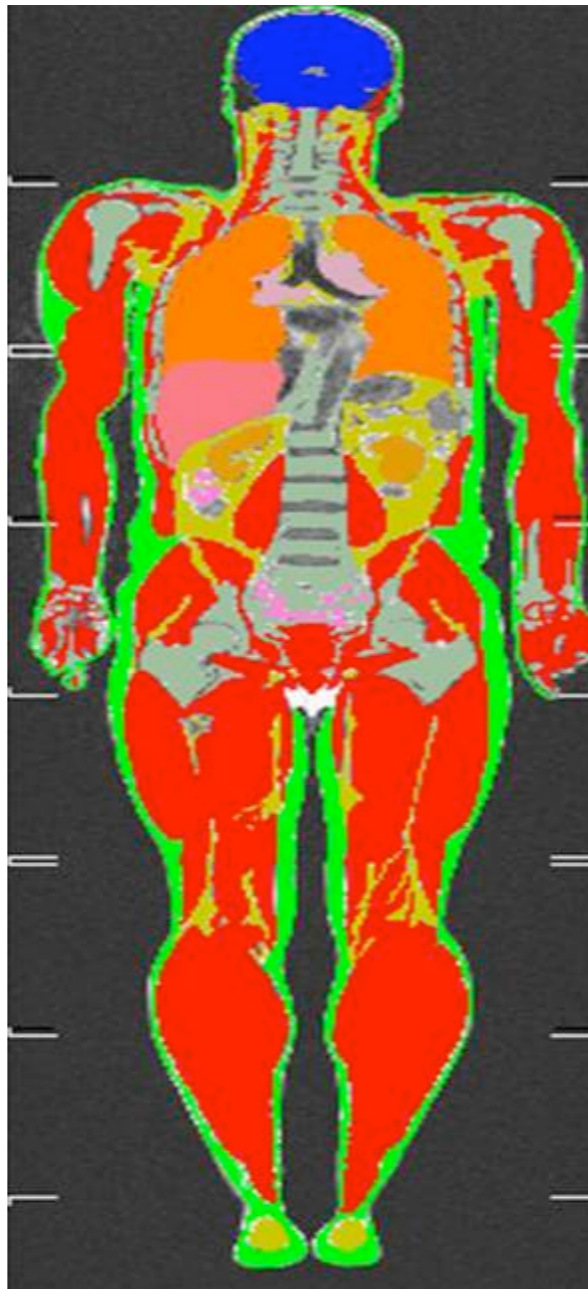
Energy density ρ_M converts energy to mass

Energy density

Fat
37.7 kJ/g

Carbs
(glycogen)
16.8 kJ/g

Protein
16.8 kJ/g

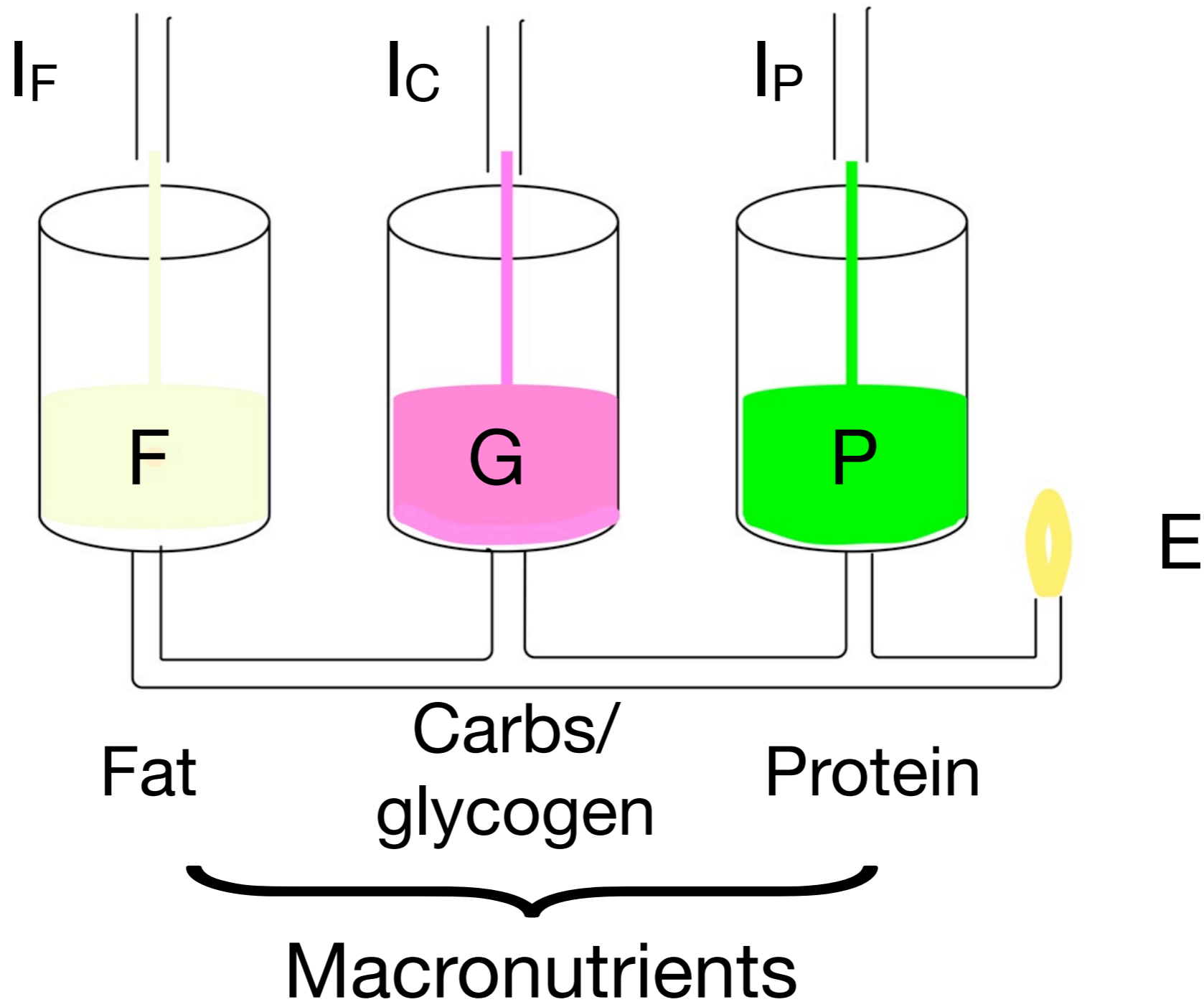


Water

Bone

Minerals

Multiple fuel sources



Macronutrient flux

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

Macronutrient flux

$$\rho_F \frac{dF}{dt} + \rho_P \frac{dP}{dt} + \rho_G \frac{dG}{dt} = I - E$$

Macronutrient flux

$$\rho_F \frac{dF}{dt} + \rho_P \frac{dP}{dt} + \rho_G \frac{dG}{dt} = I_F + I_C + I_P - E$$

Macronutrient flux

$$\begin{aligned} \rho_F \frac{dF}{dt} \\ \rho_G \frac{dG}{dt} \\ \rho_P \frac{dP}{dt} \end{aligned} = I_F + I_C + I_P - E$$

Macronutrient flux

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

$$\rho_G \frac{dG}{dt} = I_C - E$$

$$\rho_P \frac{dP}{dt} = I_P$$

Macronutrient flux

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

Macronutrient flux

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

f_F = fraction of fat utilized

f_C = fraction of carbs utilized

Macronutrient flux

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E$$

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f_F = fraction of fat utilized

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Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

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Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_G \frac{dG}{dt} = I_C - f_C E = 0$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$f_C = \frac{I_C}{E}$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F - f_C) E$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_P \frac{dP}{dt} = I_P - \left(1 - f_F - \frac{I_C}{E}\right) E$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_P \frac{dP}{dt} = I_P - (1 - f_F) E + I_C$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_P \frac{dP}{dt} = I_P + I_C - (1 - f_F) E$$

Glycogen supply small, \sim fixed on long time scales

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_P \frac{dP}{dt} = I_P + I_C - (1 - f_F) E$$

Divide mass into lean and fat $M = L + F$

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\rho_P \frac{dP}{dt} = I_P + I_C - (1 - f_F) E$$

Divide mass into lean and fat $M = L + F$

Change in L due to change
in P and water $\frac{dP}{dt} = \frac{1}{1 + h_P} \frac{dL}{dt}$

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\frac{\rho_P}{1 + h_P} \frac{dL}{dt} = I_P + I_C - (1 - f_F) E$$

Divide mass into lean and fat $M = L + F$

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\frac{\rho_P}{1 + h_P} \frac{dL}{dt} = I_P + I_C - (1 - f_F) E$$

Divide mass into lean and fat $M = L + F$

Lean intake = carbs + protein $I_P + I_C = I_L$

Reduction to $2D$

$$\rho_F \frac{dF}{dt} = I_F - f_F E$$

$$\frac{\rho_P}{1 + h_P} \frac{dL}{dt} = I_L - (1 - f_F) E$$

Divide mass into lean and fat $M = L + F$

Body composition model

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

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

Body composition model

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

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$$\rho_L = \rho_P / (1 + h_P)$$

h_p protein hydration coefficient

Body composition model

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$$\rho_L = \rho_P / (1 + h_P)$$

h_p protein hydration coefficient

f is fraction of energy use that is fat

Body composition model

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

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

$$\rho_L = \rho_P / (1 + h_P)$$

h_p protein hydration coefficient

f is fraction of energy use that is fat

E and f are functions of F and L

Dynamical systems

Infer global dynamics from local information

Dynamical systems

$$\frac{dx}{dt} = x(1 - x)$$

Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0 \quad \text{Fixed points}$$

Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0$$

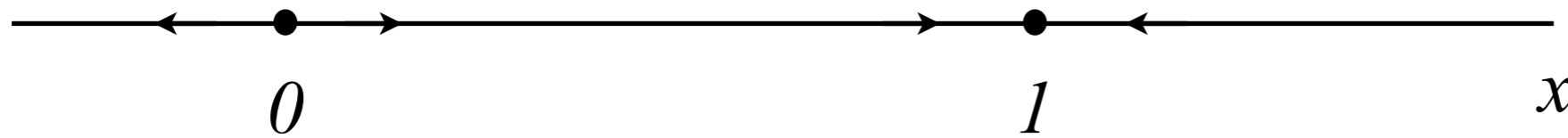
Fixed points

$$x = 0, 1$$

Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0 \quad \text{Fixed points}$$
$$x = 0, 1$$

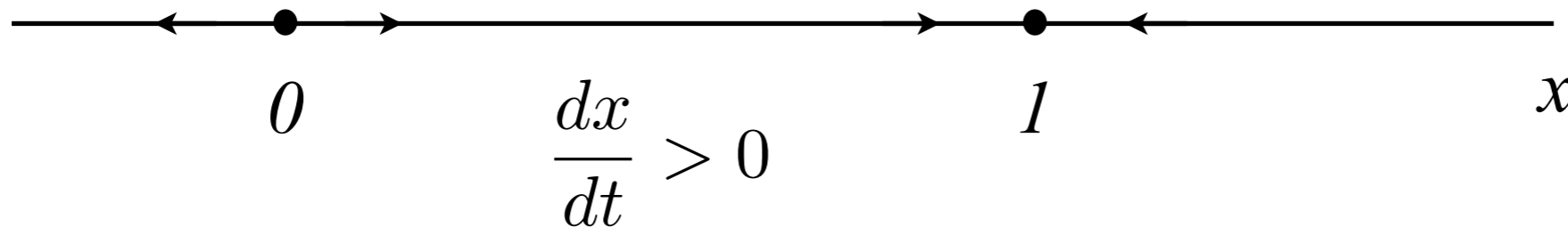
Represent geometrically in phase plane



Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0 \quad \text{Fixed points}$$
$$x = 0, 1$$

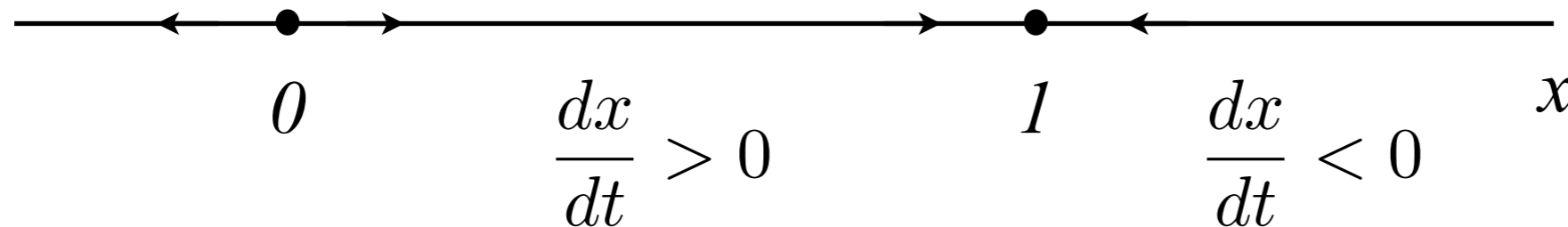
Represent geometrically in phase plane



Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0 \quad \text{Fixed points}$$
$$x = 0, 1$$

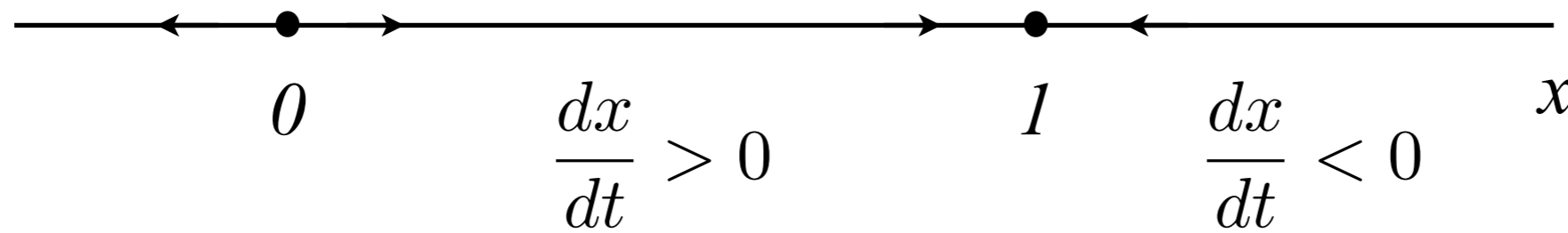
Represent geometrically in phase plane



Dynamical systems

$$\frac{dx}{dt} = x(1 - x) = 0 \quad \text{Fixed points}$$
$$x = 0, 1$$

Represent geometrically in phase plane



vector field

Fixed points

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

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

Fixed points

vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E \end{array} \right.$$

Fixed points

Nullclines

vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE = 0 \quad \text{L - Nullcline} \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E = 0 \quad \text{F - Nullcline} \end{array} \right.$$

Fixed points

Nullclines

vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE = 0 \quad \text{L - Nullcline} \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E = 0 \quad \text{F - Nullcline} \end{array} \right.$$

$$E(F, L) = I$$

Fixed points

Nullclines

vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE = 0 \quad \text{L - Nullcline} \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E = 0 \quad \text{F - Nullcline} \end{array} \right.$$

$$E(F, L) = I \quad \text{energy balance}$$

Fixed points

Nullclines

vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE = 0 \quad \text{L - Nullcline} \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E = 0 \quad \text{F - Nullcline} \end{array} \right.$$

$$E(F, L) = I \quad \text{energy balance}$$

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

Fixed points

Nullclines

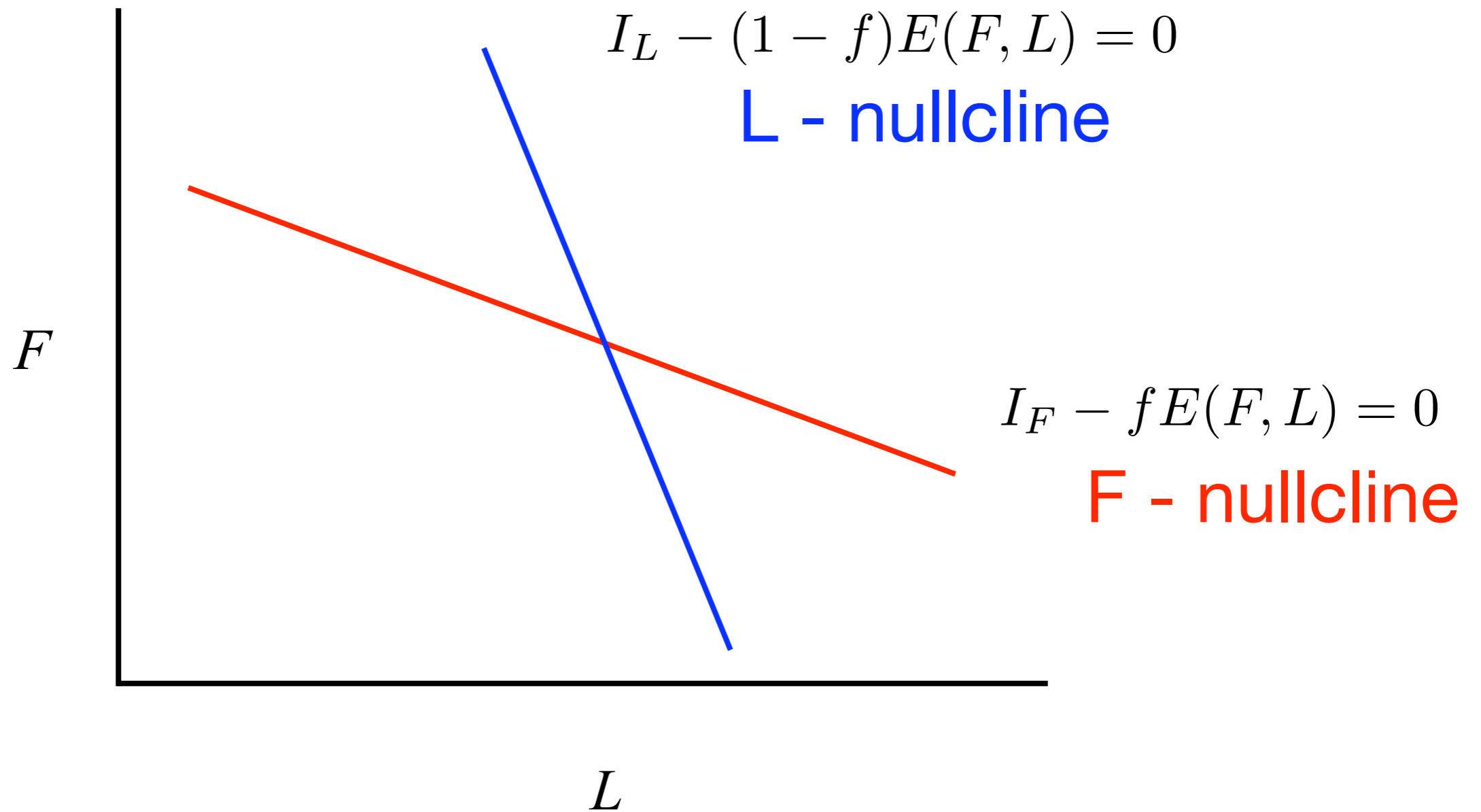
vector field

$$\left\{ \begin{array}{l} \rho_F \frac{dF}{dt} = I_F - fE = 0 \quad \text{L - Nullcline} \\ \rho_L \frac{dL}{dt} = I_L - (1 - f)E = 0 \quad \text{F - Nullcline} \end{array} \right.$$

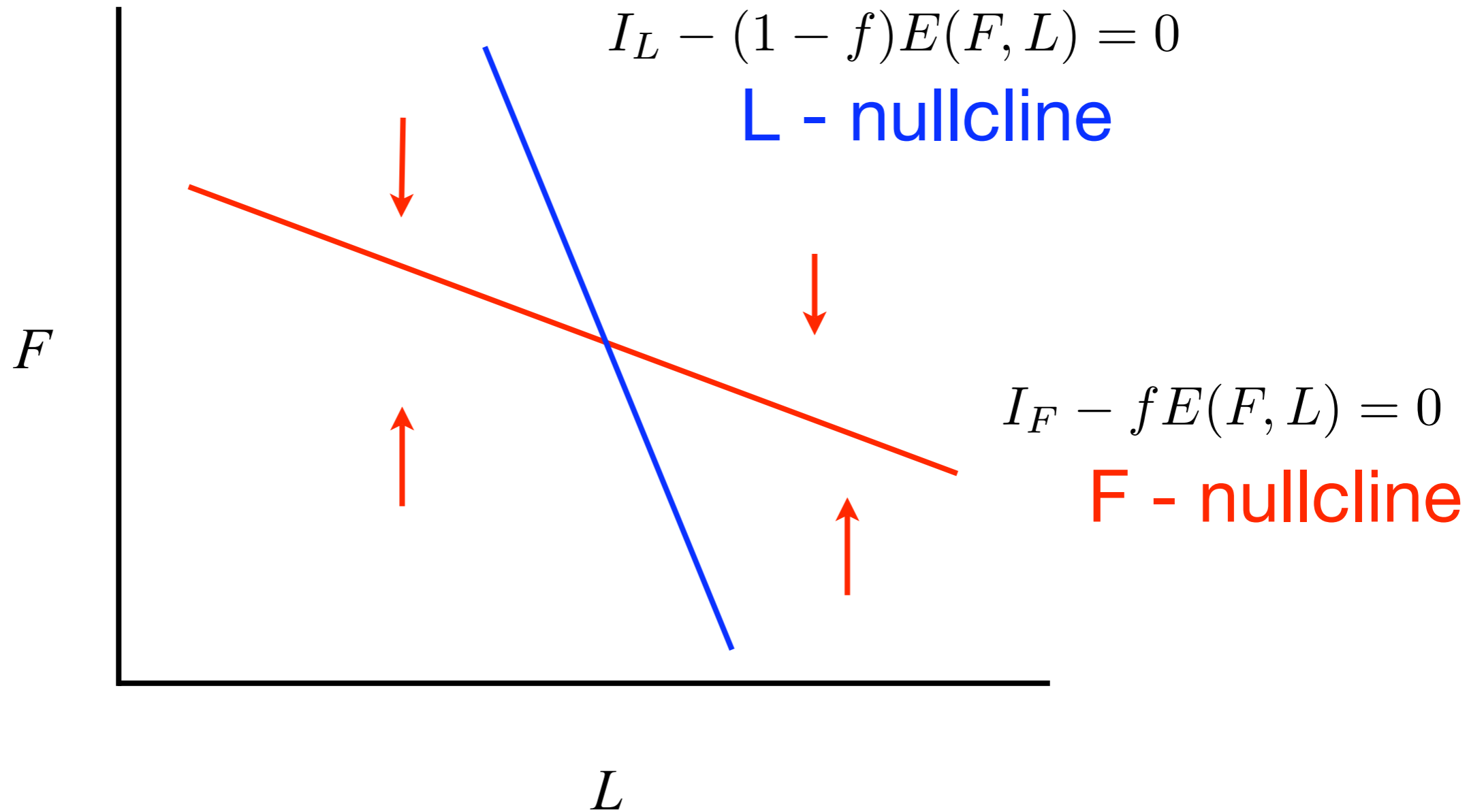
$$E(F, L) = I \quad \text{energy balance}$$

$$f(F, L) = \frac{I_F}{I} \quad \text{fat balance}$$

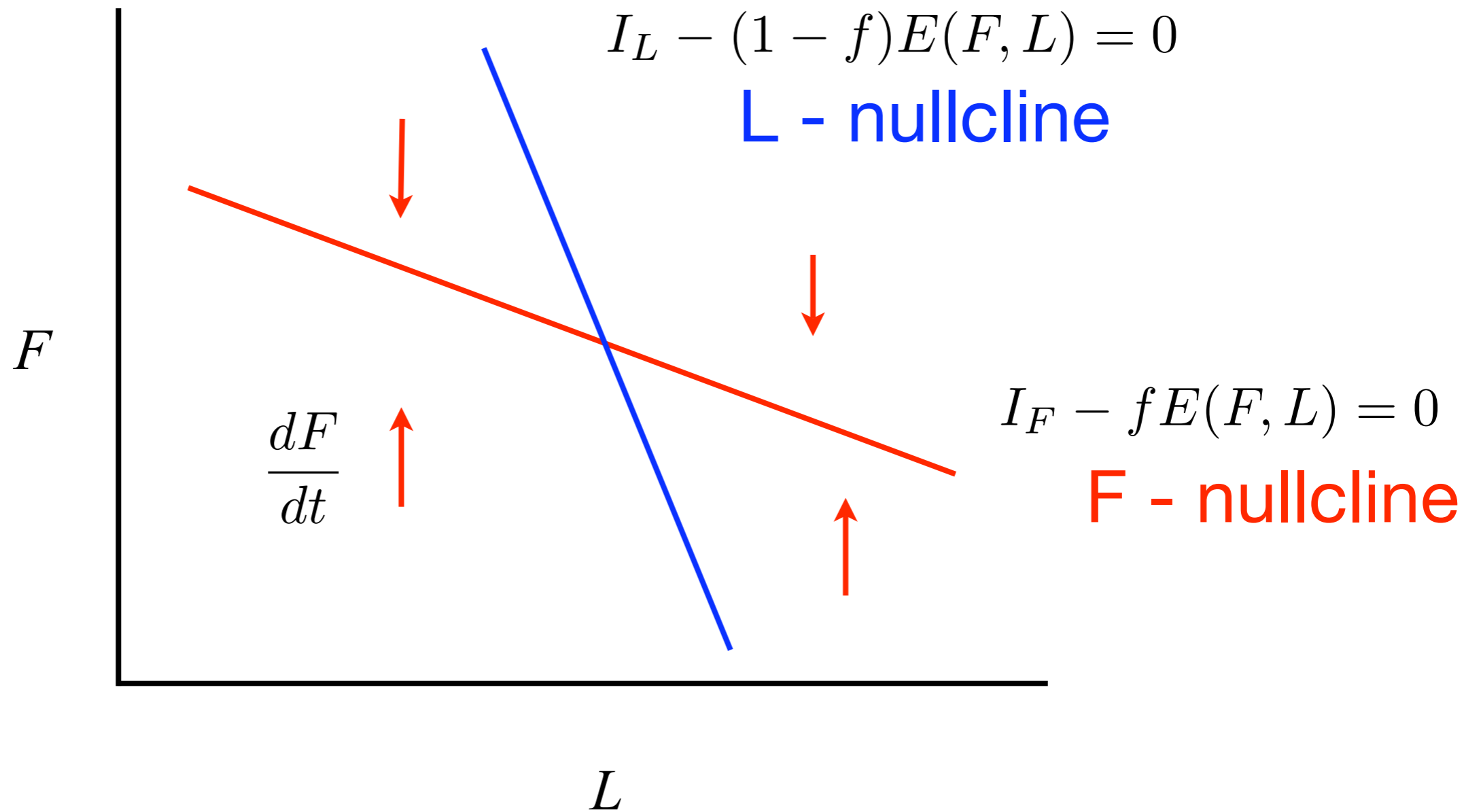
Phase plane



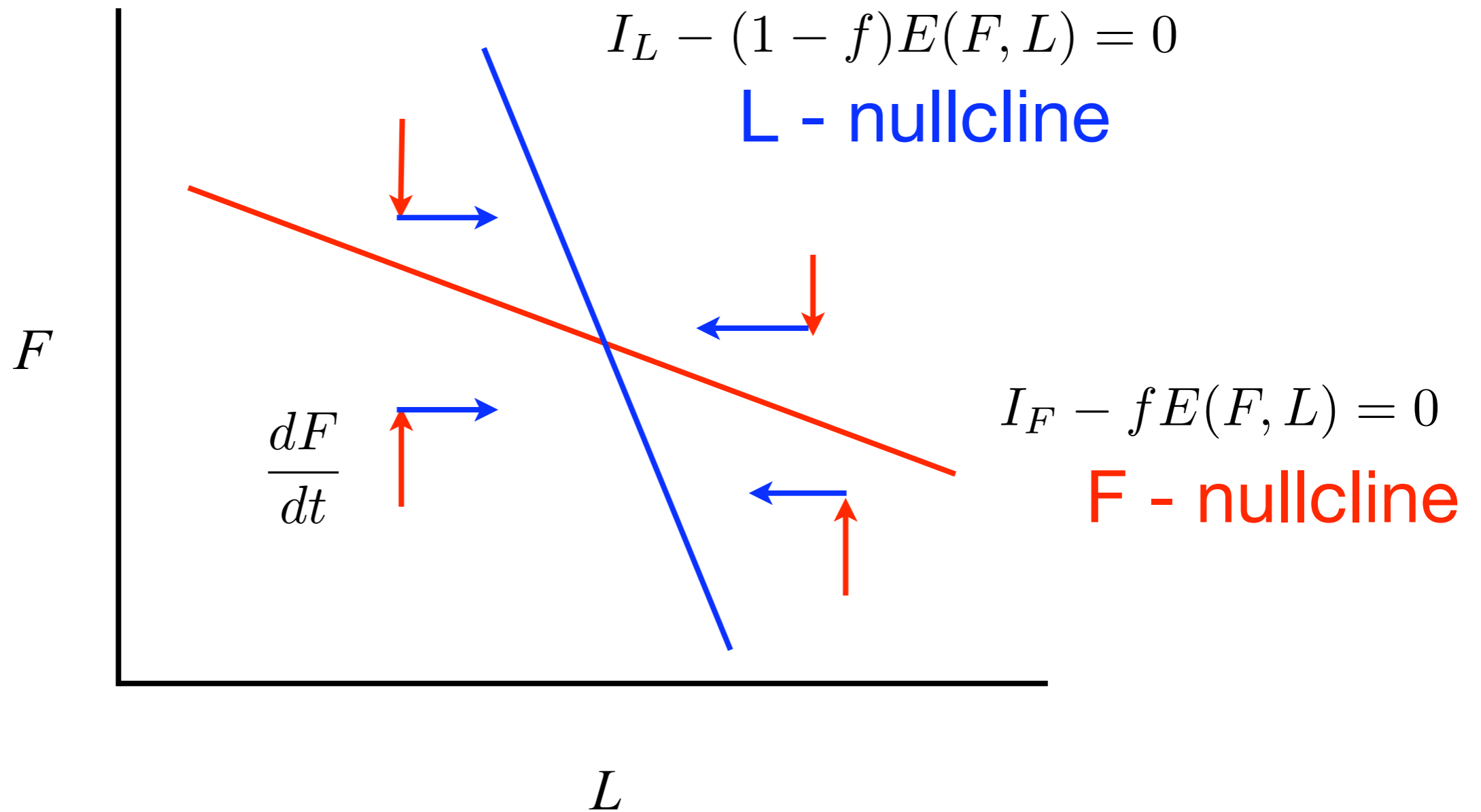
Phase plane



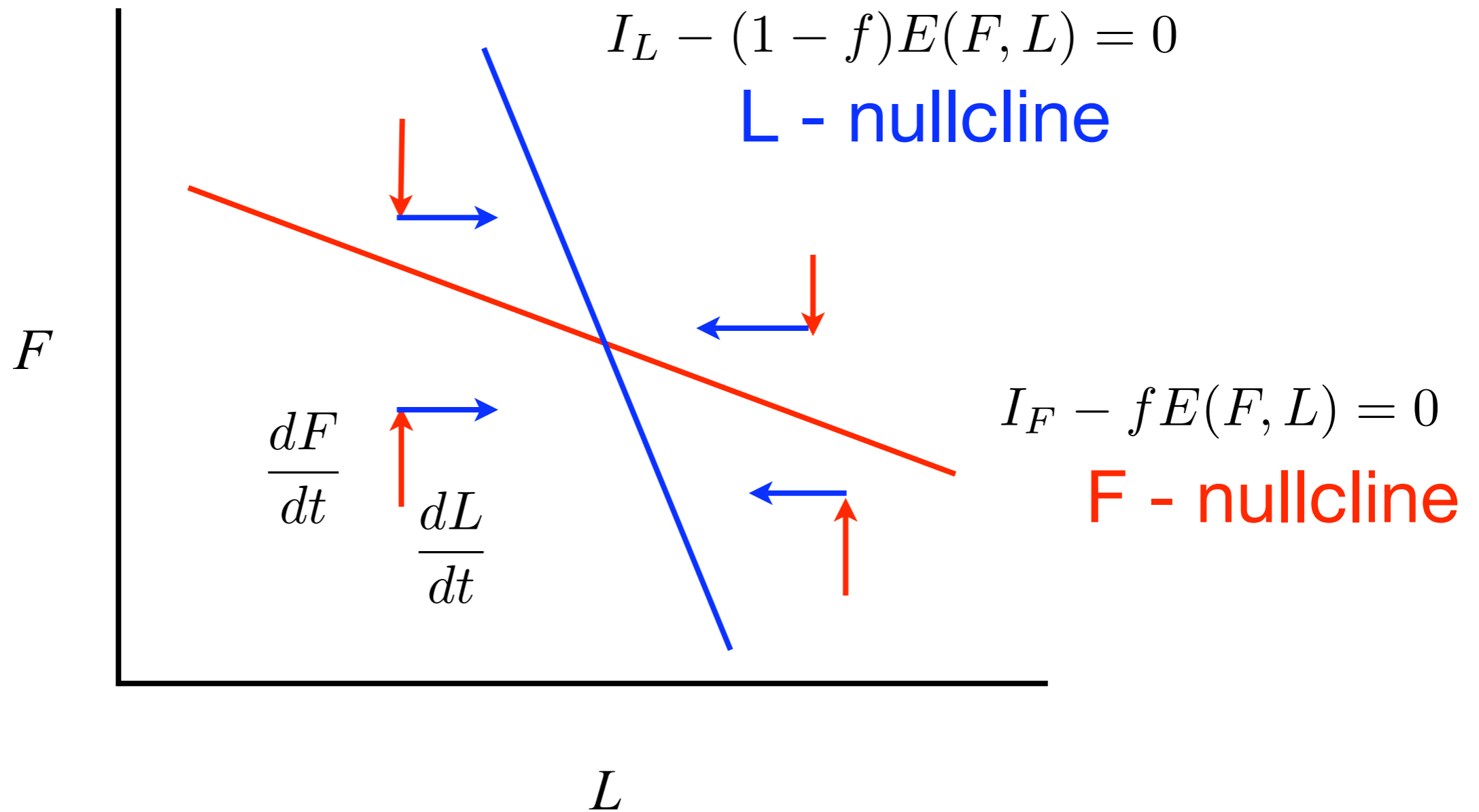
Phase plane



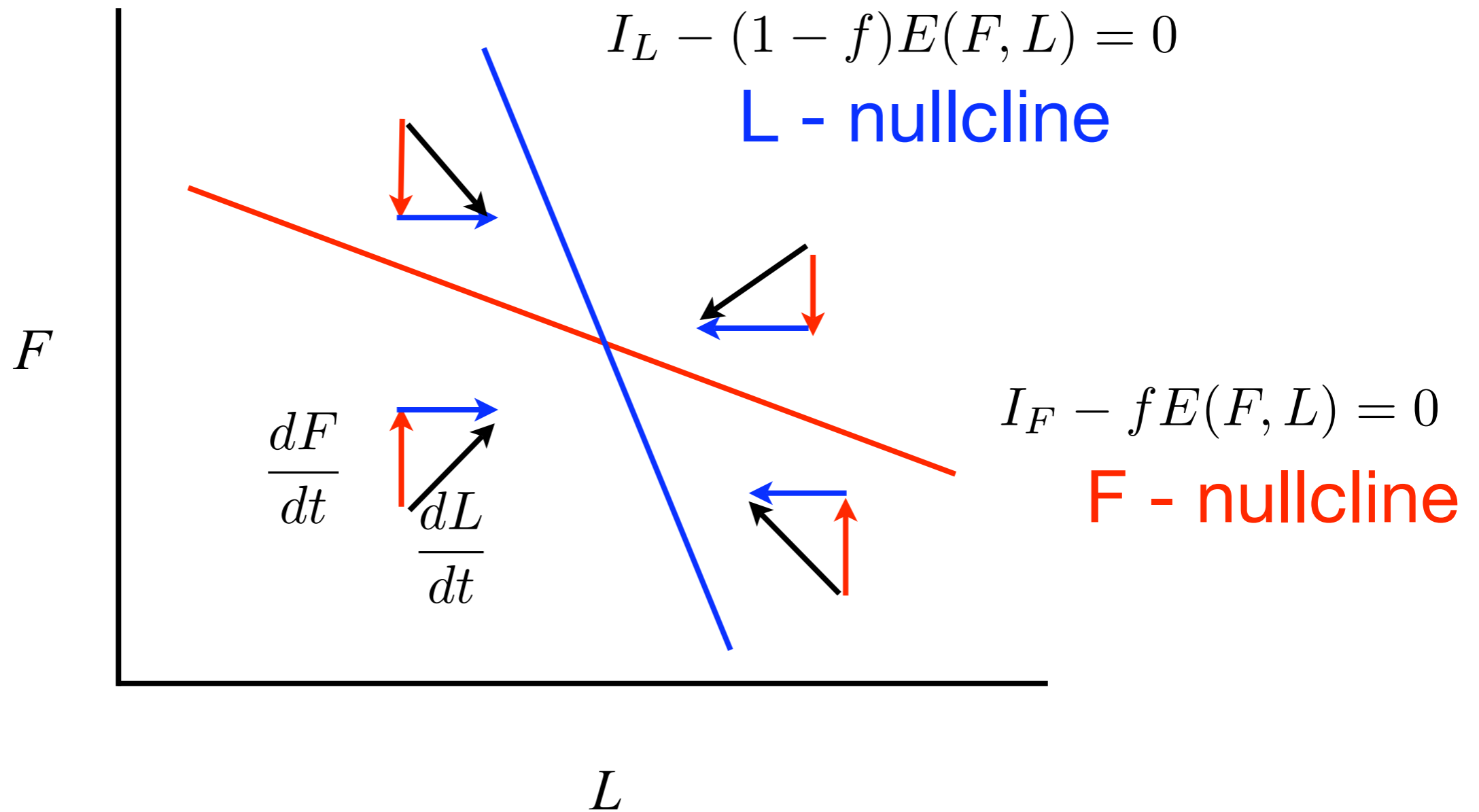
Phase plane



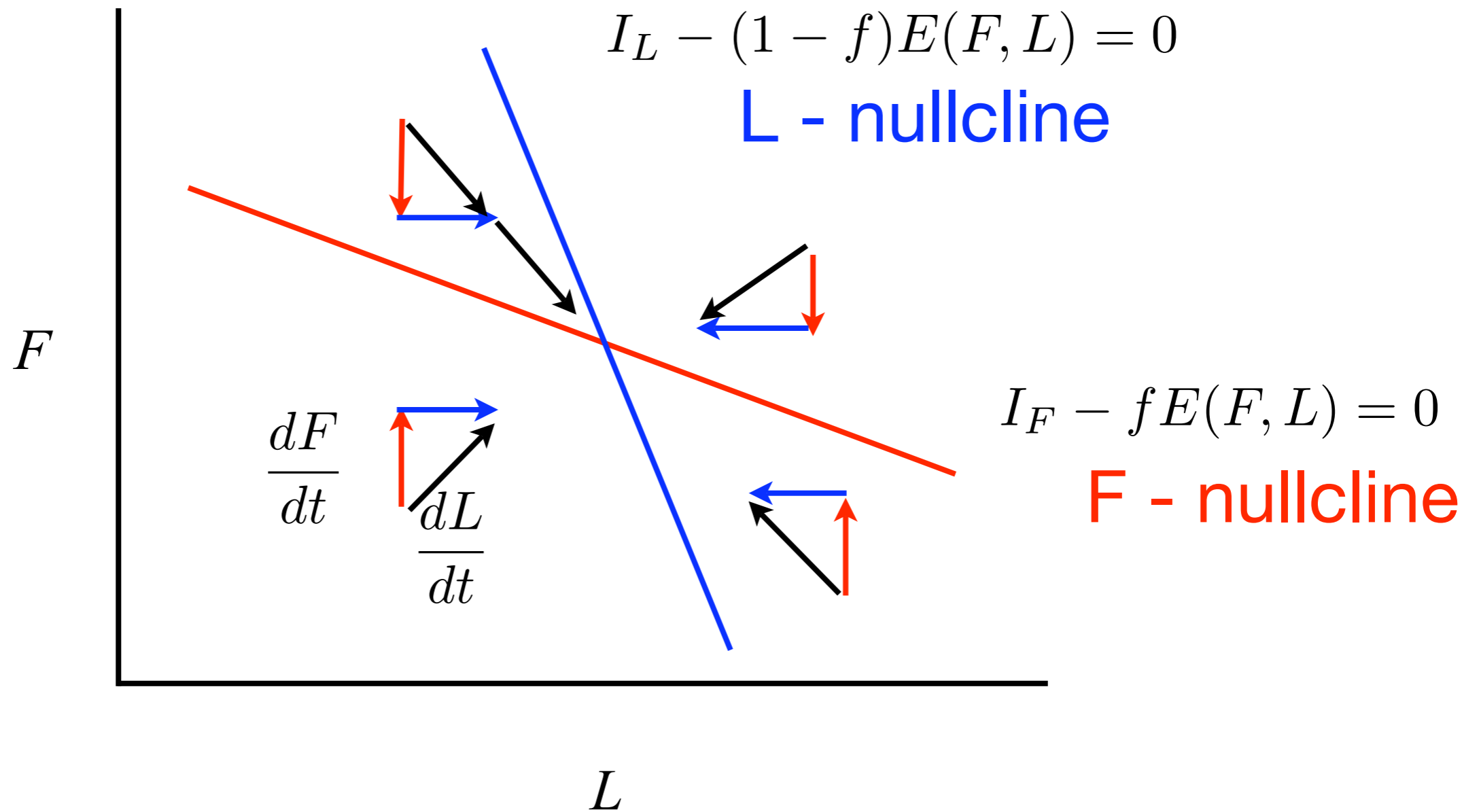
Phase plane



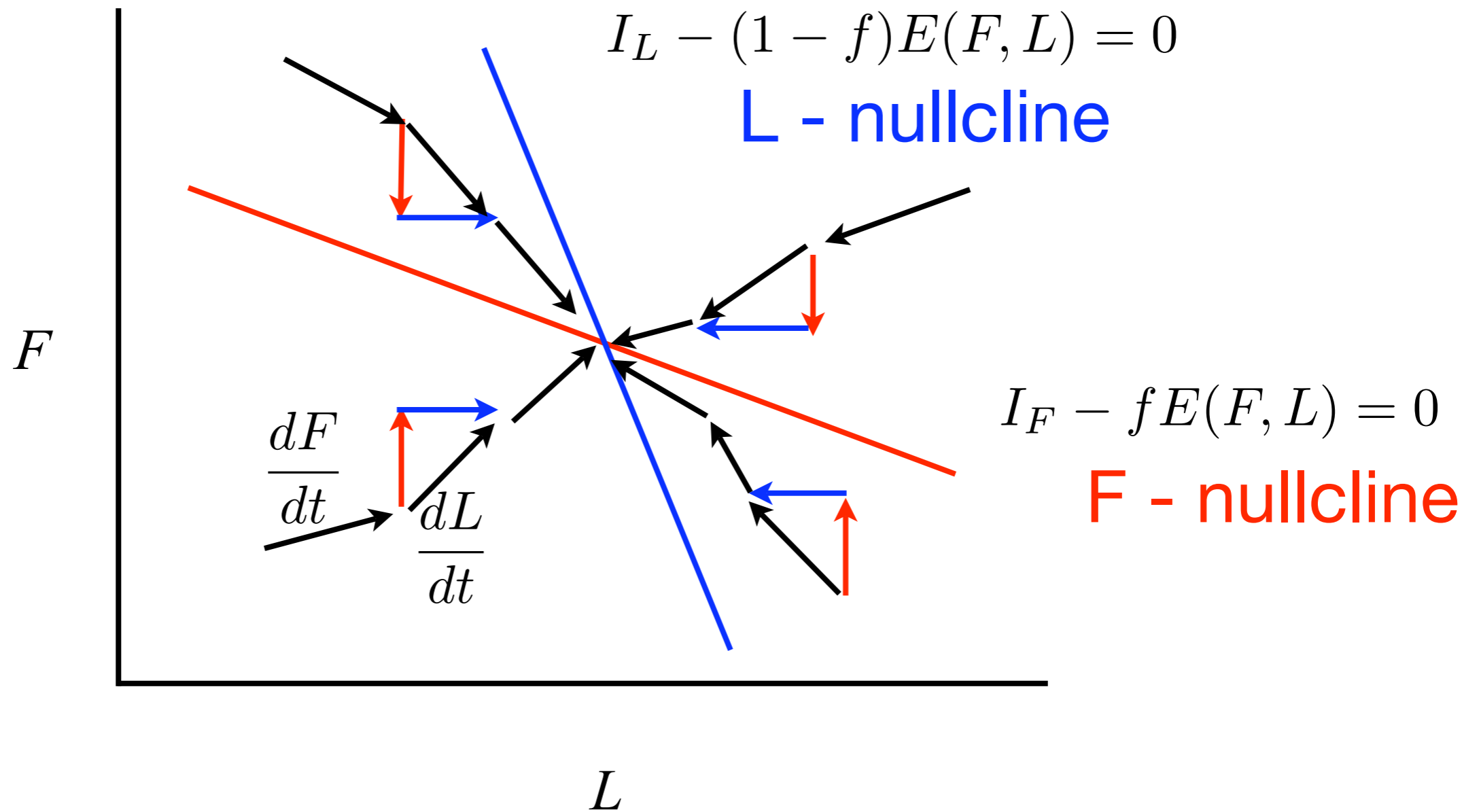
Phase plane



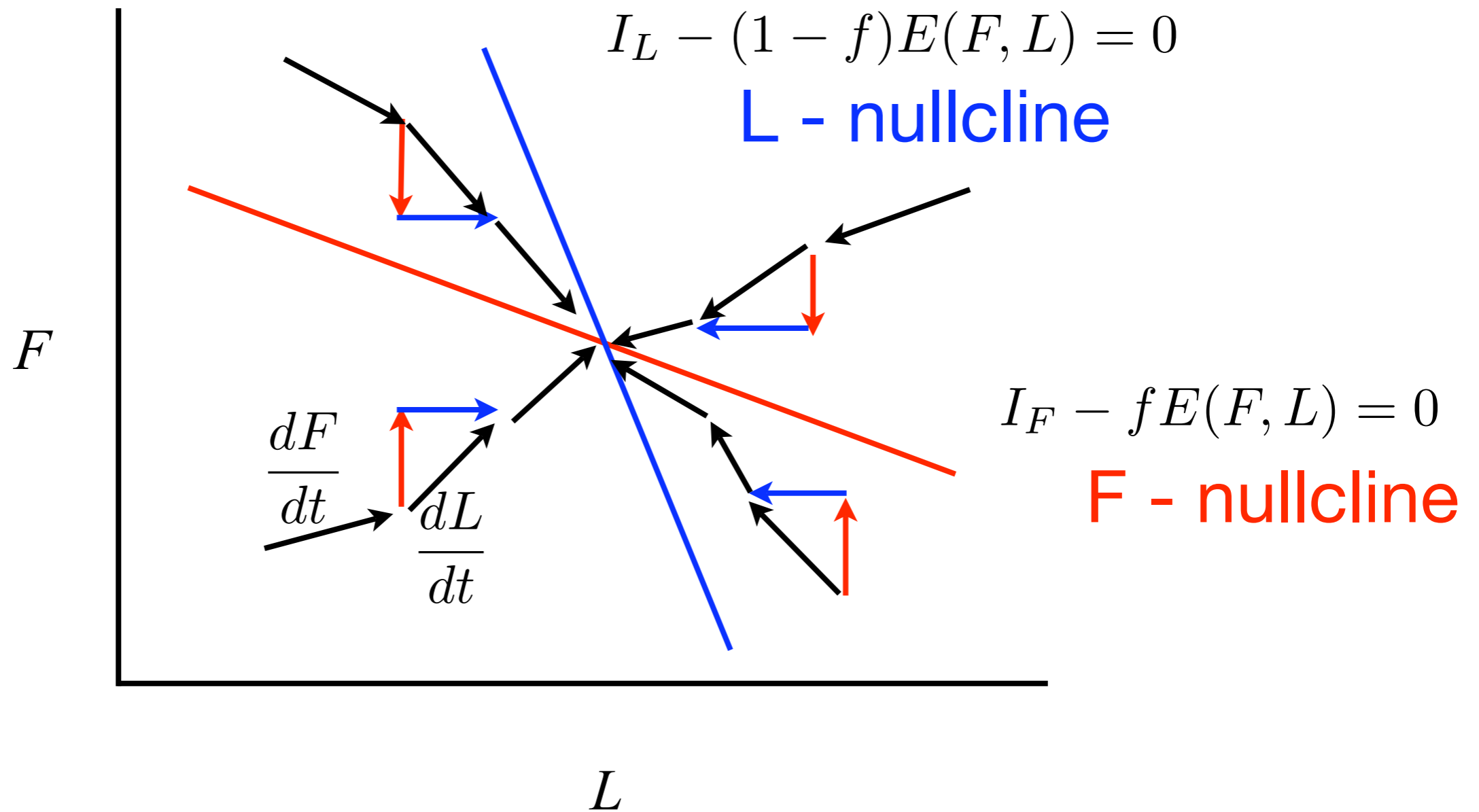
Phase plane



Phase plane

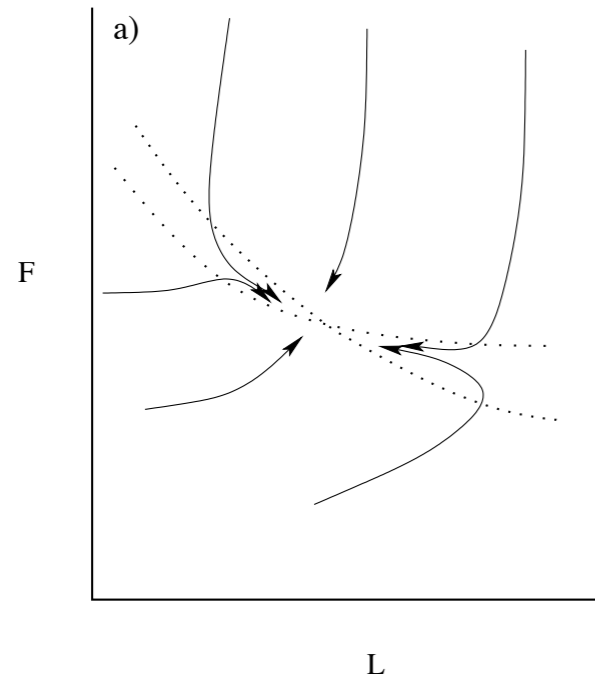


Phase plane

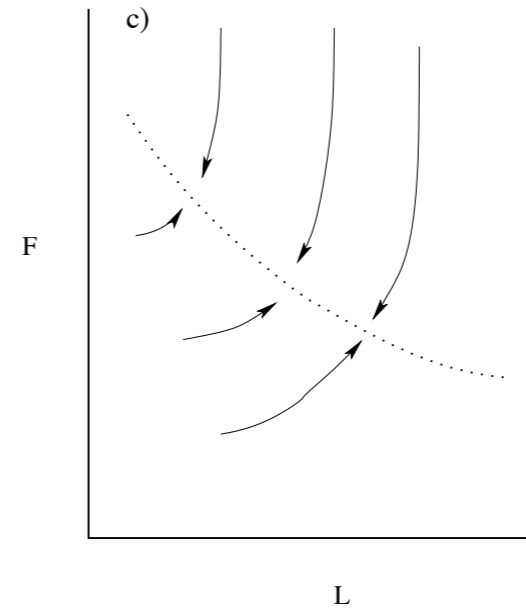


Fate of all initial conditions is known

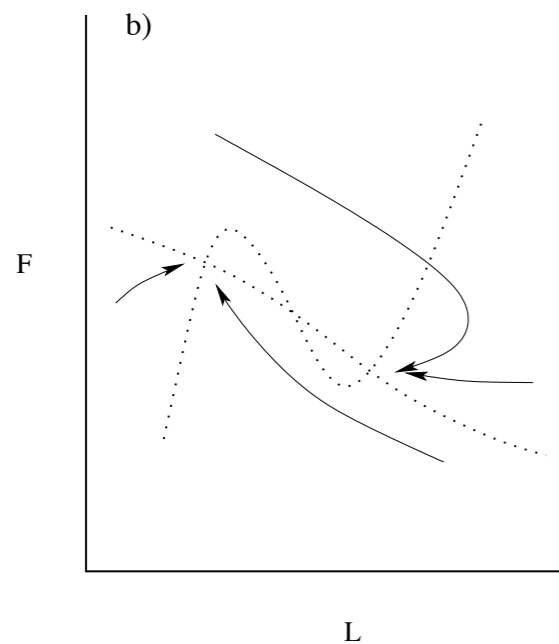
Possible phase plane dynamics



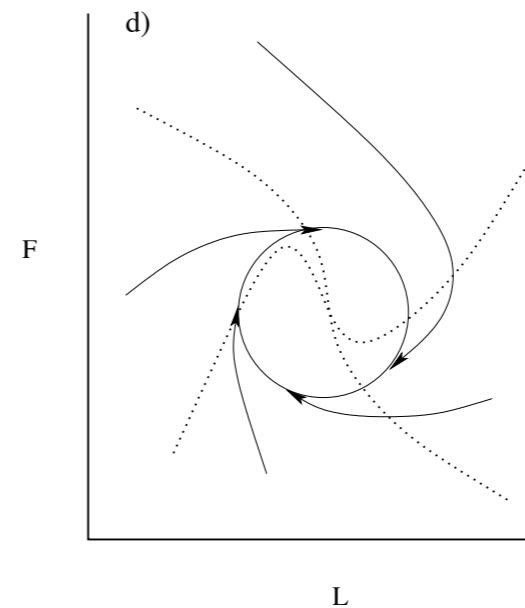
Fixed point



Line attractor

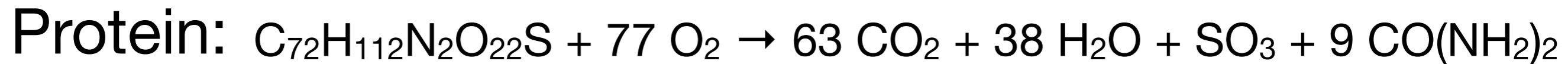
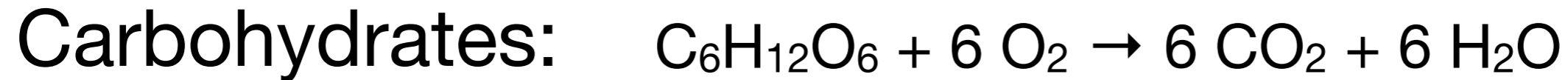


Multiple fixed points



Limit cycle

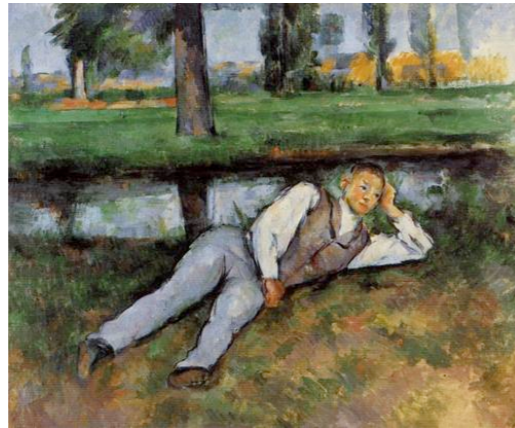
Indirect calorimetry



Flux of CO_2 and $O_2 \Rightarrow E$

Energy expenditure rate E

$E =$



+

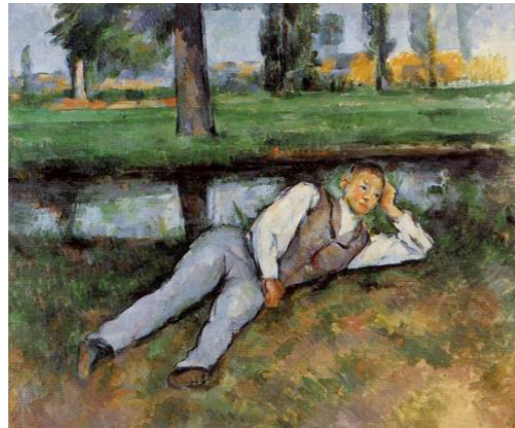


Basal metabolic rate (BMR)

Physical activity

Energy expenditure rate E

$E =$



+



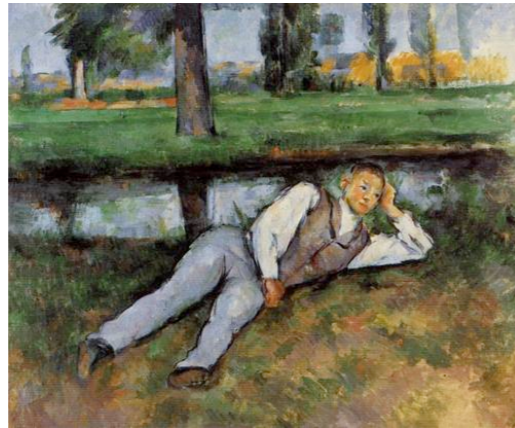
Basal metabolic rate (BMR)

Physical activity

$E \sim 10 \text{ MJ/day}$

Energy expenditure rate E

$E =$



+



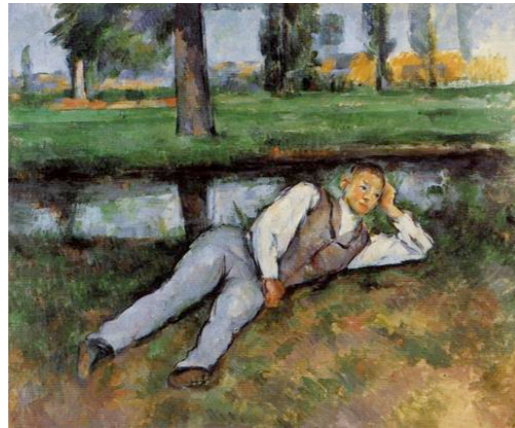
Basal metabolic rate (BMR)

Physical activity

$$E \sim 10 \text{ MJ/day} \sim 115 \text{ W}$$

Energy expenditure rate E

$E =$



+

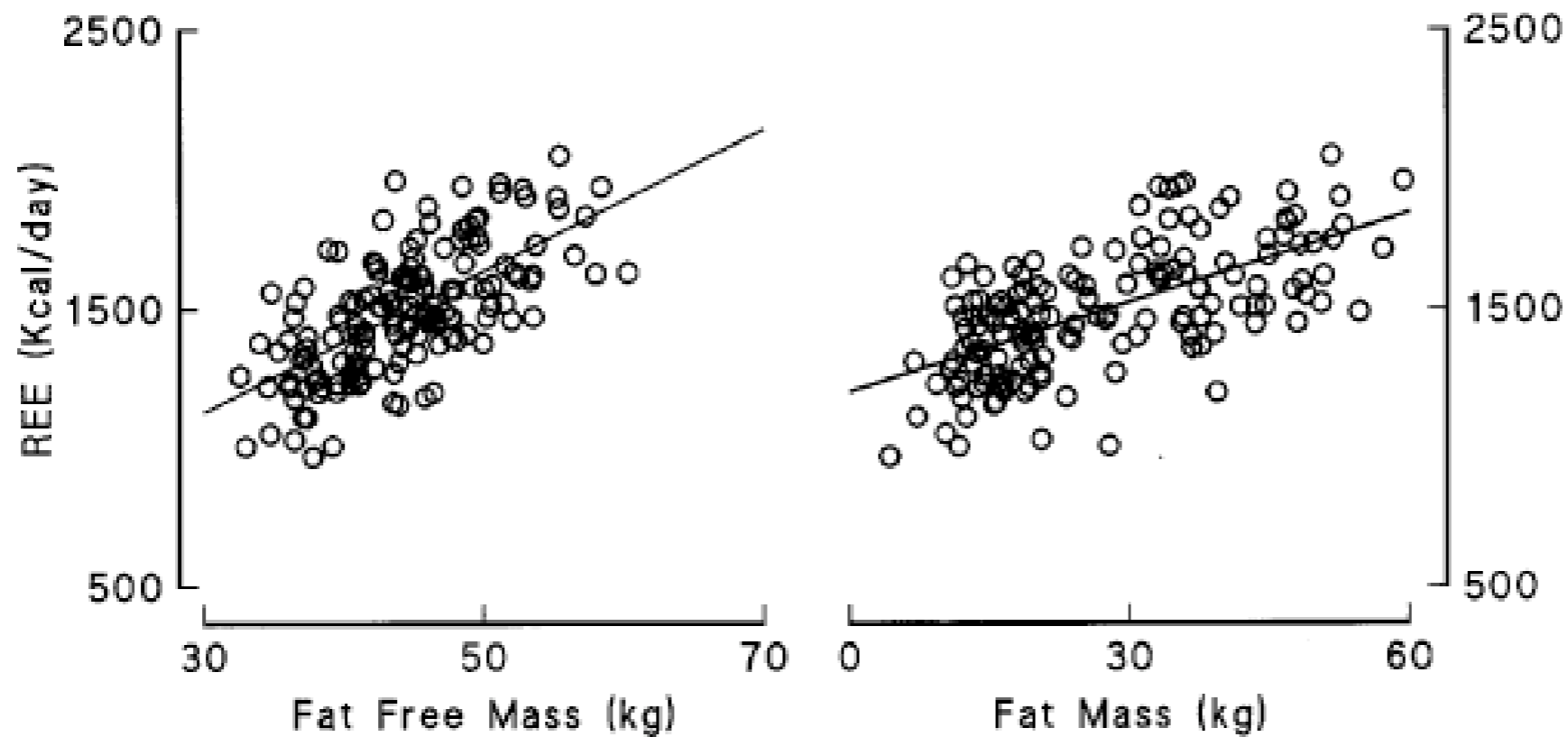


Basal metabolic rate (BMR)

Physical activity

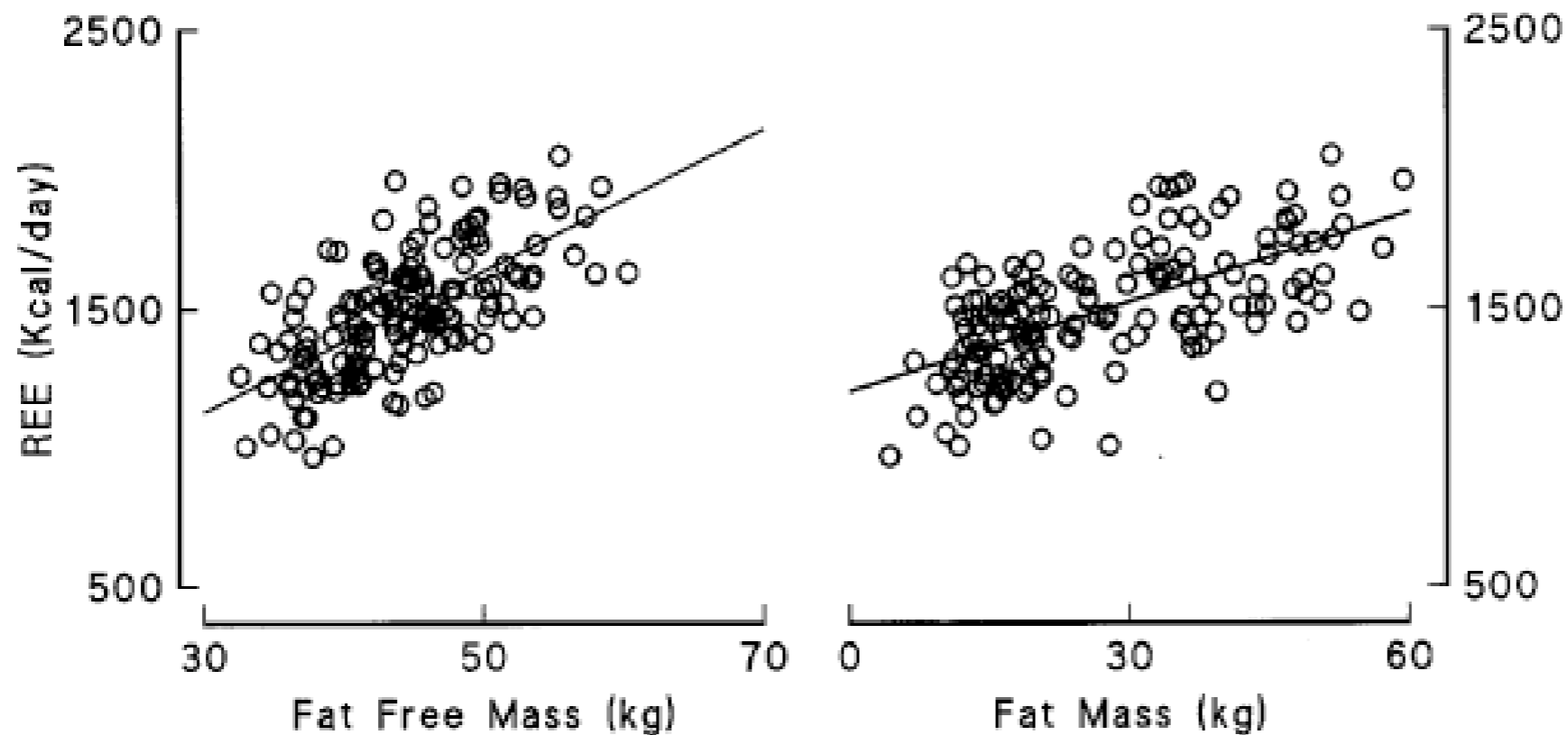
$$E \sim 10 \text{ MJ/day} \quad \sim 115 \text{ W} \quad \sim 3 \text{ KWH/day}$$

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 \propto Mass

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

a ranges from 0 to 0.1 MJ/kg/day

Physical activity

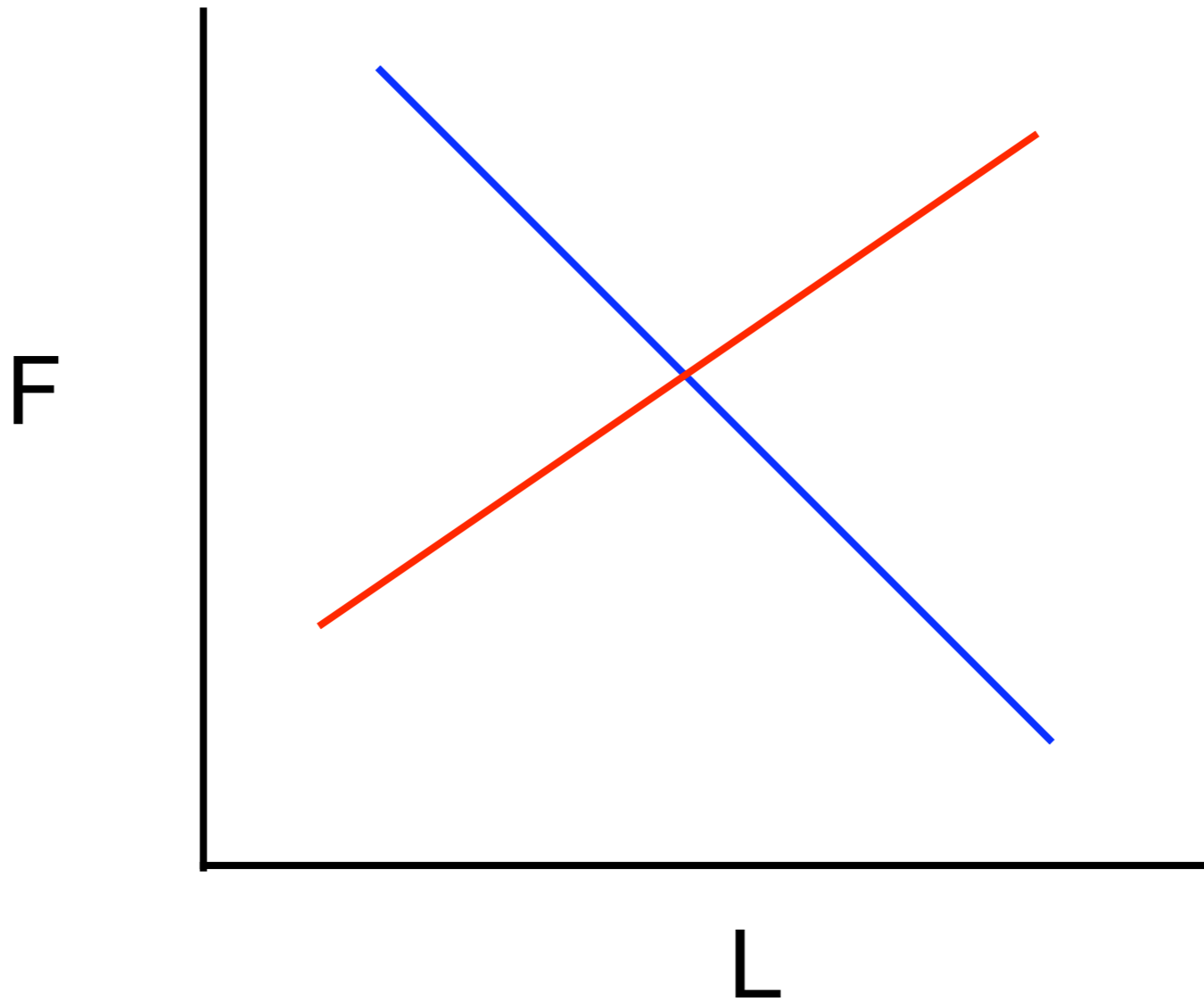
Energy due to PA \propto Mass

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

a ranges from 0 to 0.1 MJ/kg/day

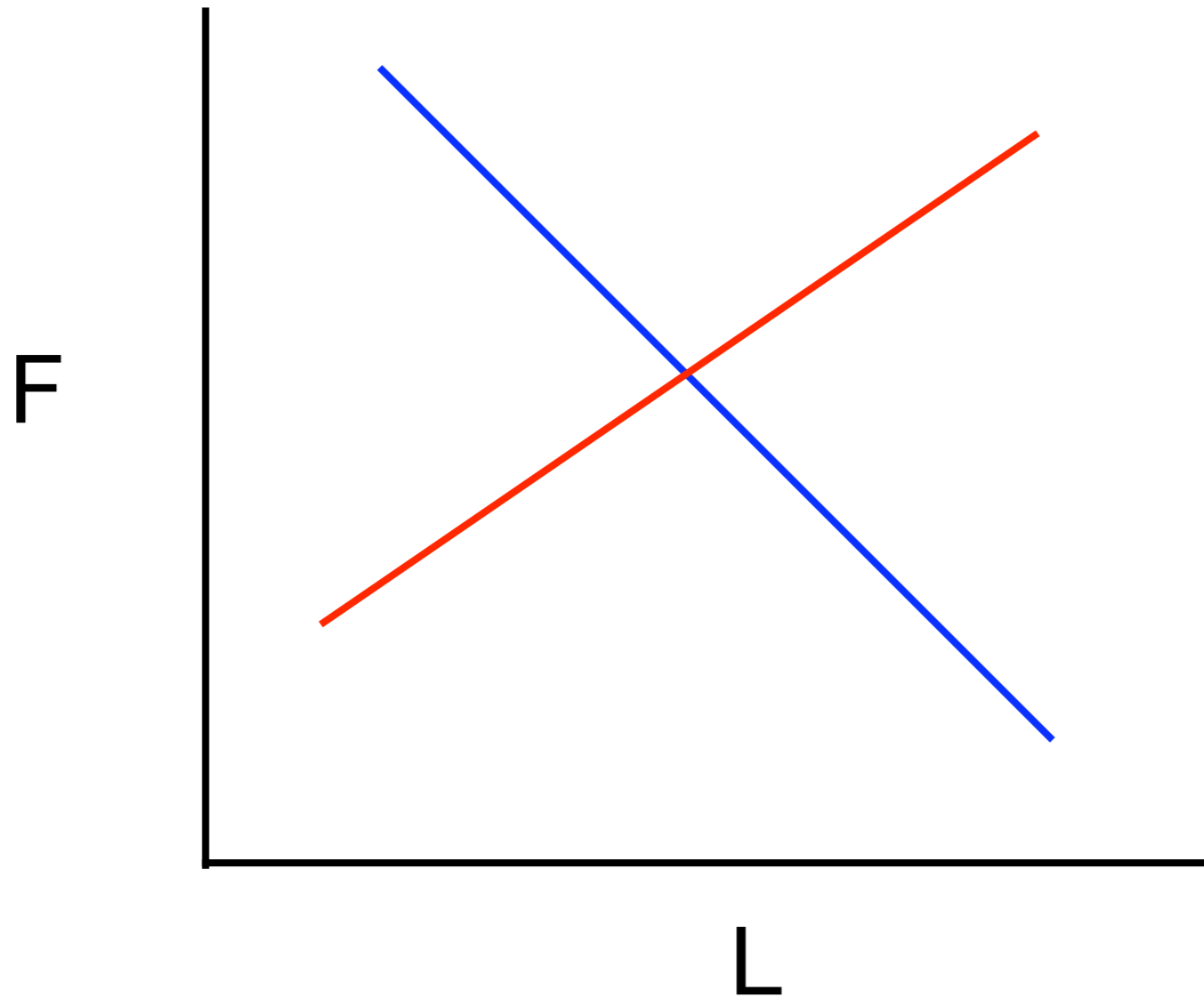
$\therefore E$ is linear in F and L

$$E(F, L) = bF + cL + d = I$$



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

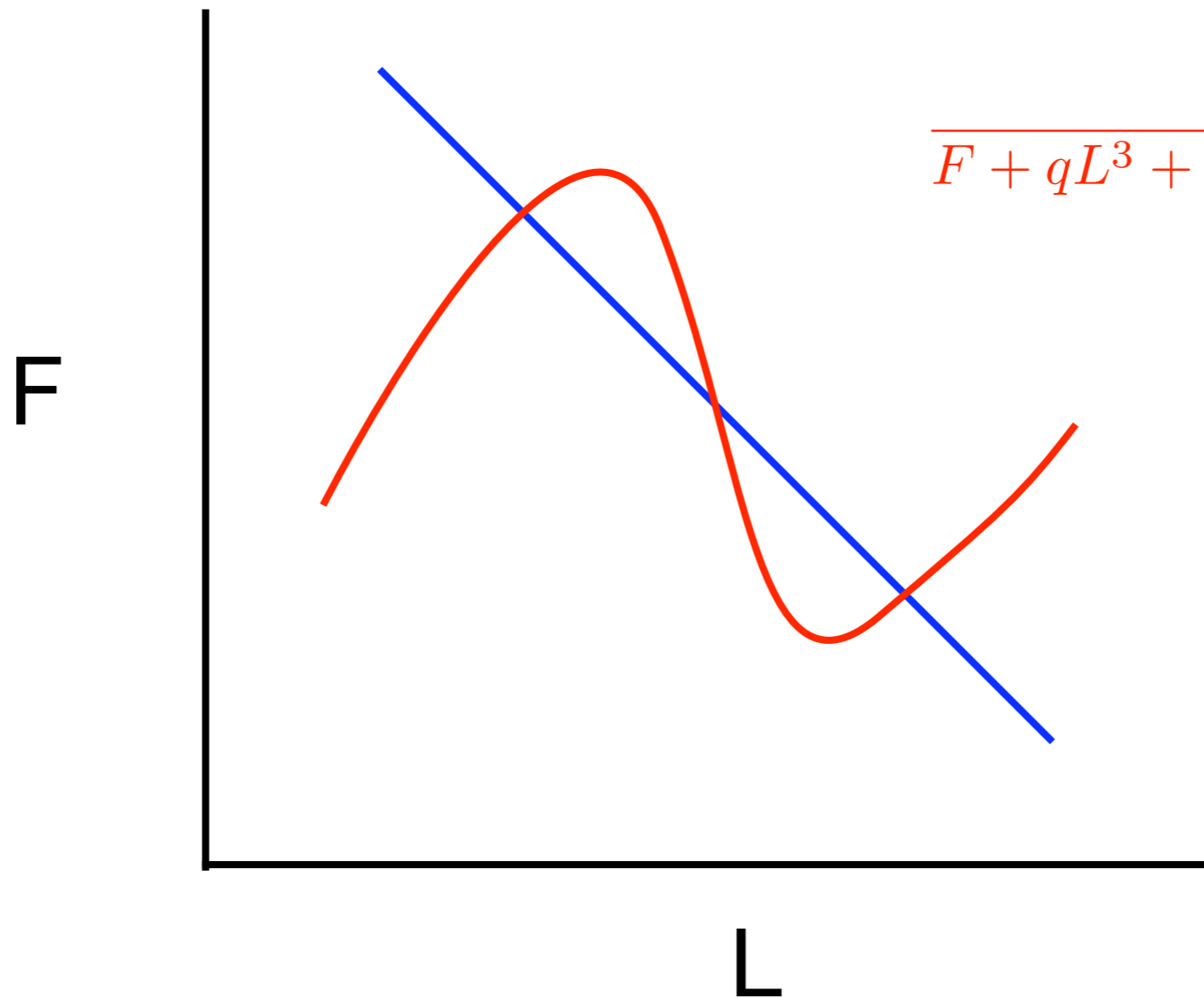
$$E(F, L) = bF + cL + d = I$$



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

Single fixed point is generic

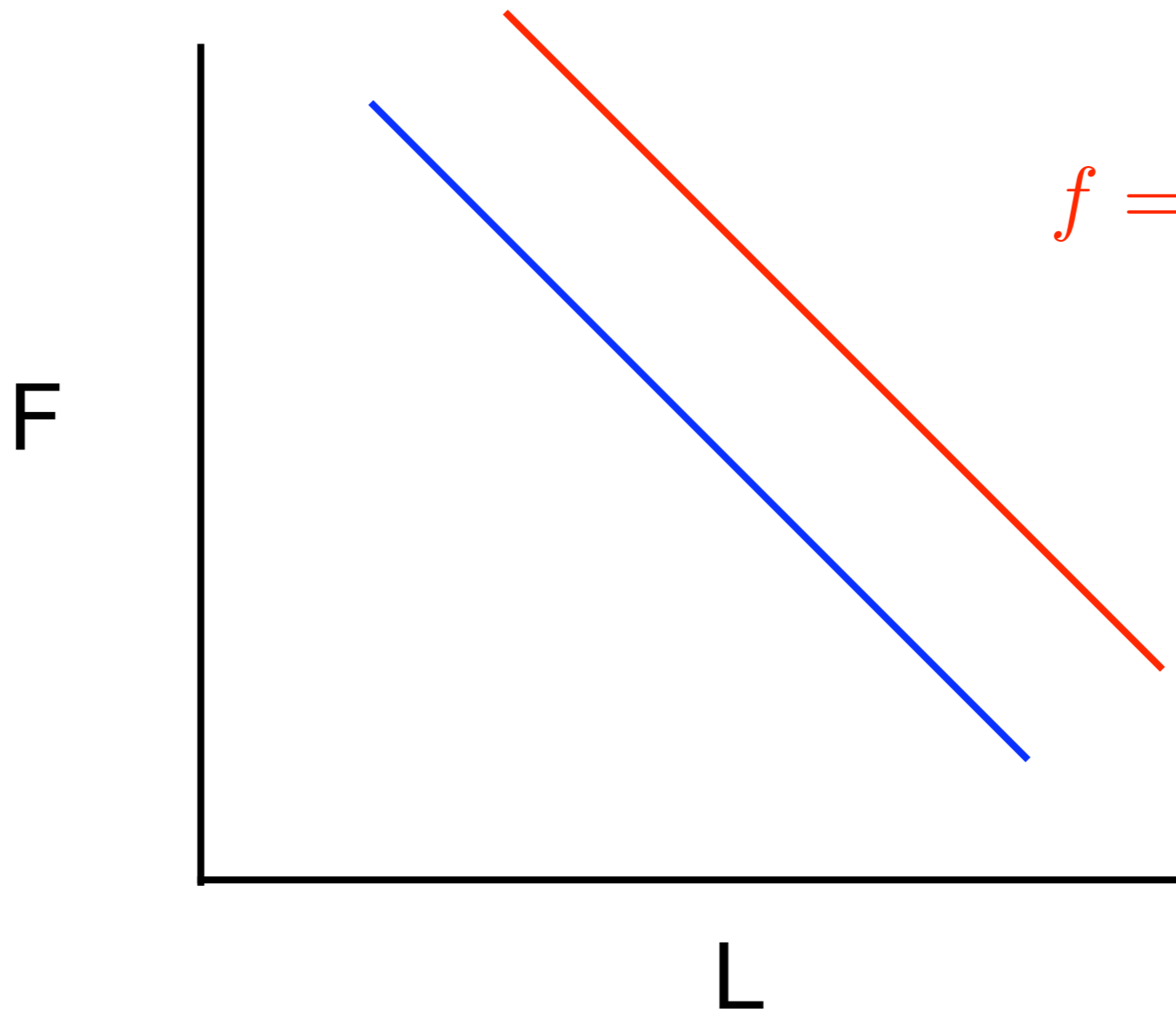
$$E(F, L) = bF + cL + d = I$$



$$\frac{F}{F + qL^3 + rL^2 + sL + t} = \frac{I_F}{E}$$

Multi-stability or limit cycle requires fine tuning

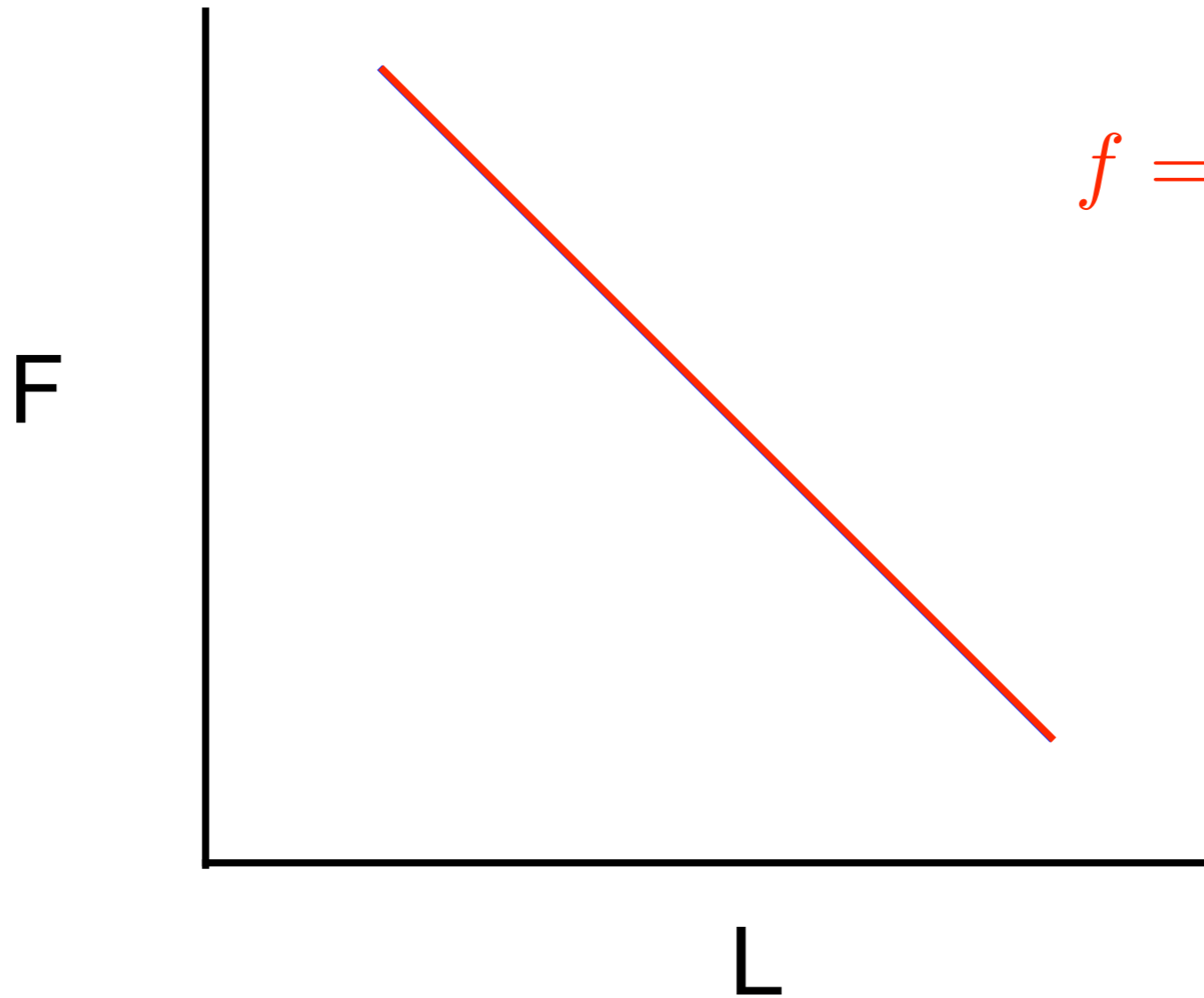
$$E(F, L) = bF + cL + d = I$$



$$f = \frac{I_F}{E} + \psi(I - E)$$

Line attractor requires special form

$$E(F, L) = bF + cL + d = I$$



$$f = \frac{I_F}{E} + \psi(I - E)$$

Line attractor requires special form

The problem with f

In energy balance, f reflects diet

The problem with f

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

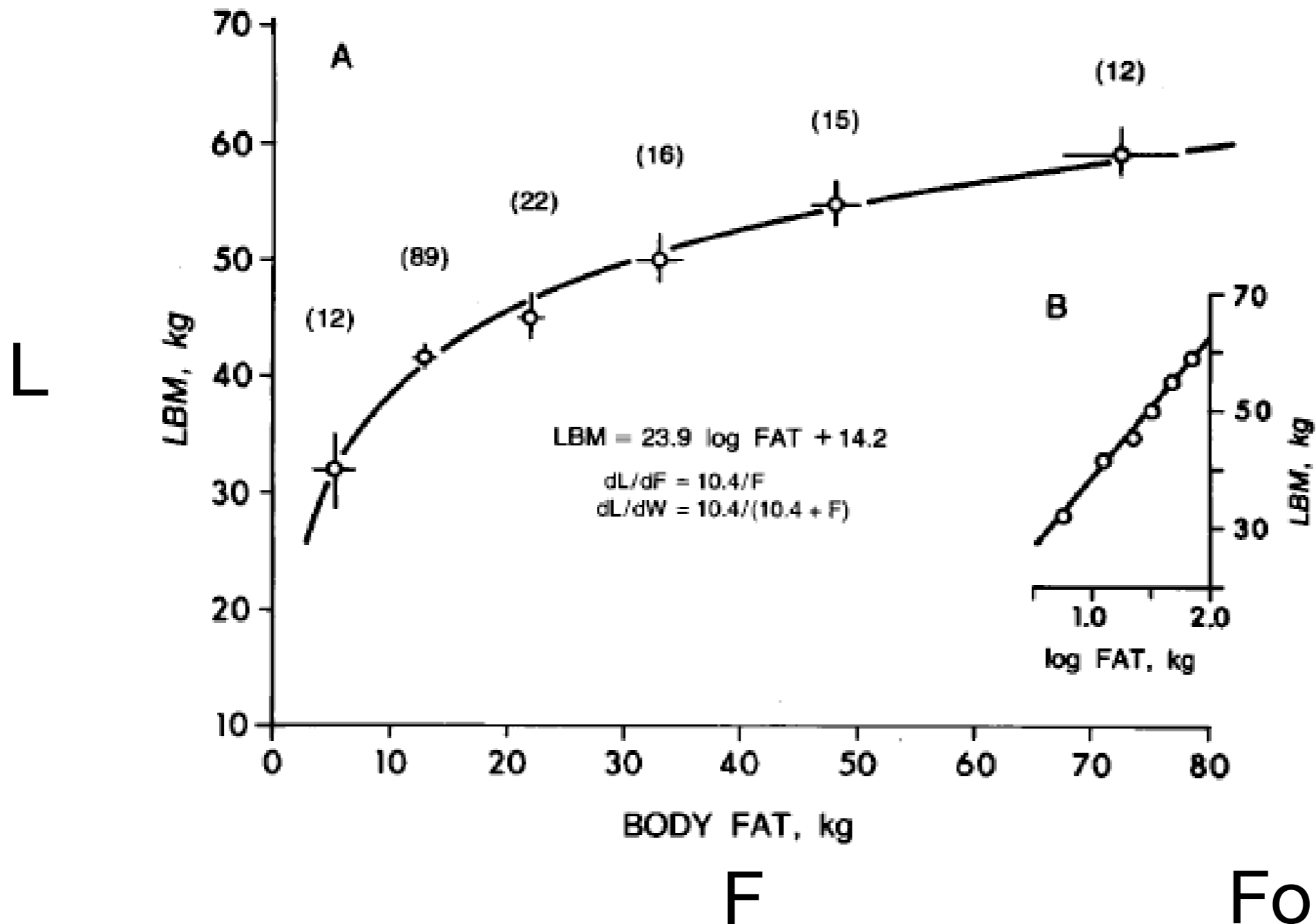
The problem with f

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

Must invert in dynamic situation

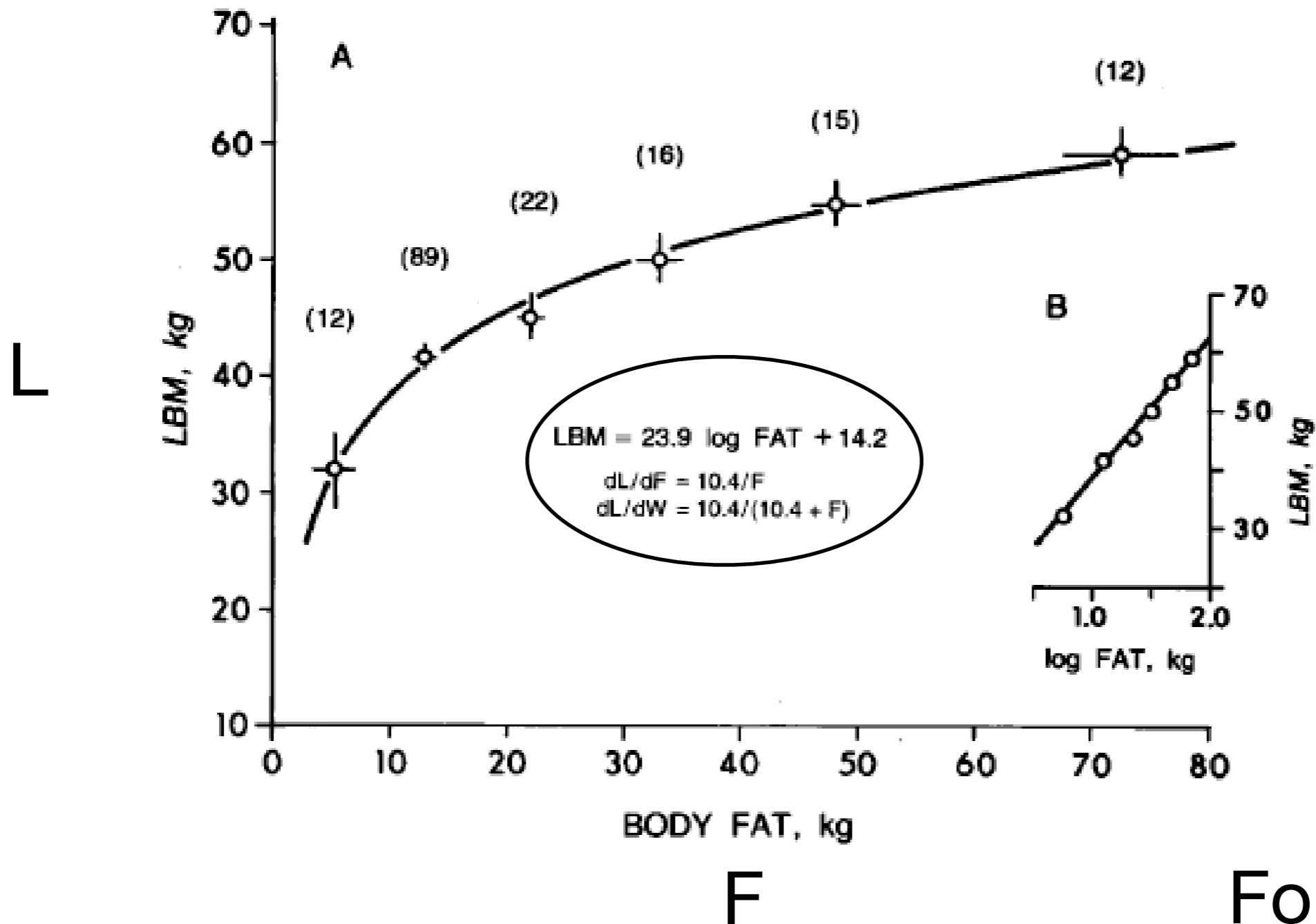
$$\rho_F \frac{dF}{dt} = I_F - fE$$
$$\rho_L \frac{dL}{dt} = I_L - (1 - f)E$$

Body composition



Forbes, 2000

Body composition



Forbes, 2000

Apply Forbes law to model

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

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

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

Apply Forbes law to model

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

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

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

Apply Forbes law to model

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

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

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

Apply Forbes law to model

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

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

Apply Forbes law to model

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

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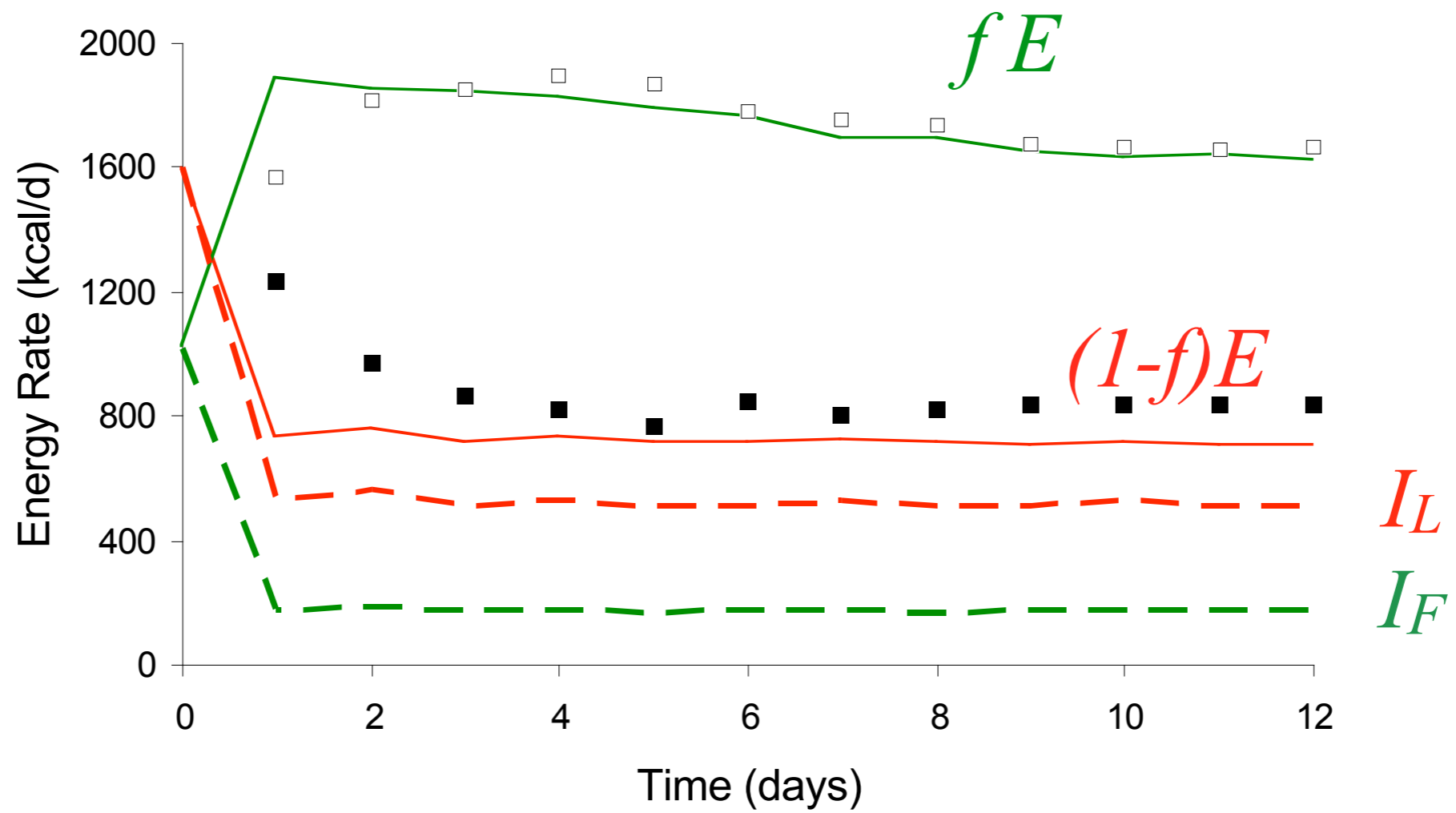
$$f = \frac{I_F - (1 - p)(I - E)}{E} \quad p = \frac{1}{1 + \frac{\rho_F}{\rho_L} \frac{F}{10.4}}$$

Apply Forbes law to model

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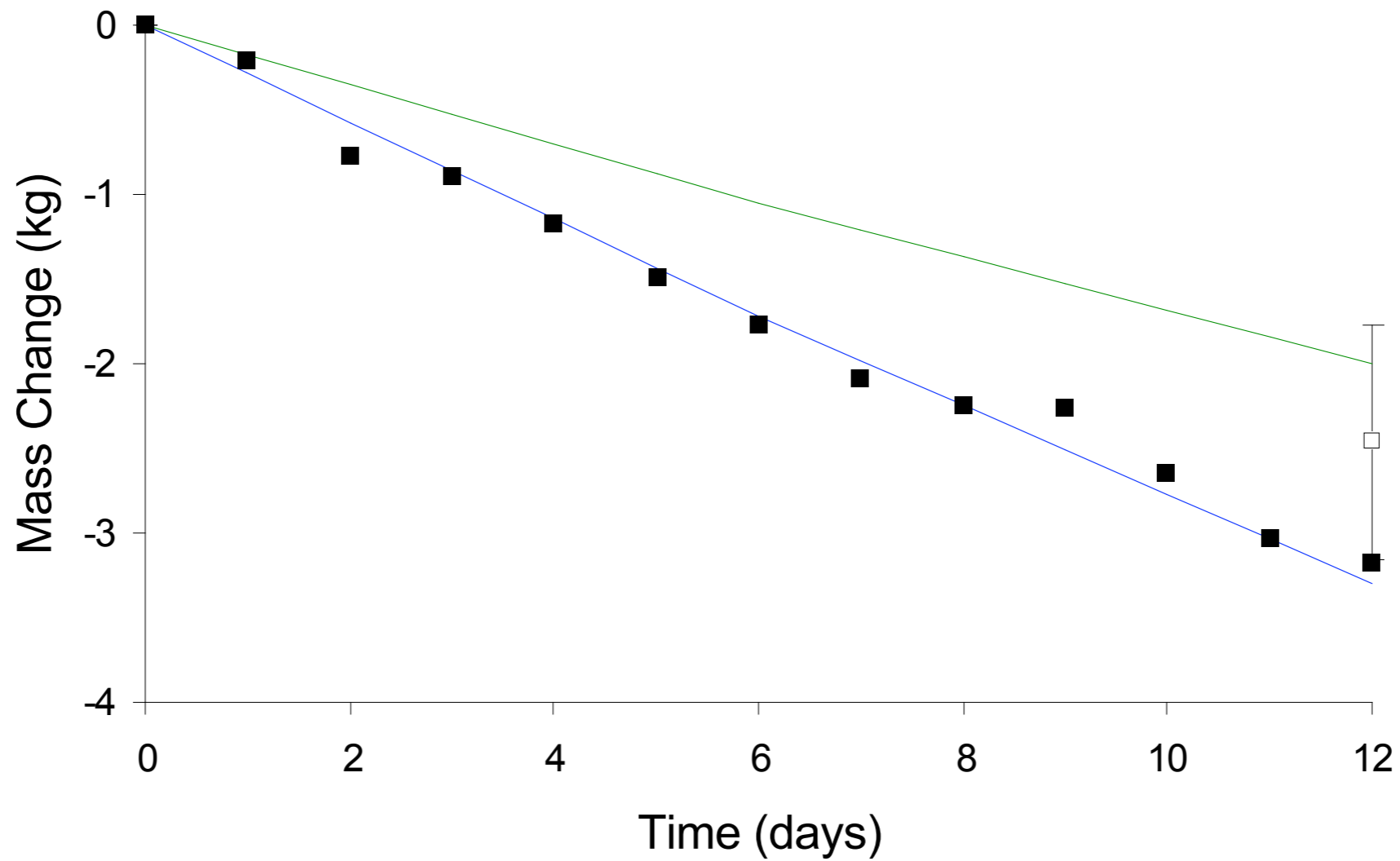
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Matches data



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

Weight and fat loss



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

Energy partition model

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

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

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Energy partition model

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

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

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

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

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

Energy partition model

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

Energy partition model

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

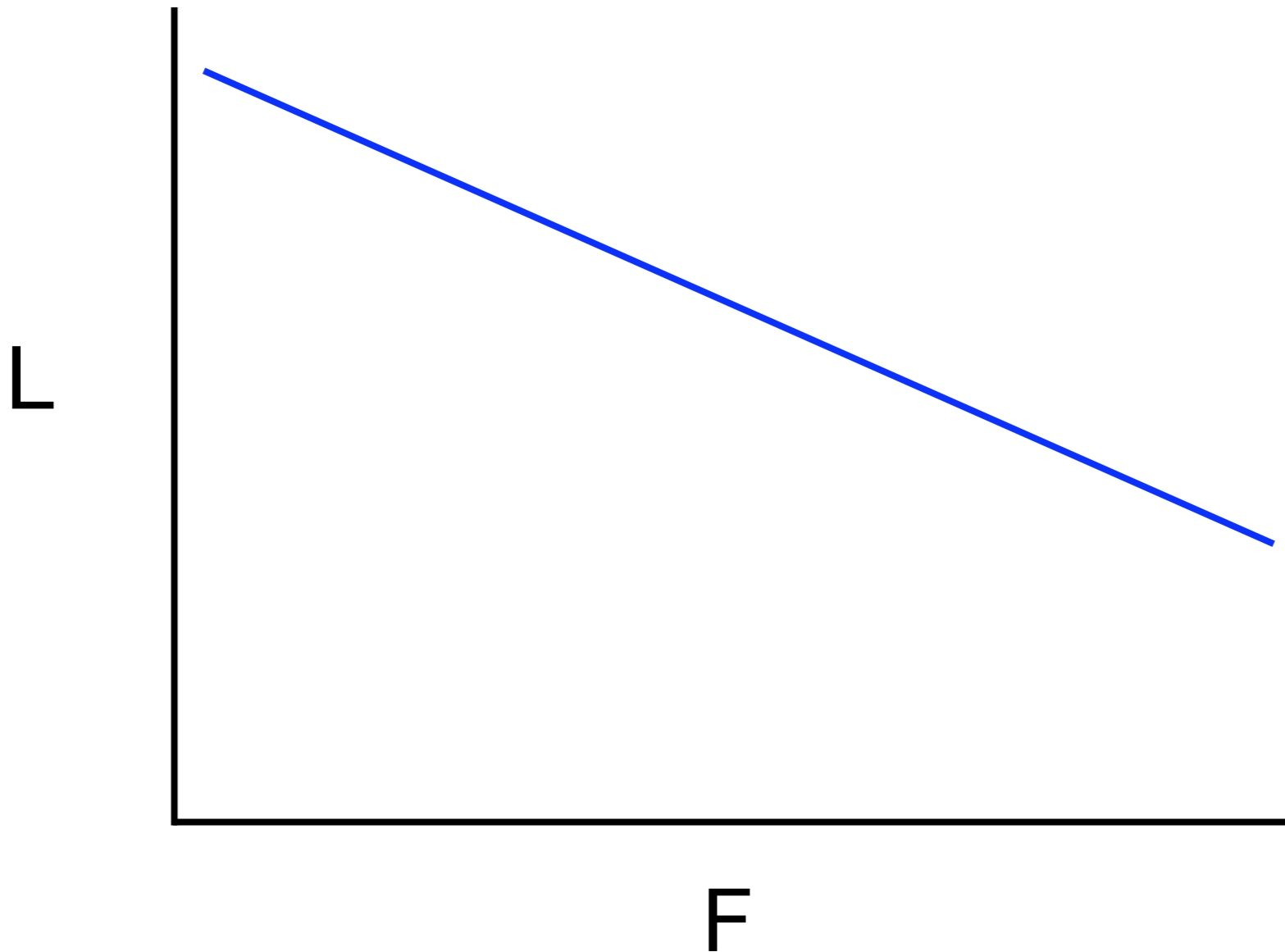
$$\rho_L \frac{dL}{dt} = p(I - E)$$

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

Almost all previous models use energy partition

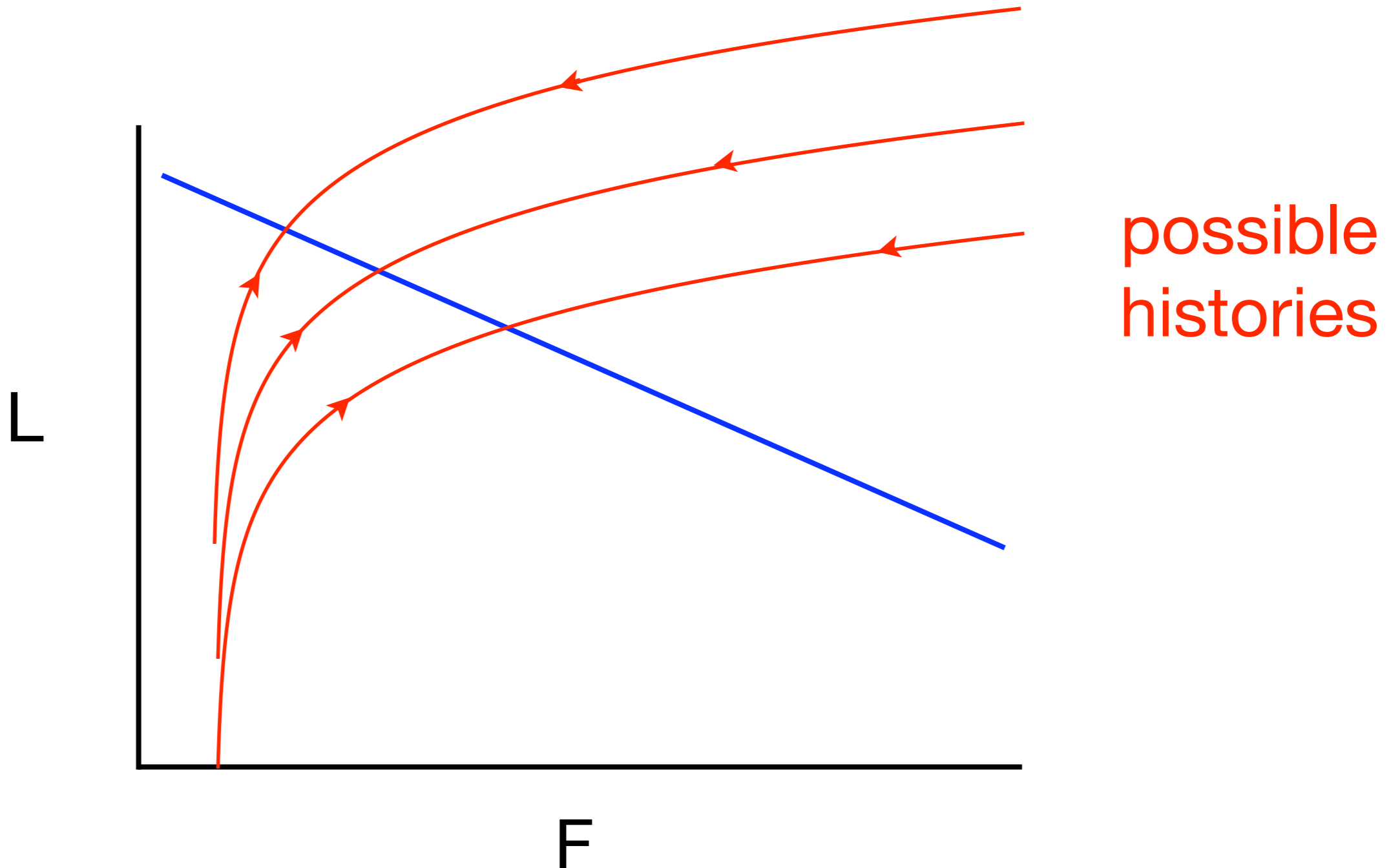
Consequences of line attractor

$$E(F,L)=I$$



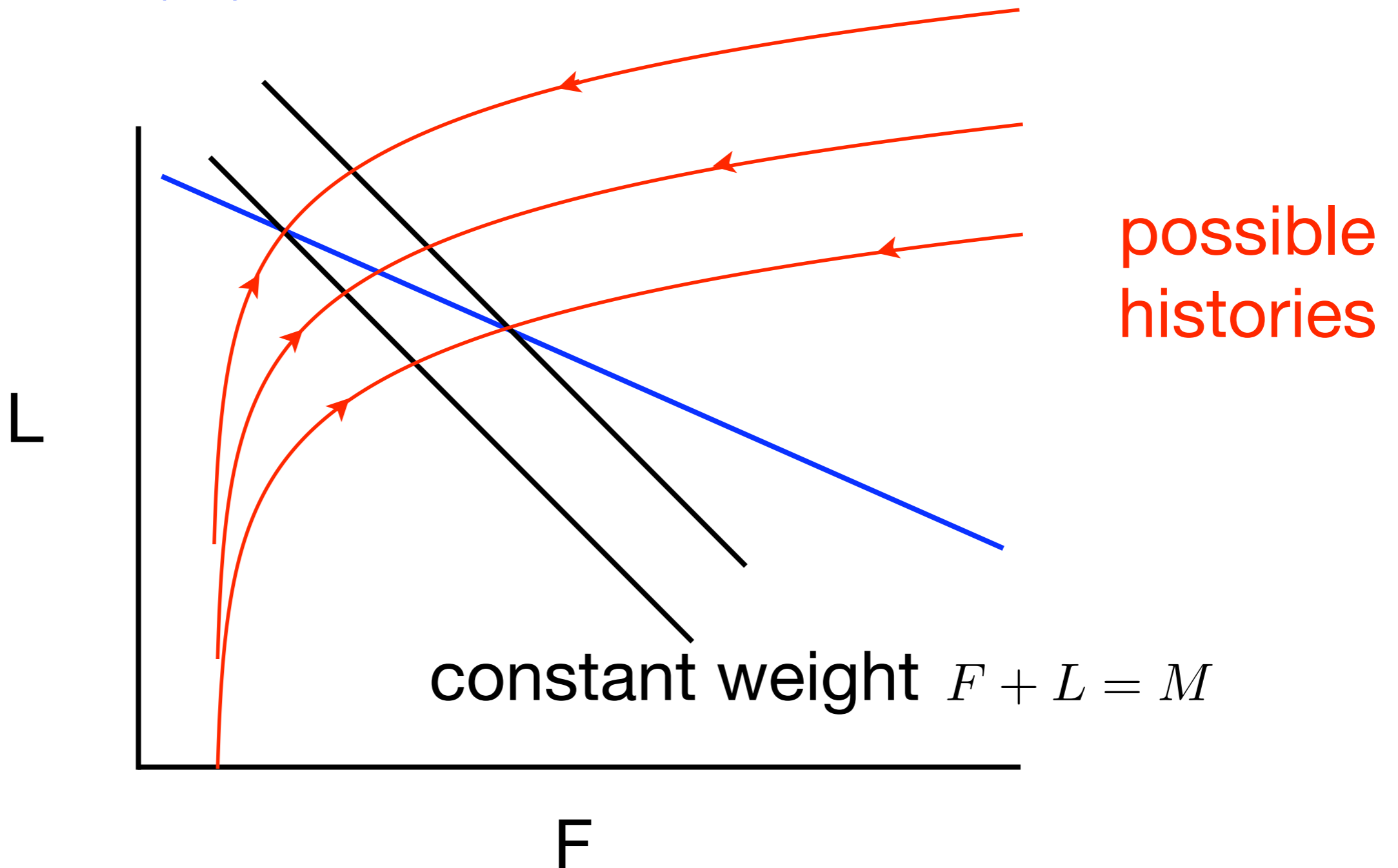
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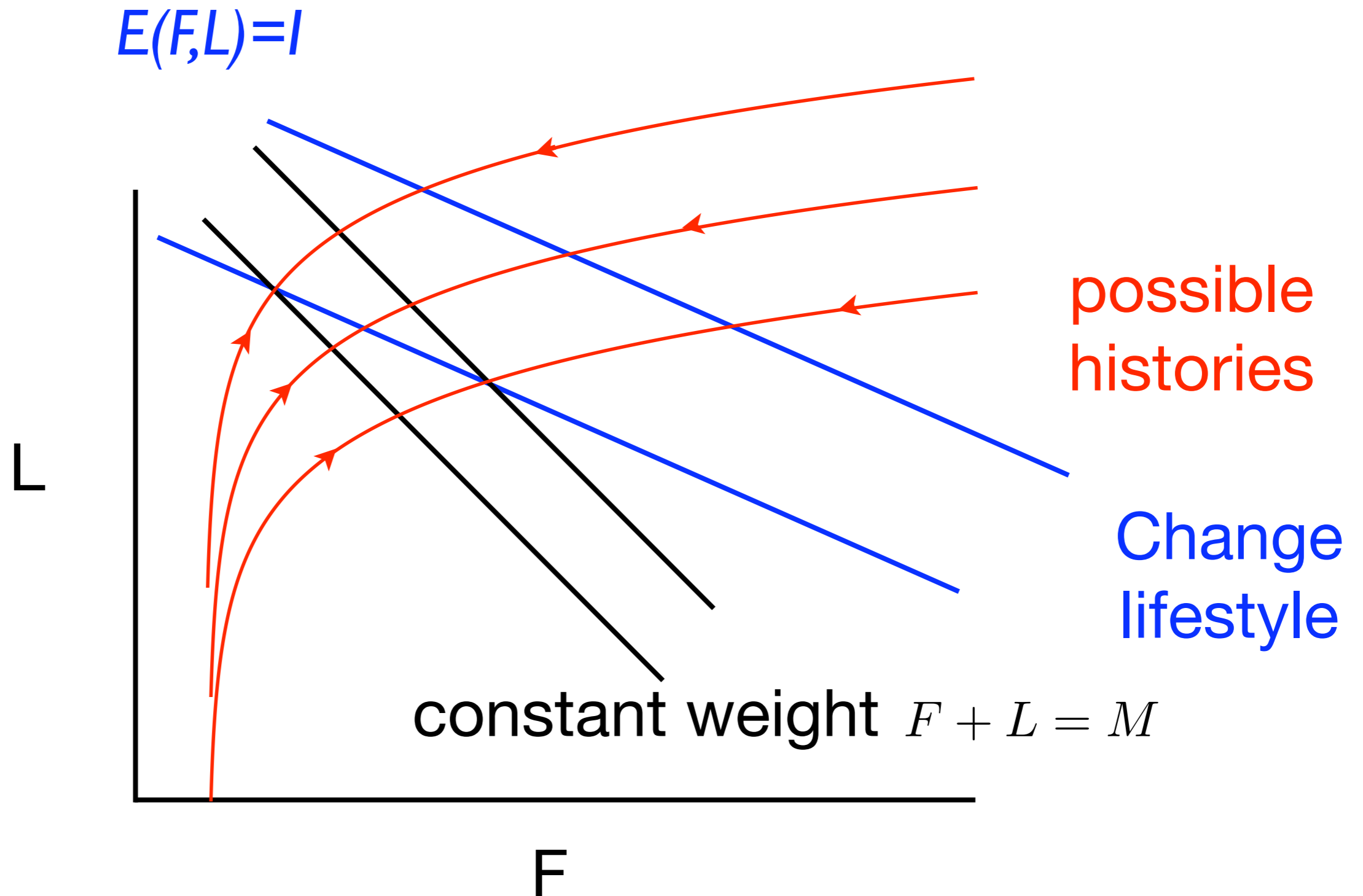


Consequences of line attractor

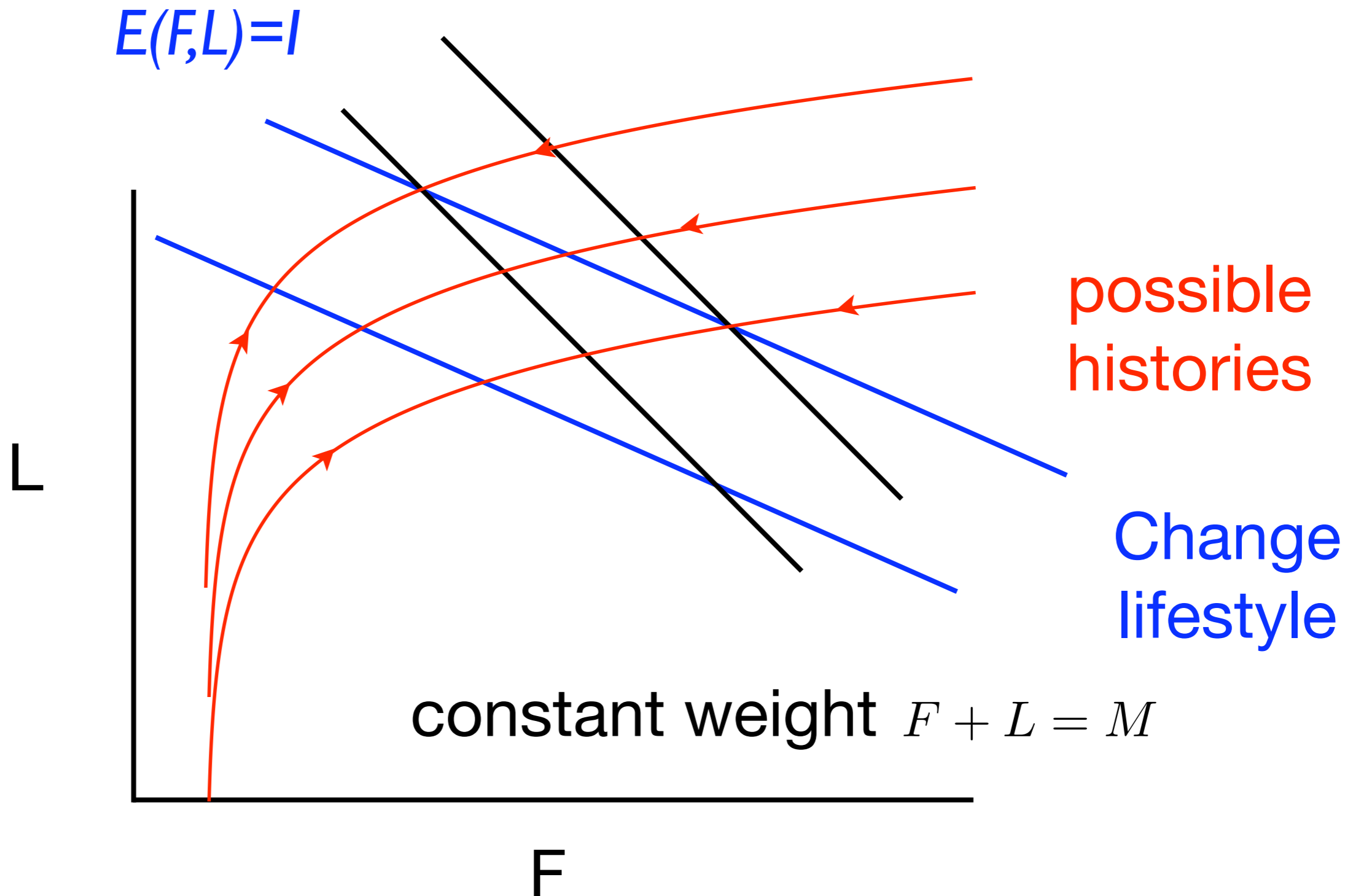
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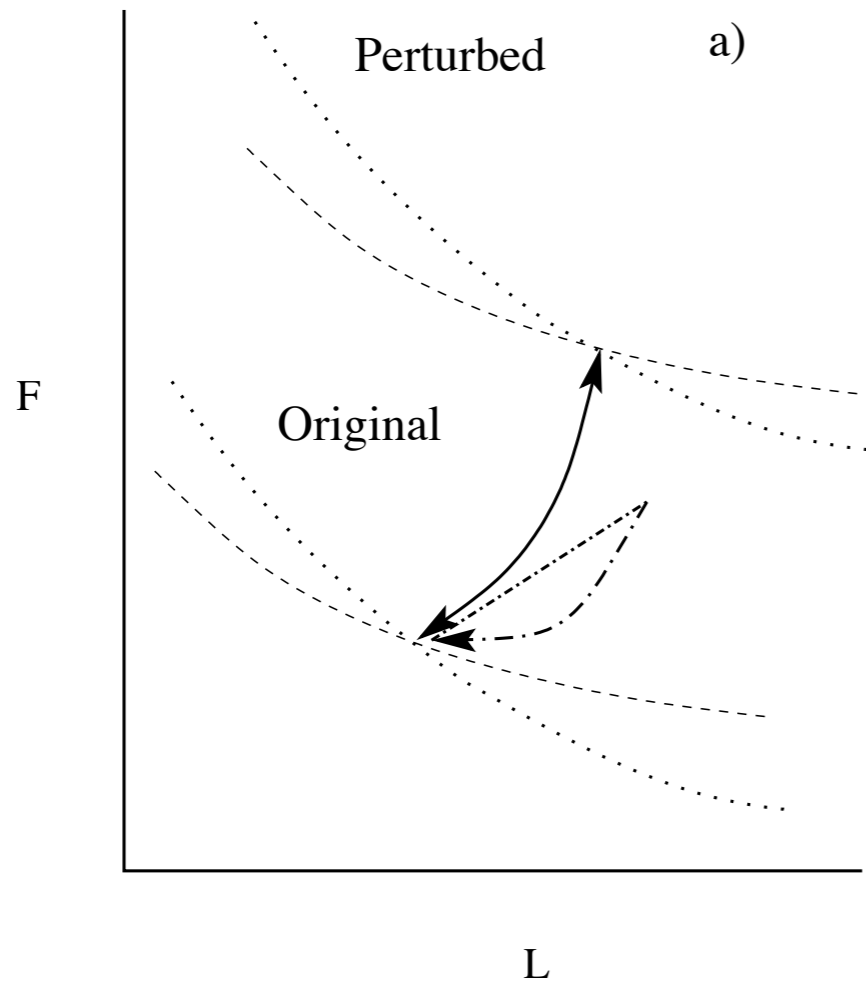
Consequences of line attractor



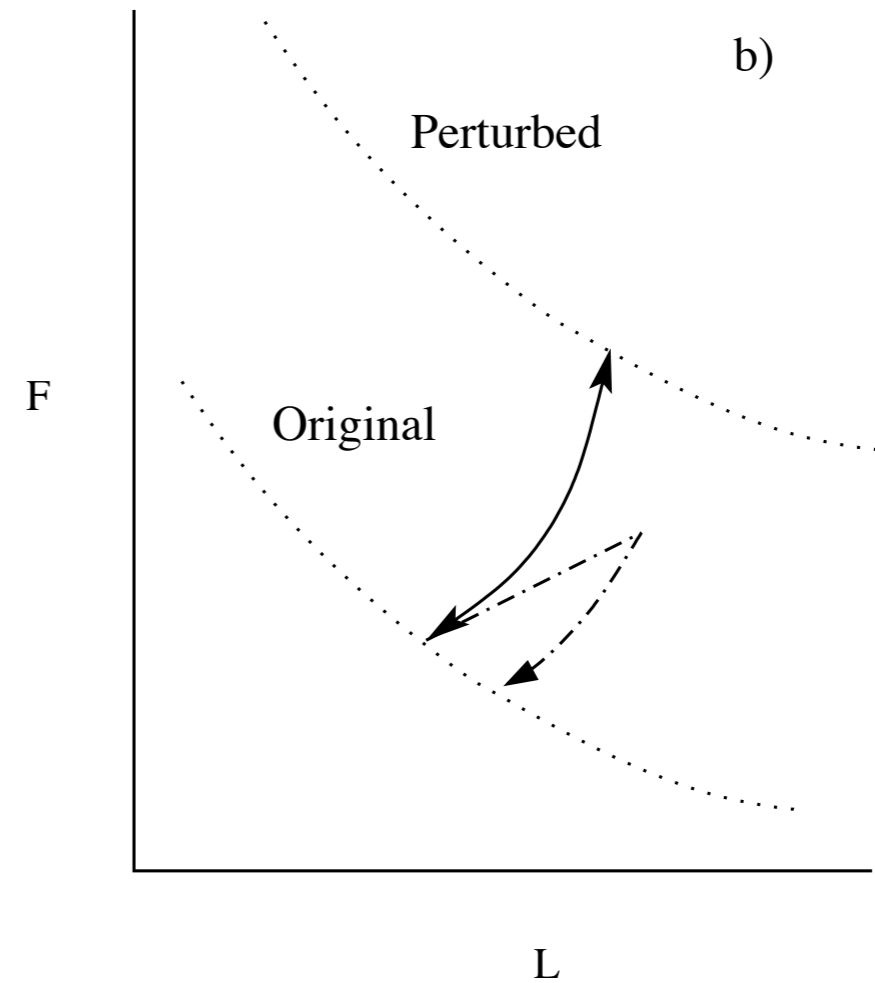
Consequences of line attractor



Effect of perturbations



fixed point



line attractor

Numerical example

$$\rho_F \frac{dF}{dt} = I_F - fE \quad \rho_F = 37.7 \text{ MJ/kg}$$

$$\rho_L \frac{dL}{dt} = I_L - (1 - f)E \quad \rho_L = 7.6 \text{ MJ/kg}$$

$$E \text{ (MJ/Day)} = 0.14 L \text{ (kg)} + 0.05 F \text{ (kg)} + 1.55$$

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

Numerical example

$$\rho_F \frac{dF}{dt} = (1 - p)(I - E) + \psi \quad \rho_F = 37.7 \text{ MJ/kg}$$

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$$\psi = \begin{cases} 0.05(F - 0.4 \exp(L/10.4))/F \\ 0 \end{cases}$$

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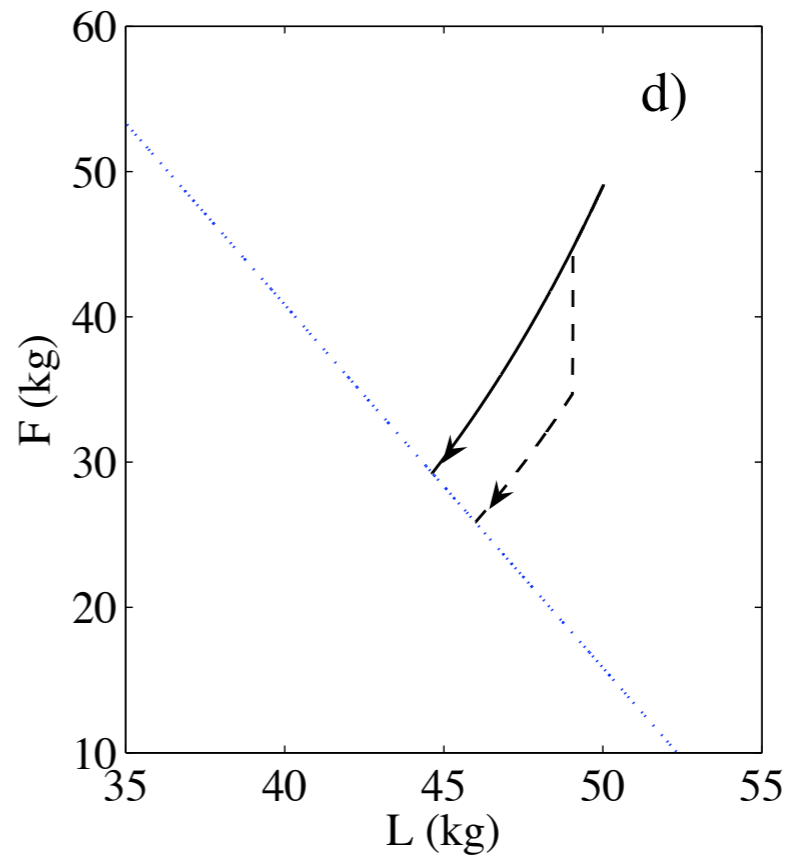
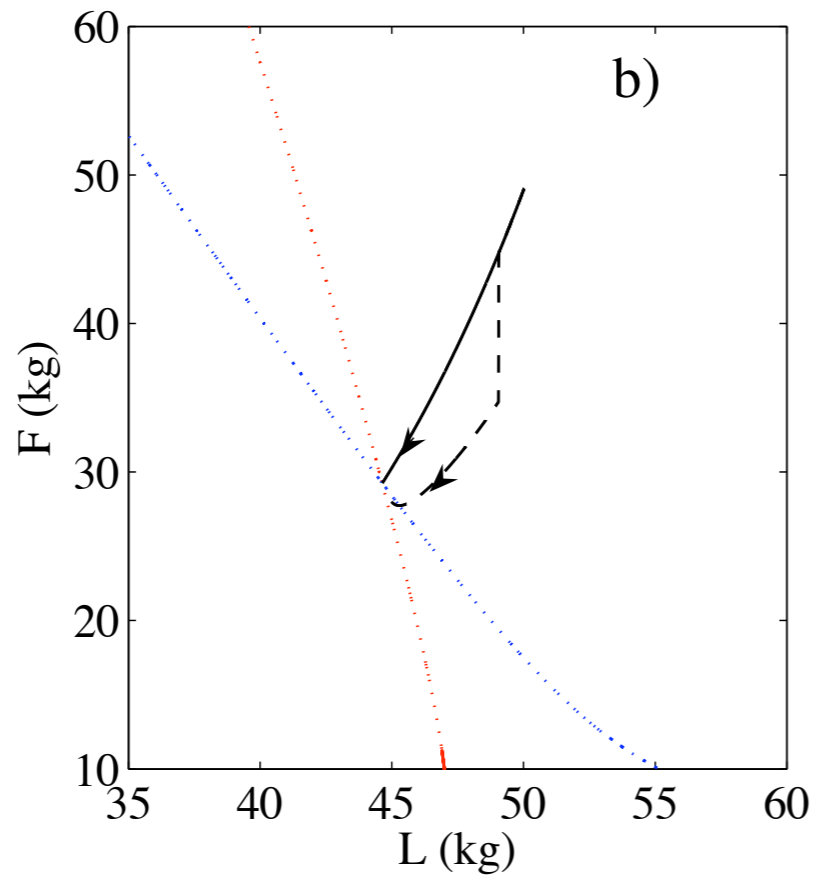
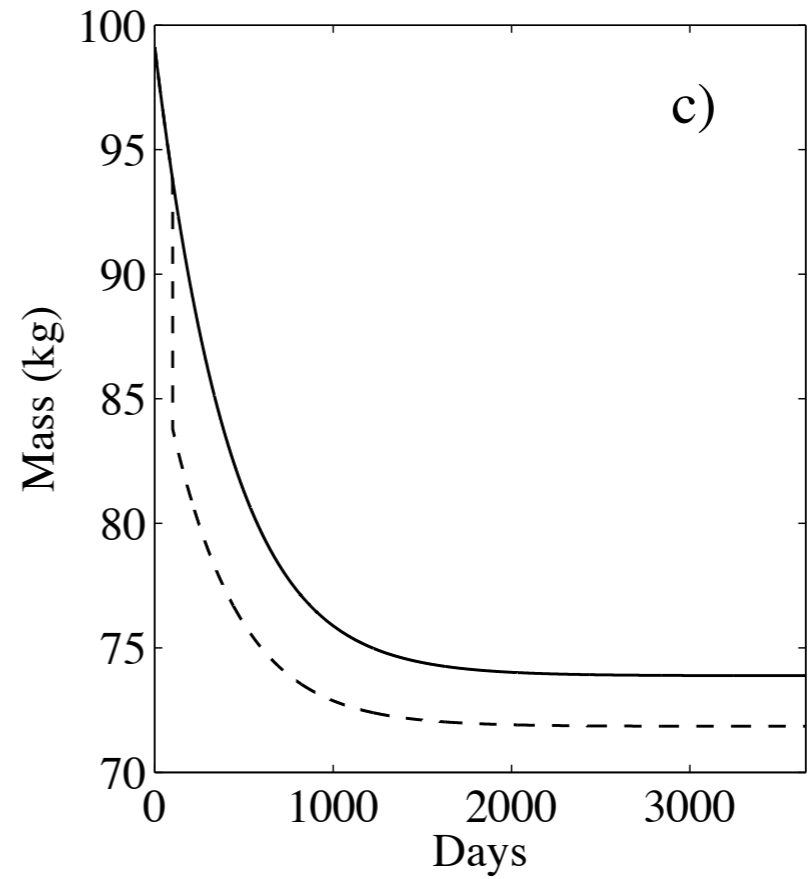
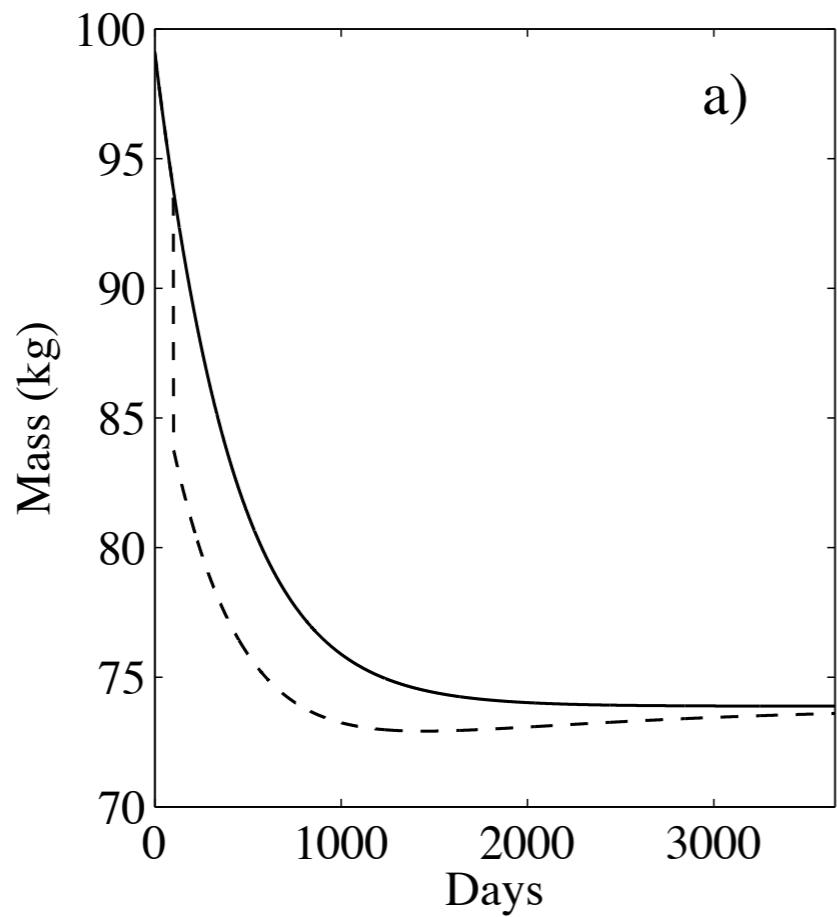
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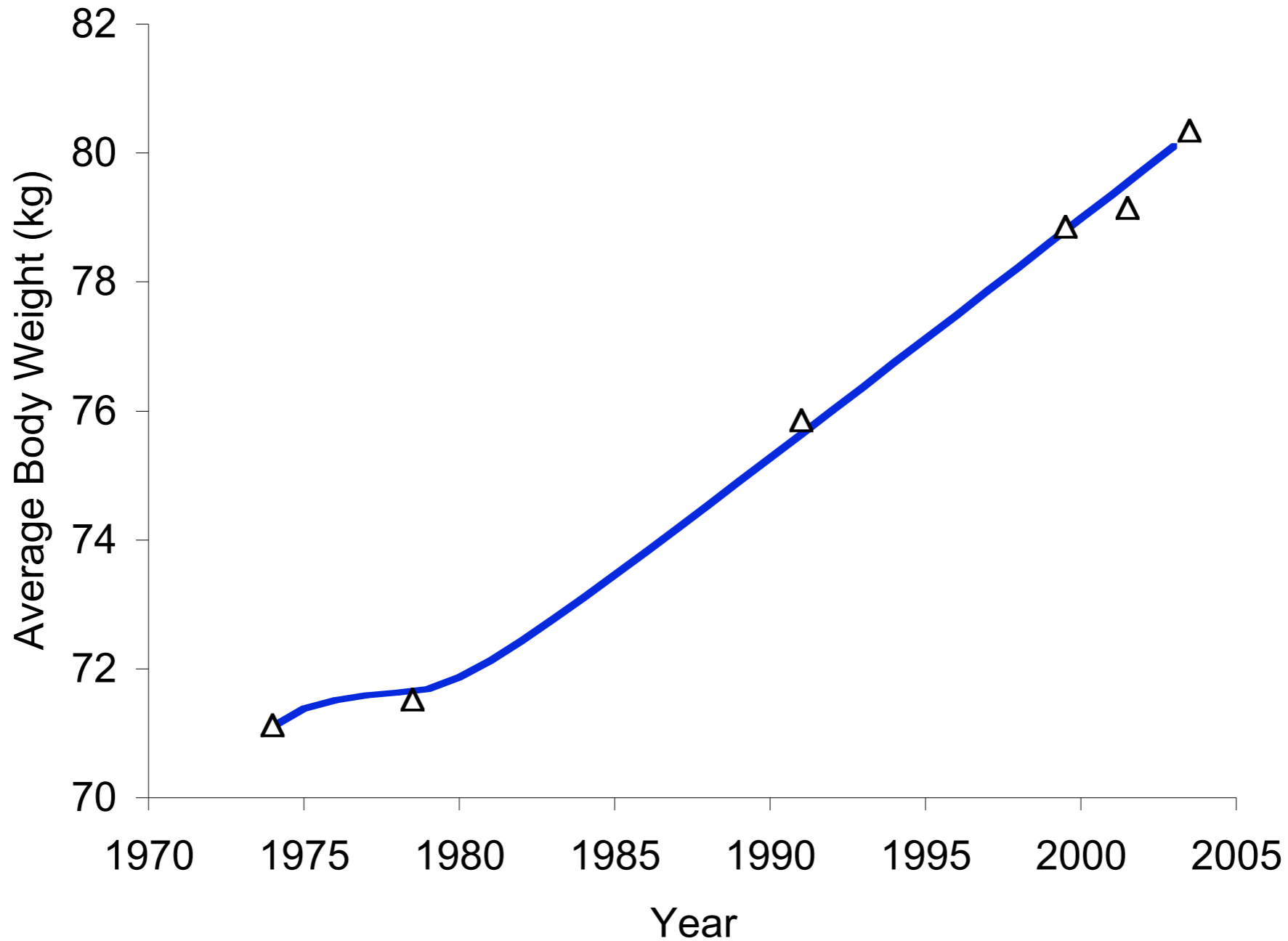
fixed point

$$\psi = \begin{cases} 0.05(F - 0.4 \exp(L/10.4))/F \\ 0 \end{cases}$$

invariant manifold

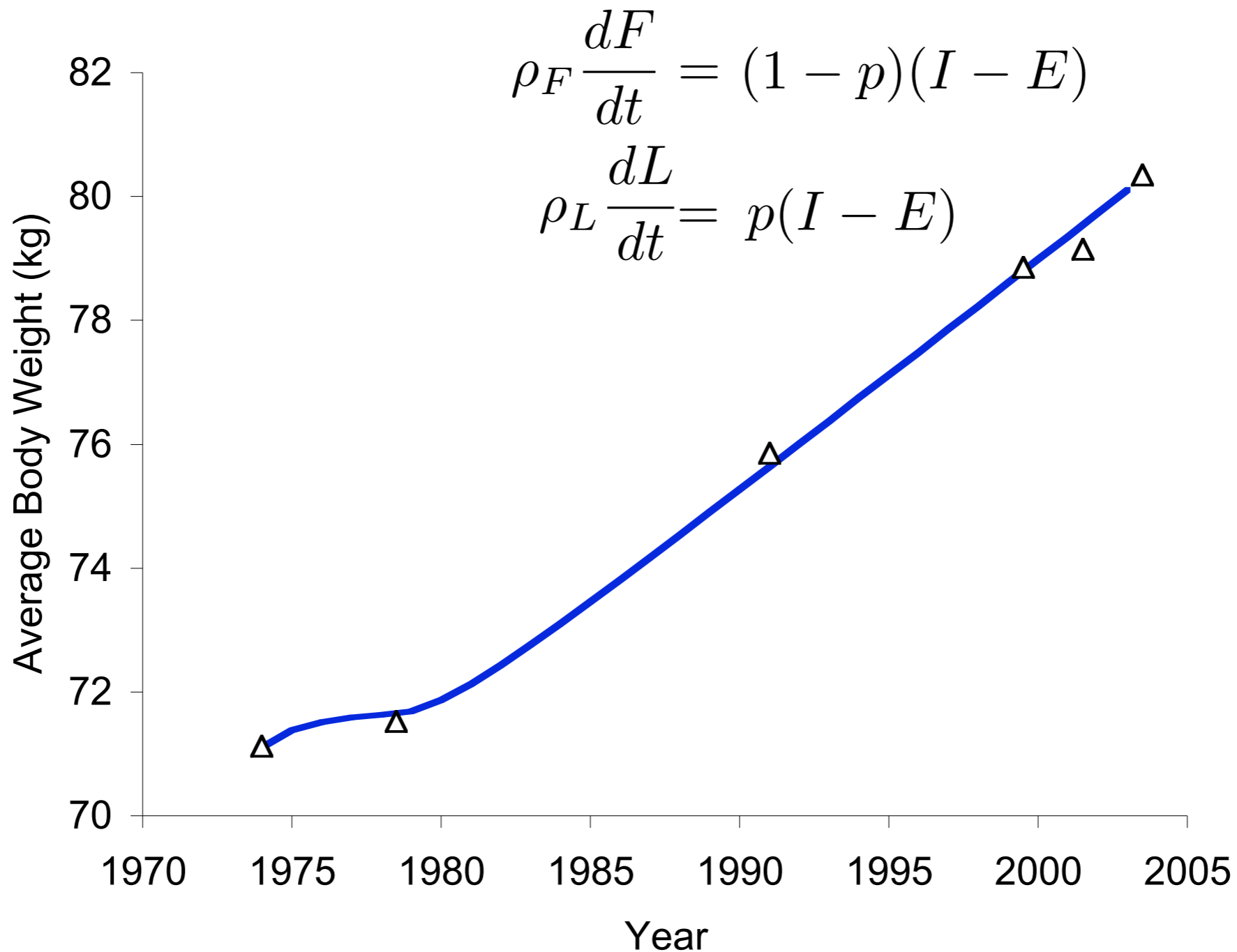


Mean US body weight



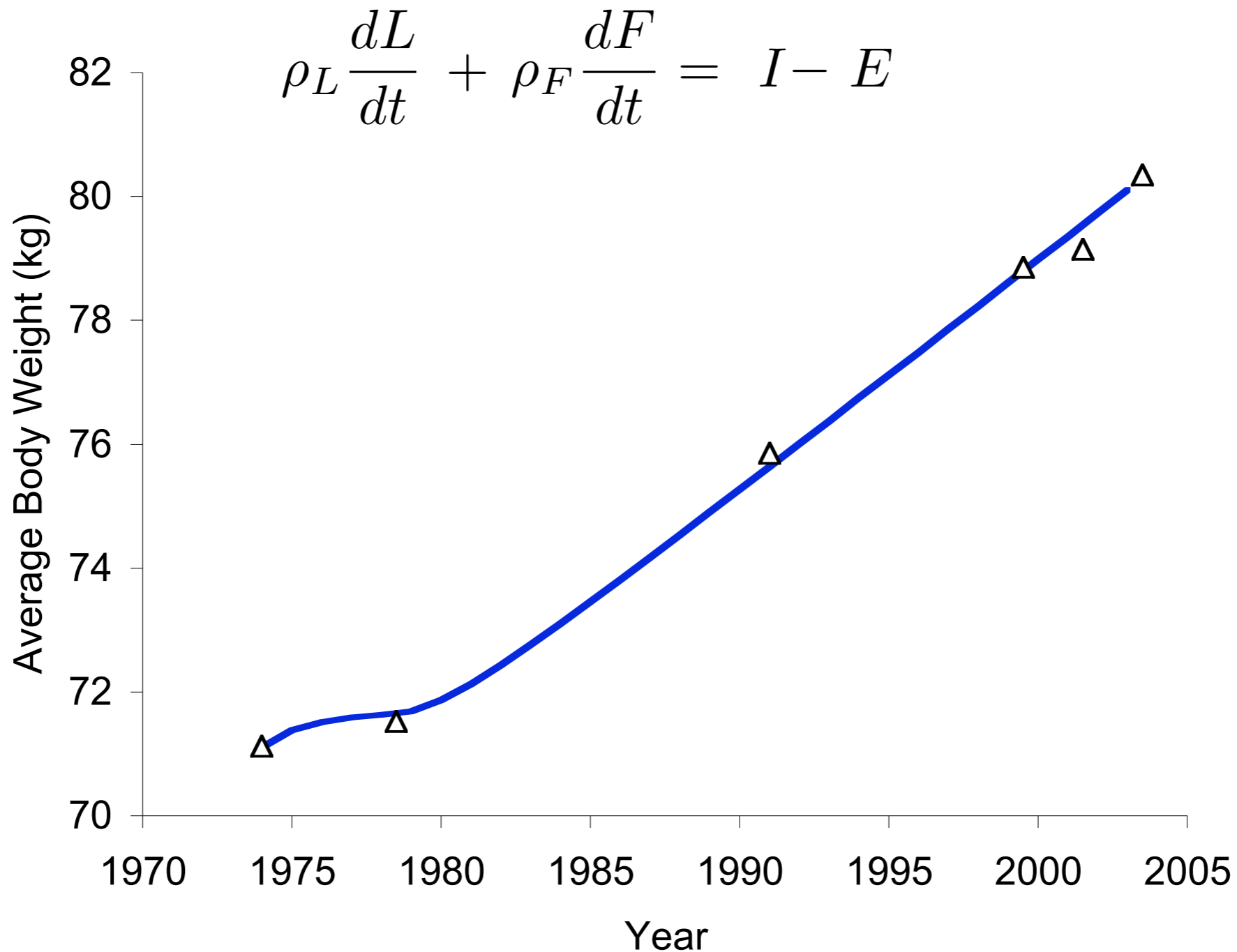
Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight



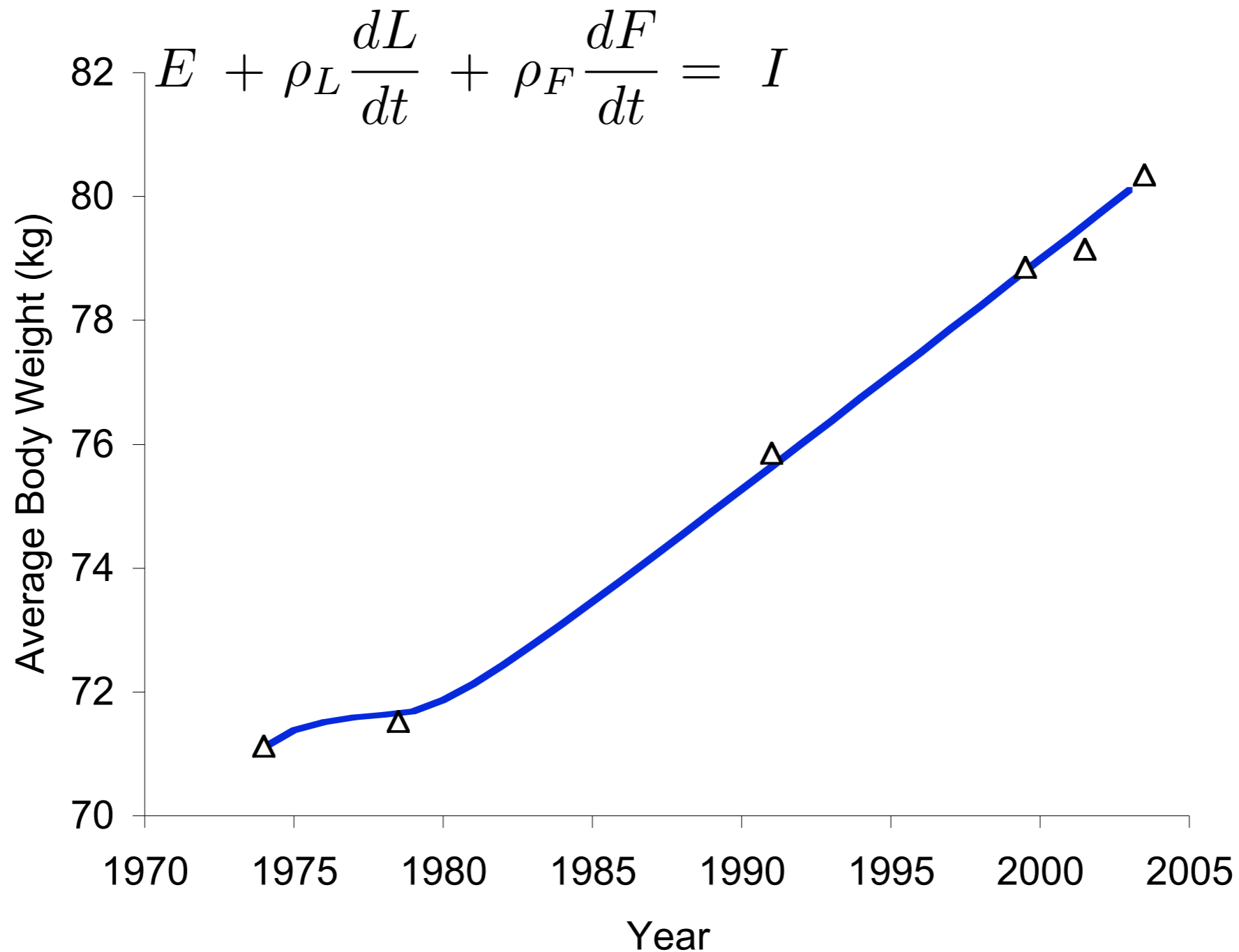
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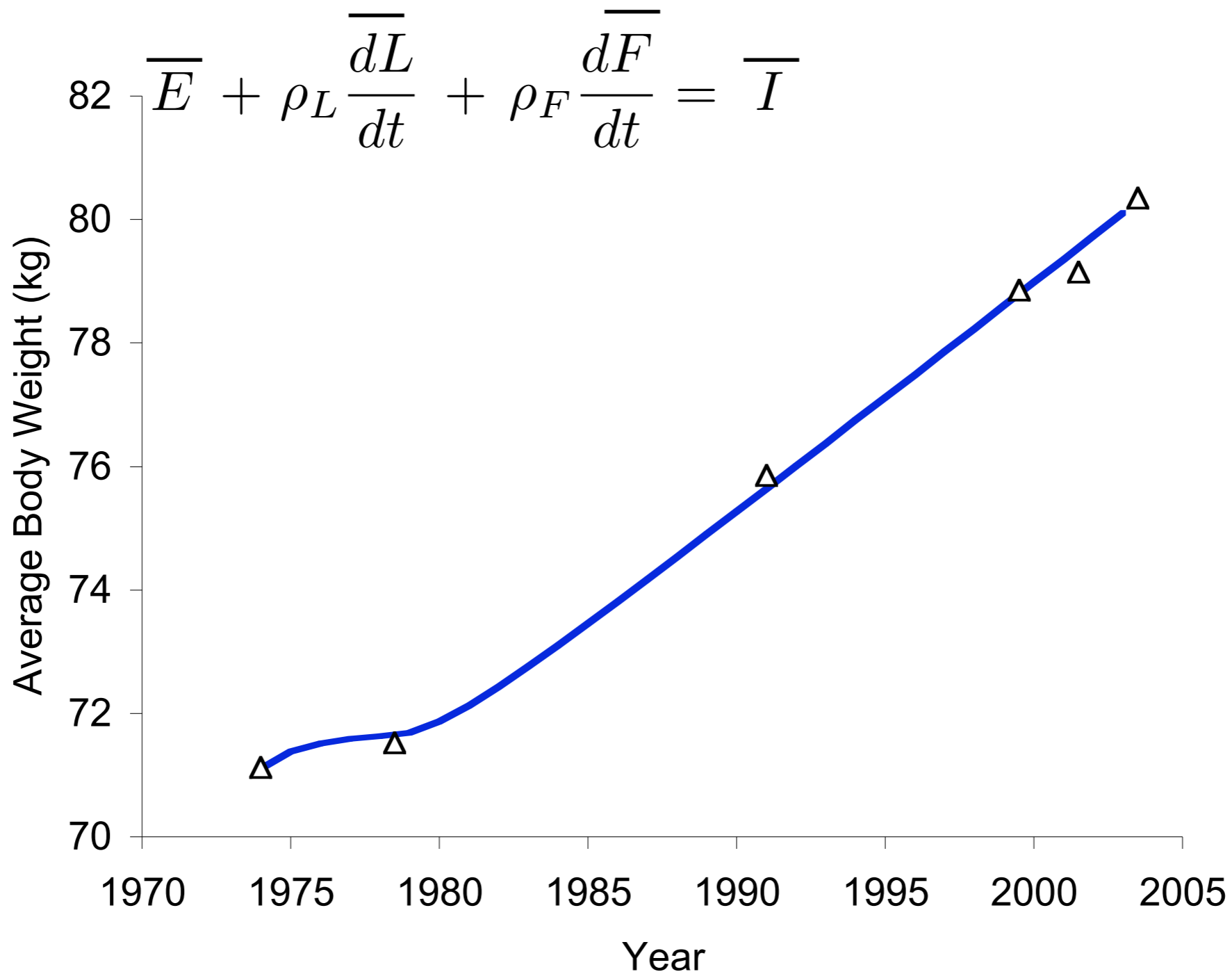
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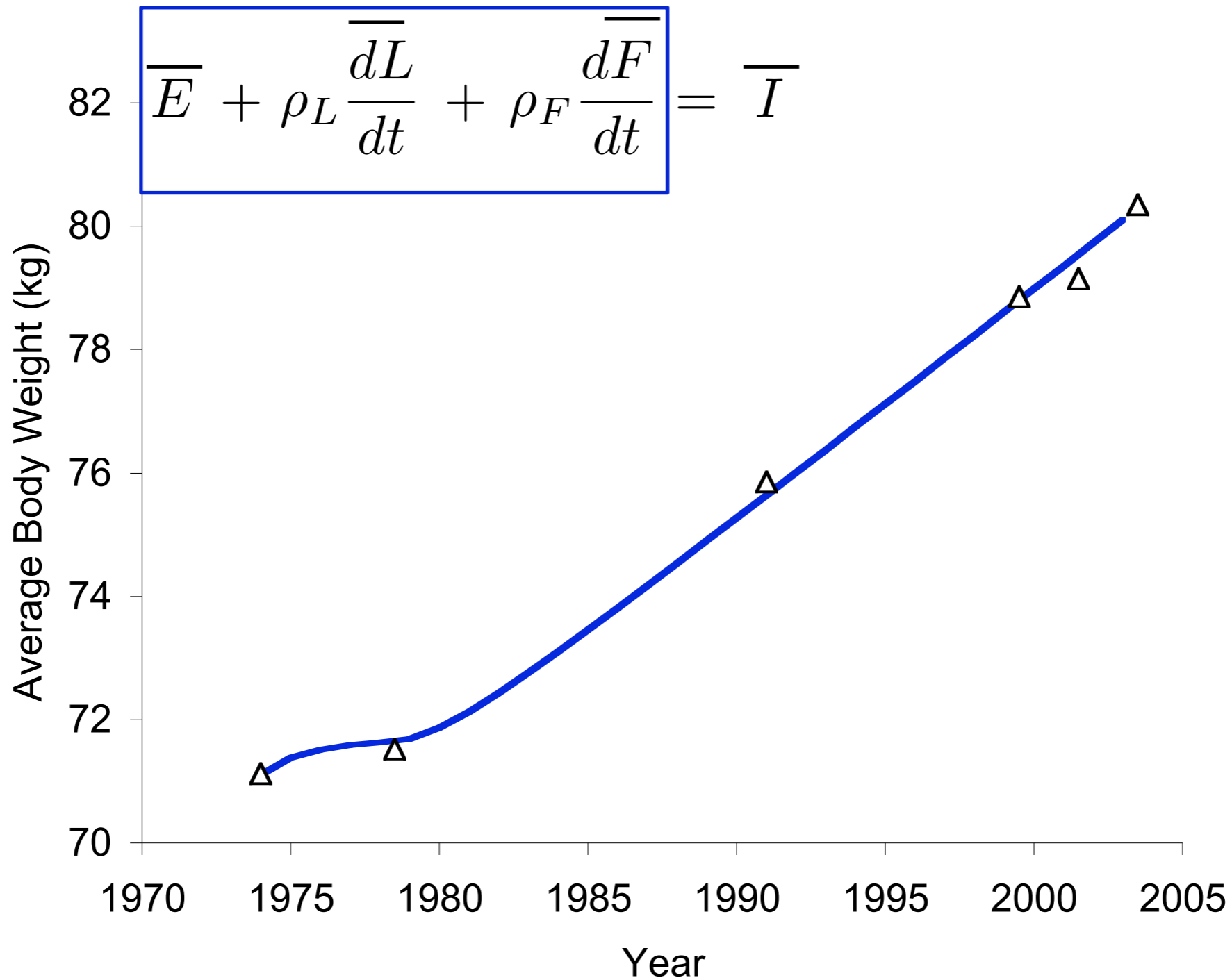
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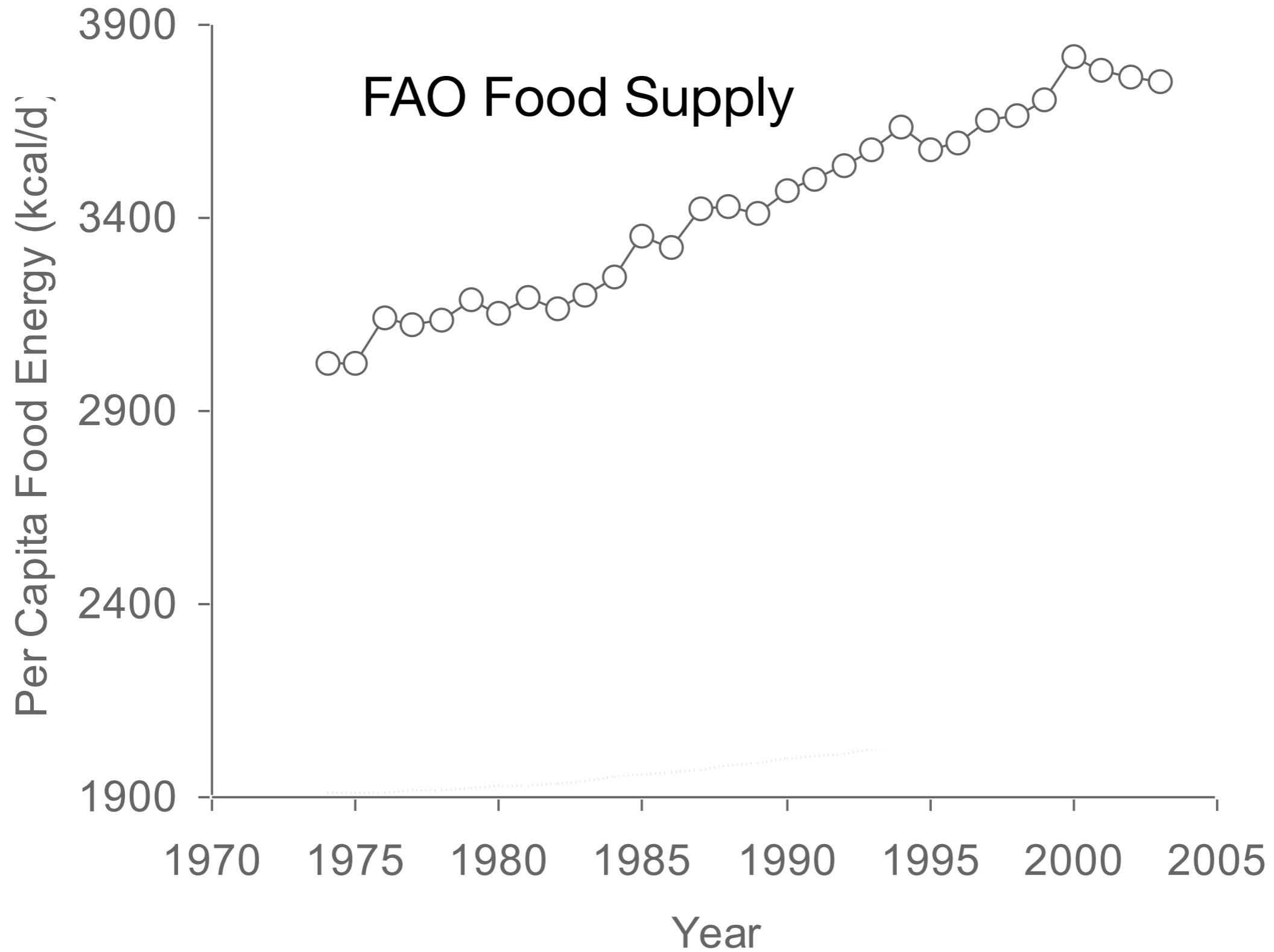
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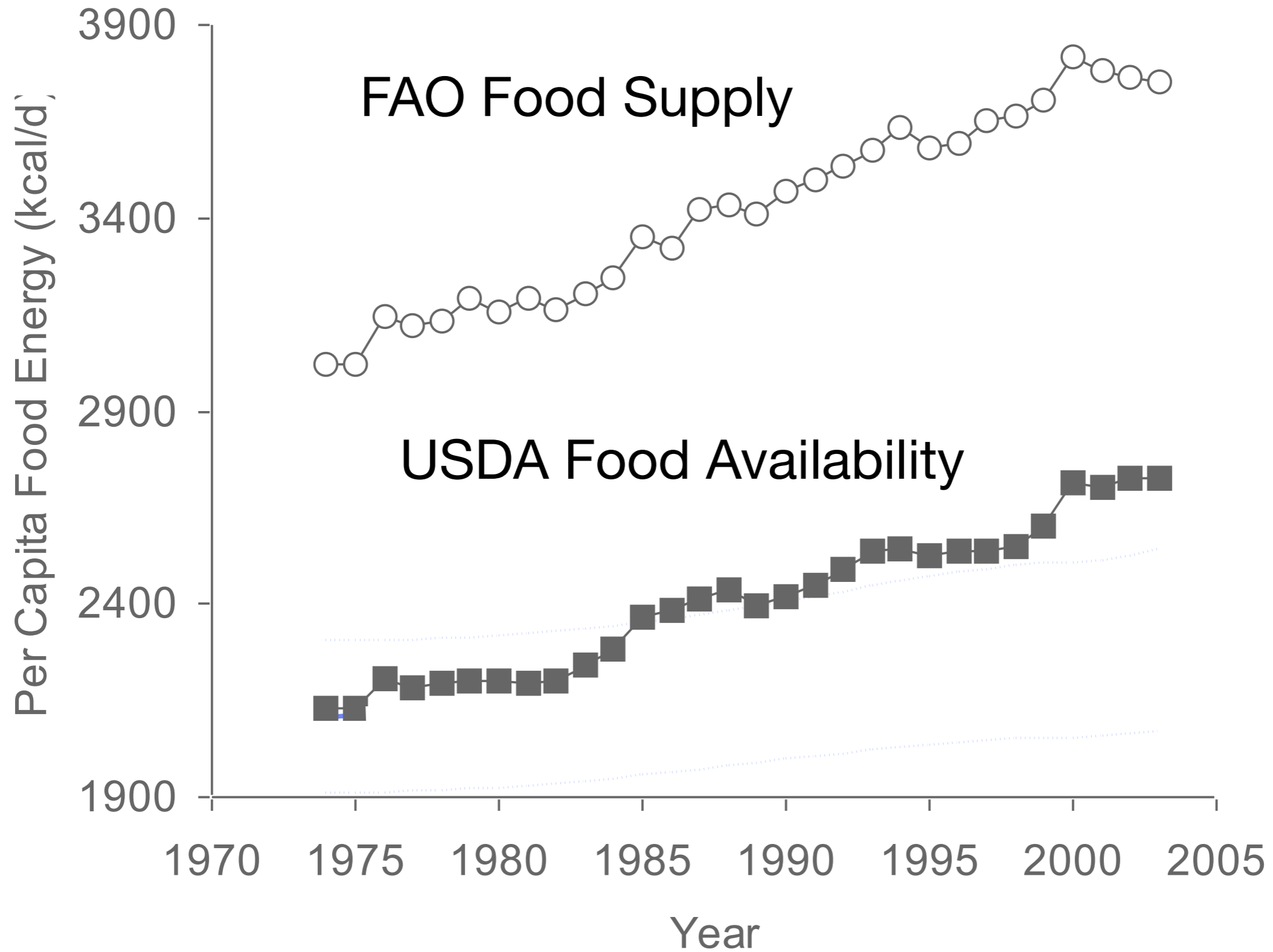
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U.S. Food Supply



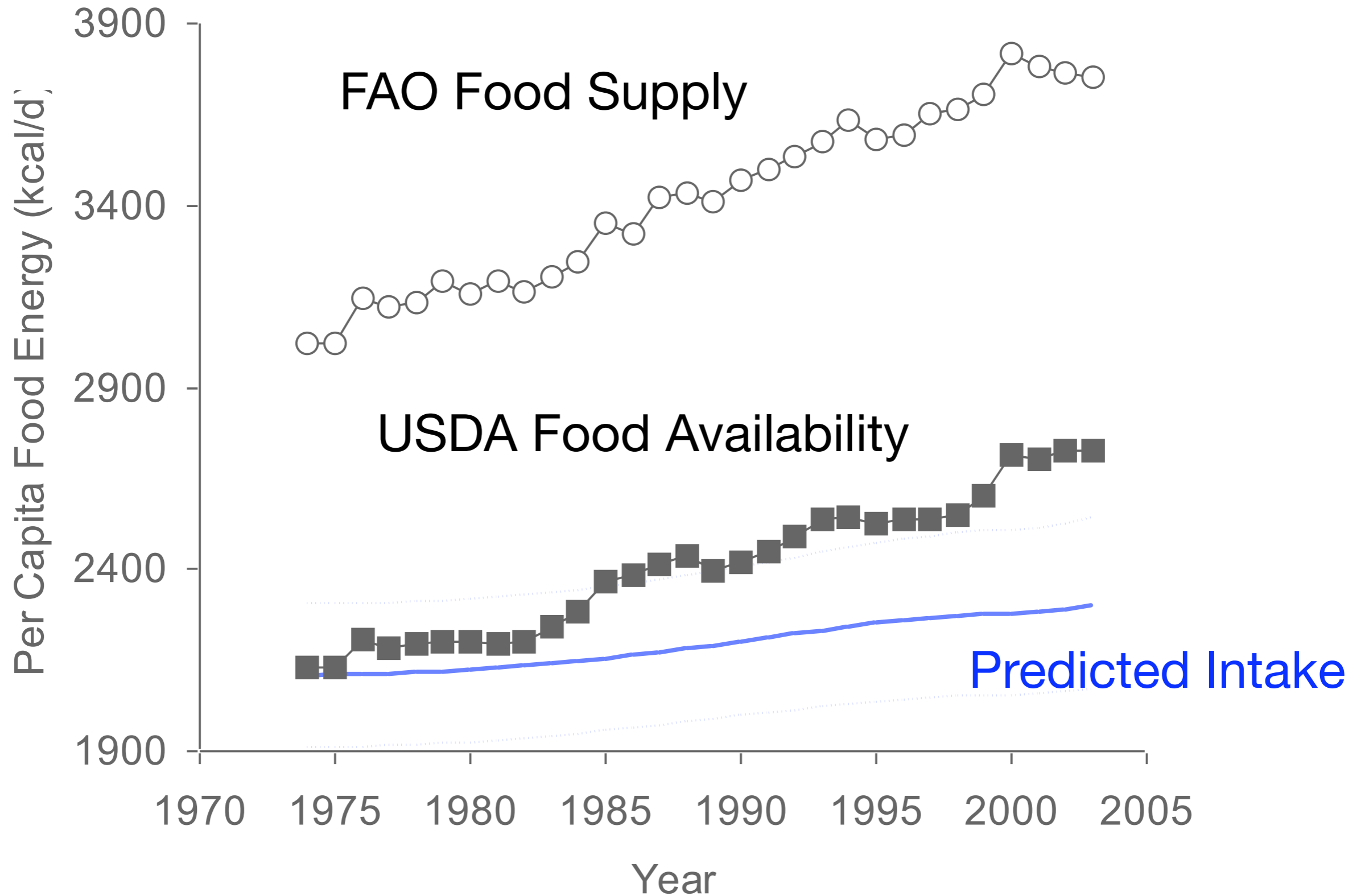
Hall, Guo, Dore, Chow. *PLoS One* (2009)

U.S. Food Supply



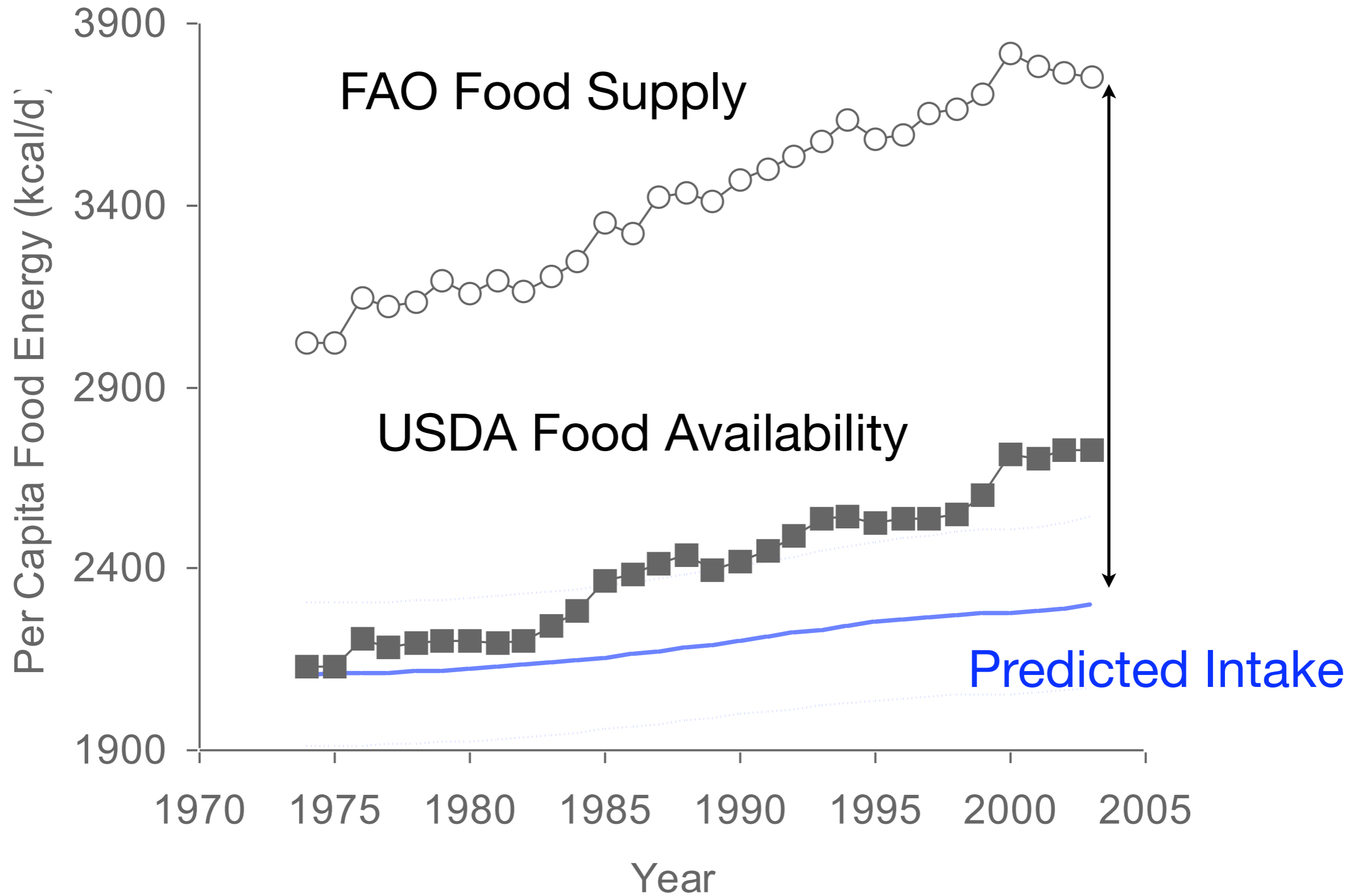
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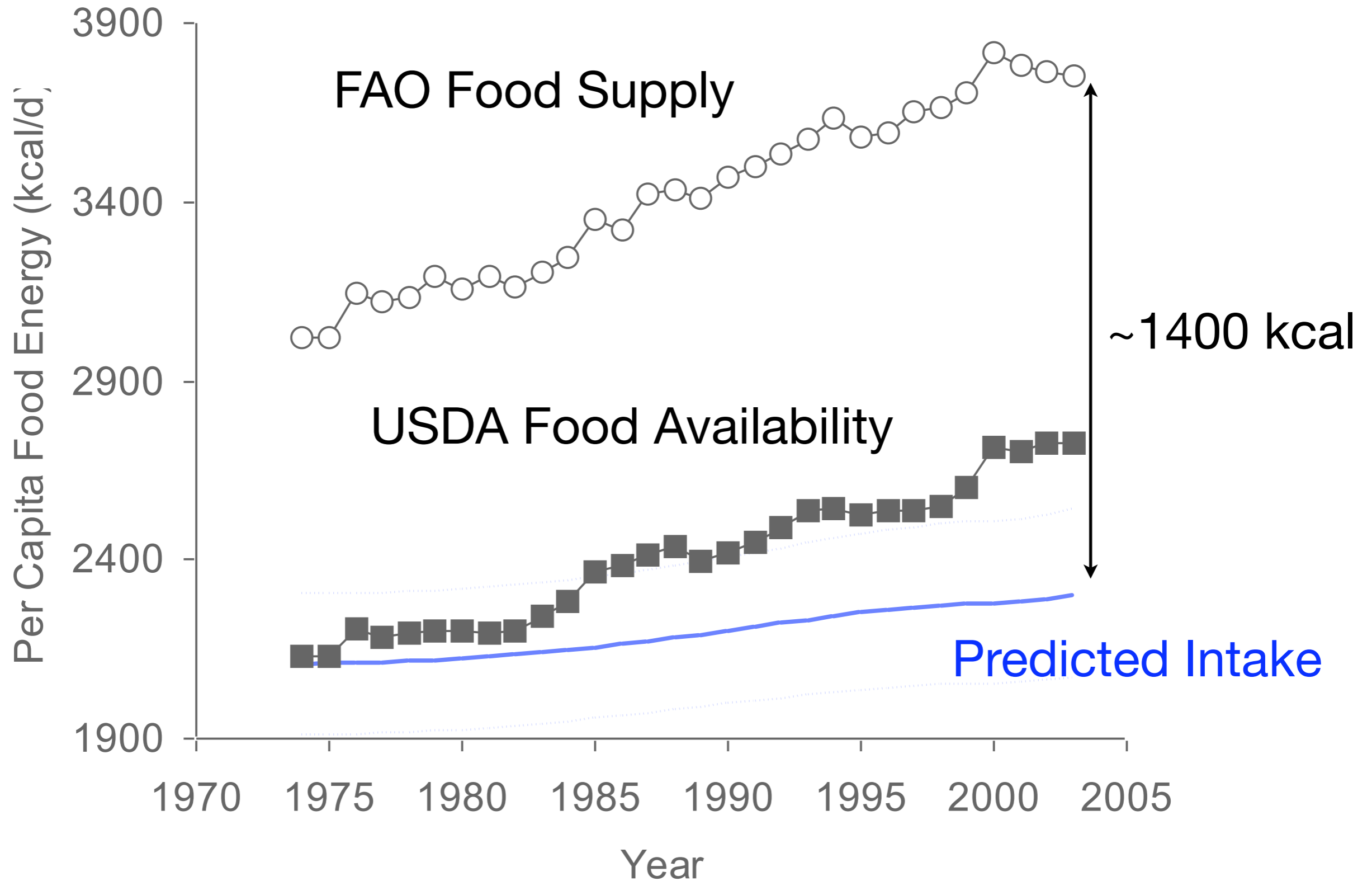
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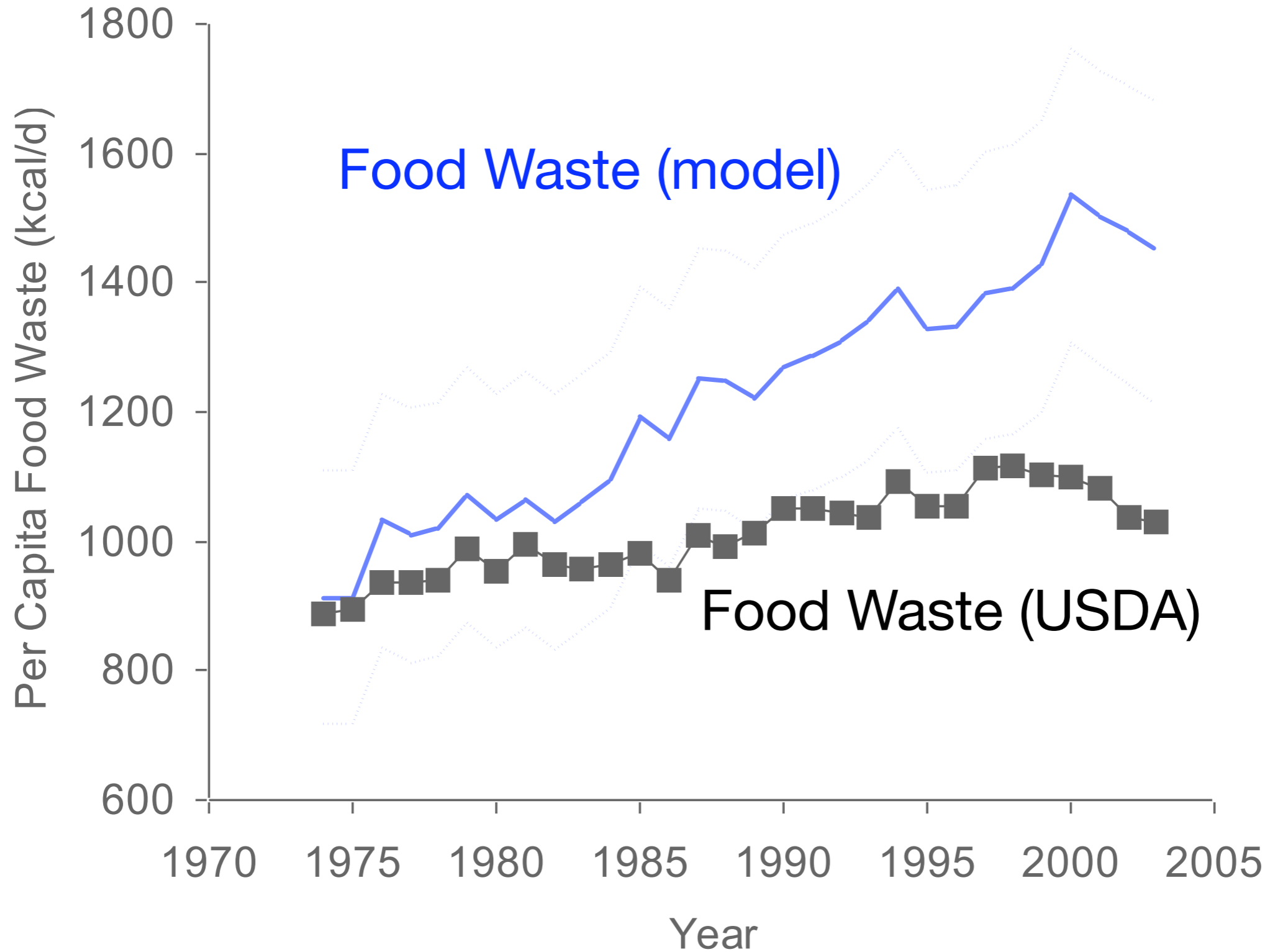
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U.S. Food Supply



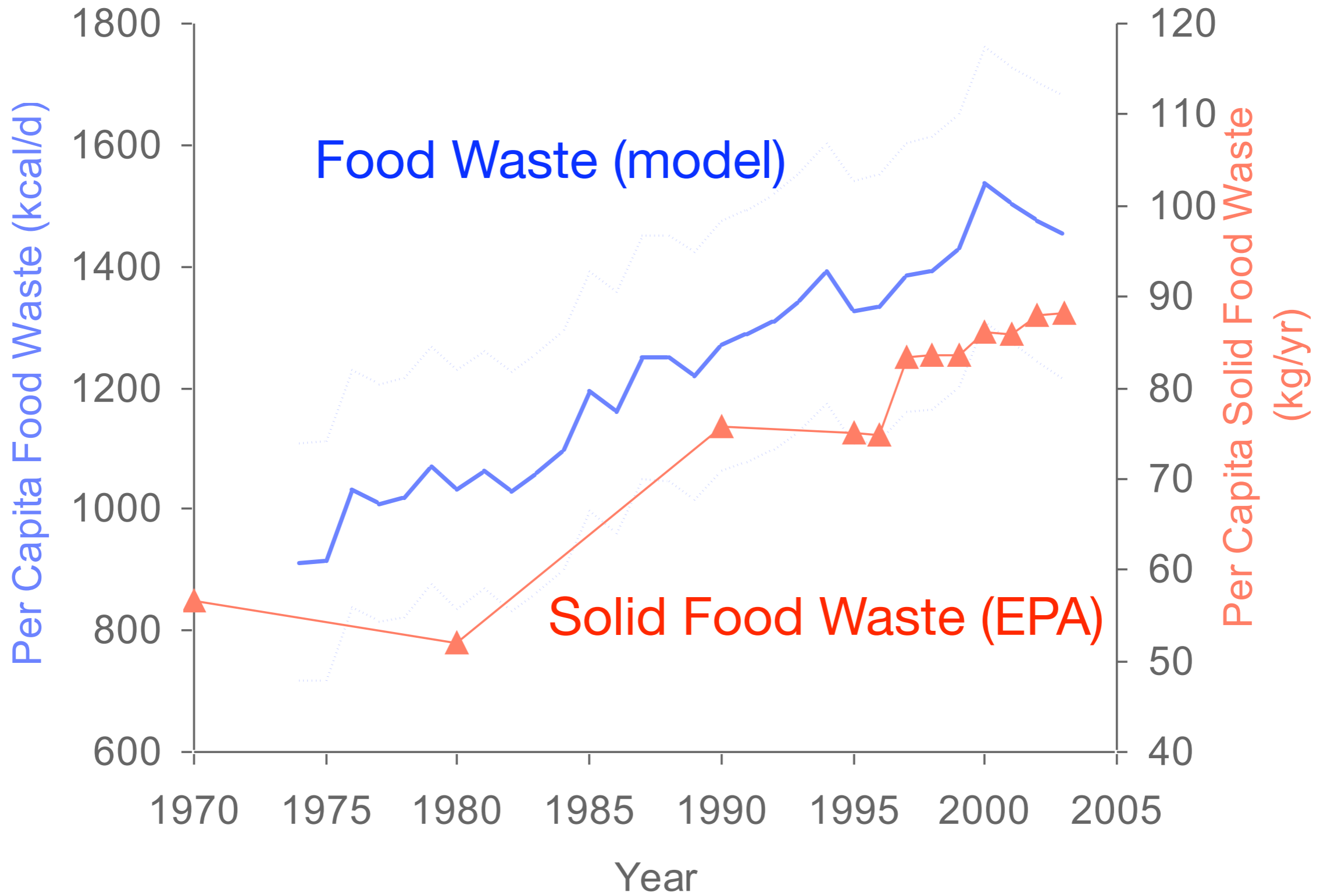
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U.S. Food Waste



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U.S. Food Waste



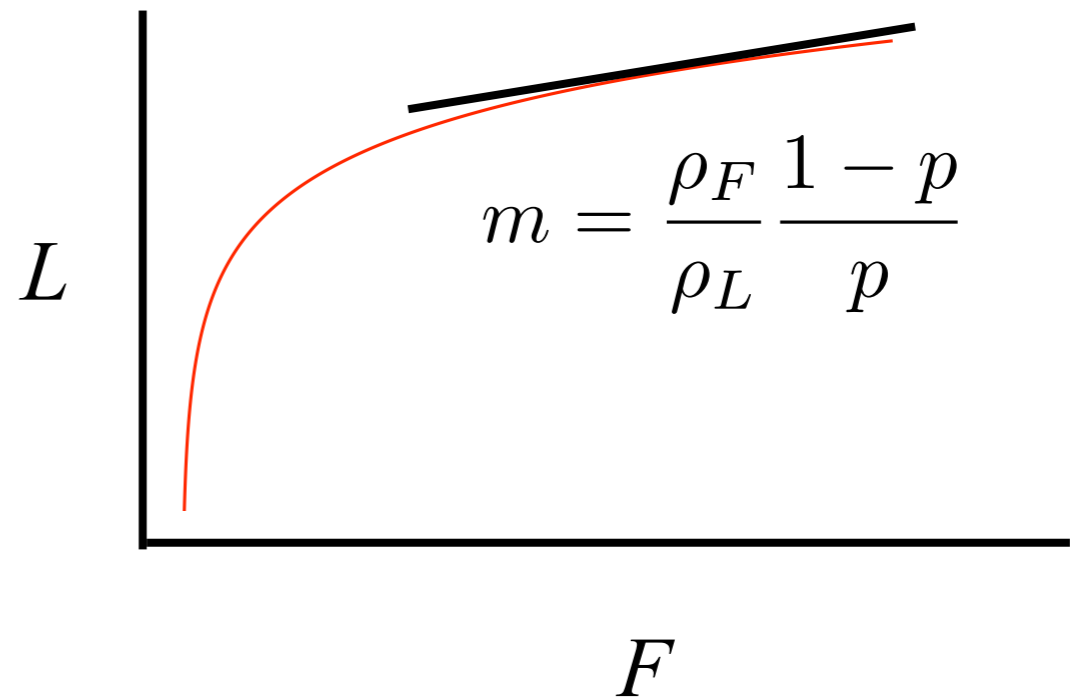
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One dimensional models

Energy partition models are effectively *1D*

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

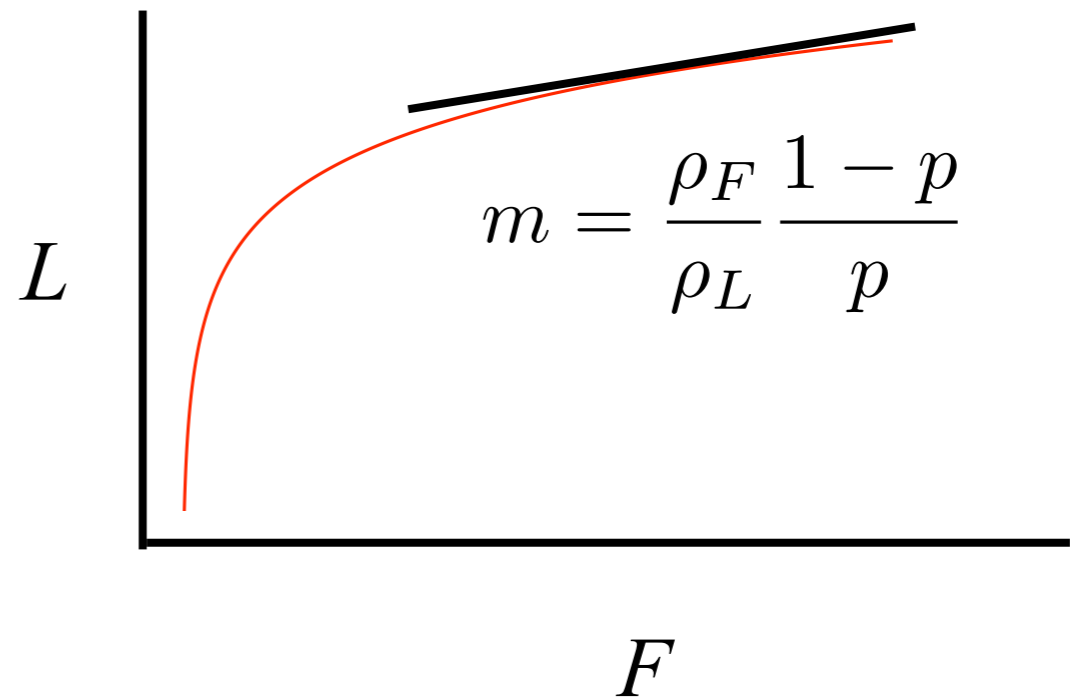
$$\rho_L \frac{dL}{dt} = p(I - E)$$



One dimensional models

Energy partition models are effectively *1D*

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

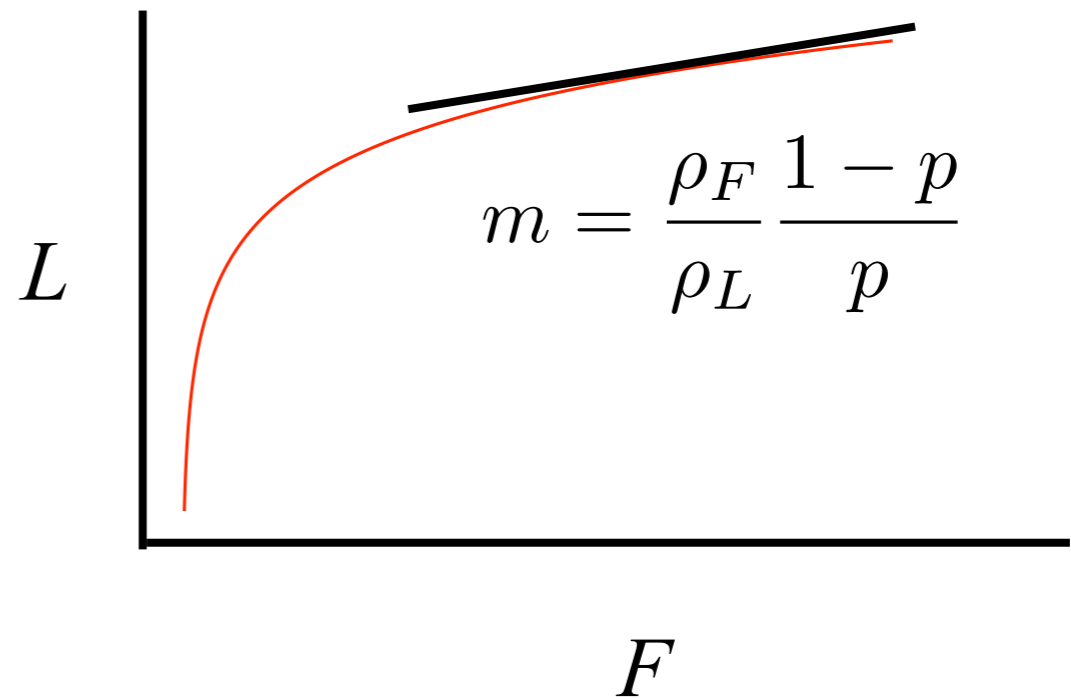


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$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E$$

$$L \approx mF + b$$

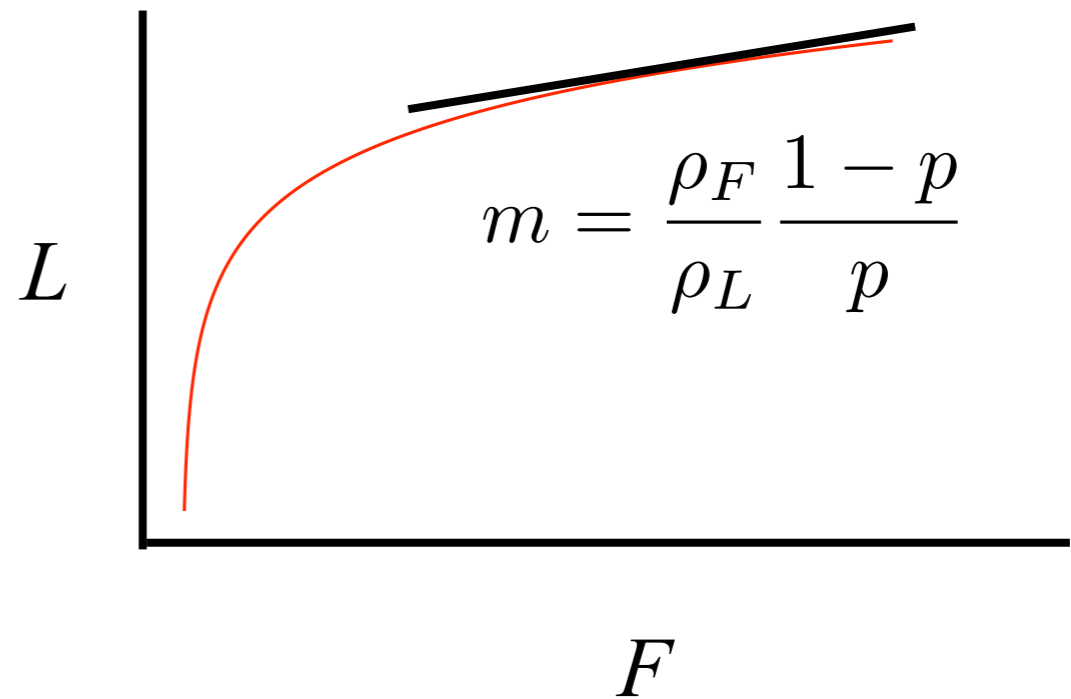


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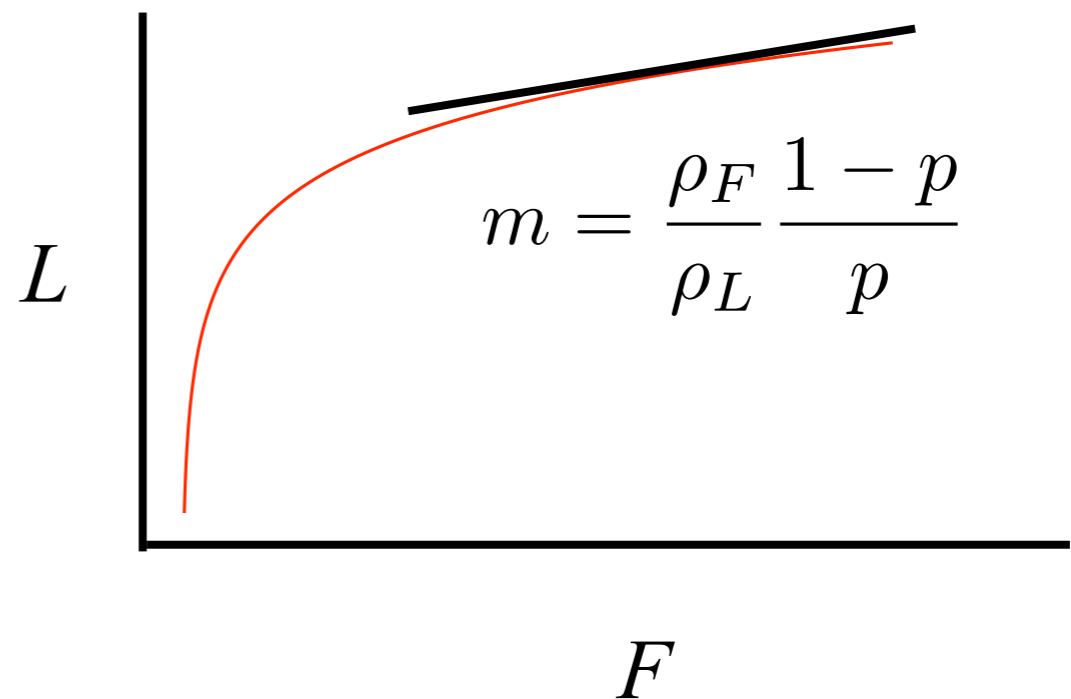
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$$F = \frac{M - b}{1 + m}$$



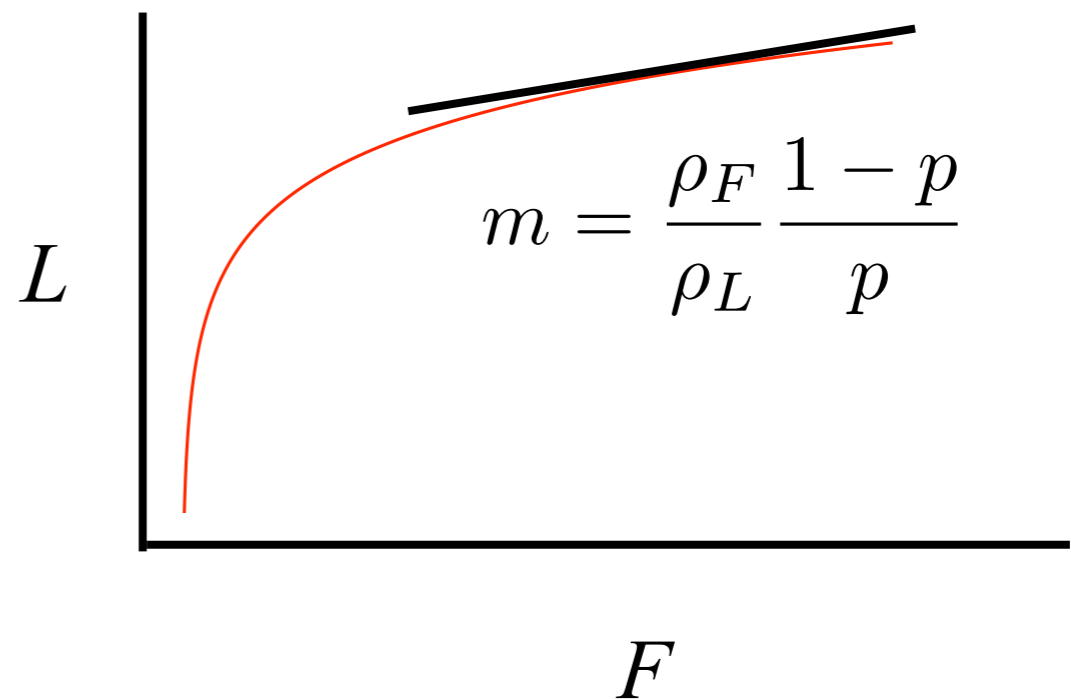
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$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E$$

$$L \approx mF + b \quad F = M - L$$

$$L = \frac{mM + b}{1 + m} \quad F = \frac{M - b}{1 + m}$$



One dimensional models

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

$$\rho_M = \frac{\rho_F \rho_L}{\rho_L + (\rho_F - \rho_L)p}$$

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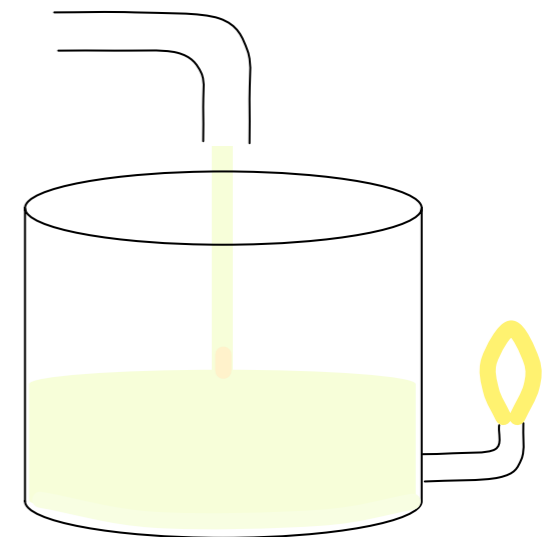
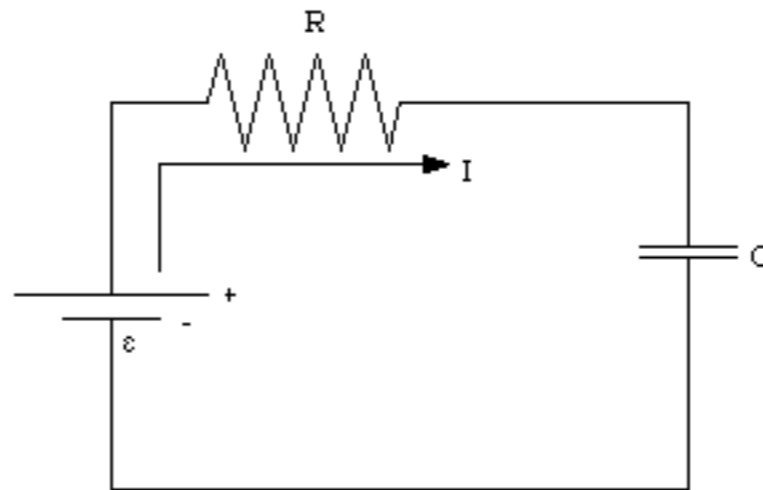
Leaky integrator

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Leaky integrator



$$C \frac{dV}{dt} = I - \frac{1}{R} V$$

Steady state

$$\rho_M \frac{dM}{dt} = I - \epsilon M - b = 0$$

$$M = (I - b)/\epsilon \qquad \Delta M \sim \frac{1}{\epsilon} \Delta I$$

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ϵ decreases with weight and increases with activity

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$\epsilon \sim 0.1$ MJ/kg/day or 23 kcal/kg/day

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$\epsilon \sim 0.1$ MJ/kg/day or 23 kcal/kg/day

Extra ~ 23 kcal/day is an extra kg

Time Constant

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

Time constant (half-life/.69) to reach steady state:

$$\tau = \rho_M / \epsilon$$

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τ increases with weight and decreases with activity

Intake precision

To maintain weight to 2 kg requires controlling intake to ~50 kcal/day, (out of ~2500 kcal/day)

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Paradox?

Intake precision

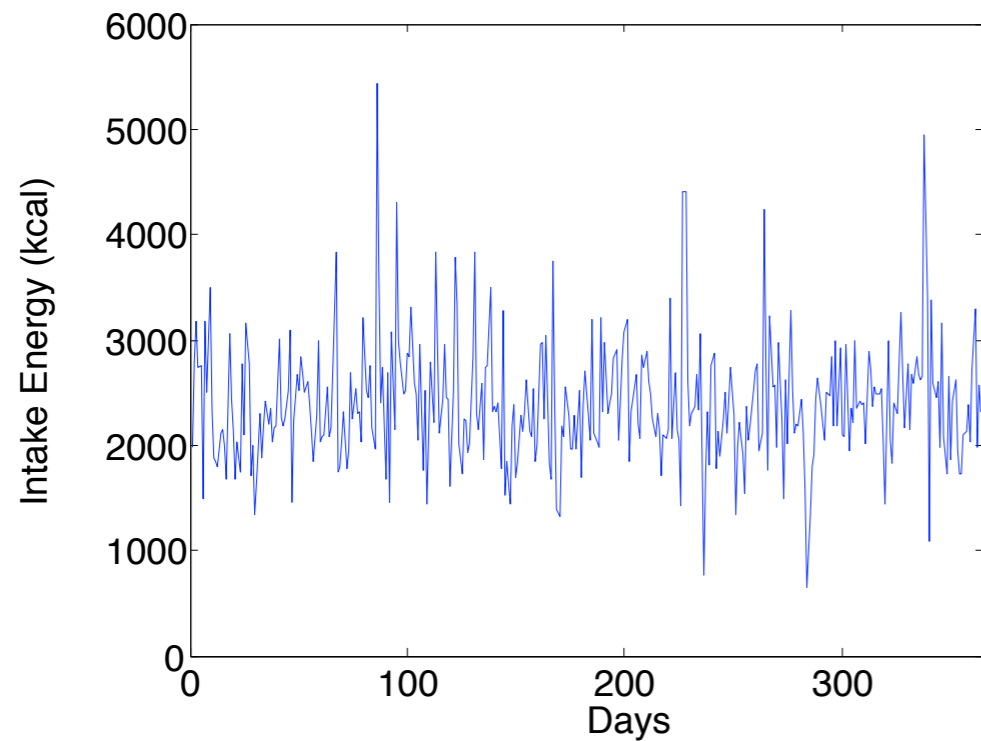
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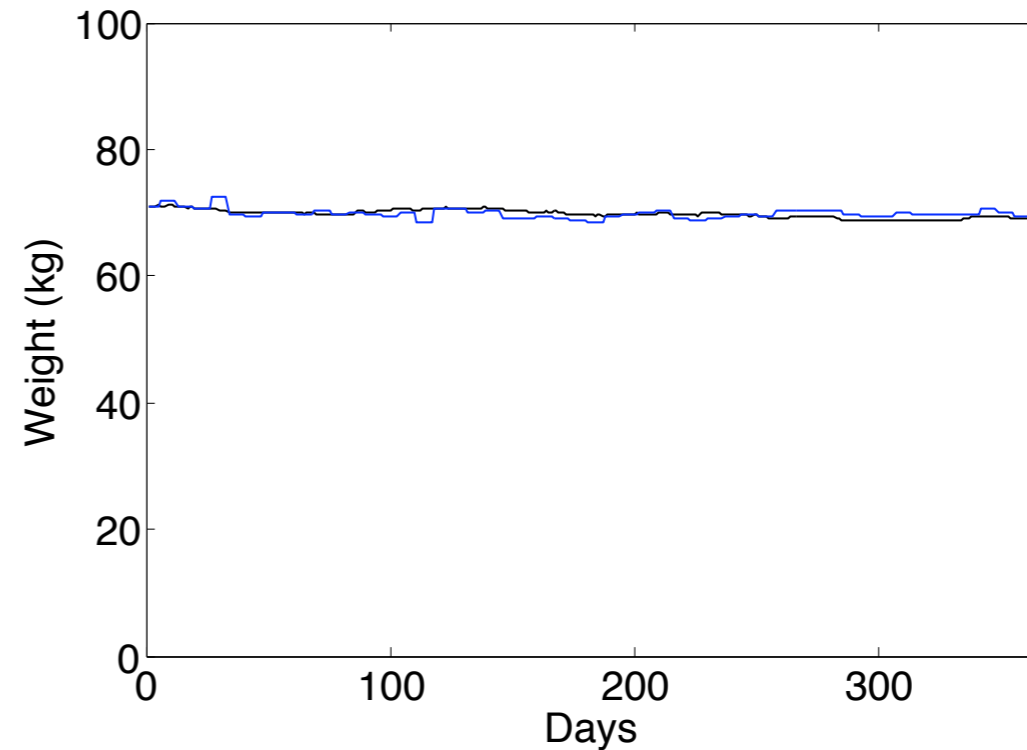
Paradox? No, because of long time constant

Example daily intake energy

Beltsville one year intake study (courtesy of W. Rumpler)



$CV \sim 24\%$



$CV \sim 1\%$

Intake variations have little effect on weight

Time varying intake

$$I(t) = \bar{I} + \eta(t)$$

Noisy intake

$$\langle \eta(t)\eta(t') \rangle = \sigma^2 \delta(t - t')$$

White noise

$$\rho_M \frac{dM}{dt} = \bar{I} - b - \epsilon M + \eta(t)$$

Ornstein-Uhlenbeck process

$CV(I)$ is σ/\bar{I} , find $CV(M)$

$$\langle (M(t) - \langle M \rangle)^2 \rangle = \frac{\sigma^2}{2\rho_M \epsilon}$$

$$\langle M \rangle = \frac{I - b}{\epsilon}$$

$$\text{CV}(M) = \frac{1}{\sqrt{2\tau}} \frac{\bar{I}}{I - b} \text{CV}(\bar{I})$$

$$\tau = \rho_M / \epsilon$$

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For $\sqrt{2\tau} \sim 30, \bar{I} \sim 2500, b \sim 600$

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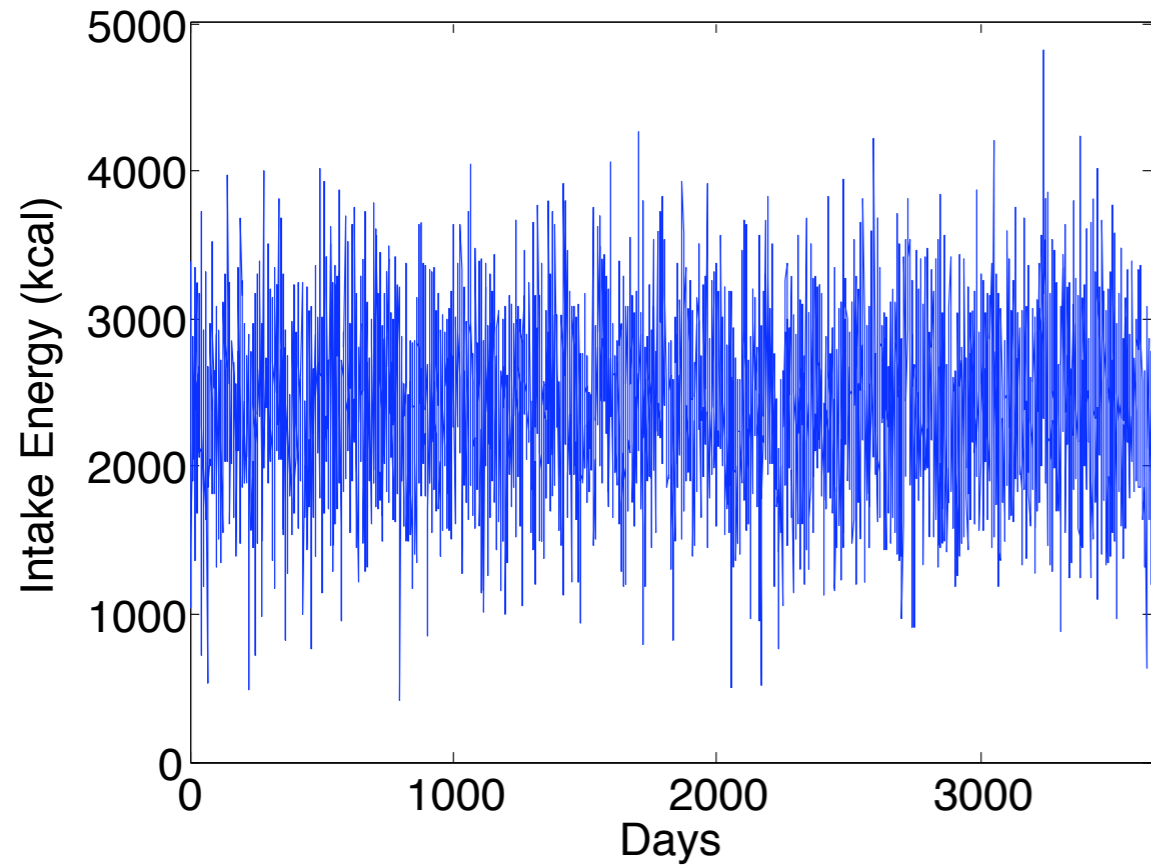
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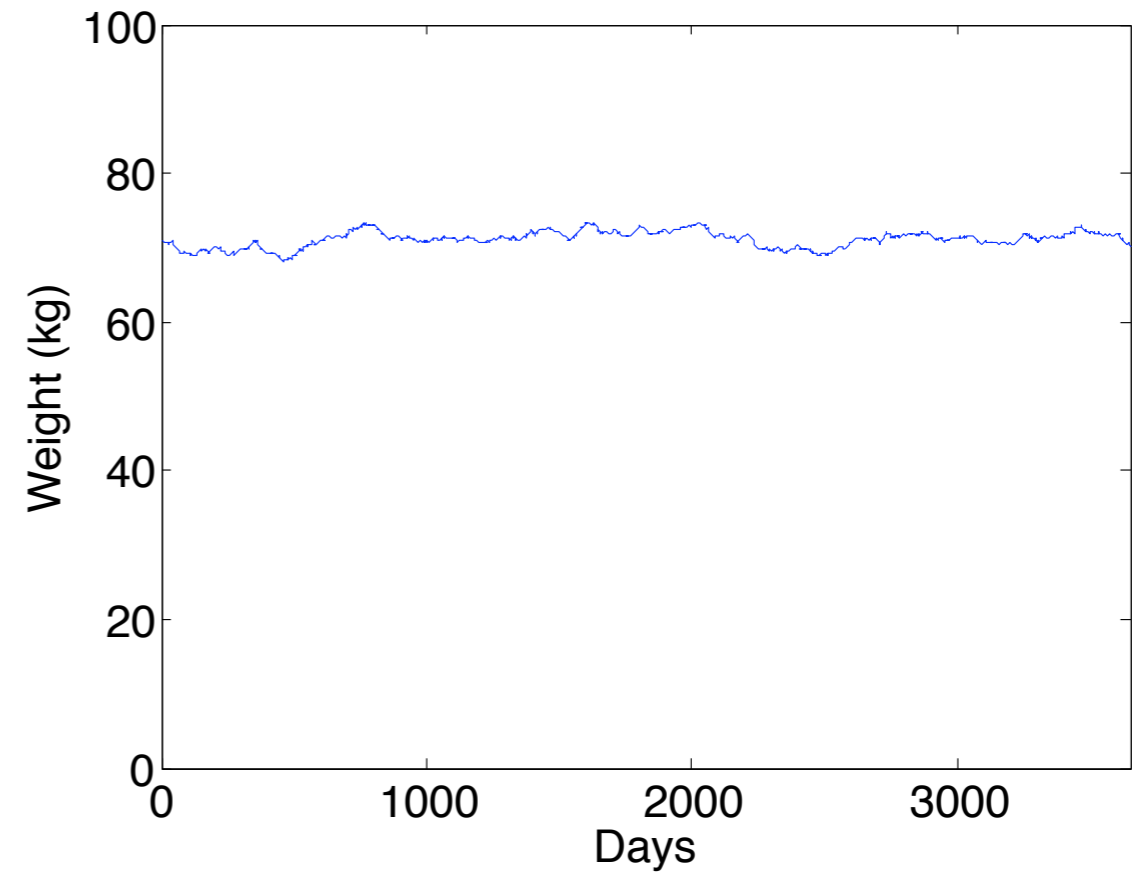
For $\sqrt{2\tau} \sim 30, \bar{I} \sim 2500, b \sim 600$

***CV* (M) reduced by factor of 15-20 vs *CV* (I)**

Simulated Beltsville data 10 years

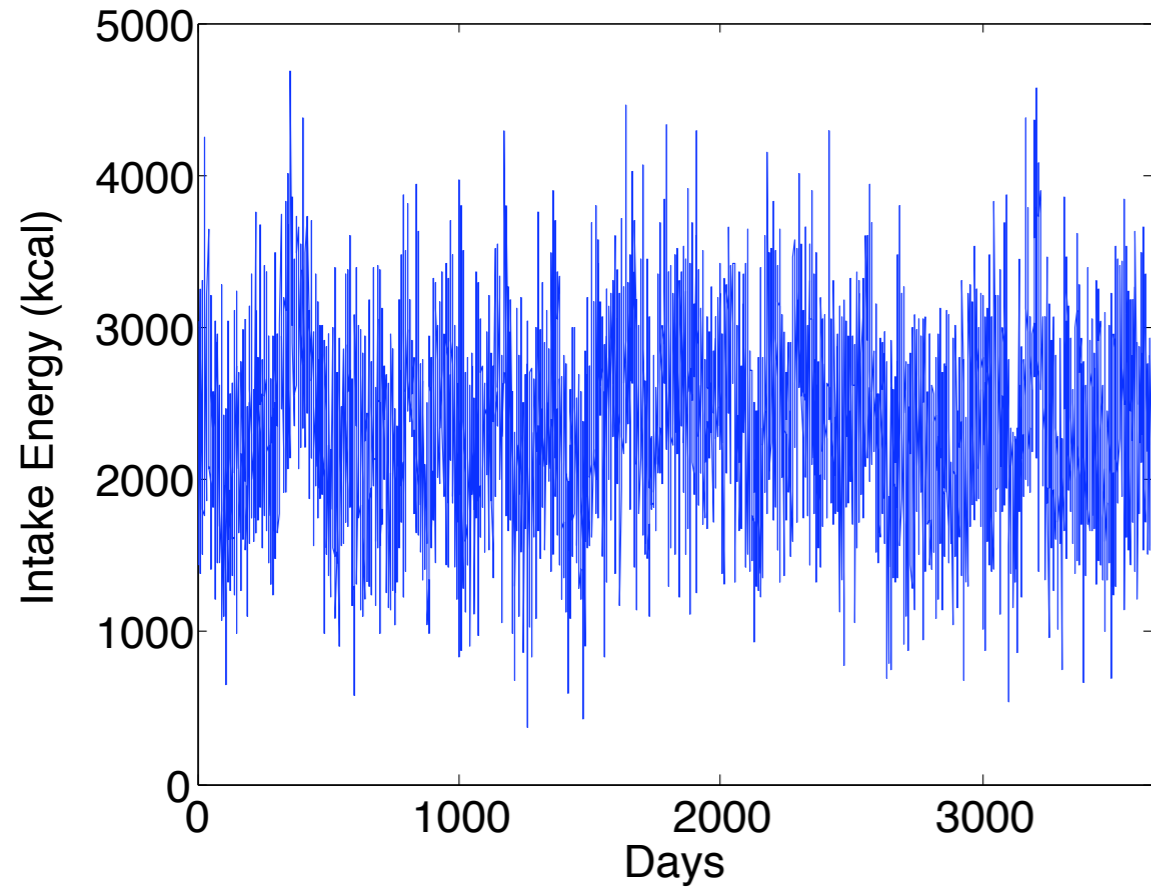


$CV \sim 23\%$

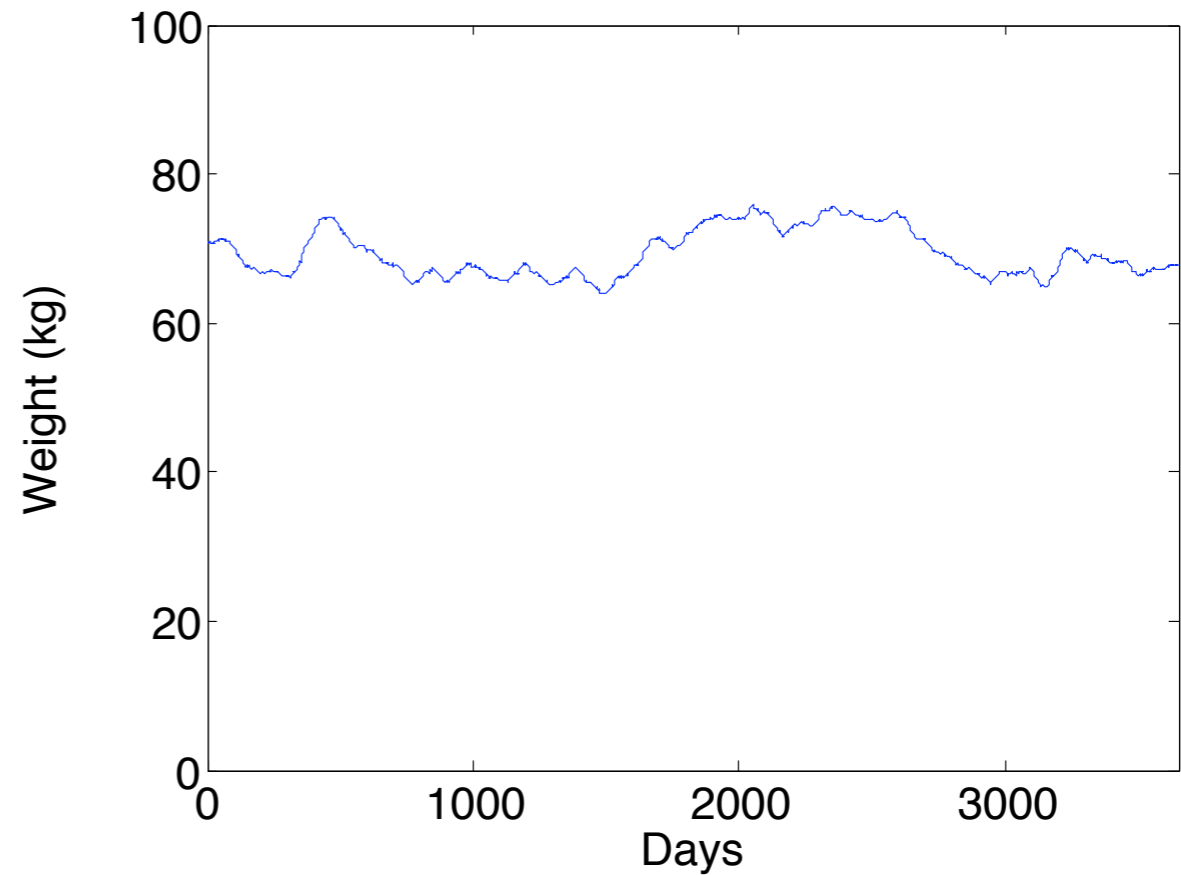


$CV \sim 2\%$

Correlations increase fluctuations

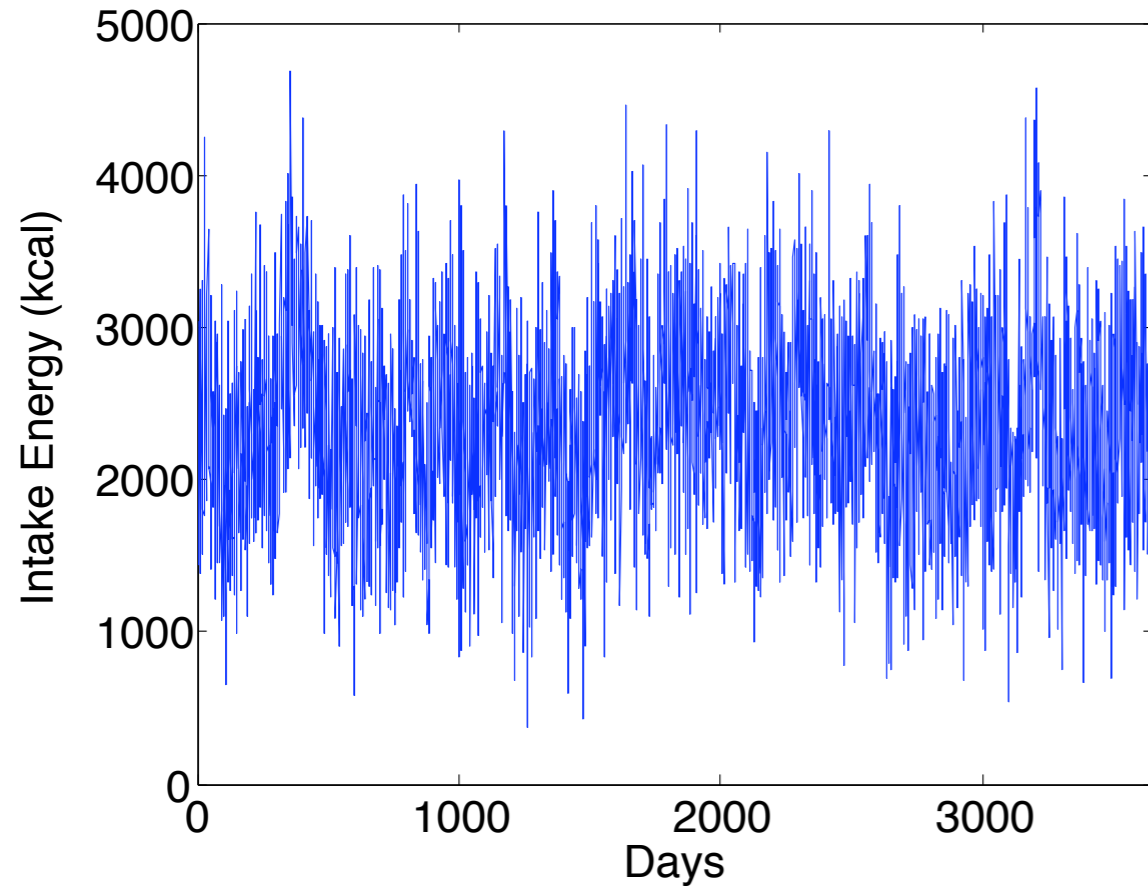


$CV \sim 26\%$

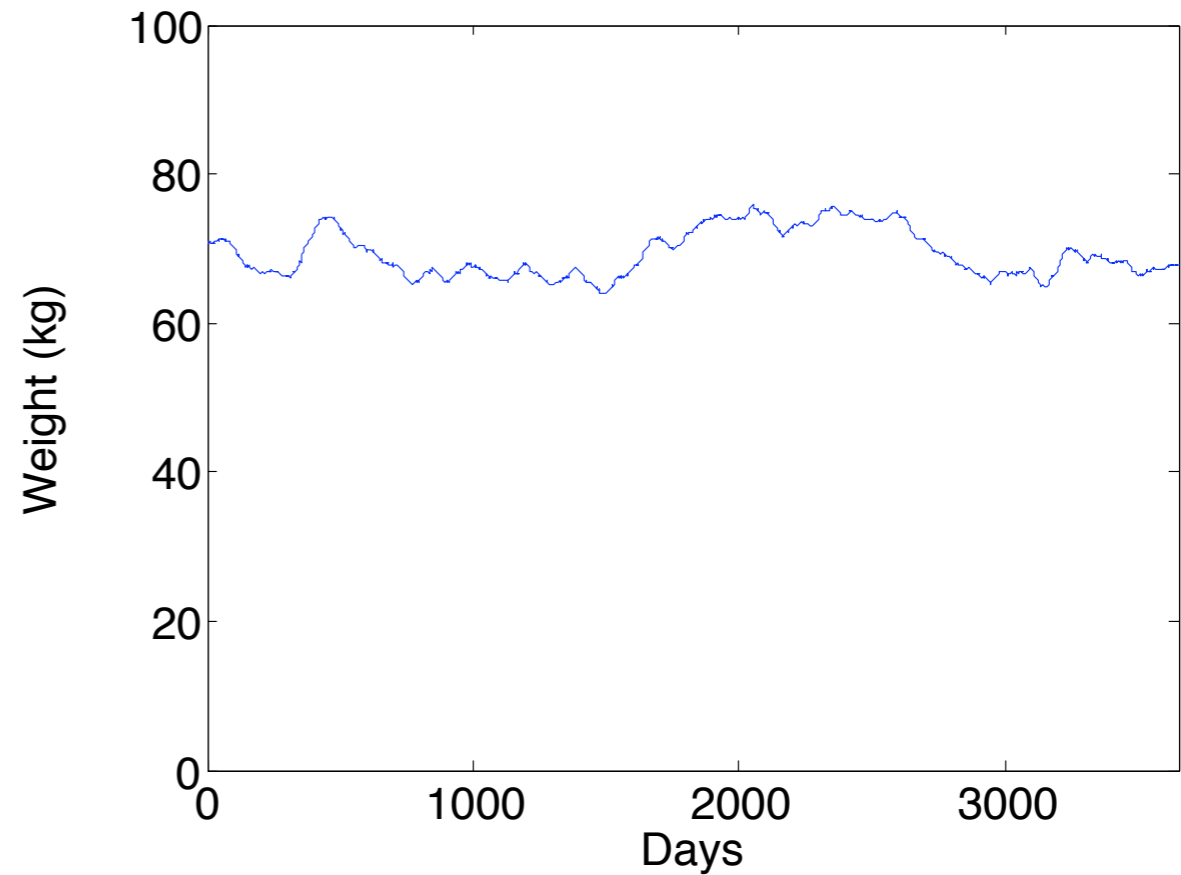


$CV \sim 5\%$

Correlations increase fluctuations



$CV \sim 26\%$



$CV \sim 5\%$

Longer correlations \Rightarrow higher BMI

Periwal and Chow, *AJP:EM*, 291:929-36 (2006)

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