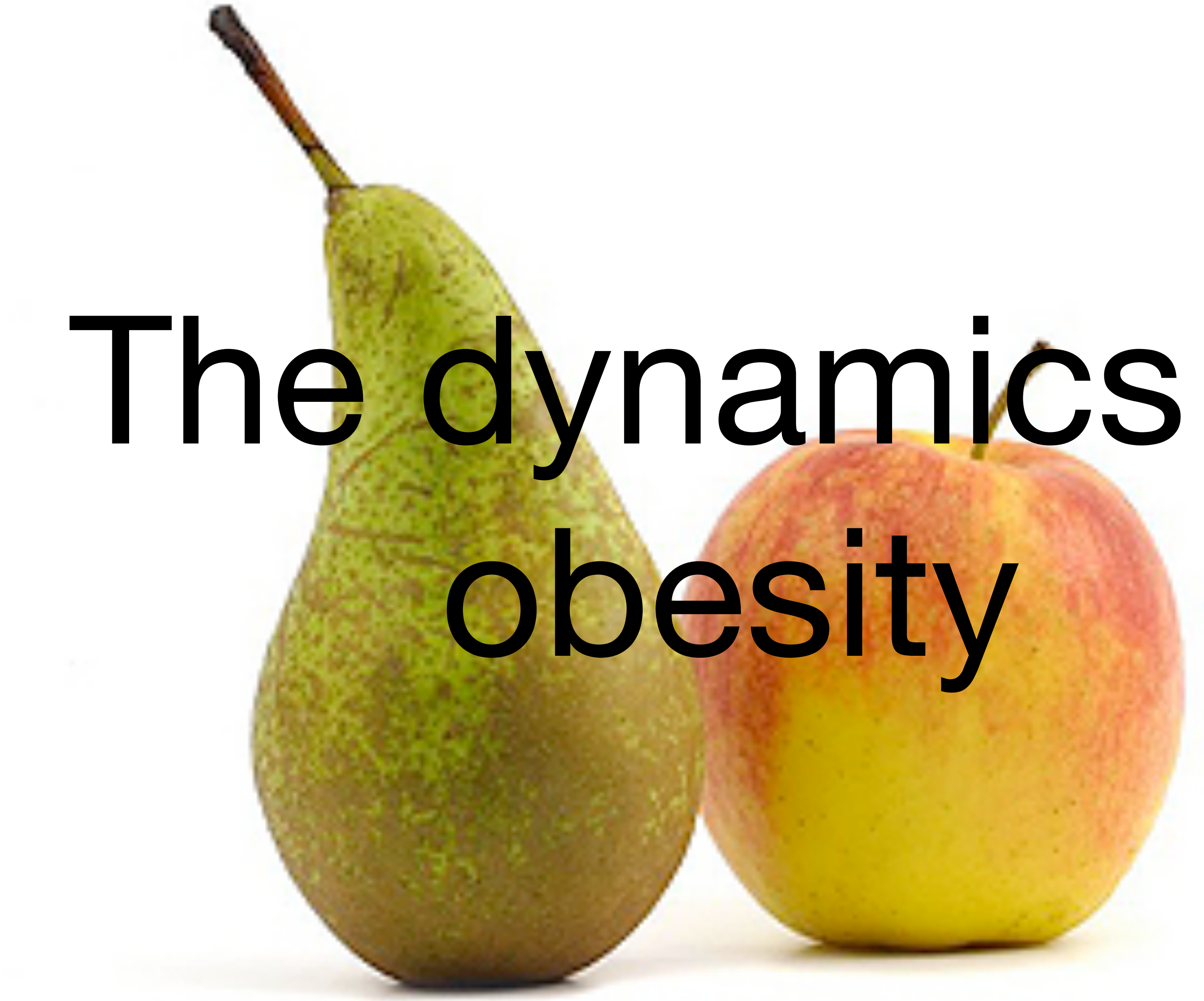
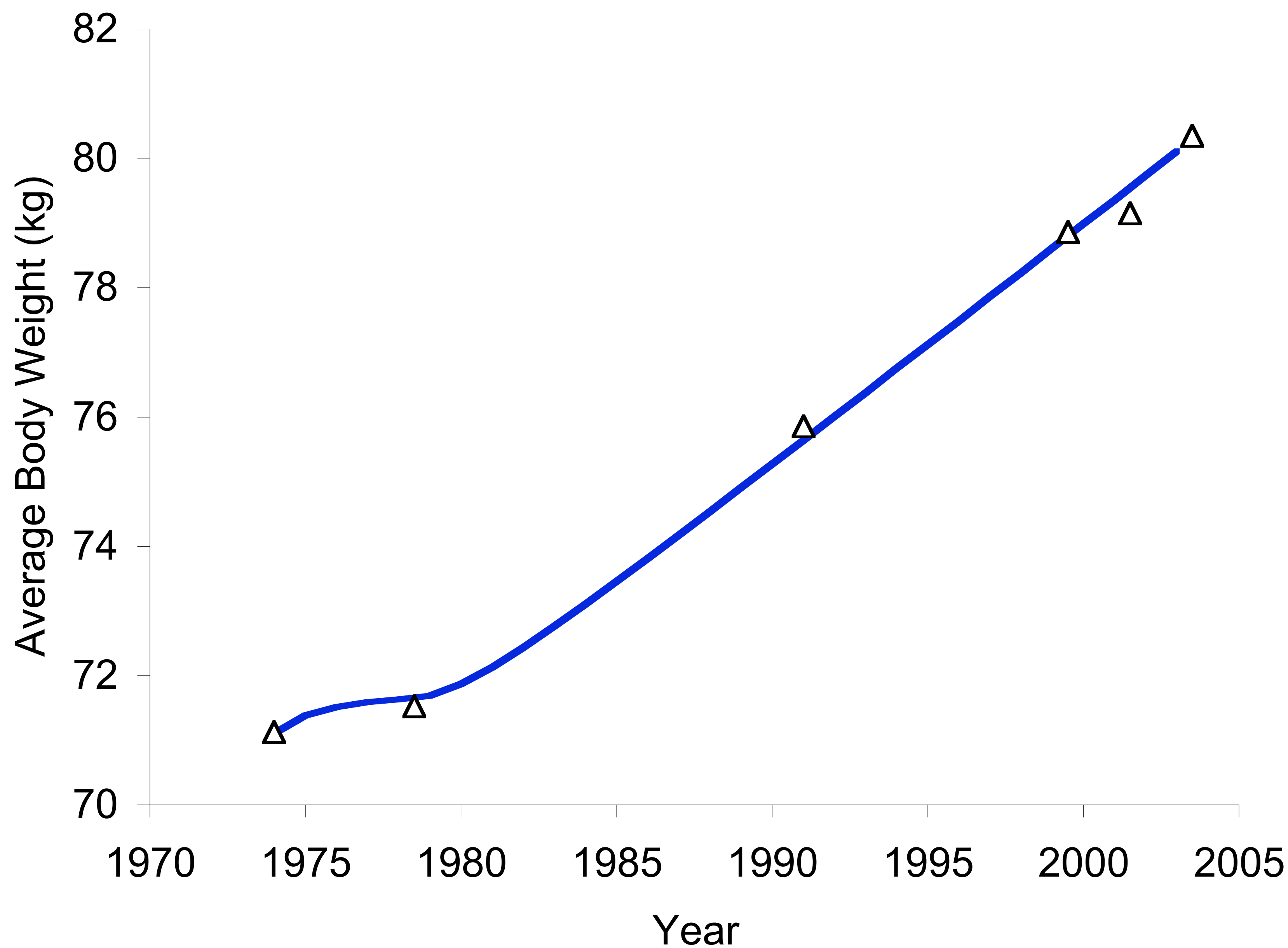
The dynamics of obesity



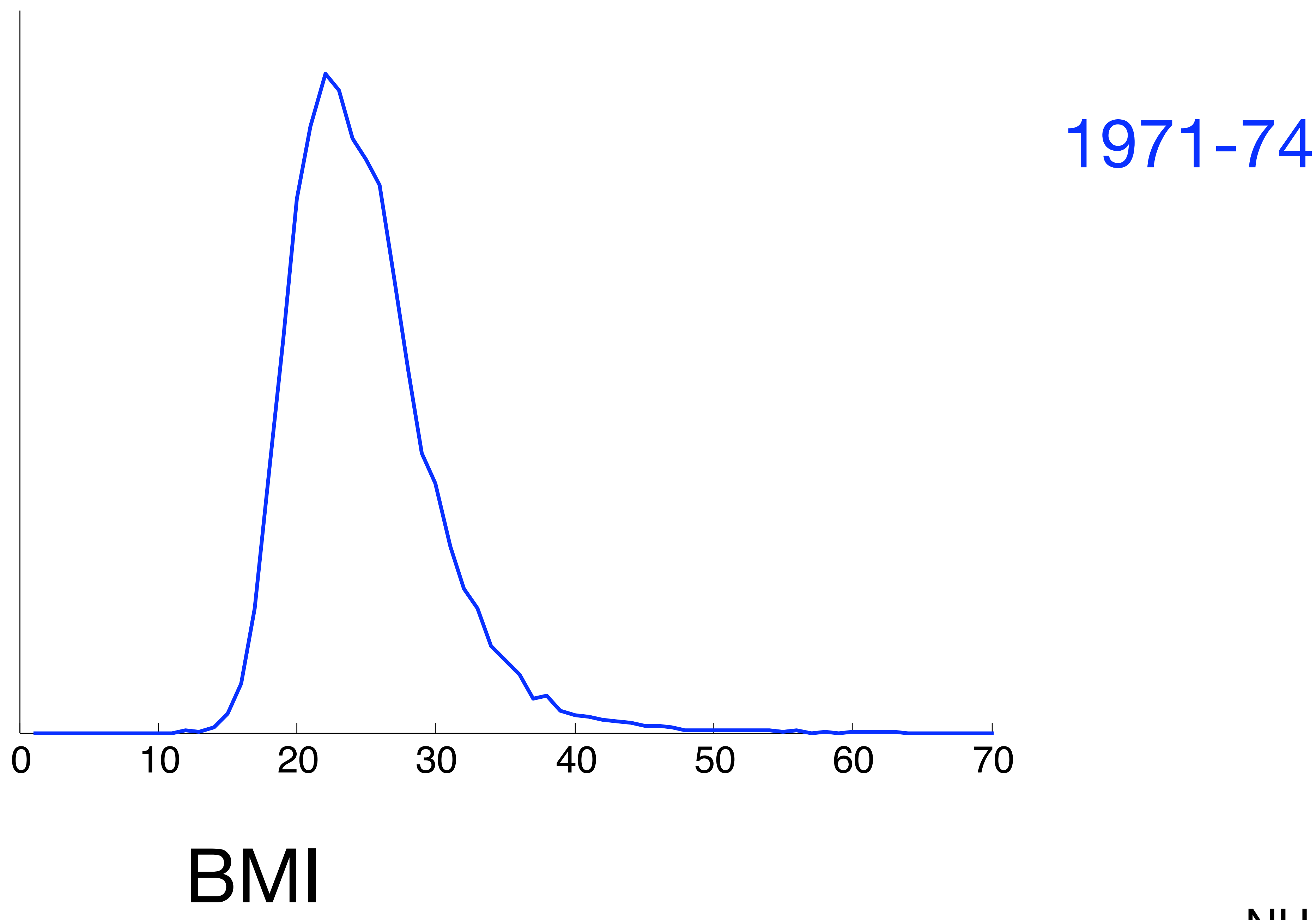
Carson C Chow
Laboratory of Biological Modeling, NIDDK, NIH

US obesity epidemic



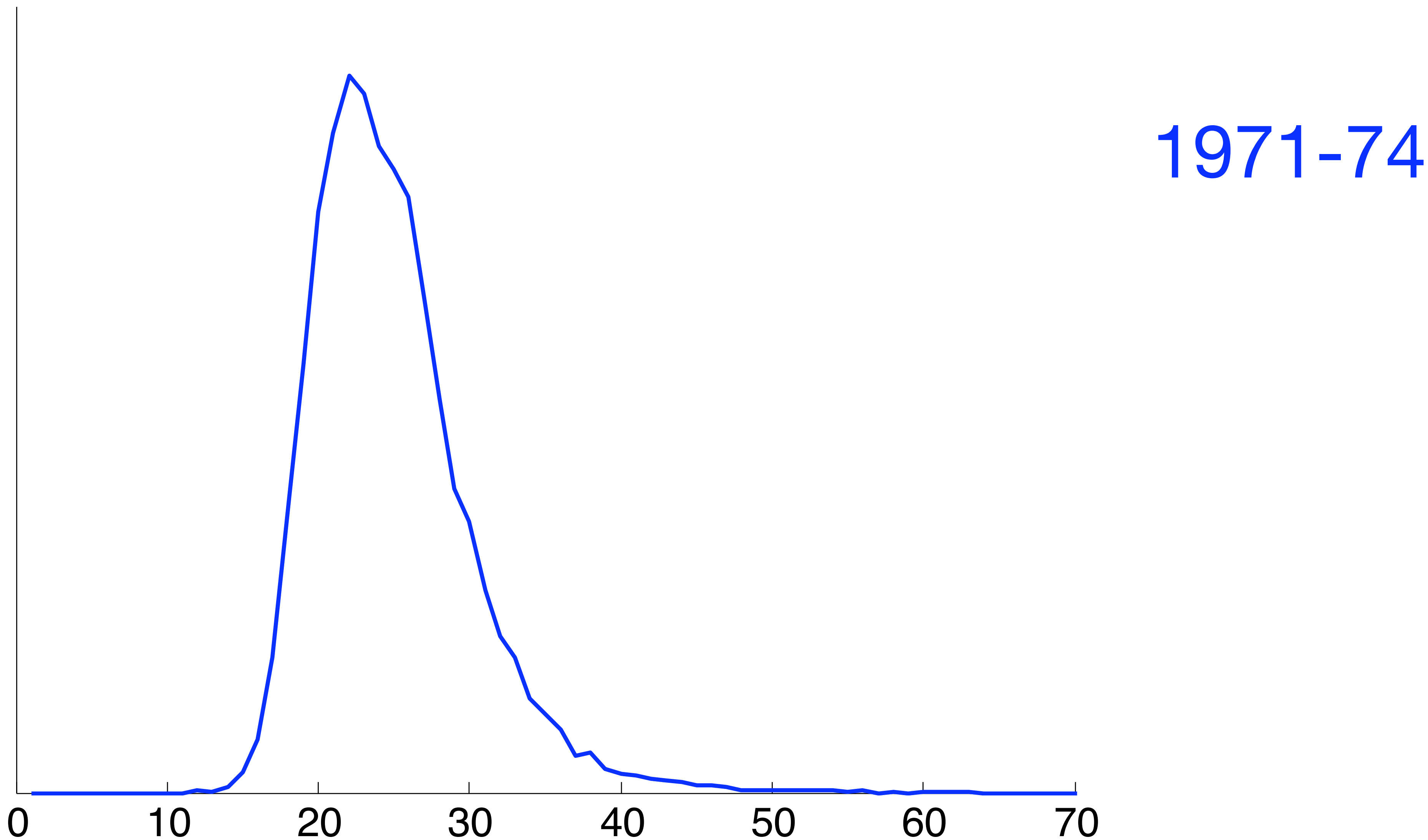
Data from National Health and Nutrition Examination Survey (NHANES)

US obesity epidemic



NHANES data

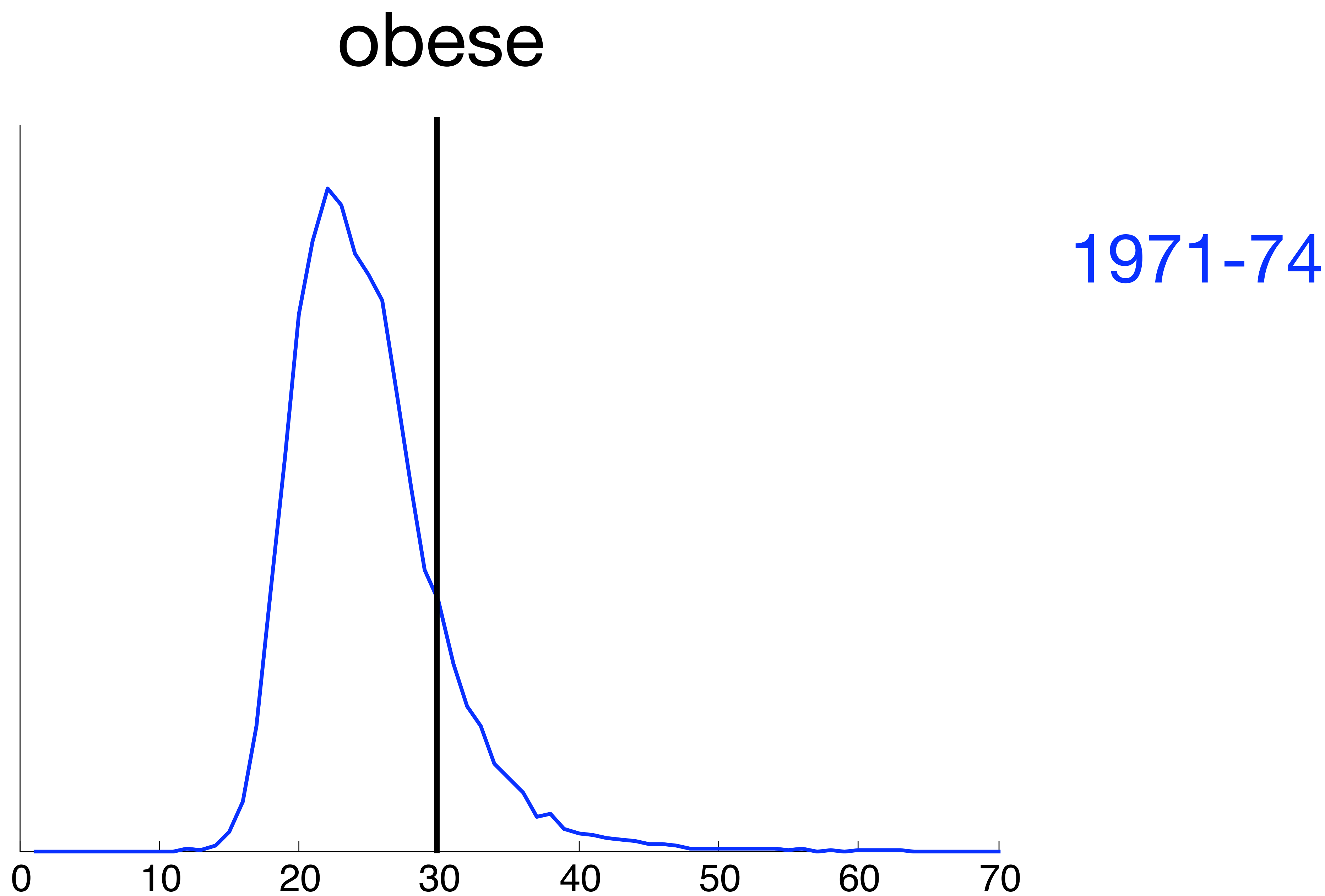
US obesity epidemic



BMI = weight / height^2

NHANES data

US obesity epidemic



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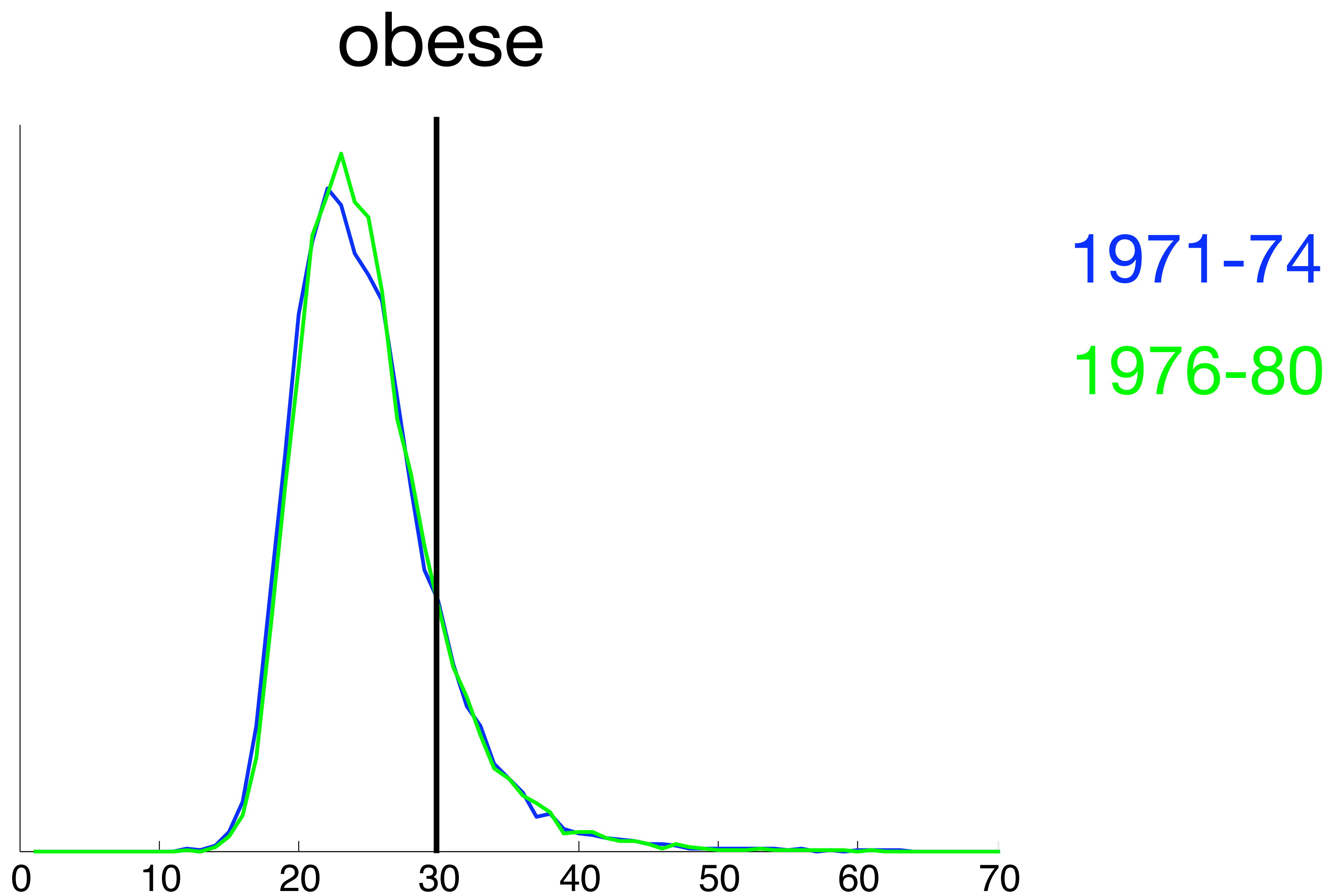
US obesity epidemic



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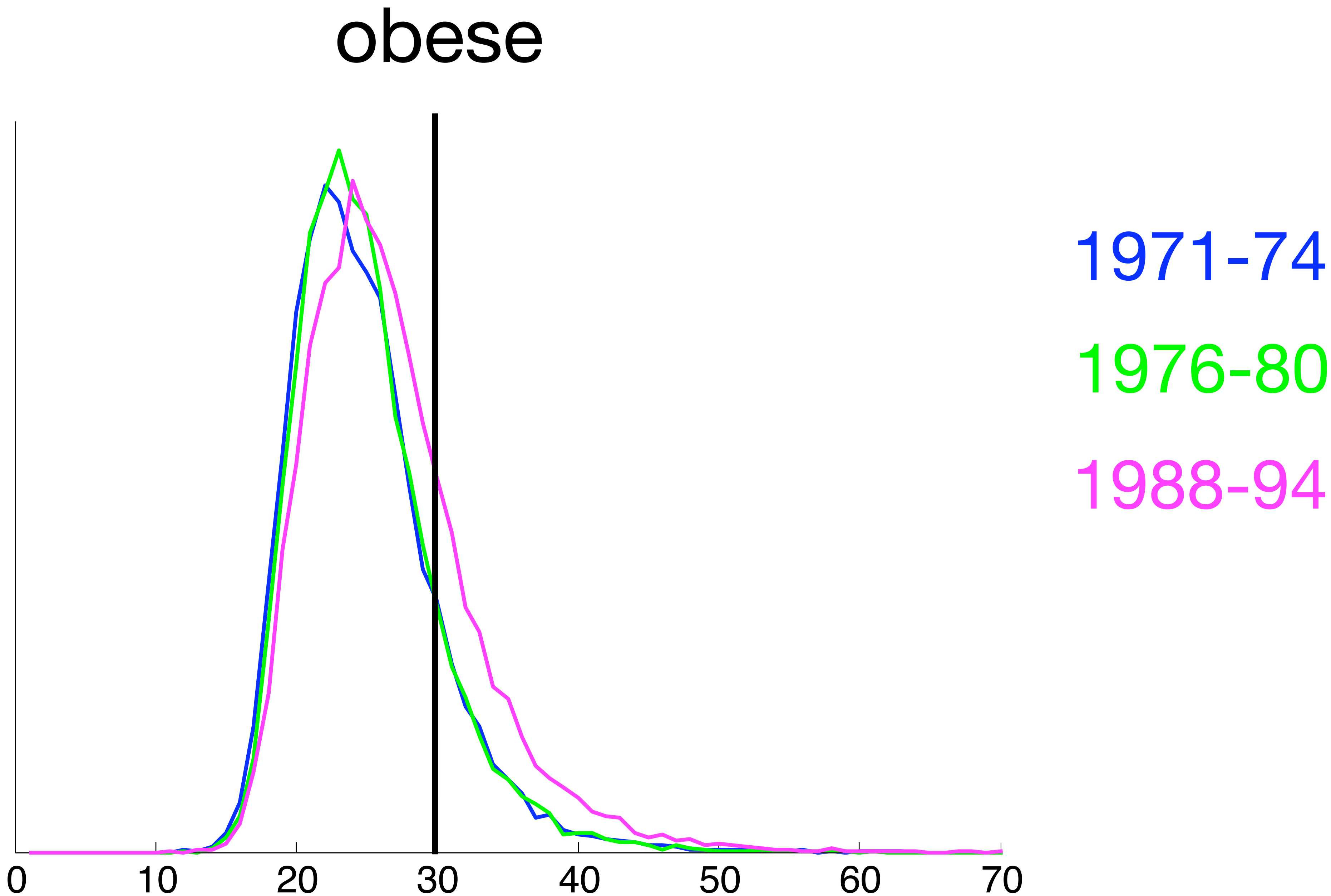
NHANES data

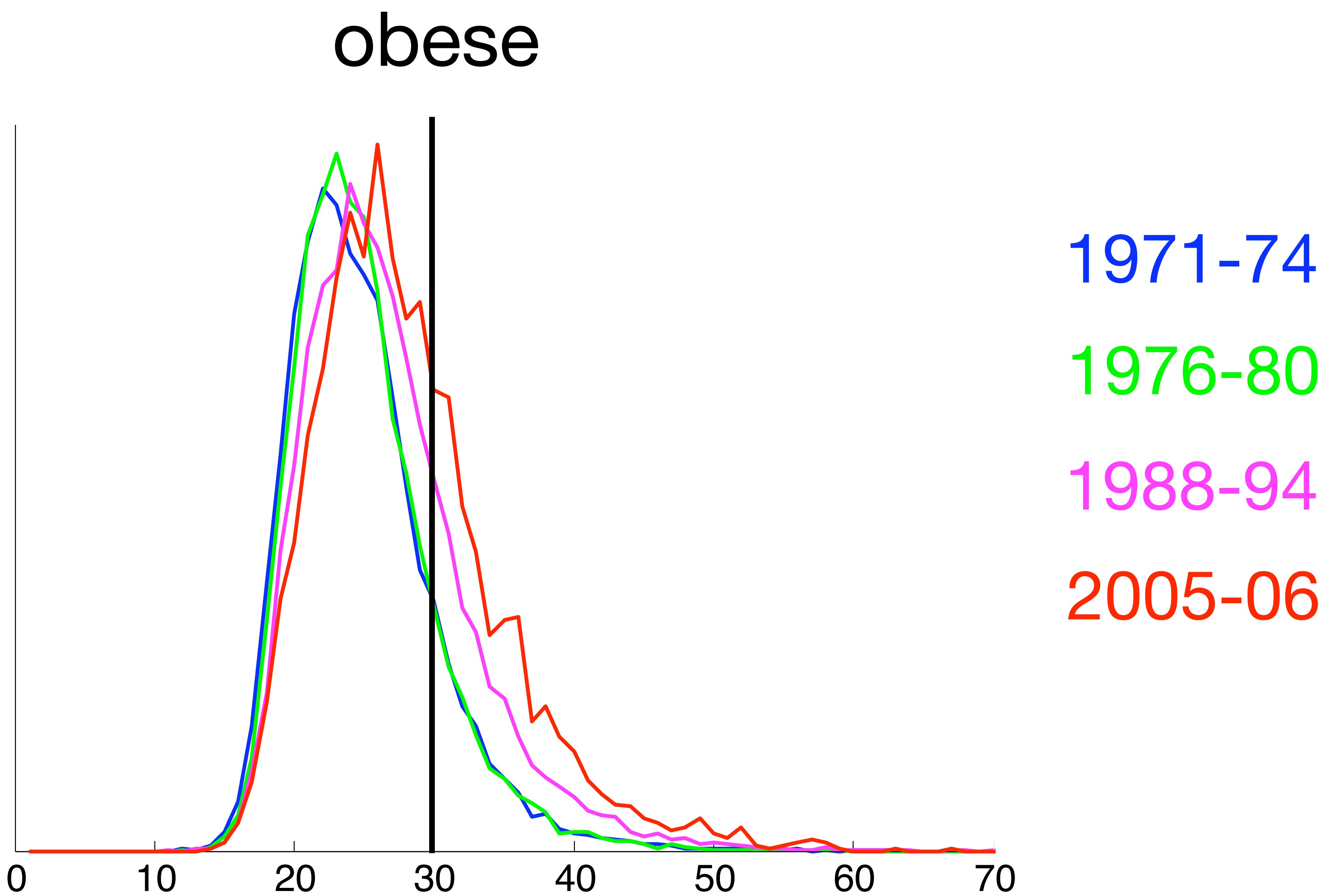
US obesity epidemic



BMI = weight / height^2

NHANES data

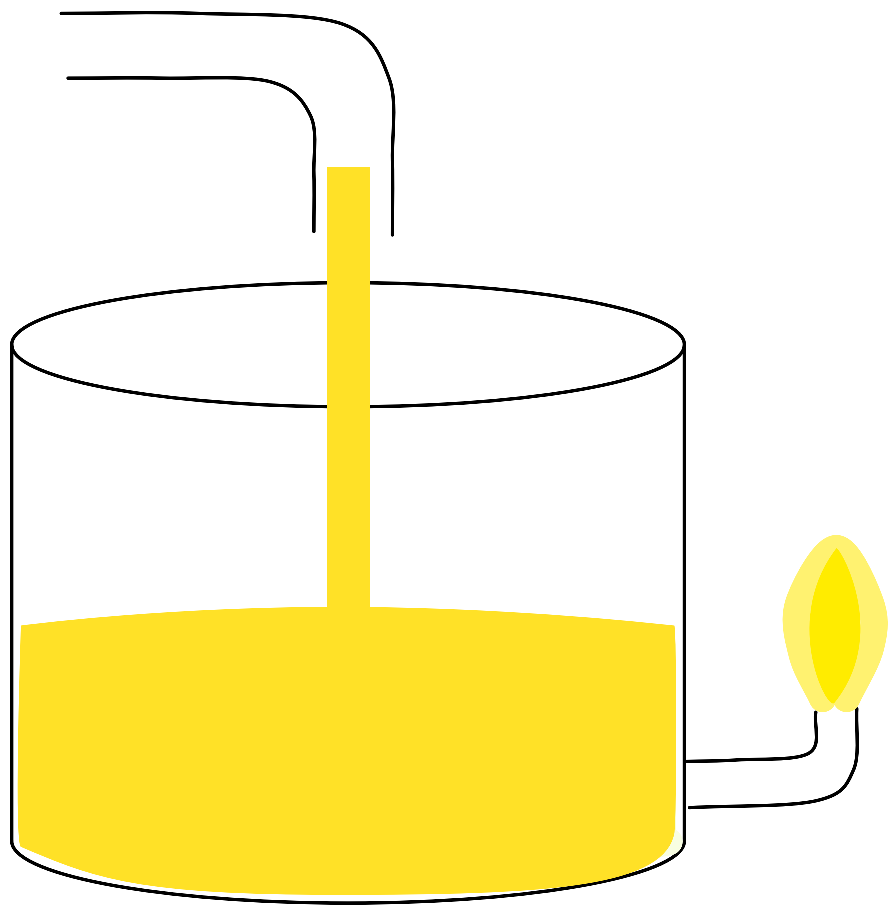
US obesity epidemic



BMI = weight / height^2

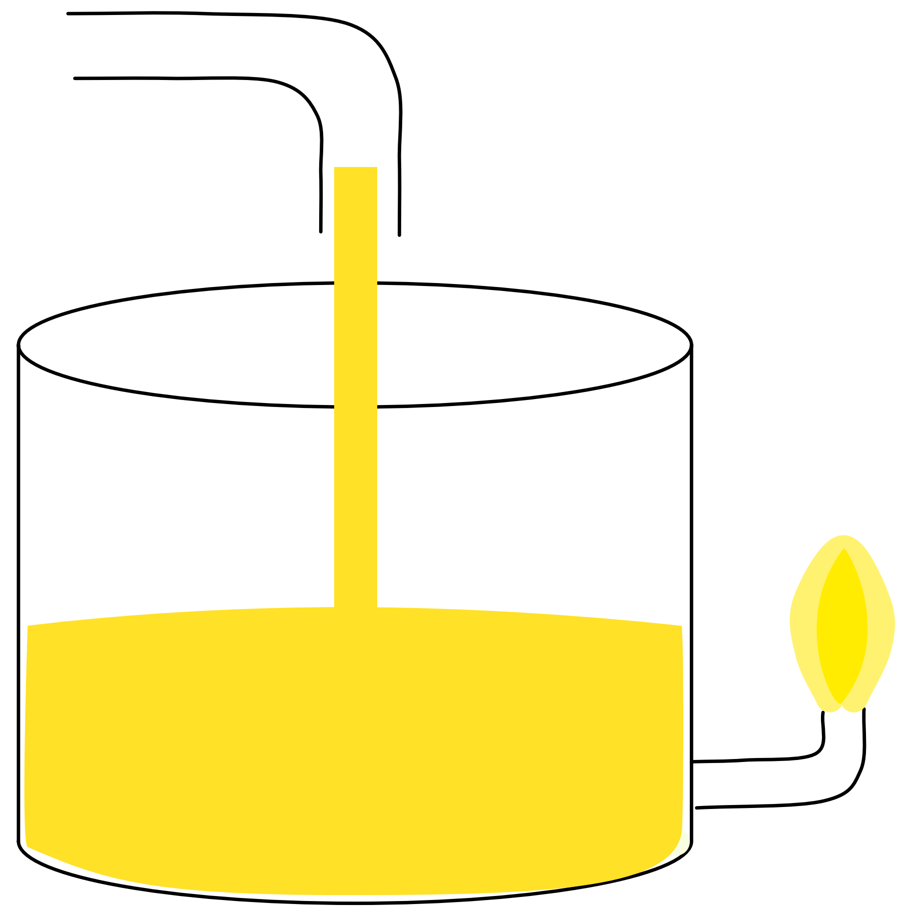
NHANES data

Conservation of energy



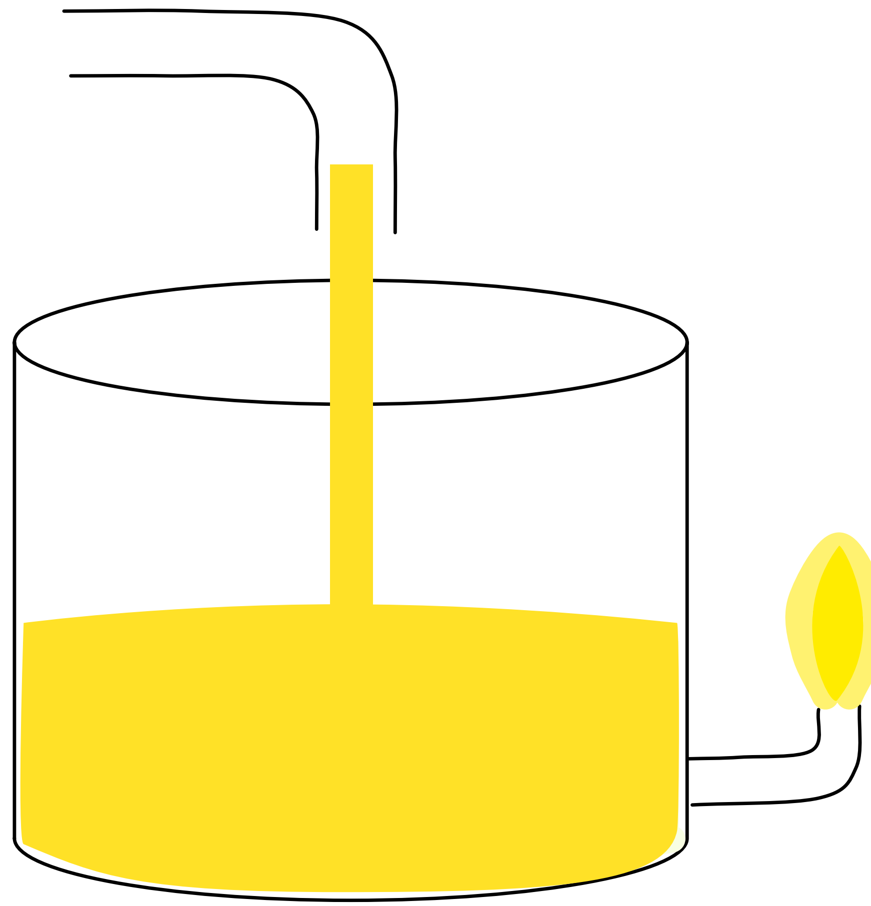
Conservation of energy

Food Intake



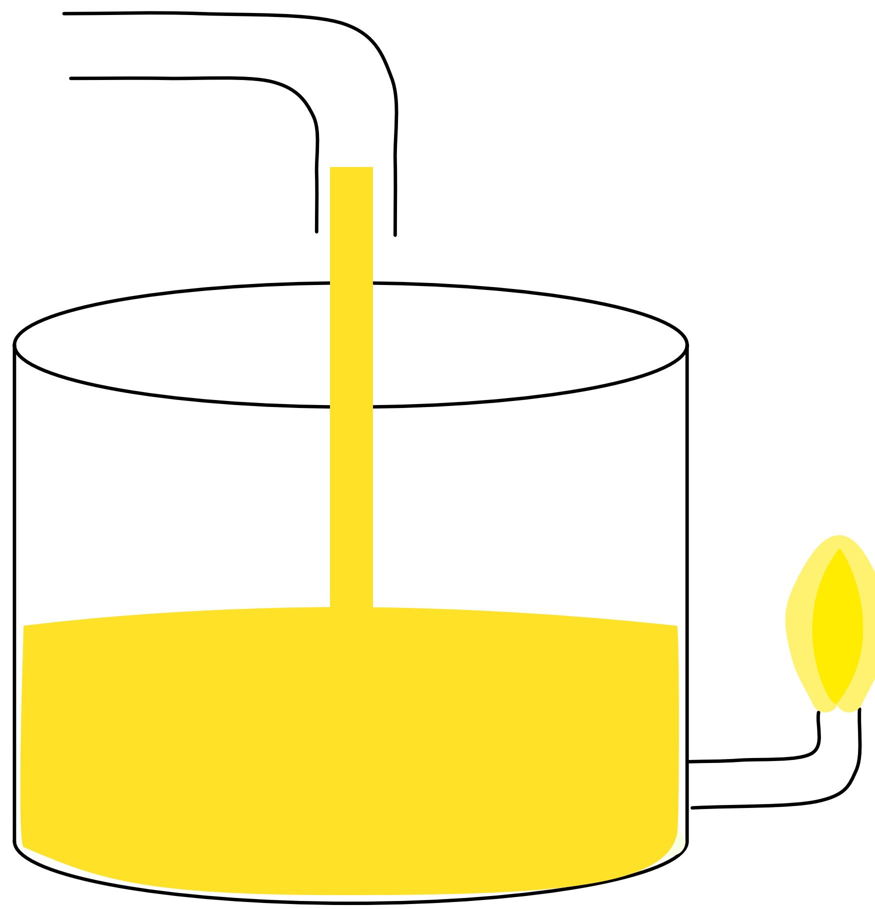
Conservation of energy

Food Intake



Conservation of energy

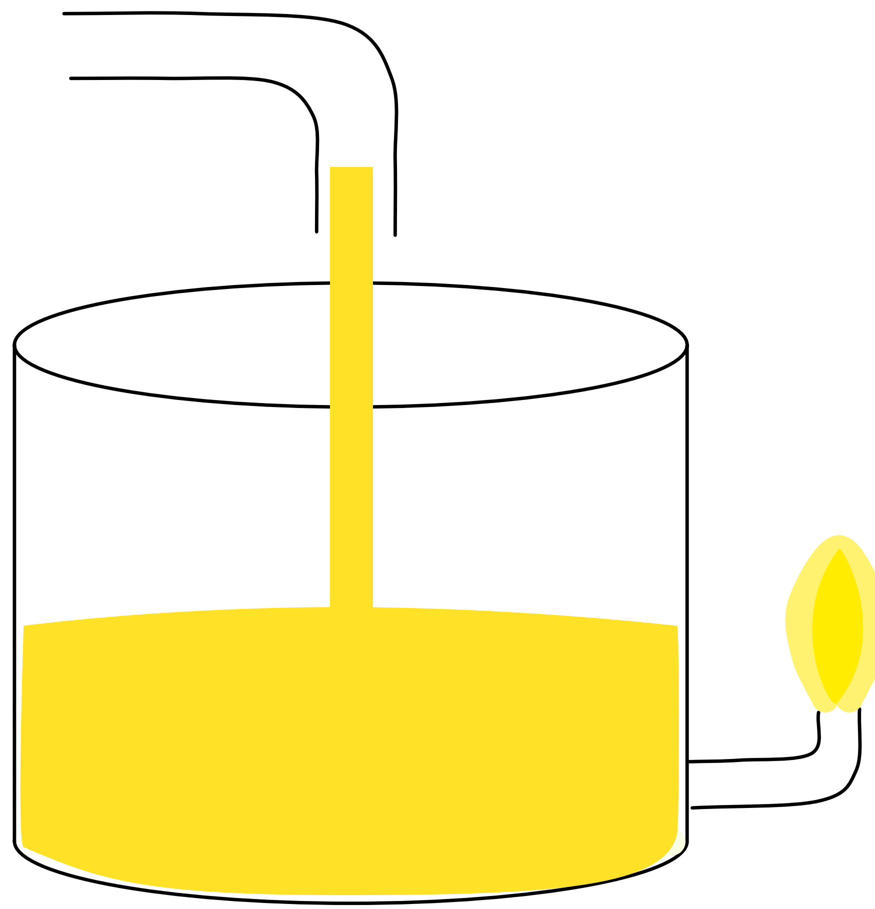
Food Intake



Energy expenditure

Conservation of energy

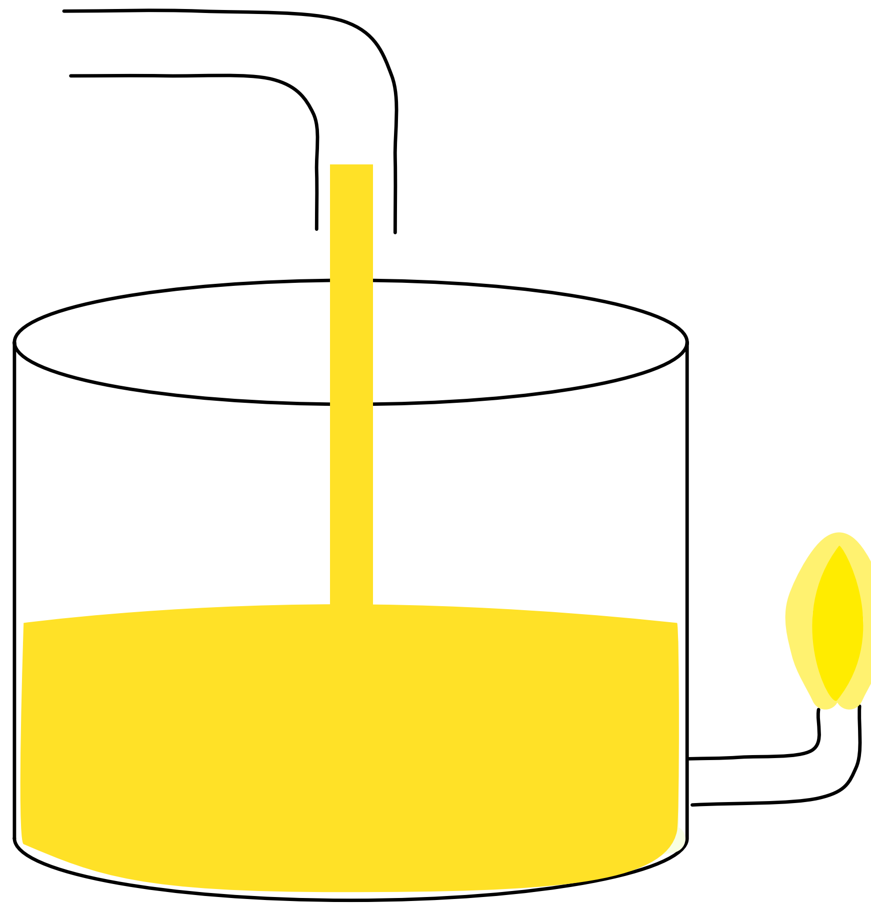
Food Intake



Energy expenditure

Conservation of energy

Food Intake

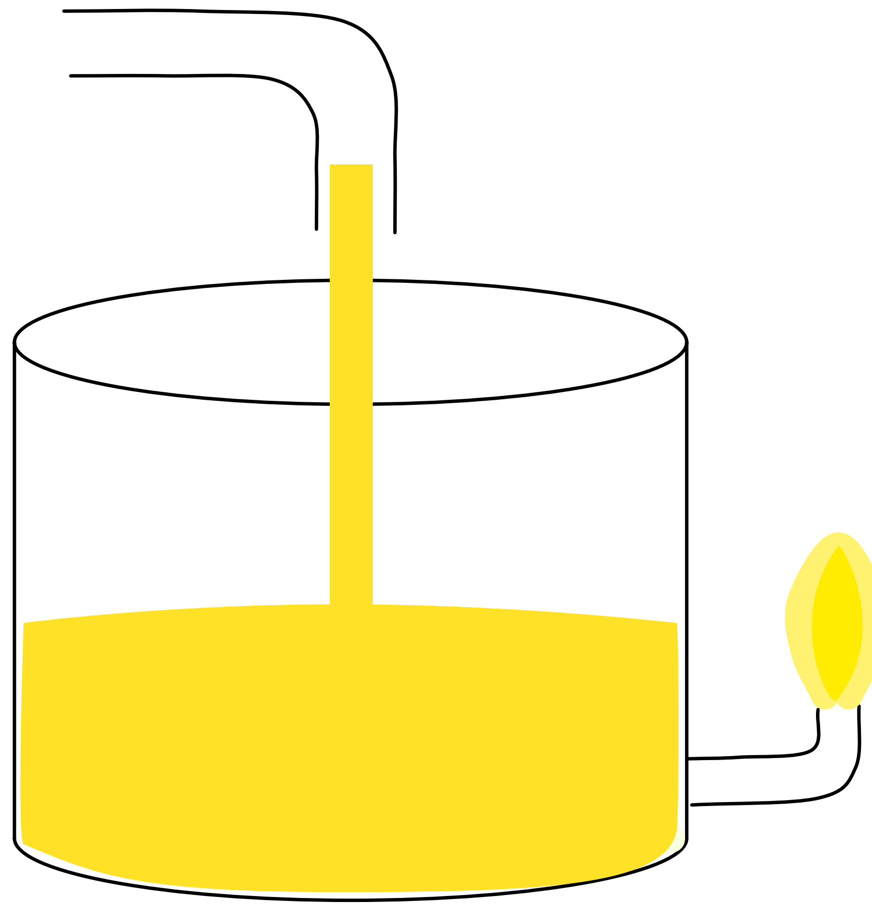


Energy storage

Energy expenditure

Conservation of energy

Food Intake

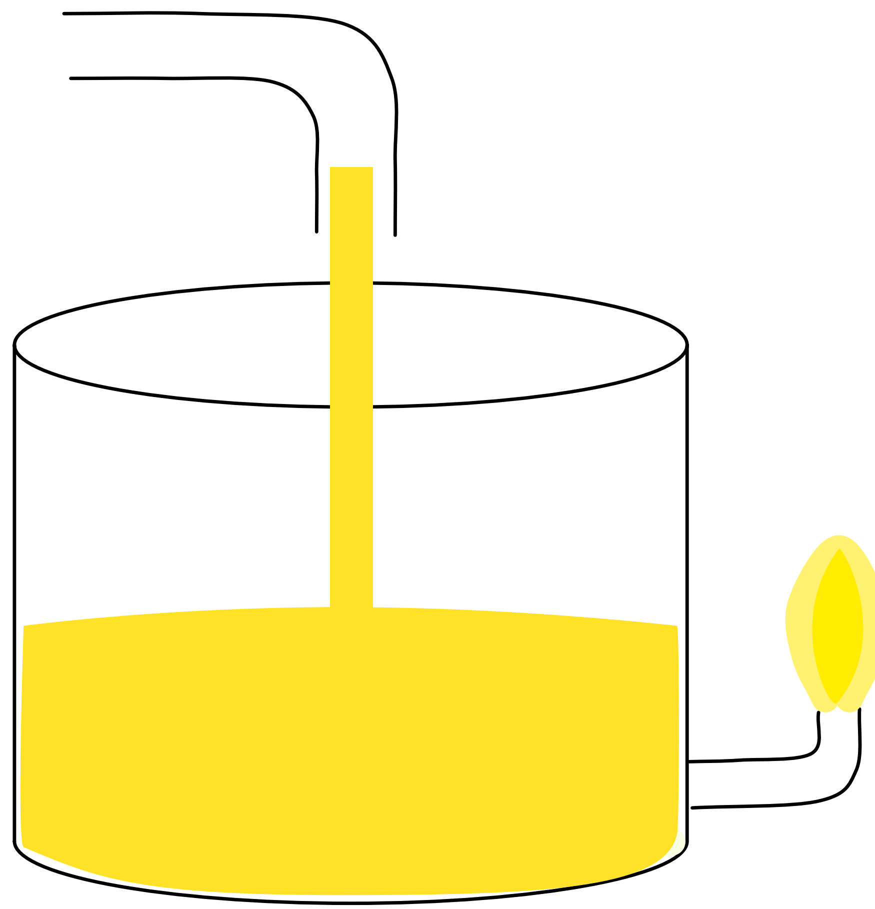


Energy expenditure

Energy storage

Conservation of energy

Food Intake



Energy expenditure

Energy storage

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

Energy flux

Rate of storage = intake rate - expenditure rate

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

M = body mass

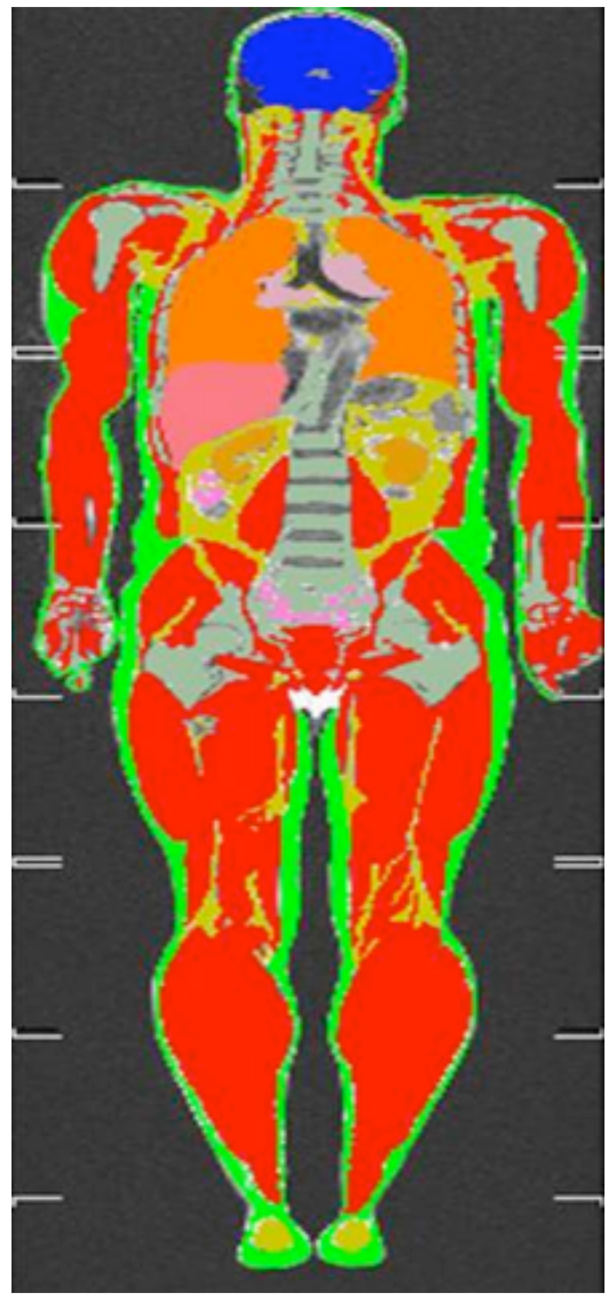
Energy density ρ_M converts energy to mass

Energy density

Fat
37.7 kJ/g

Carbs
(glycogen)
16.8 kJ/g

Protein
16.8 kJ/g

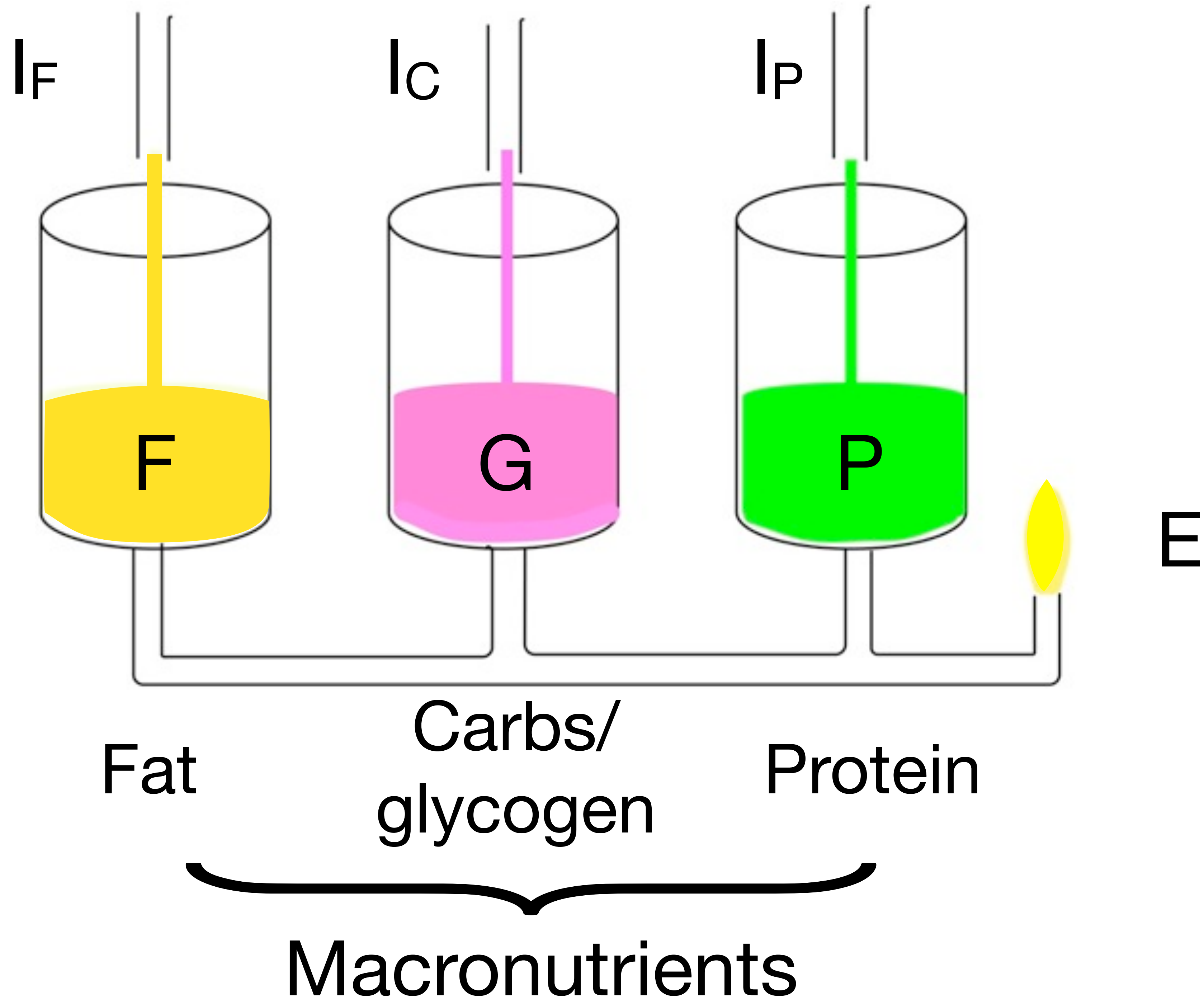


Water

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

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

$$\rho_G \frac{dG}{dt} \qquad = I_F + I_C + I_P - E$$

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

Macronutrient flux

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

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

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

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

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

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

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

f_F = fraction of fat utilized

f_C = fraction of carbs utilized

Reduction to $2D$

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

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

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

f_F = fraction of fat utilized

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

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

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

Glycogen supply small, ~ 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, ~ 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, ~ fixed on long time scales

Reduction to $2D$

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

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

Glycogen supply small, ~ 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, ~ 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, ~ 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 $\quad M = L + F$

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 $\quad M = L + F$

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

h_p protein hydration coefficient

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 $M = L + F$

h_p protein hydration coefficient

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 $\quad M = L + F$

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

h_p protein hydration coefficient

Reduction to $2D$

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

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

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

h_p protein hydration coefficient

Body composition model

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

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

Body composition model

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f is fraction of energy use that is fat

Body composition model

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

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

f is fraction of energy use that is fat

E and f are functions of F and L

Fixed points

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

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

Fixed points

$$\rho_F \frac{dF}{dt} = I_F - fE \quad = 0$$

$$\rho_L \frac{dL}{dt} = I_L - (1-f)E = 0$$

Fixed points

$$\rho_F \frac{dF}{dt} = I_F - fE \quad = 0$$

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} Nullclines

Fixed points

$$\rho_F \frac{dF}{dt} = I_F - fE \quad = 0$$

$$\rho_L \frac{dL}{dt} = I_L - (1-f)E = 0$$

Nullclines

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

energy balance

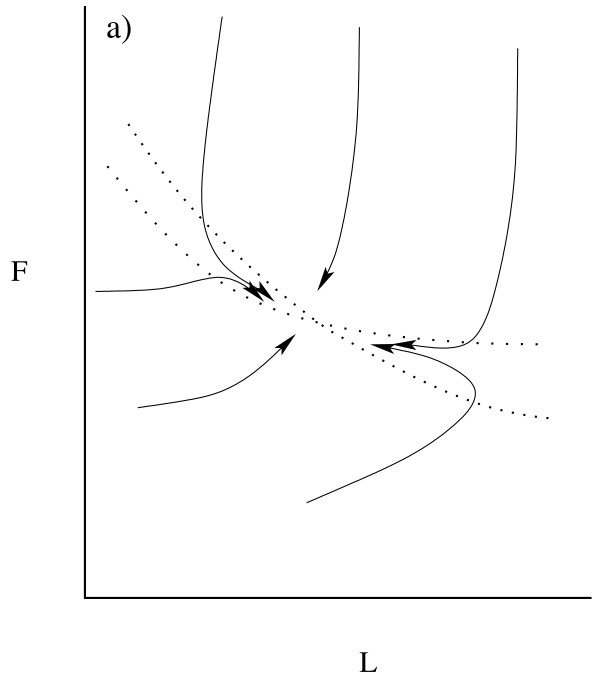
Fixed points

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

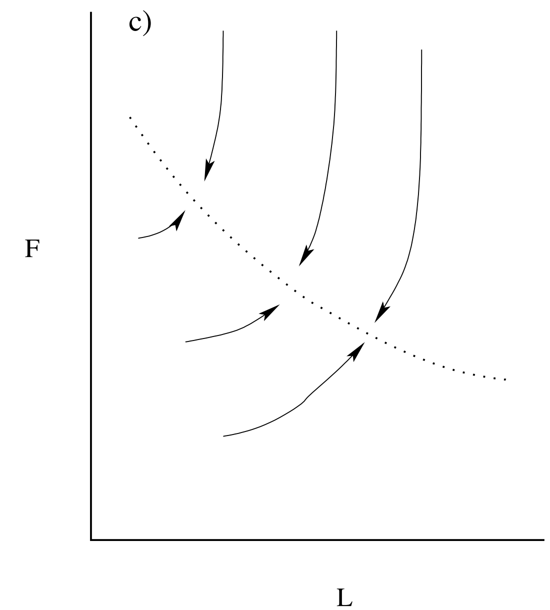
$$E(F, L) = I_F + I_L \equiv I$$ energy balance

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

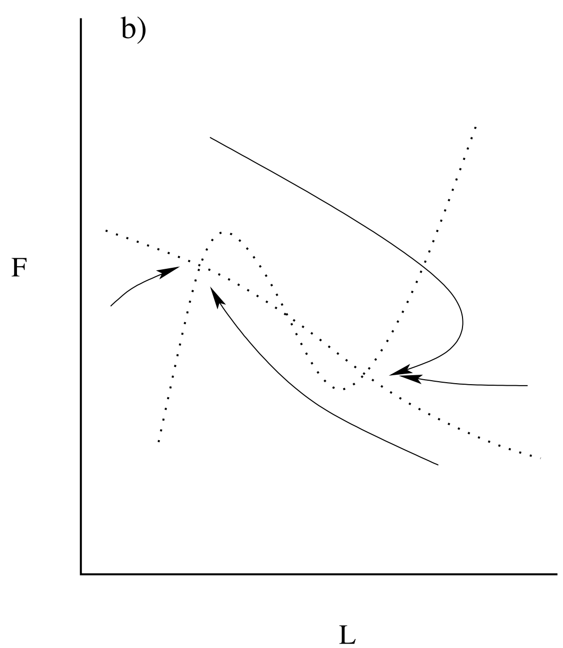
Possible phase plane dynamics



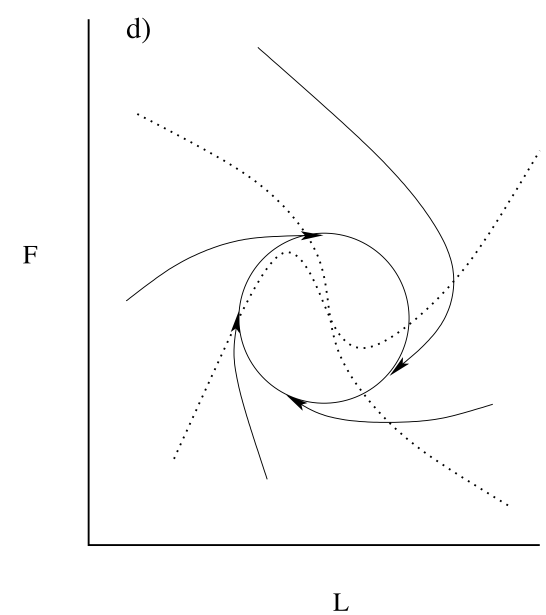
Fixed point



Invariant manifold



Multiple fixed points



Limit cycle

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

Energy expenditure rate E

Energy expenditure rate E

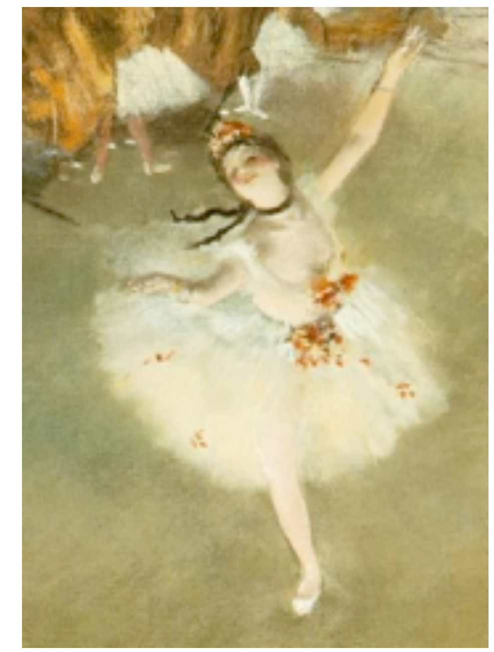
$E =$

Energy expenditure rate E

$E =$ 

Basal metabolic rate (BMR)

Energy expenditure rate E

$E =$  $+$ 

Basal metabolic rate (BMR) Physical activity

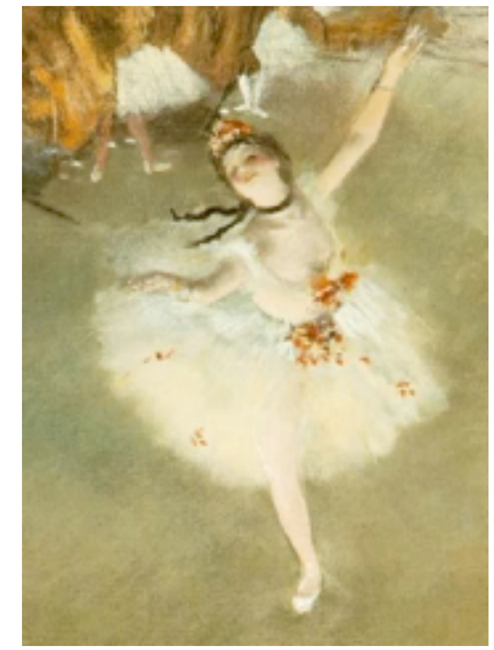
Energy expenditure rate E

$E =$  $+$ 

Basal metabolic rate (BMR) Physical activity

$E \sim$ 10 MJ/day

Energy expenditure rate E

$E =$  $+$ 

Basal metabolic rate (BMR) Physical activity

$E \sim$ 10 MJ/day ~115 W

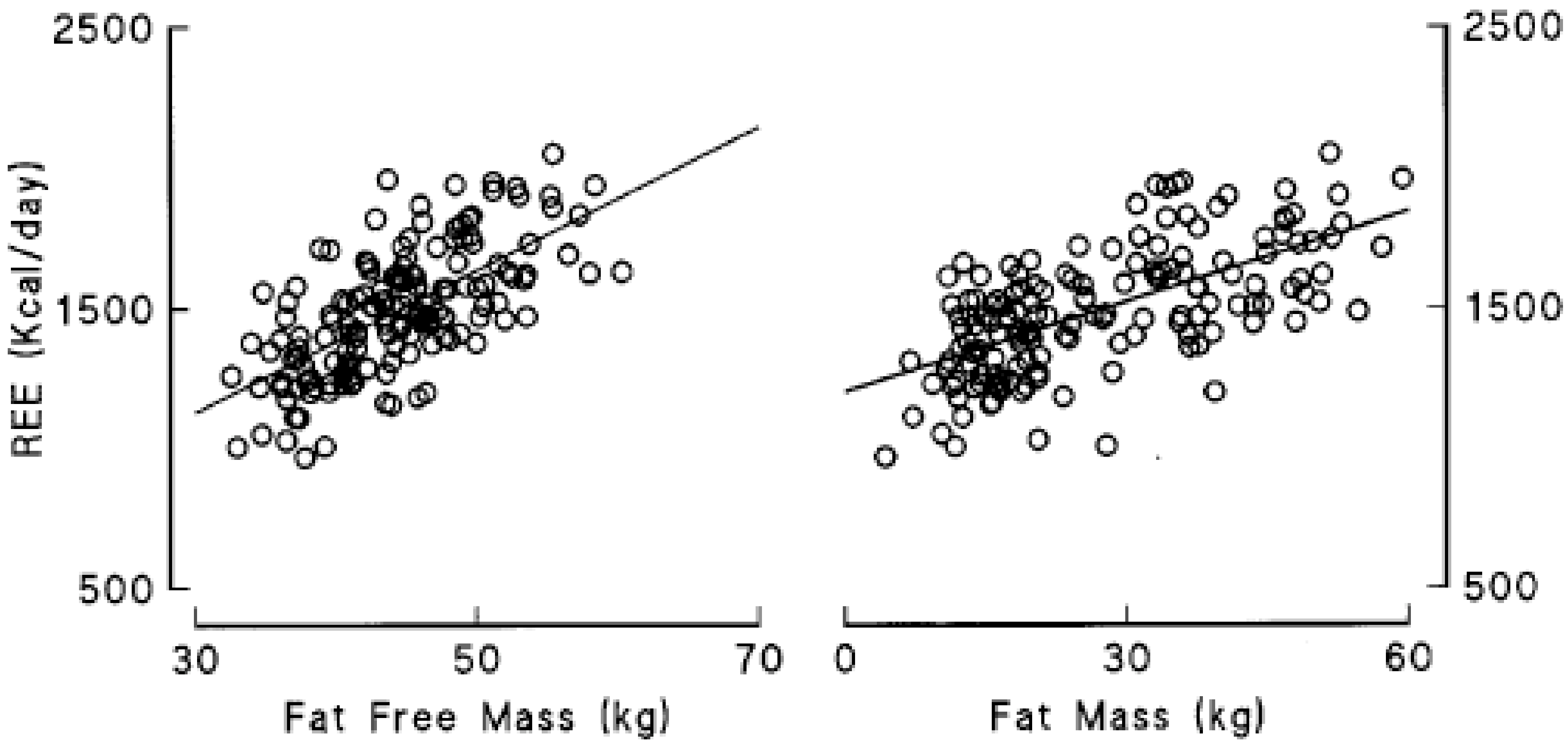
Energy expenditure rate E

$E =$  $+$ 

Basal metabolic rate (BMR) Physical activity

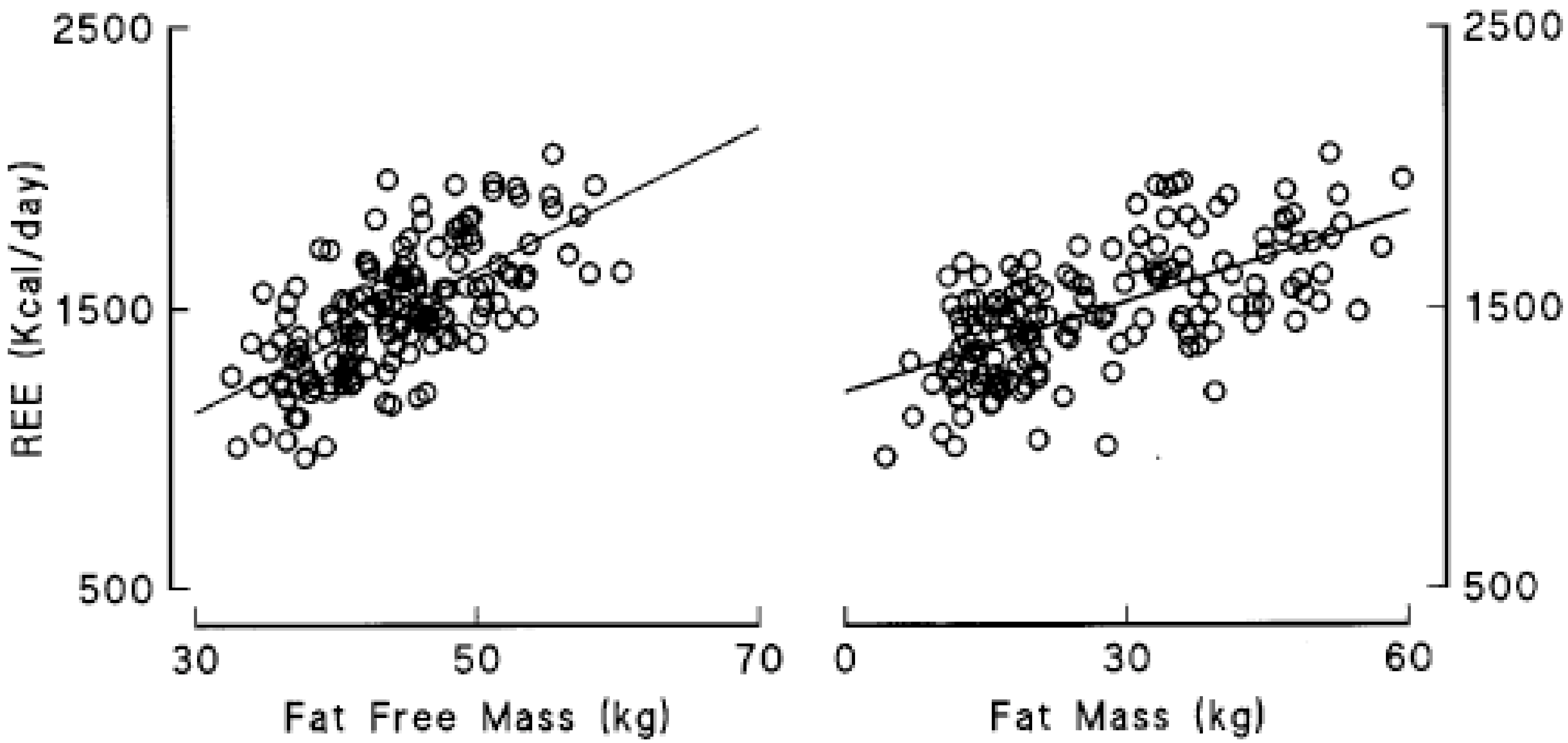
E ~ 10 MJ/day ~115 W ~ 3 KWH/day

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

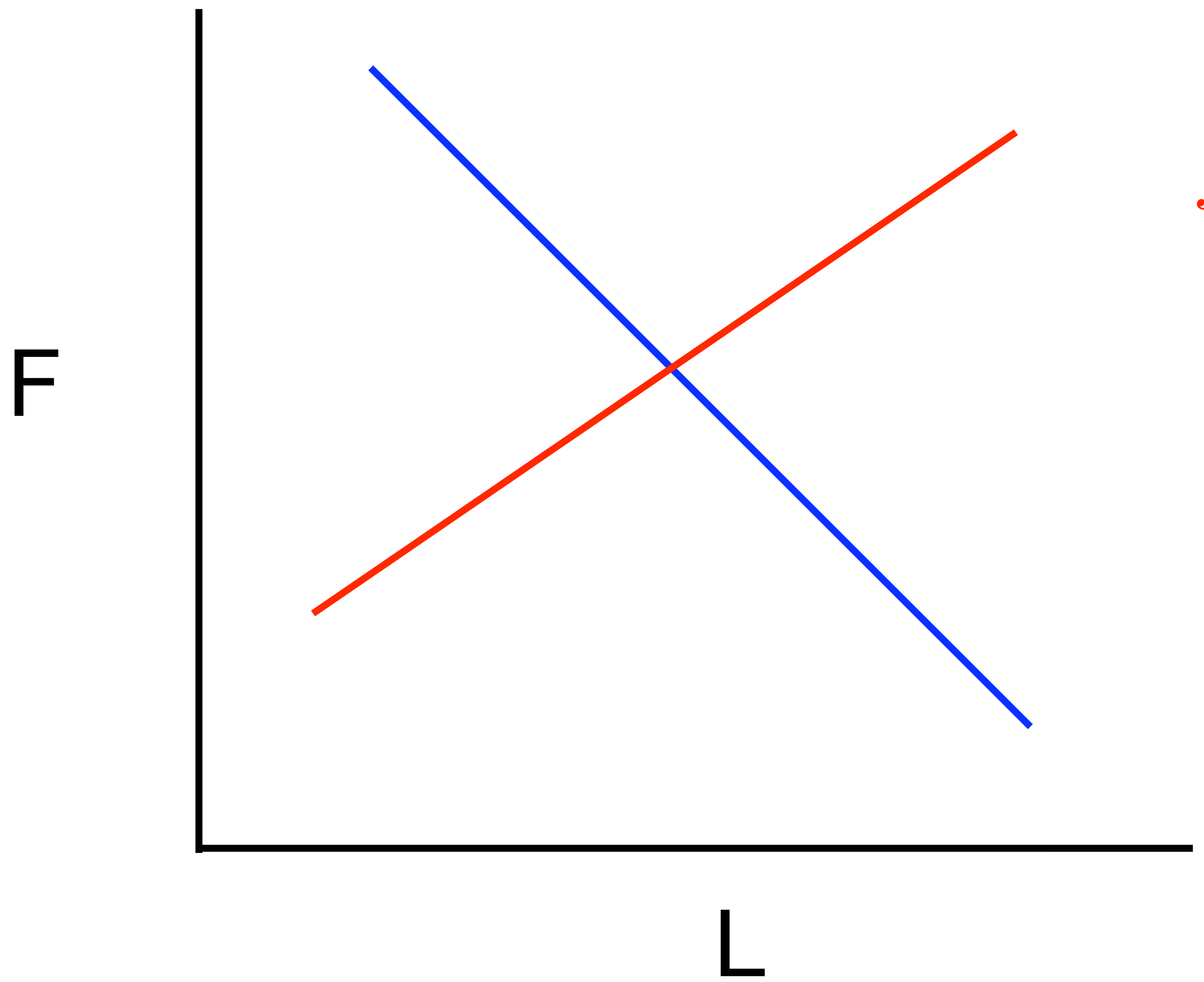
Energy due to PA ∝ Mass

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

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

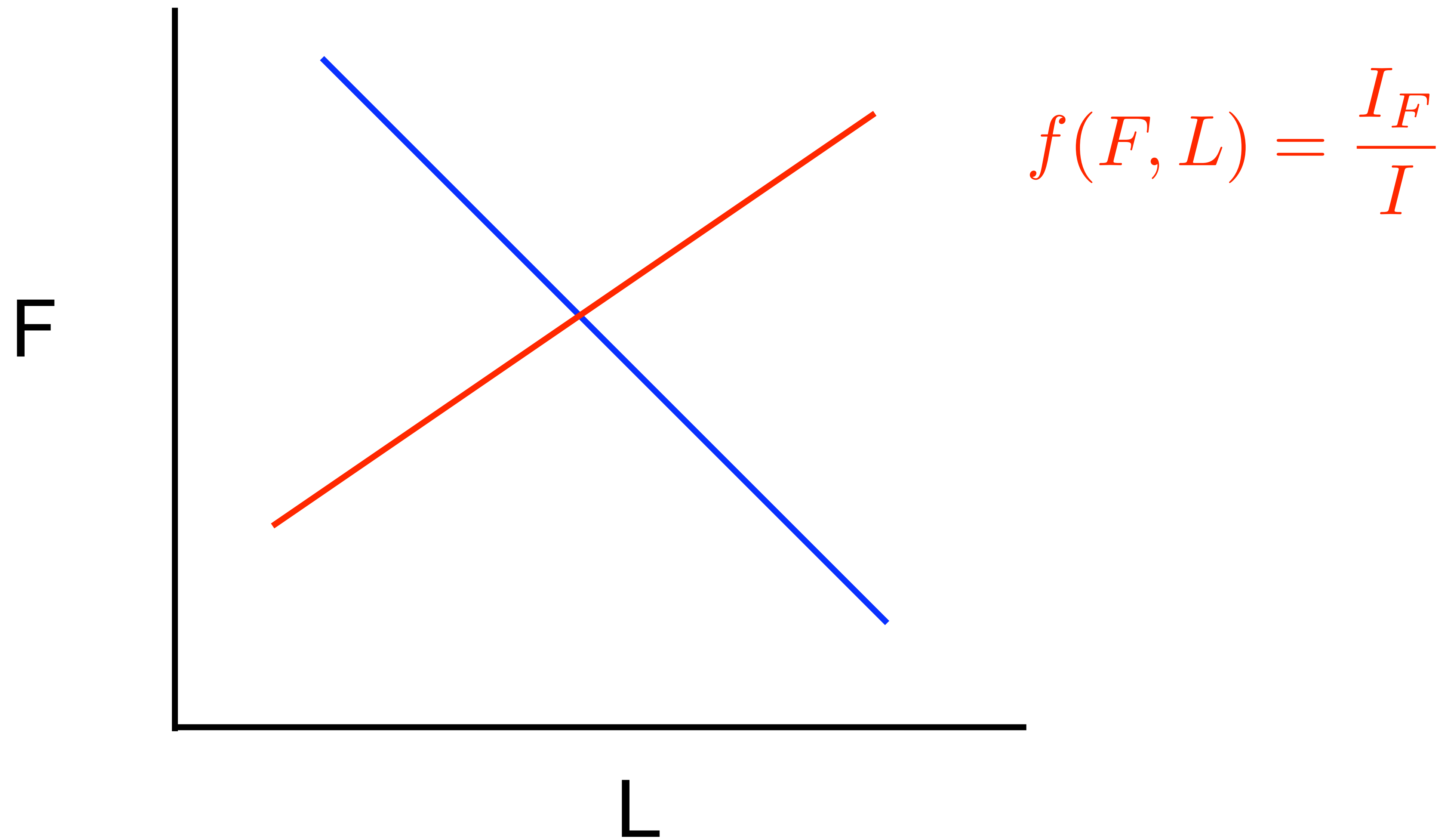
E is linear in F and L

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



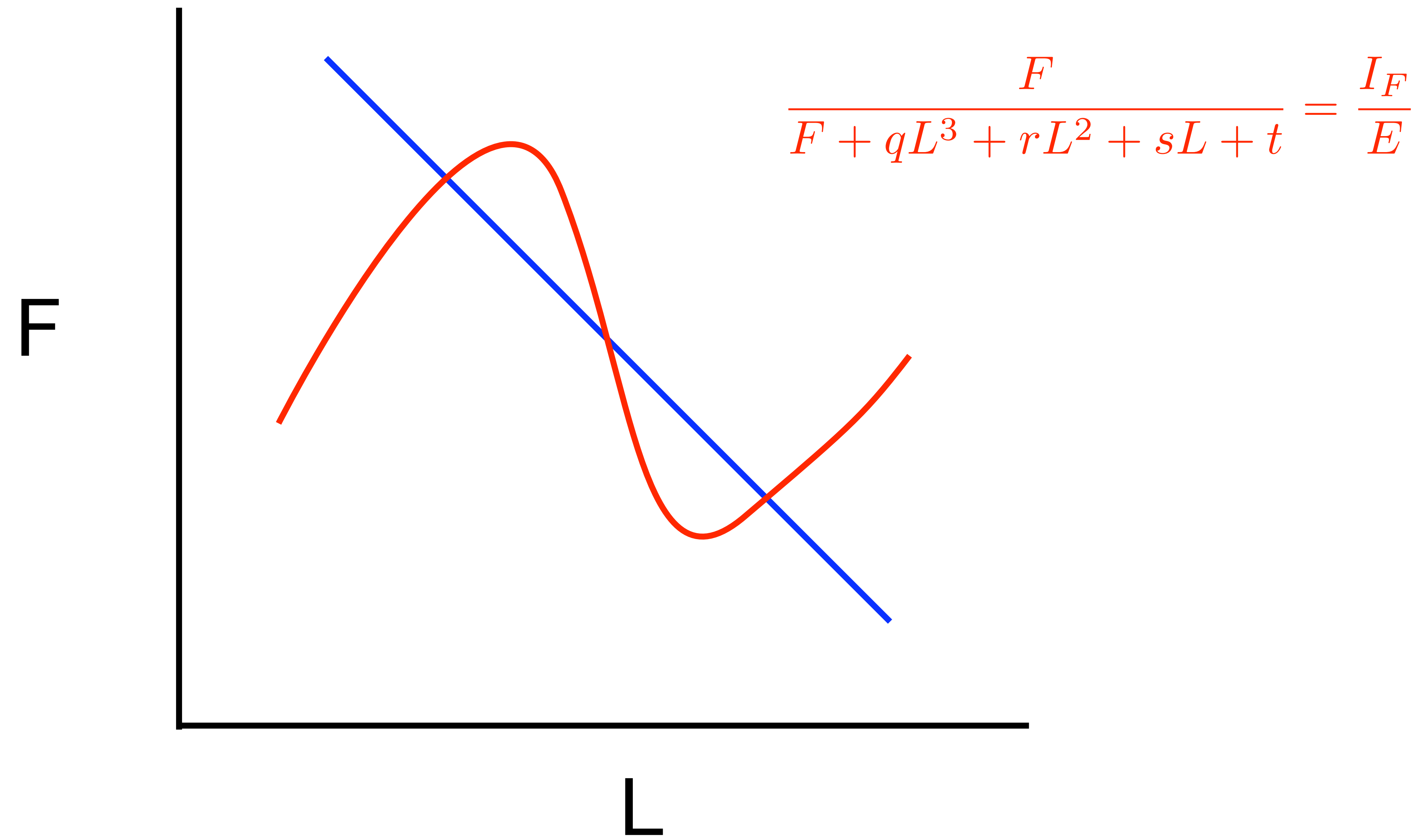
$$f(F, L) = \frac{I_F}{I}$$

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



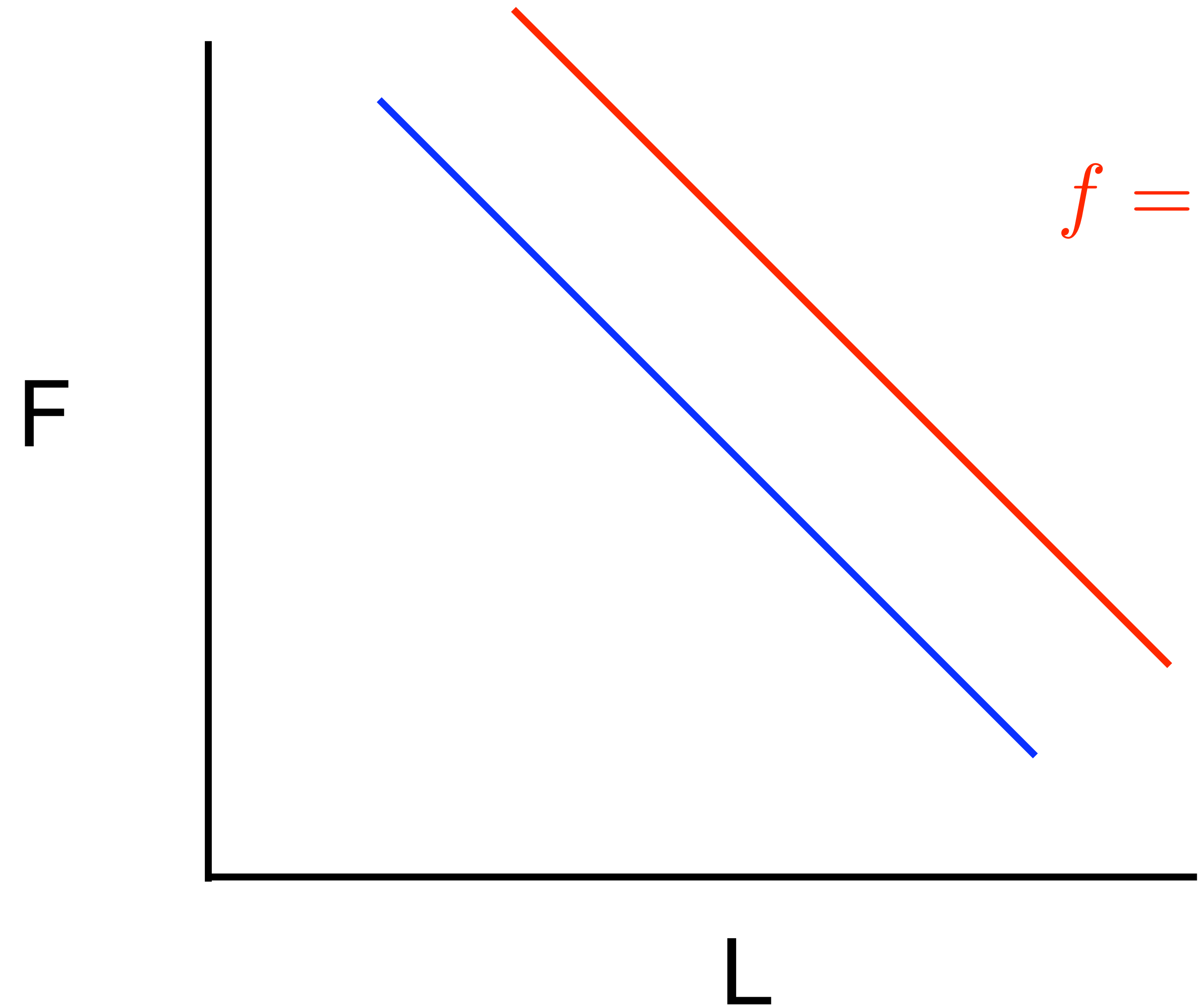
Single fixed point is generic

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



Multi-stability or limit cycle requires fine tuning

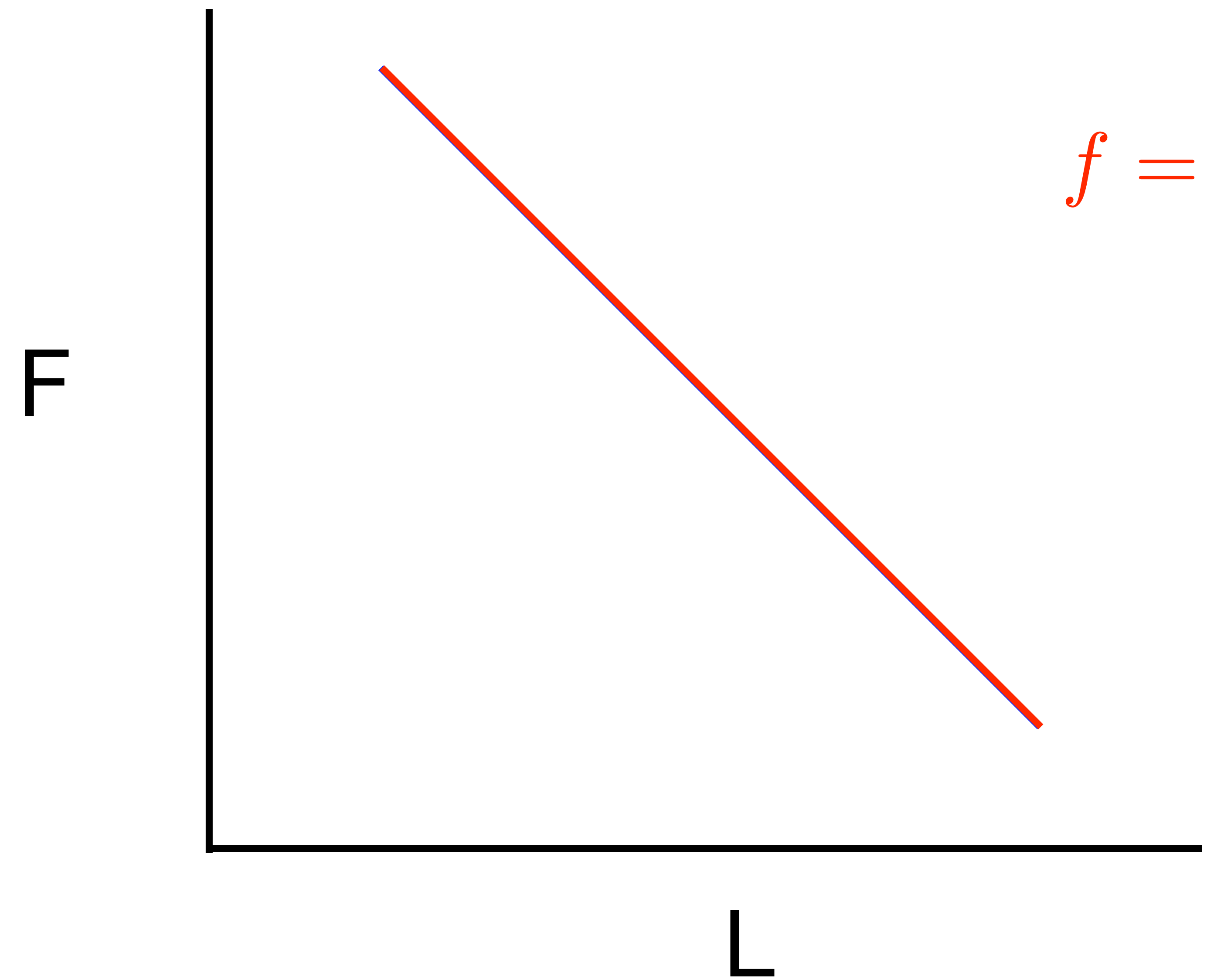
$$E(F,L) = bF + cL + d = I$$



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

Invariant manifold or line attractor requires special form

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



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

Invariant manifold or line attractor requires special form

The problem with measuring f

In energy balance, f reflects diet

The problem with measuring f

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

The problem with measuring f

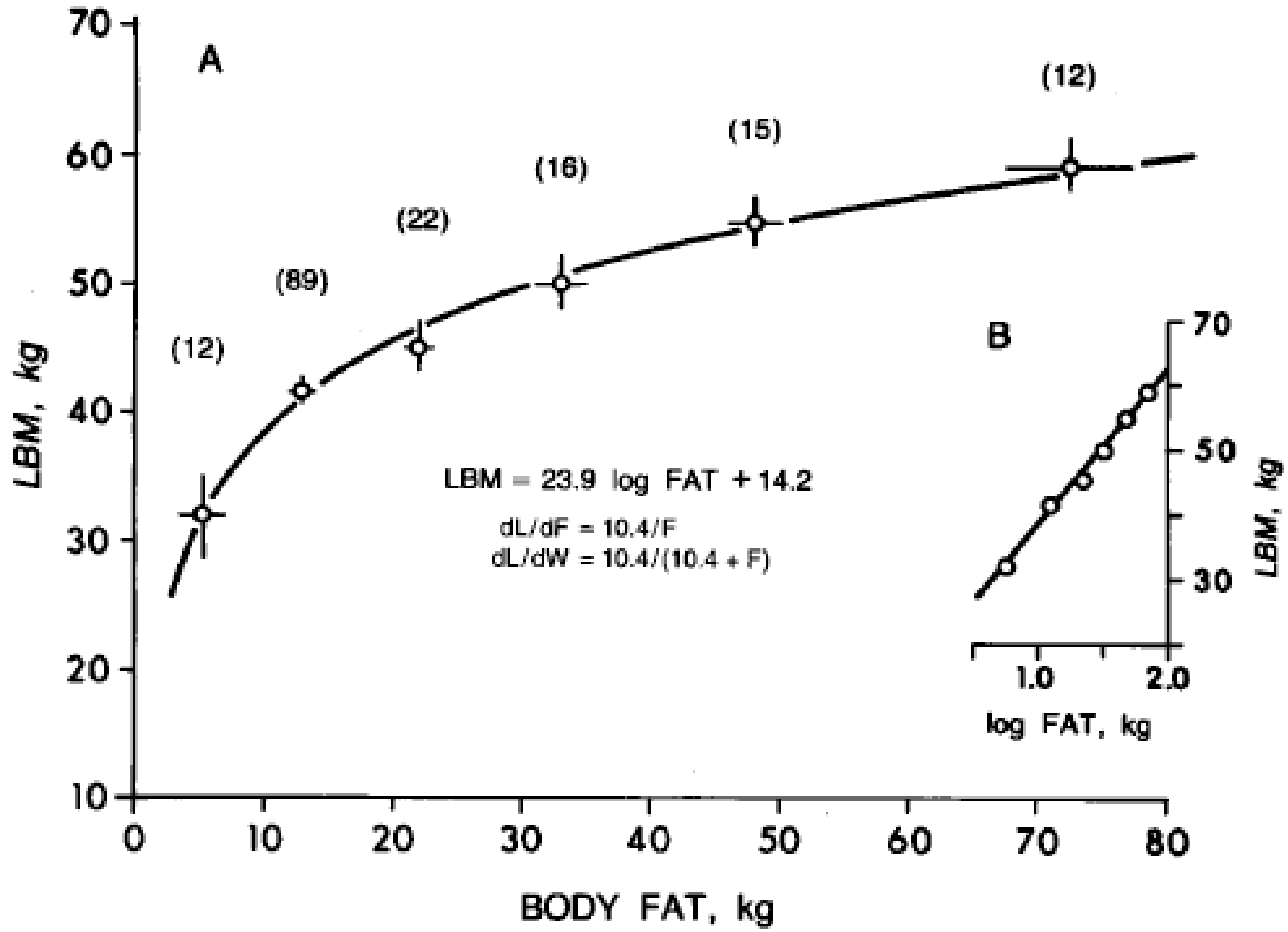
In energy balance, f reflects diet $f(F, L) = \frac{I_F}{I}$

Must invert in dynamic situation

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

Forbes Law

L

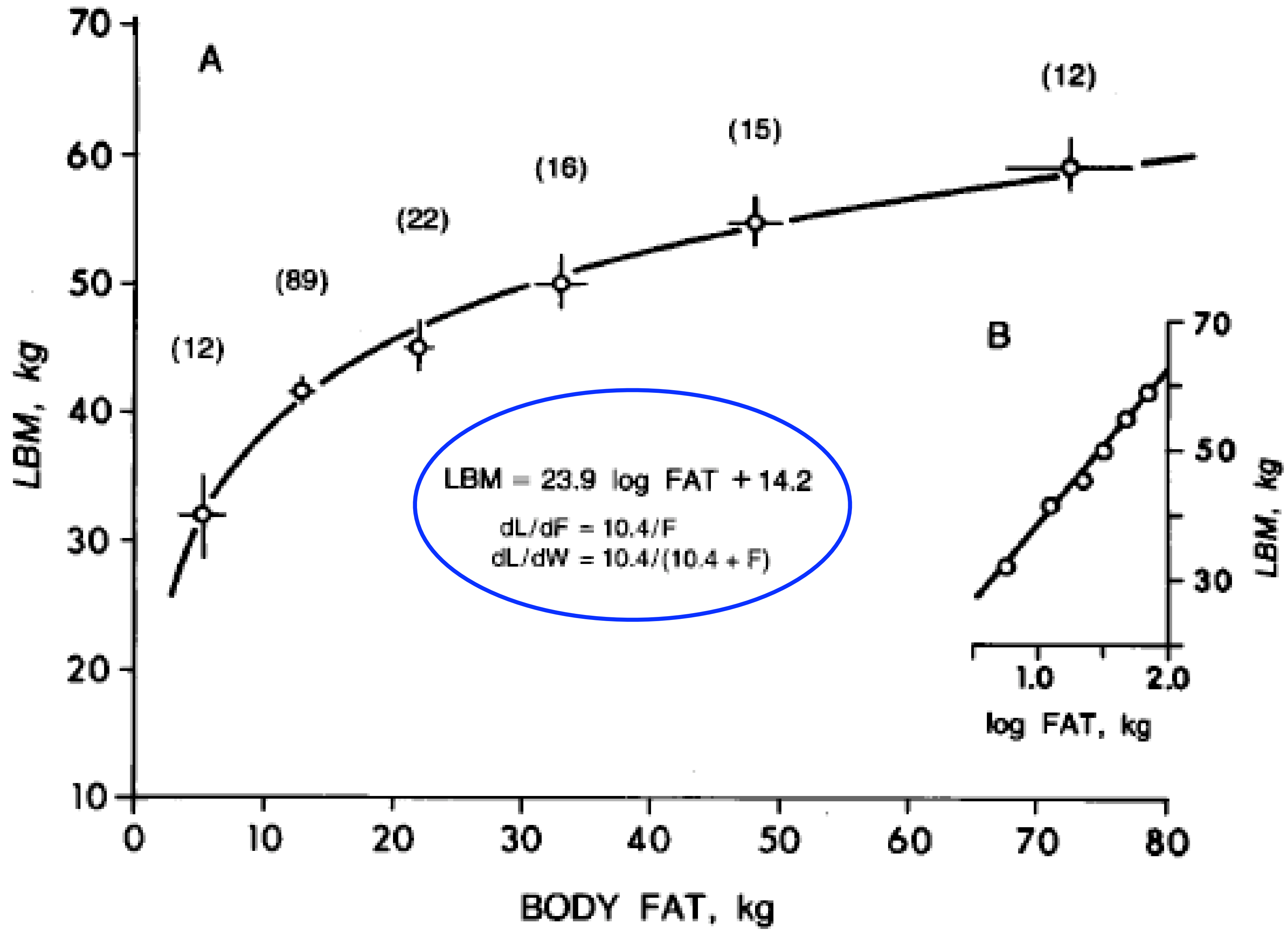


F

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

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

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

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

Impose Forbes law

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

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

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

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

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

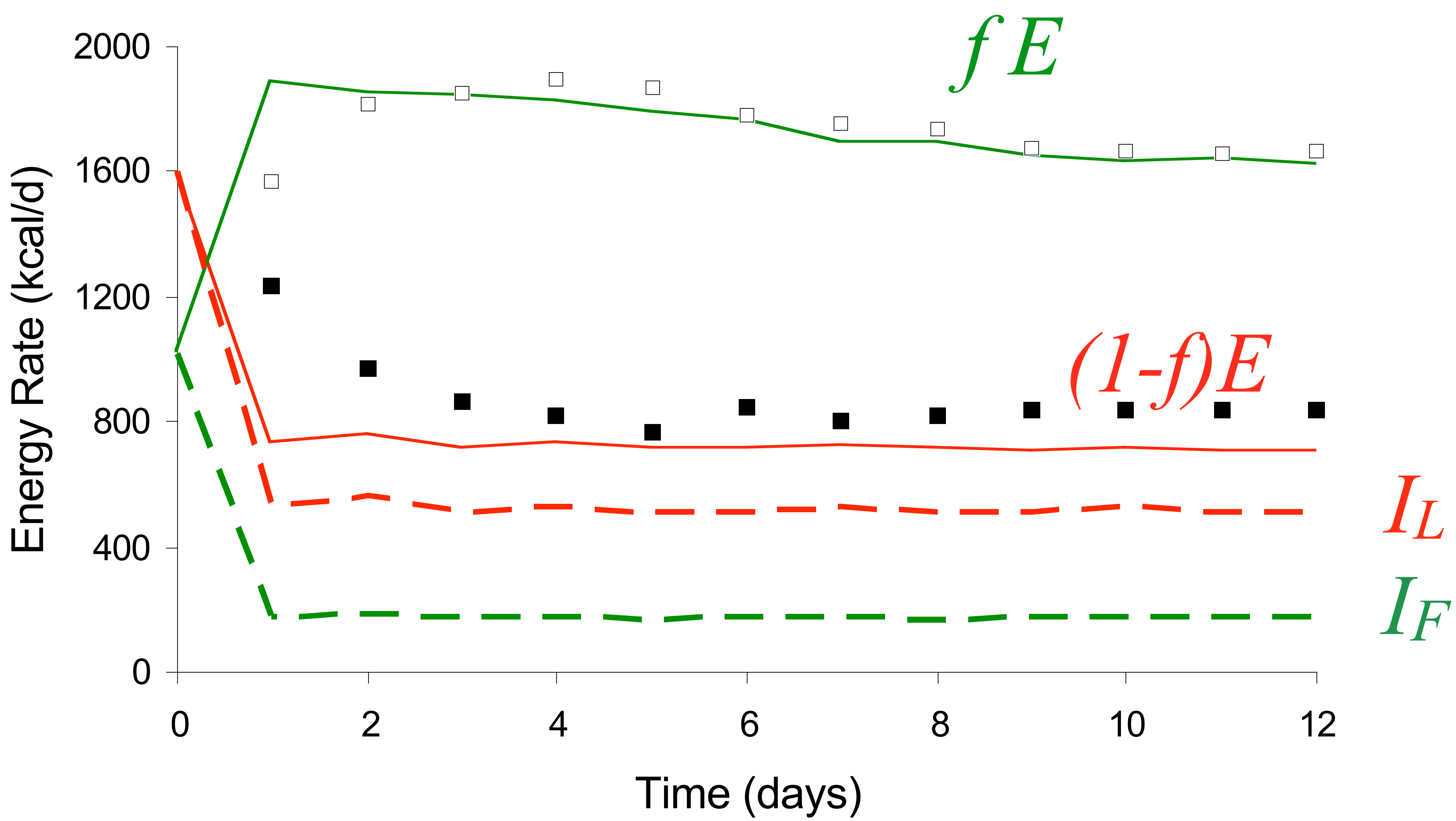
$$f = \frac{I_F - (1-p)(I-E)}{E} \qquad p = \frac{1}{1 + \frac{\rho_F}{\rho_L}\frac{F}{10.4}}$$

Impose Forbes law

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

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

Matches data



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

Energy partition model

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

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

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

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

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

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

Energy partition model

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

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

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 $E(F, L) = I$

Energy partition model

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

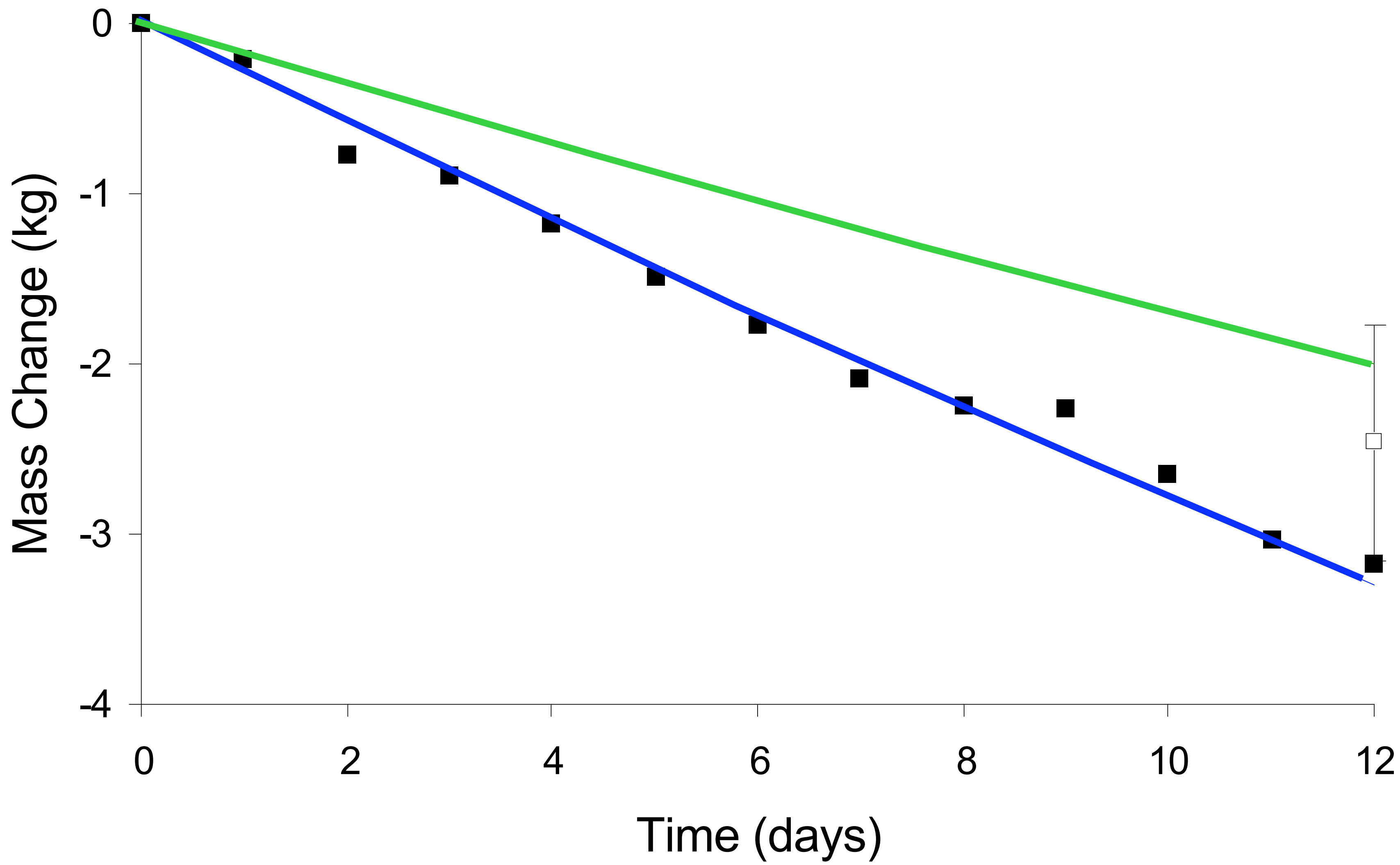
$$p = \frac{1}{1 + \frac{\rho_F}{\rho_L}\frac{F}{10.4}}$$

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

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

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

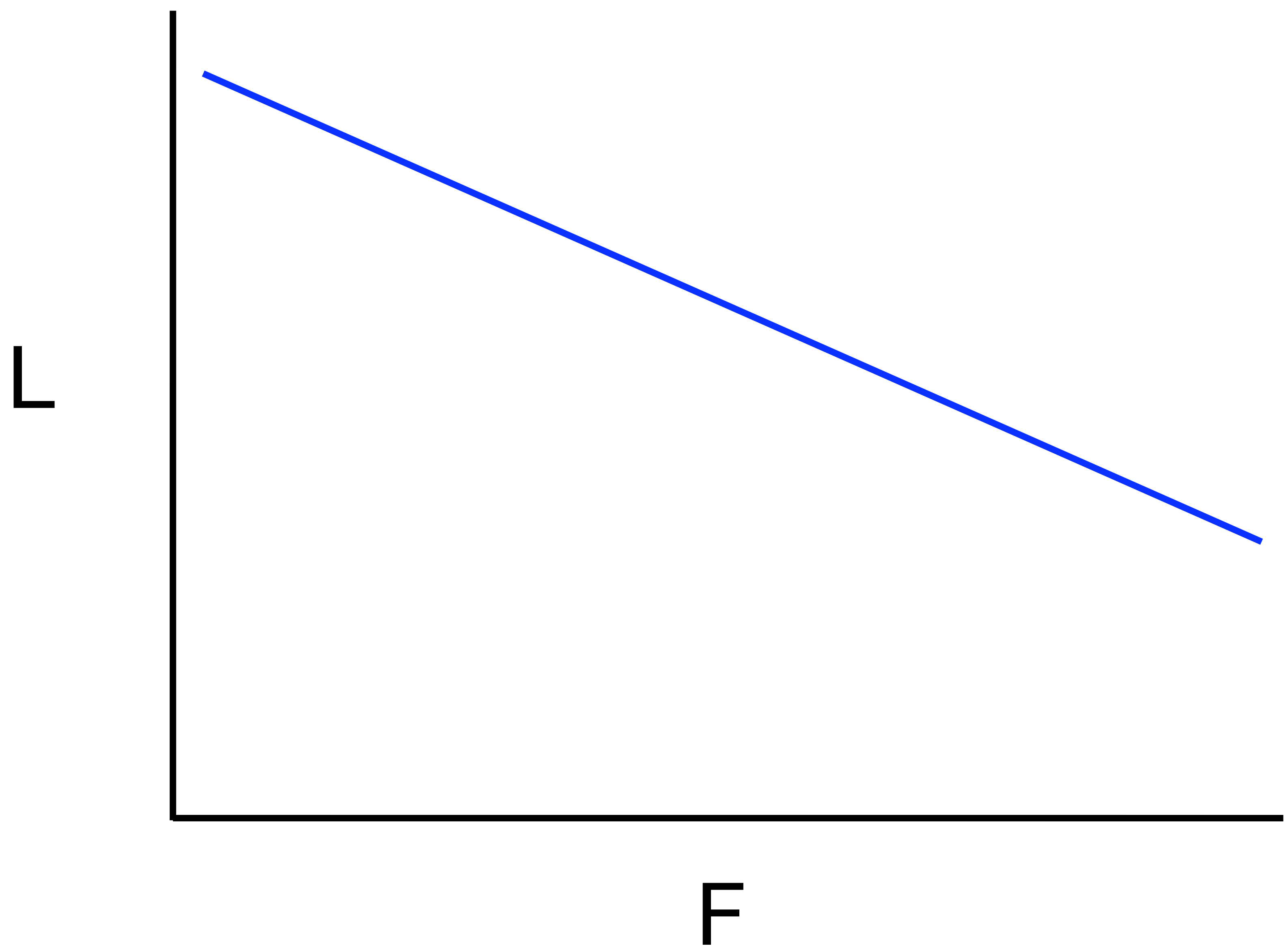
Weight and fat loss



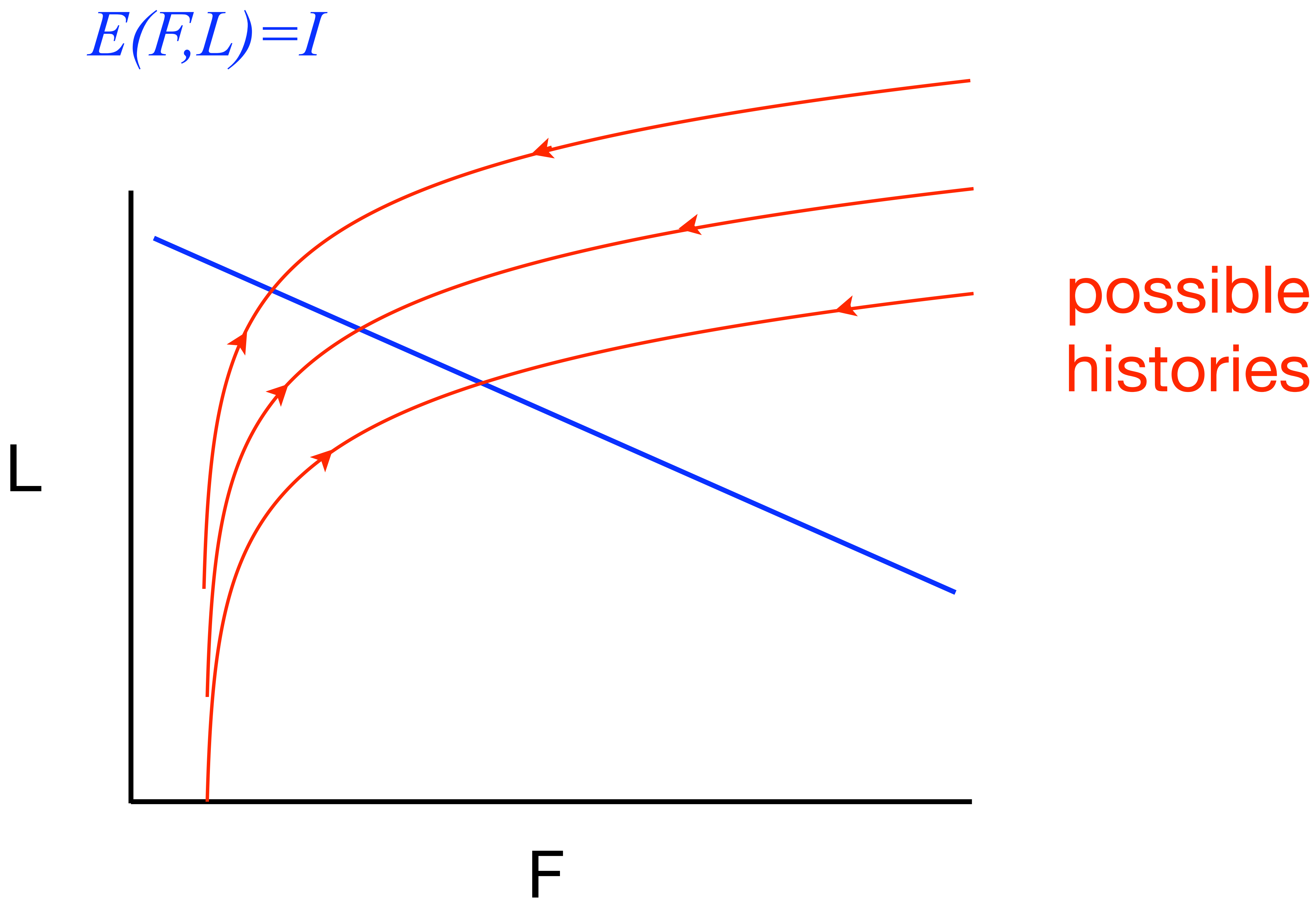
Hall, Bain, and Chow, Int J. Obesity, (2007)

Consequences of line attractor

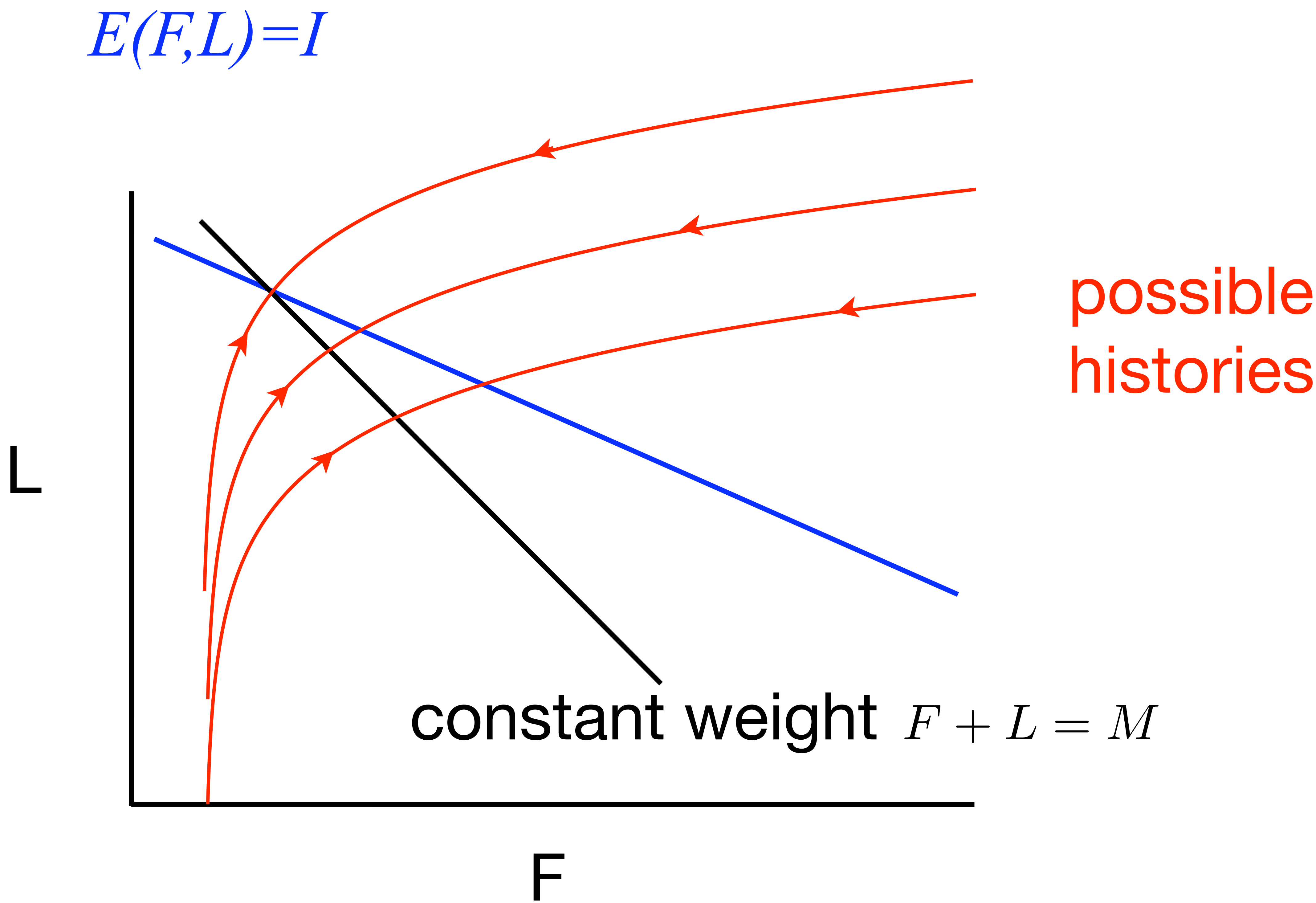
$E(F,L)=I$



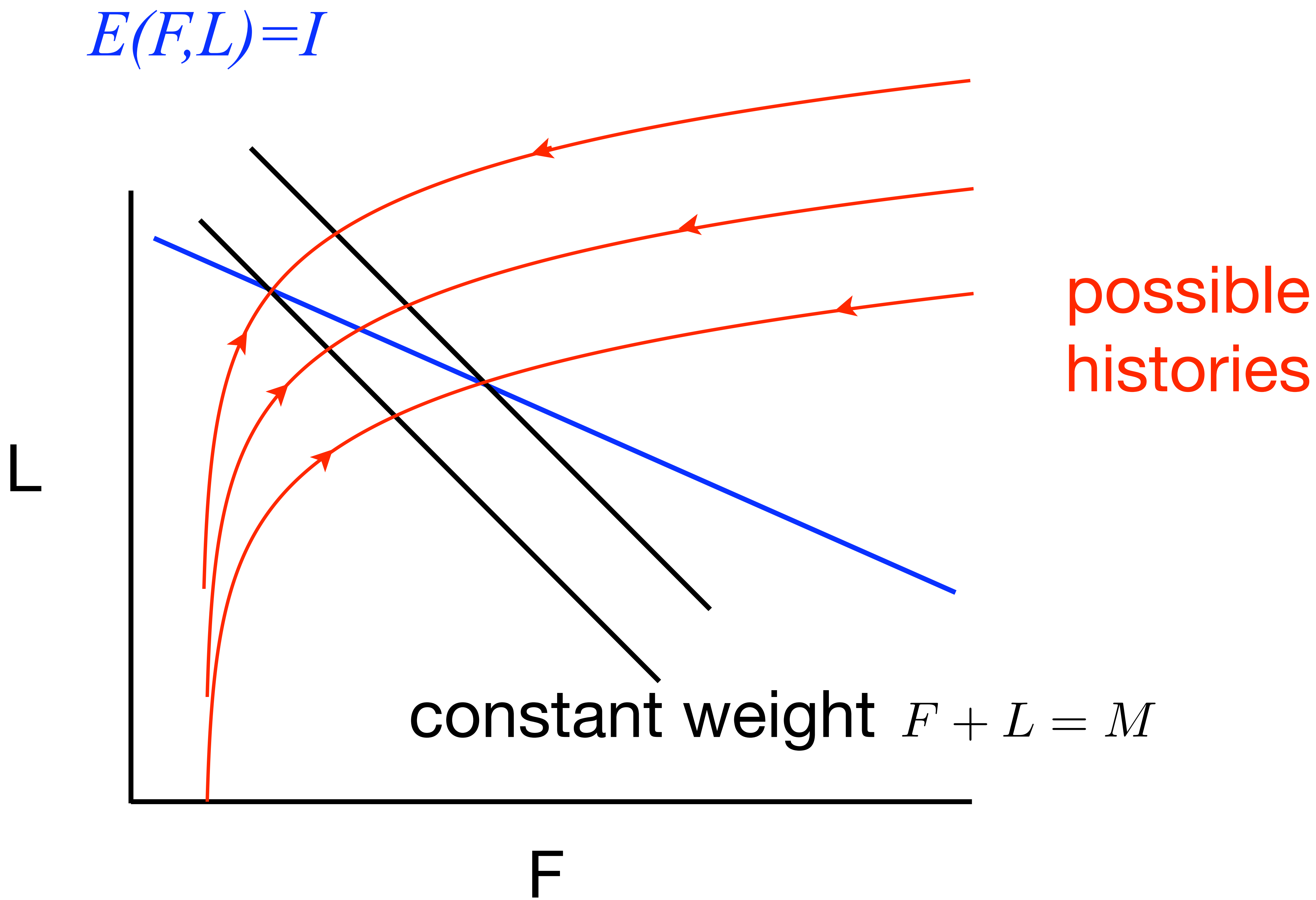
Consequences of line attractor



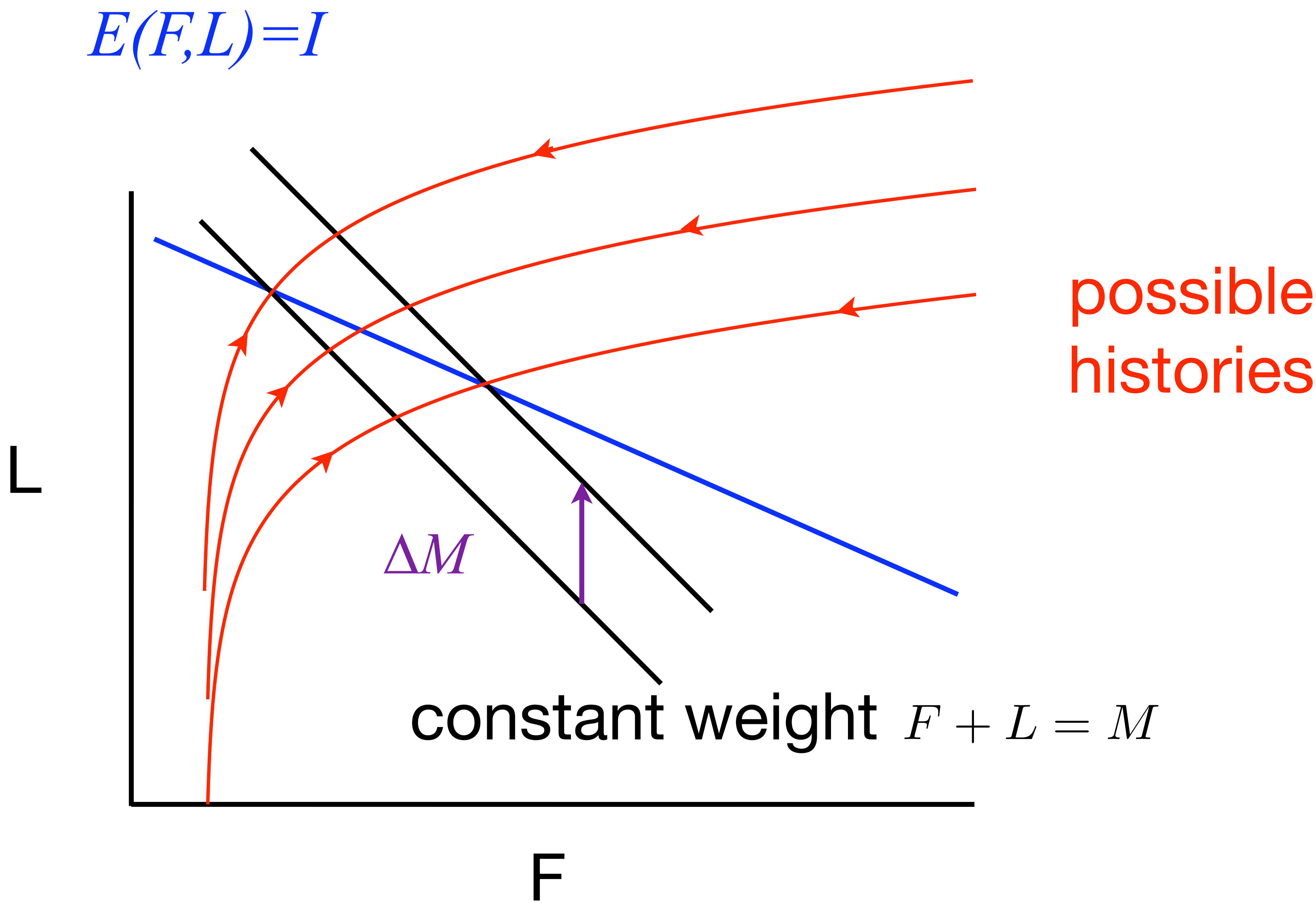
Consequences of line attractor



Consequences of line attractor



Consequences of line attractor



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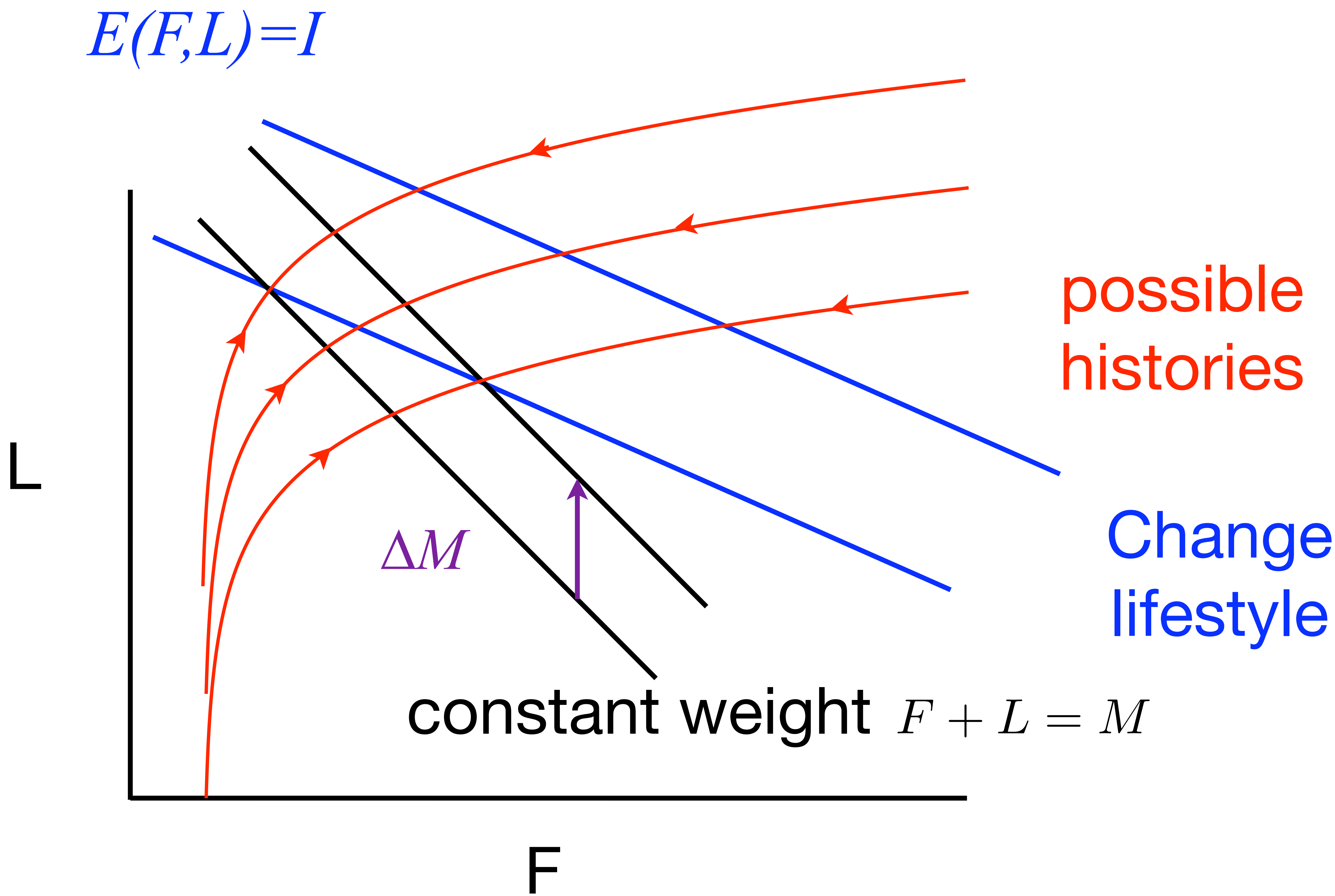
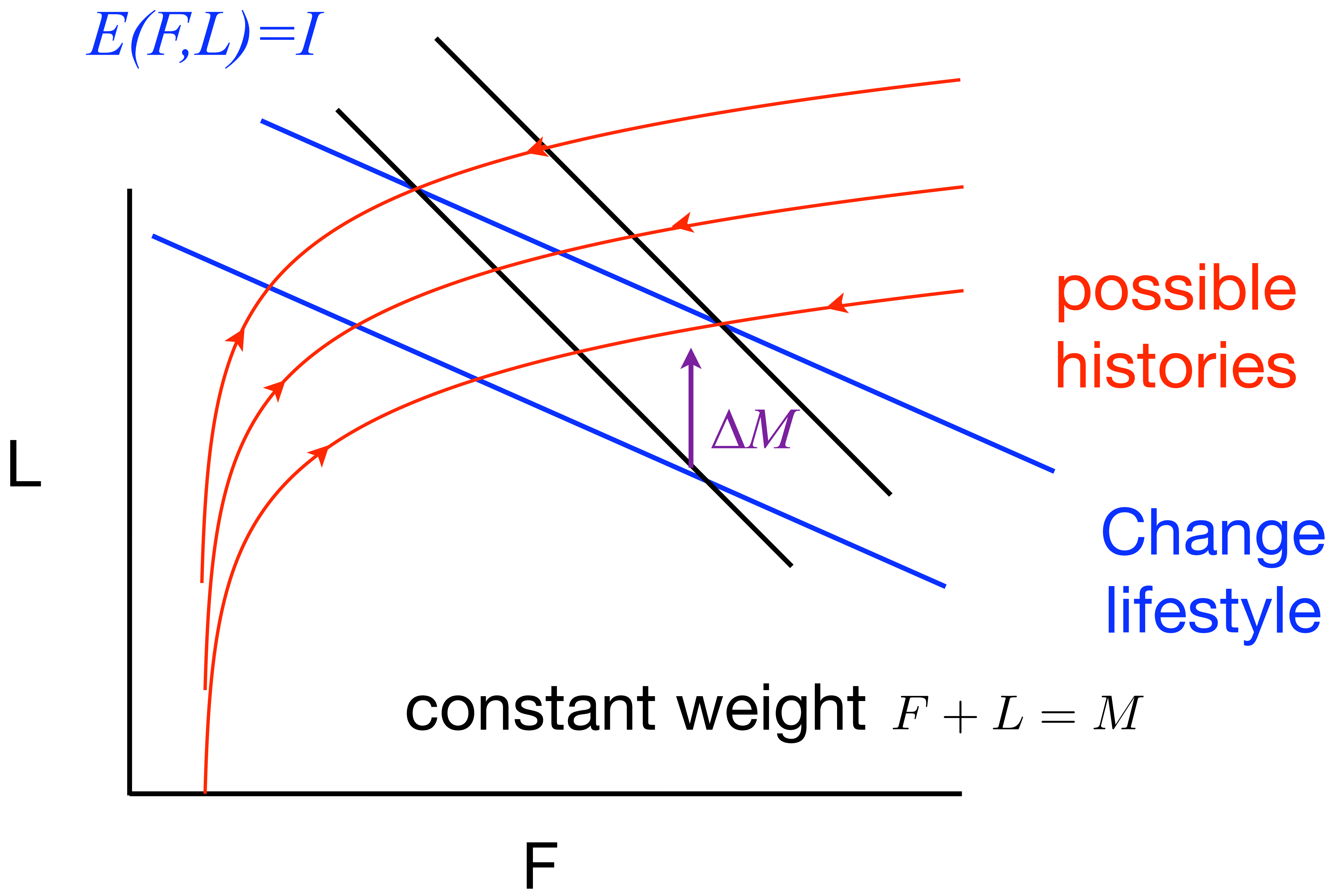
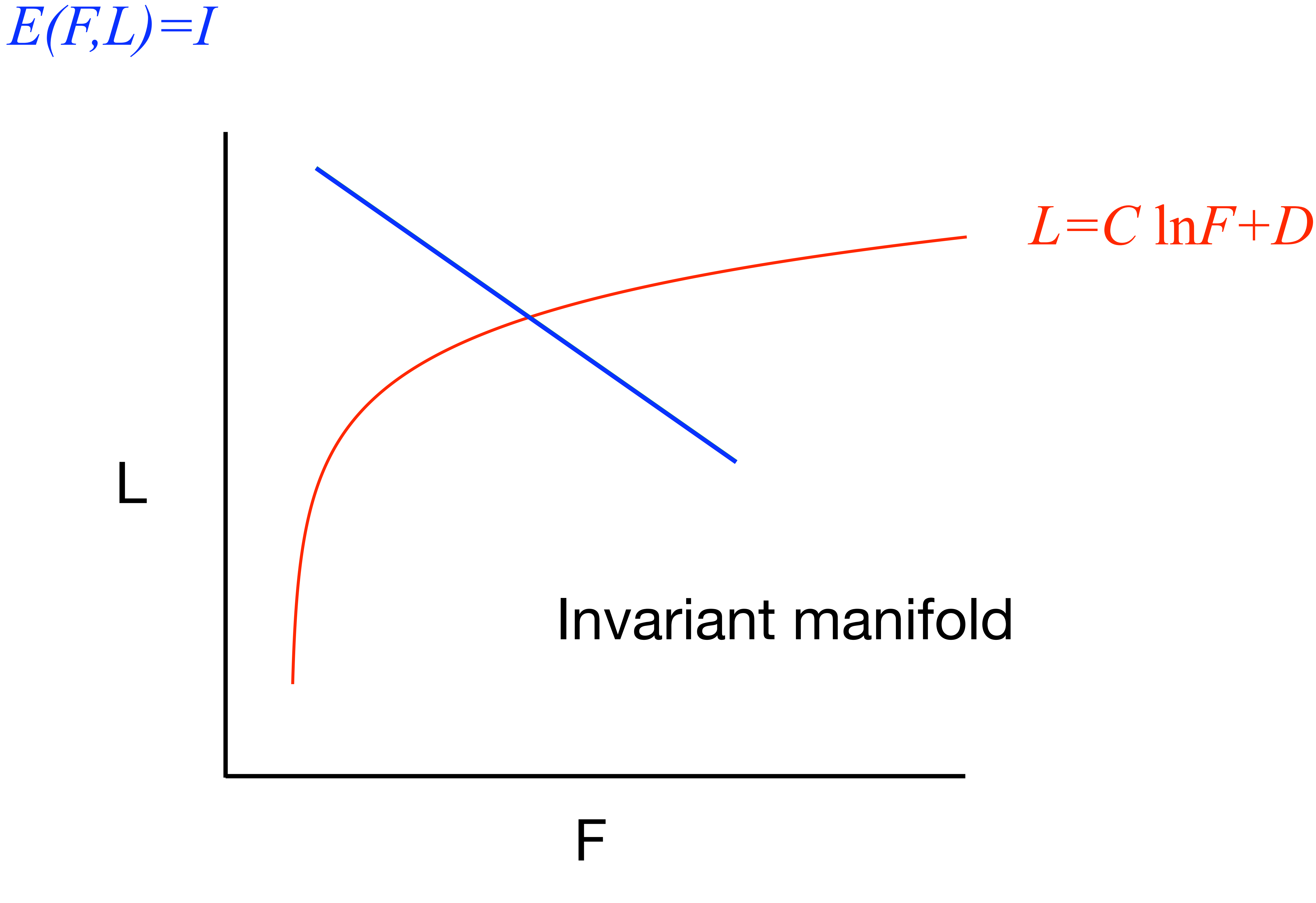
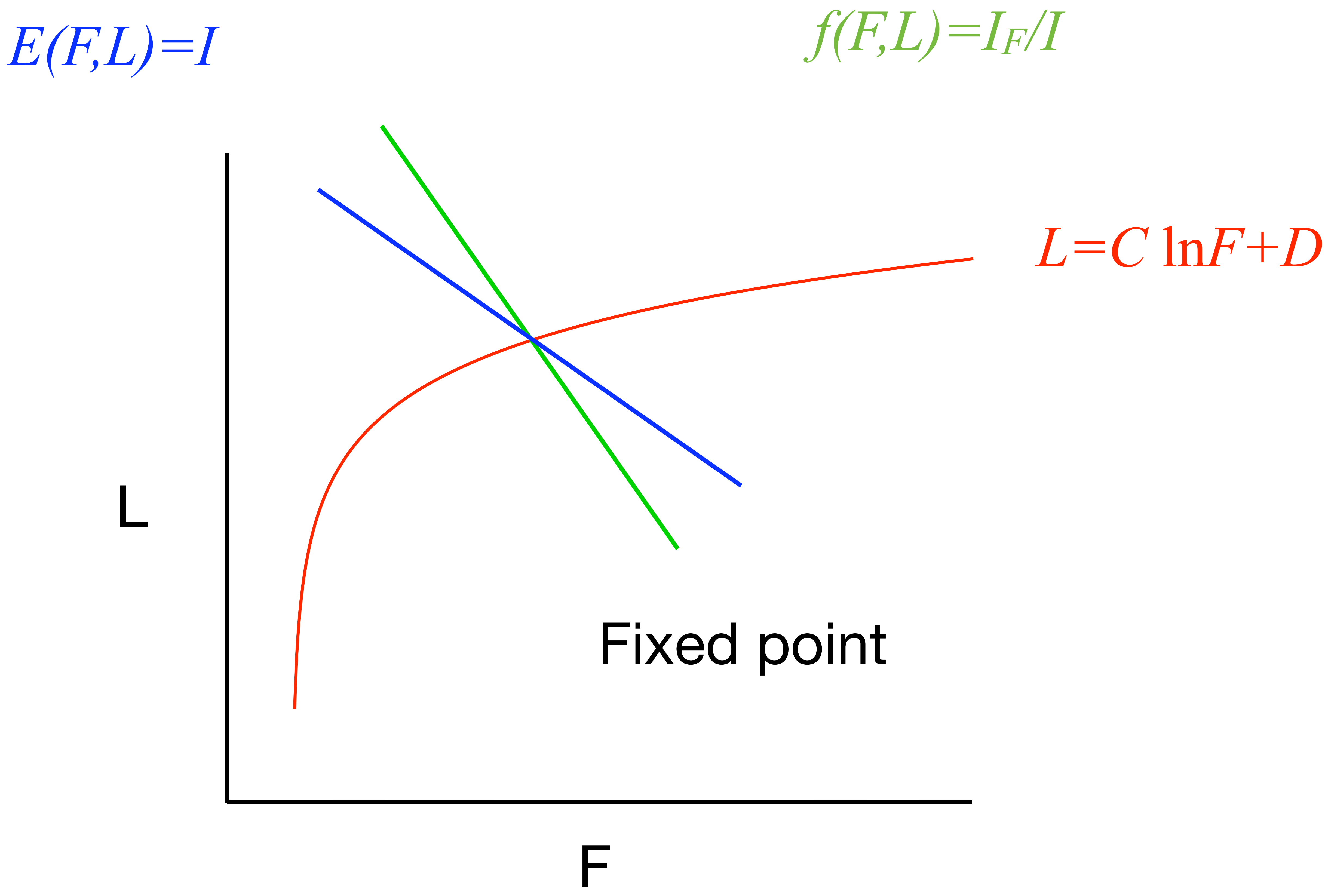


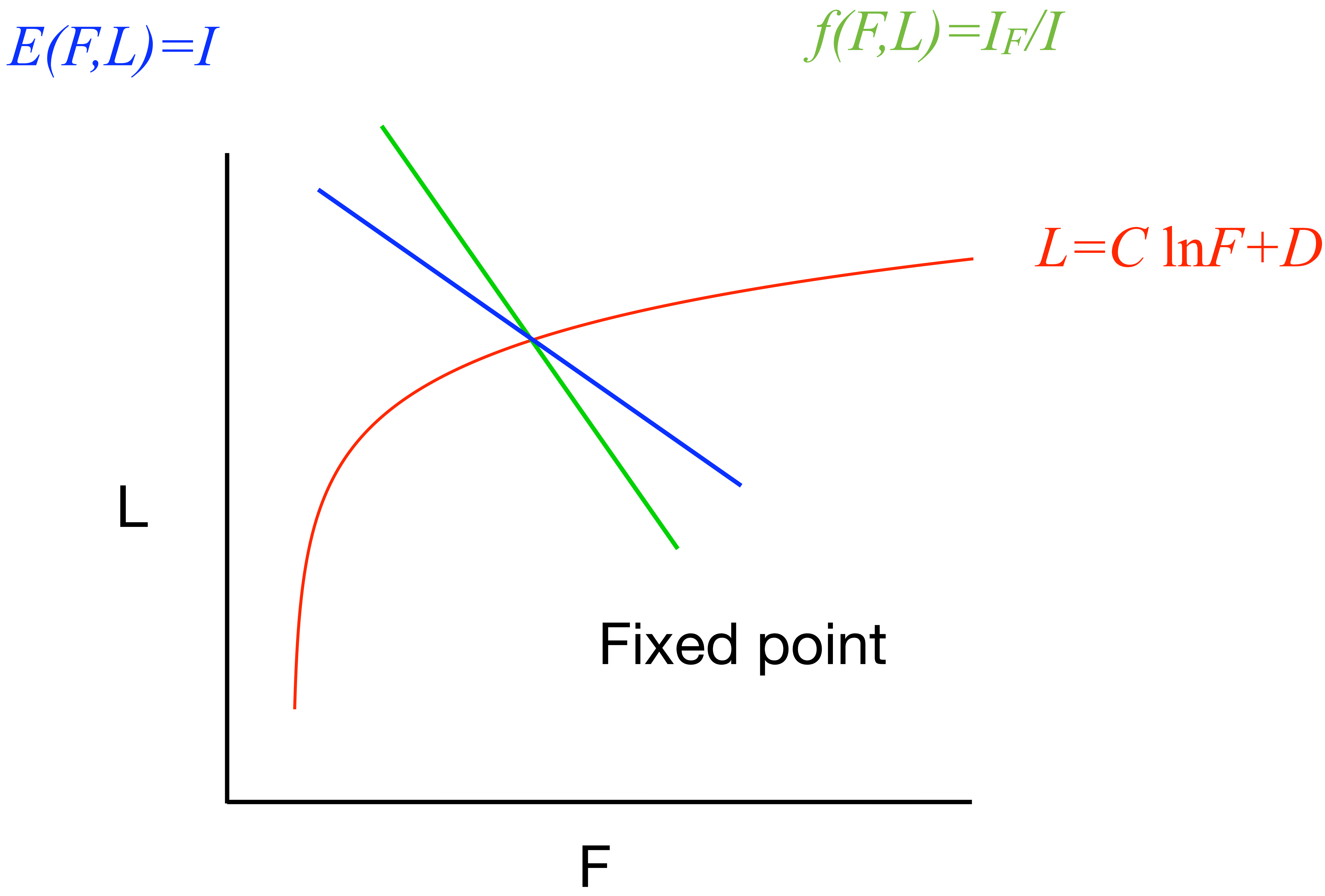
Consequences of line attractor




$E(F,L)=I$
$L=C\ln F+D$
L
Invariant manifold
F



E(F,L)=I
f(F,L)=I_F/I
L=C lnF+D
L
Fixed point
F



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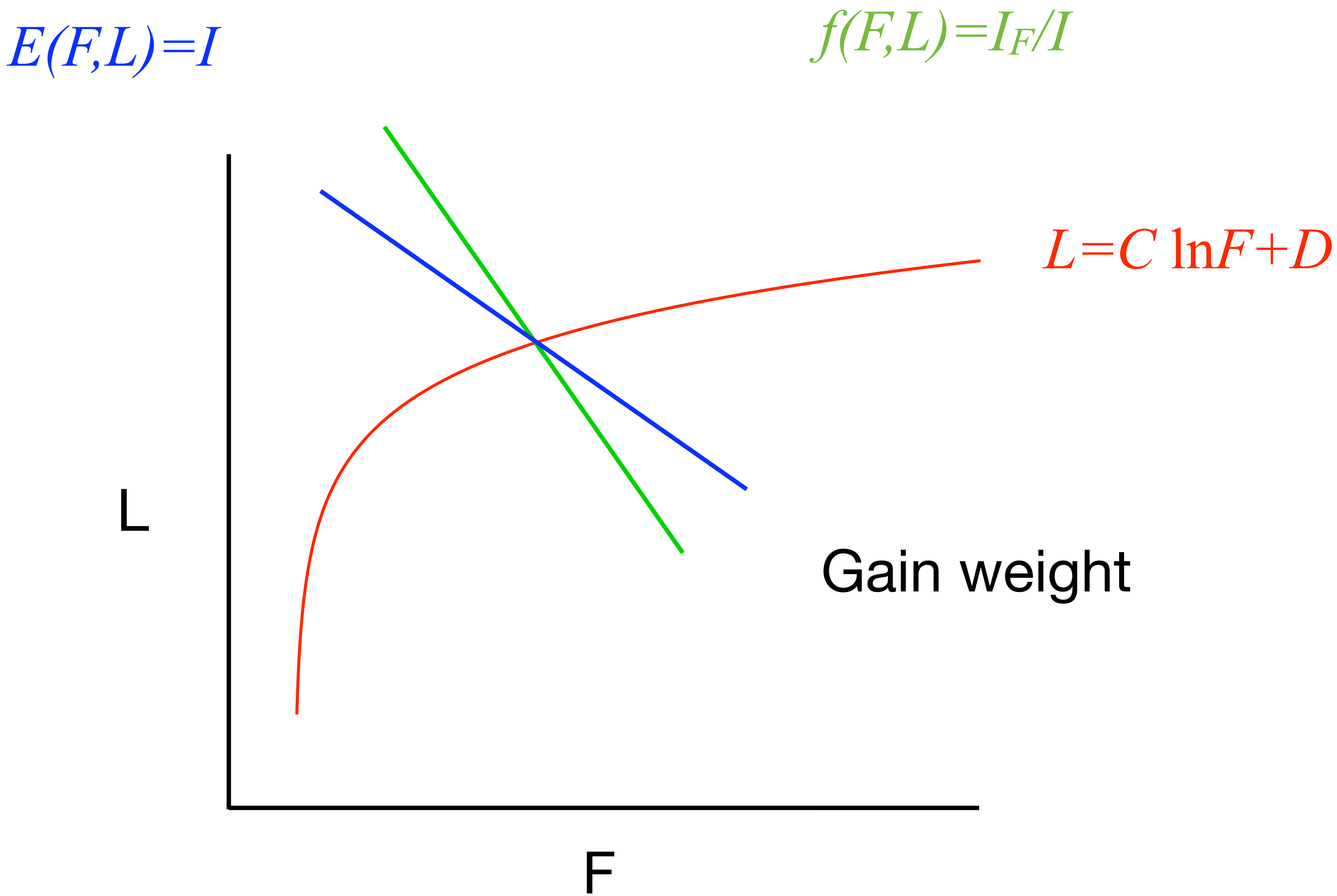
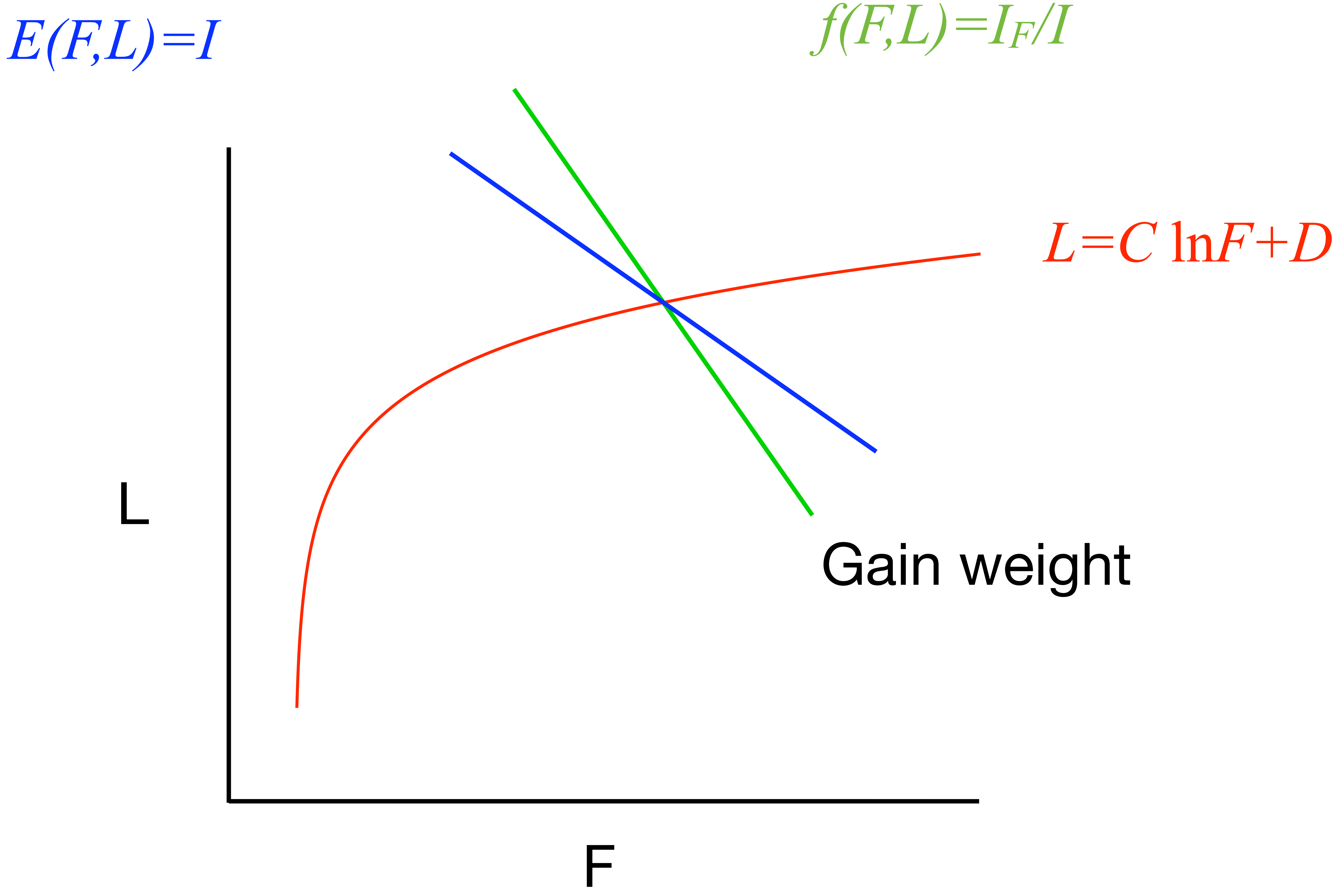
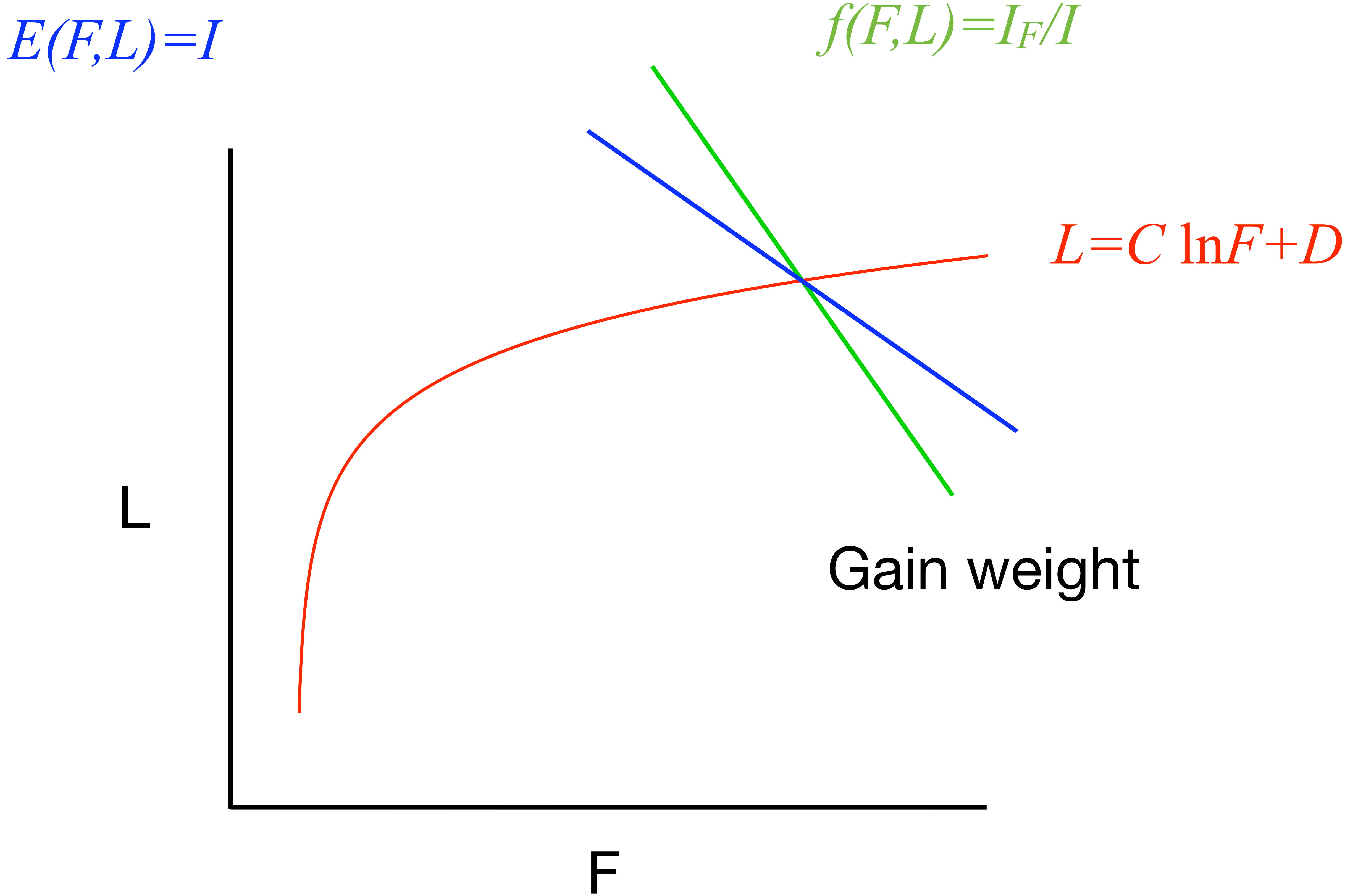
L
F
Fixed point

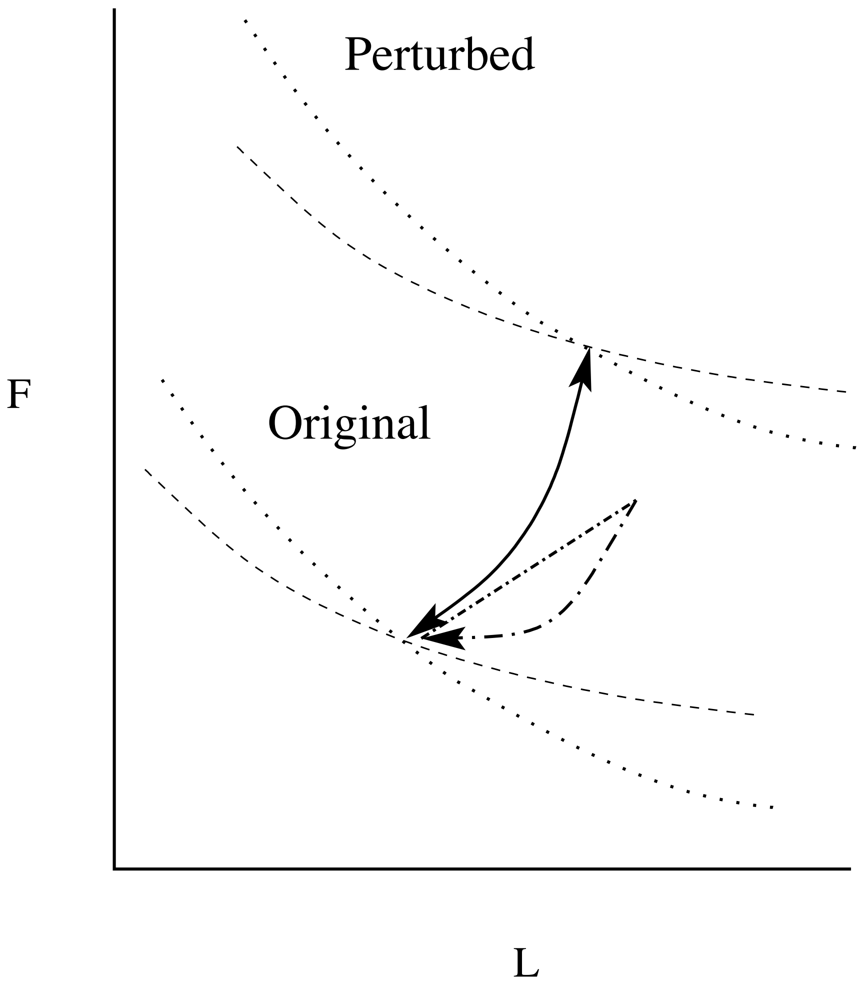


$E(F,L)=I$
$f(F,L)=I_F/I$
$L=C\ \ln F+D$
L
F
Gain weight

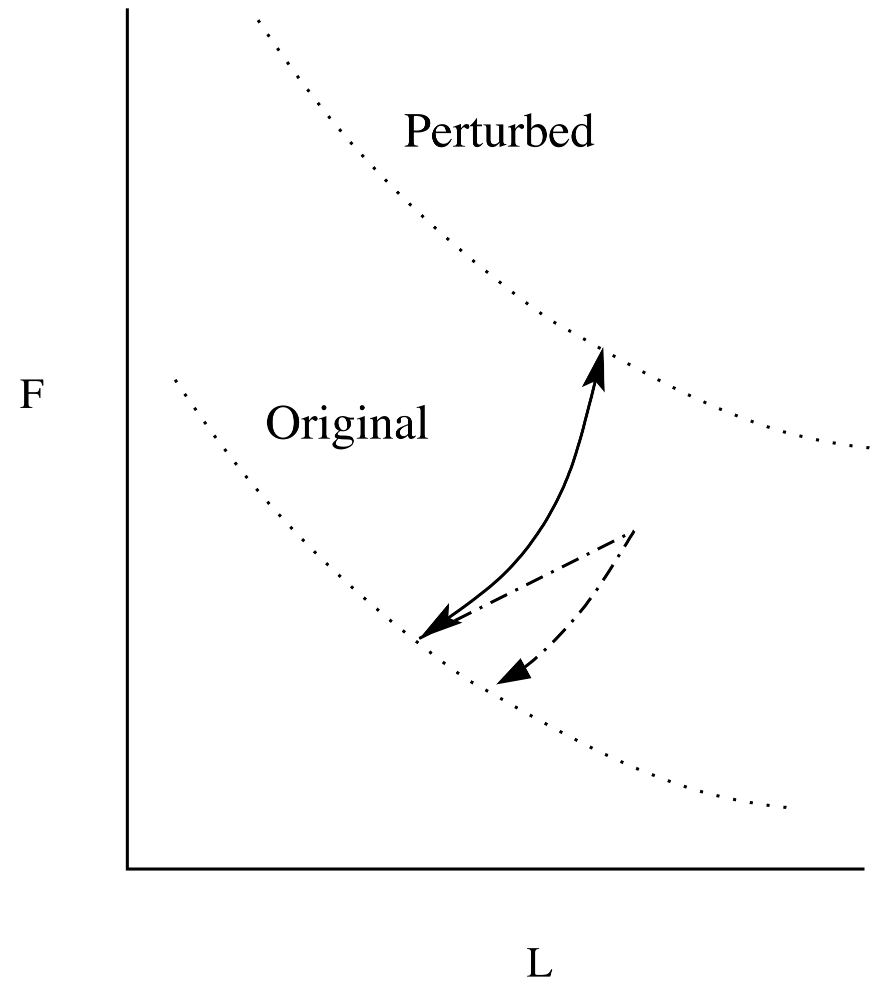

$E(F,L)=I$
$f(F,L)=I_F/I$
$L=C\ \ln F+D$
L
Gain weight
F


$E(F,L)=I$
$f(F,L)=I_F/I$
$L=C \ln F+D$
L
Gain weight
F

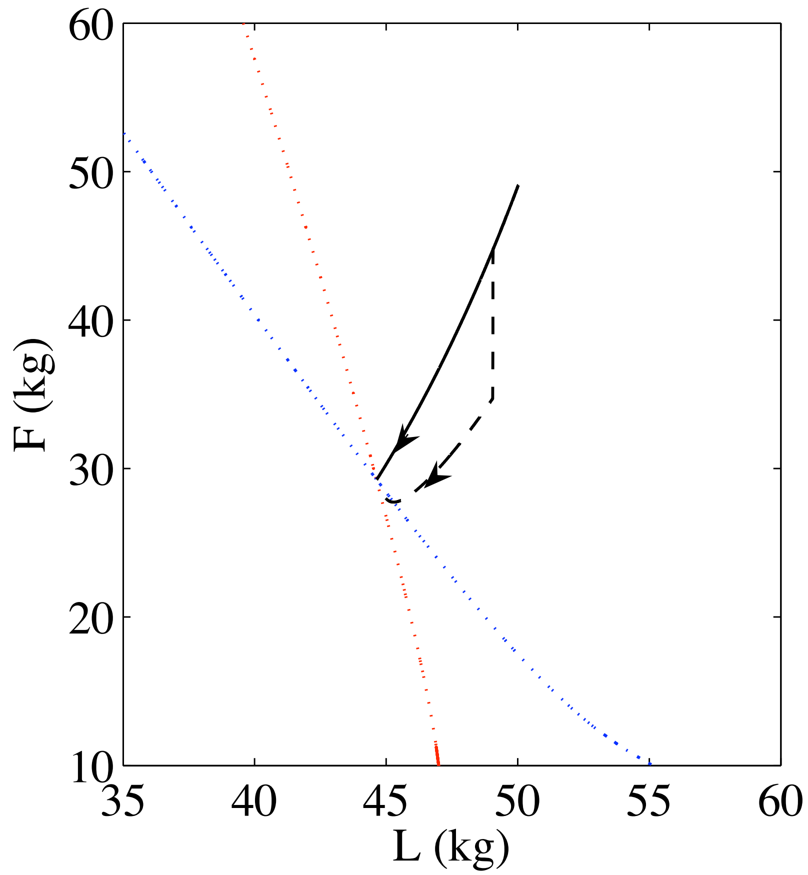
Effect of perturbations



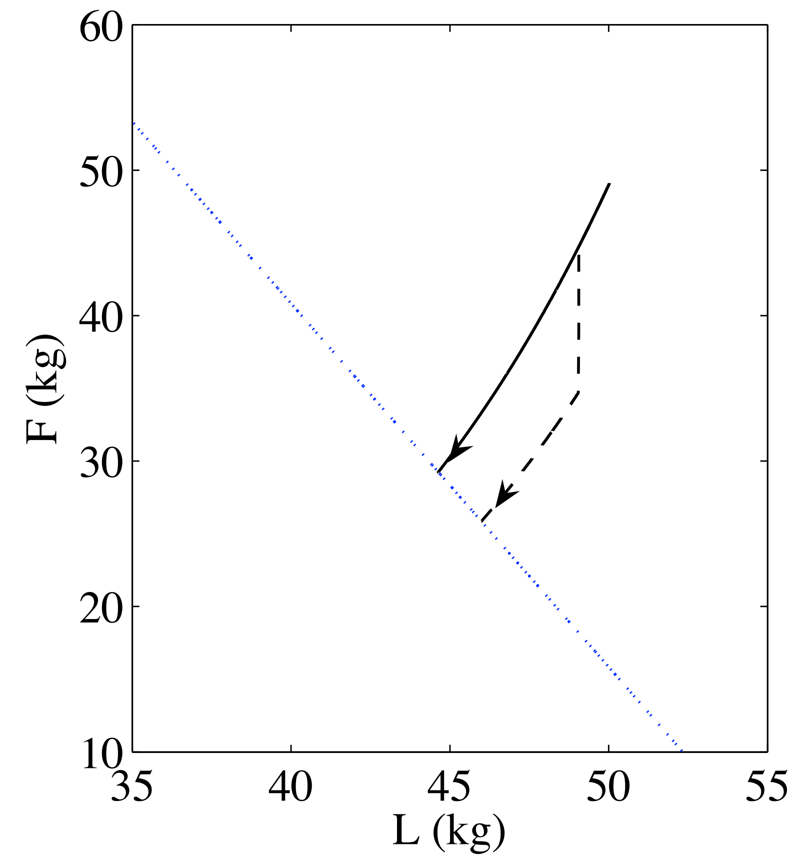
fixed point



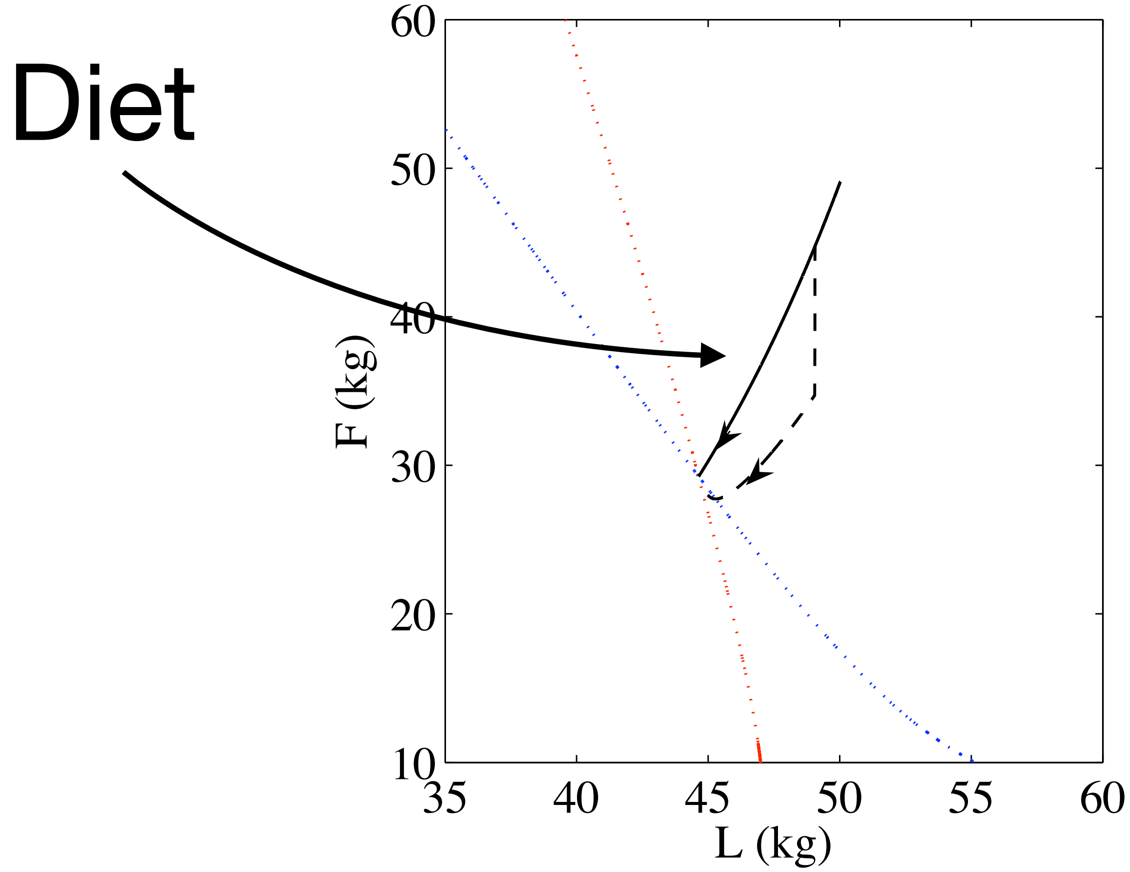
line attractor



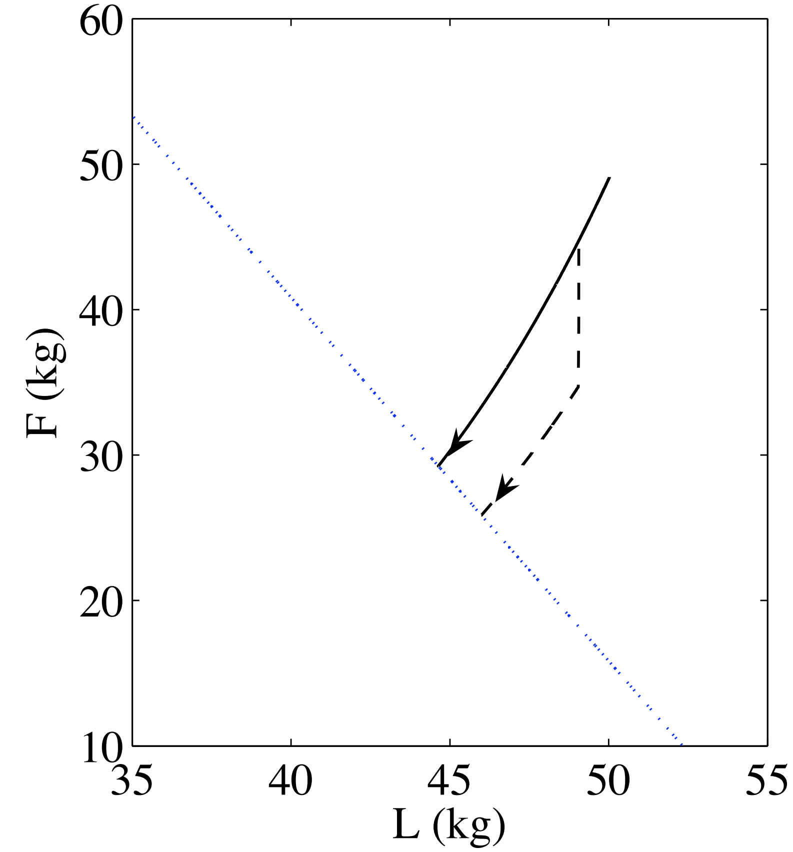
fixed point



line attractor



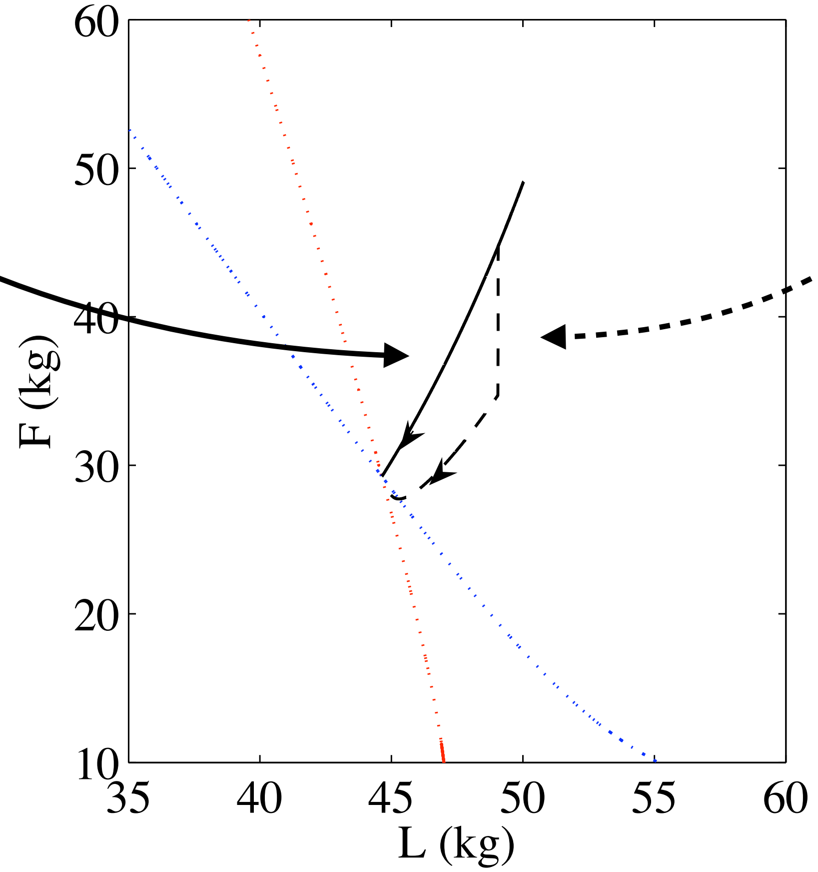
fixed point

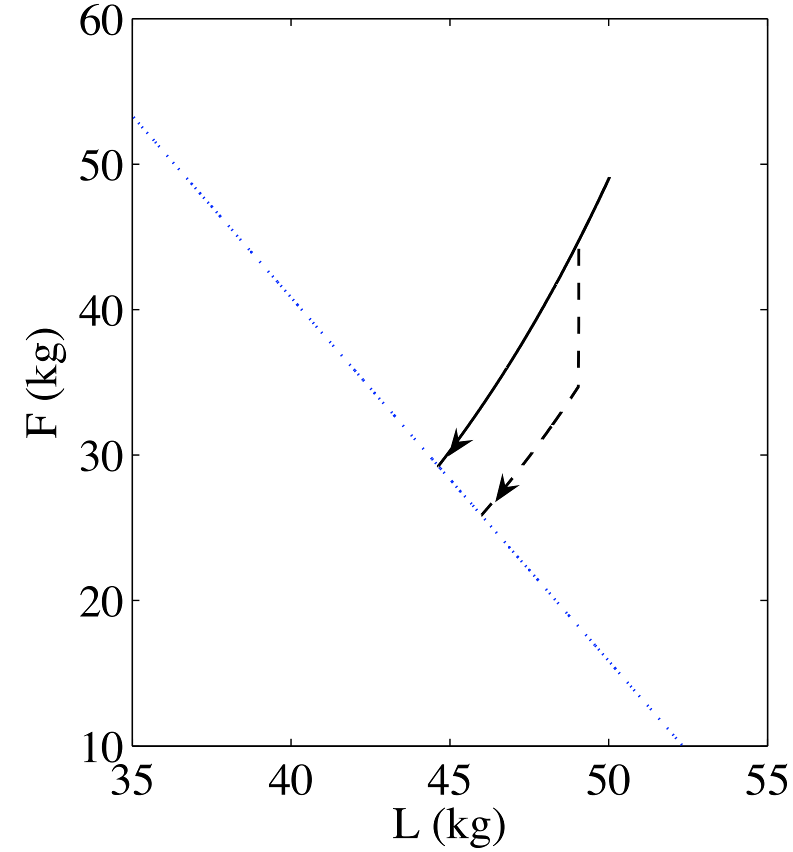


line attractor

Remove fat

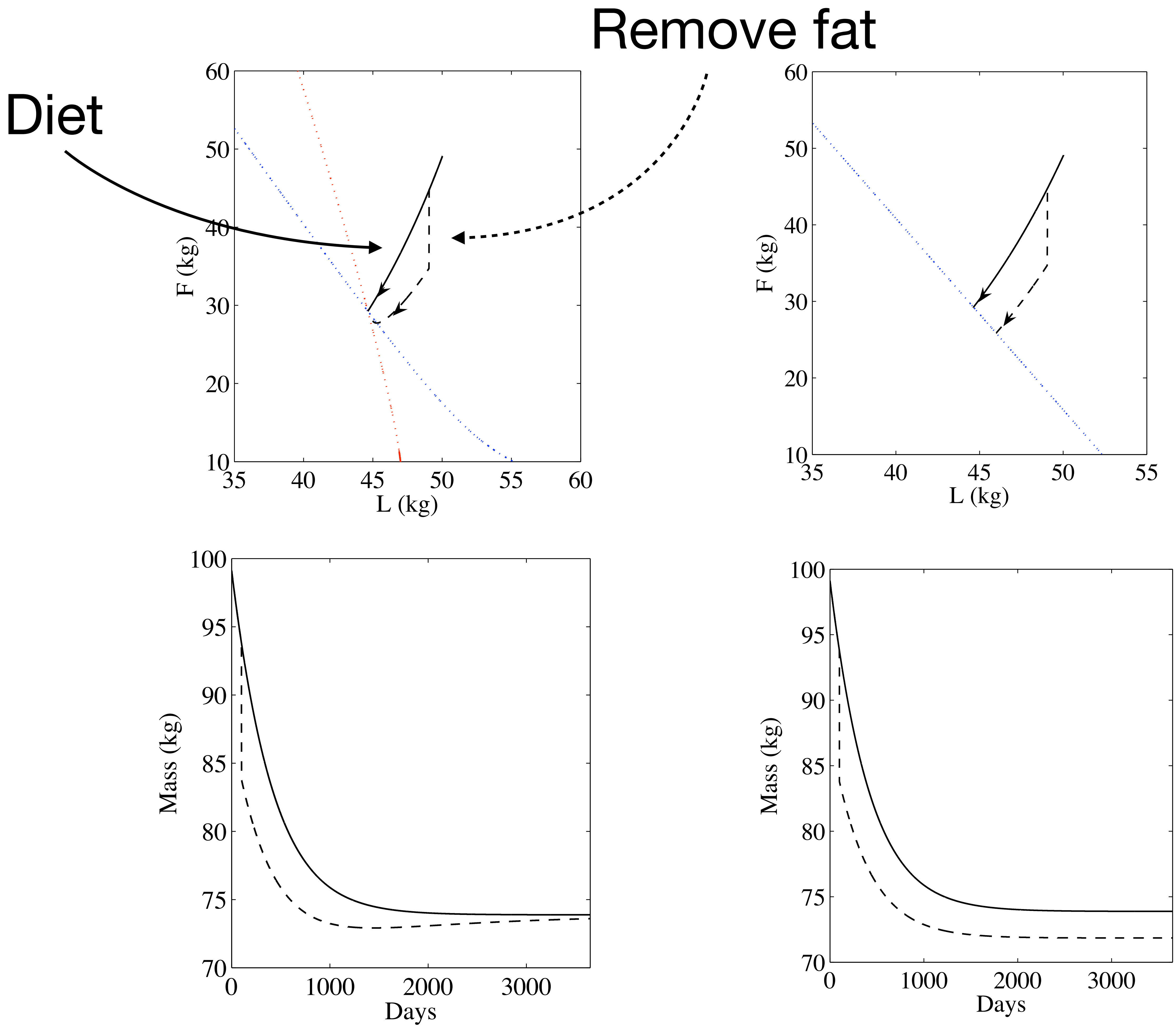
Diet





fixed point

line attractor



Remove fat
Diet
F (kg)
L (kg)
Mass (kg)
Days

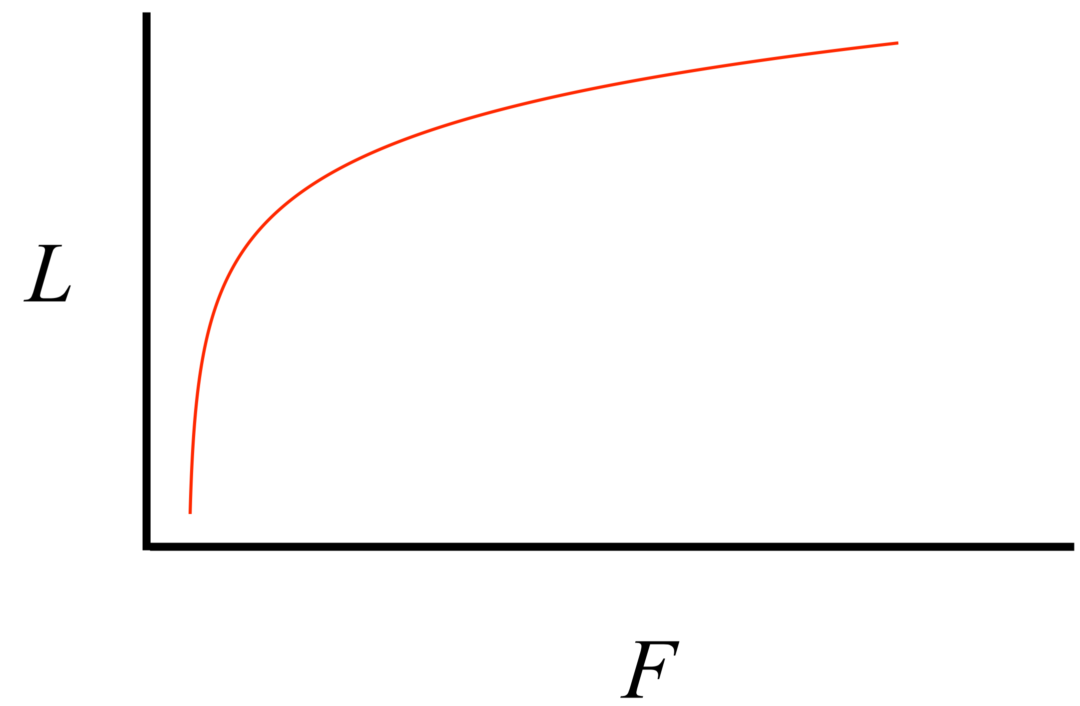
THE BIGGEST LOSER

Living on the Forbes curve

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

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

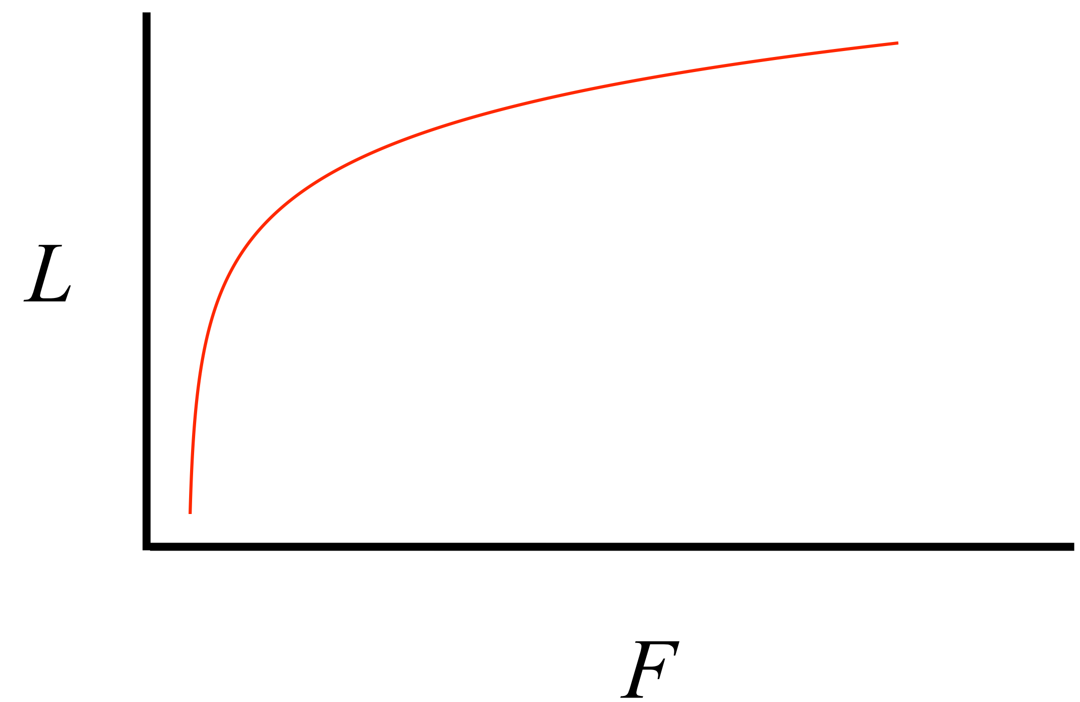
$$L = 10.4 \ln F + D$$



Living on the Forbes curve

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

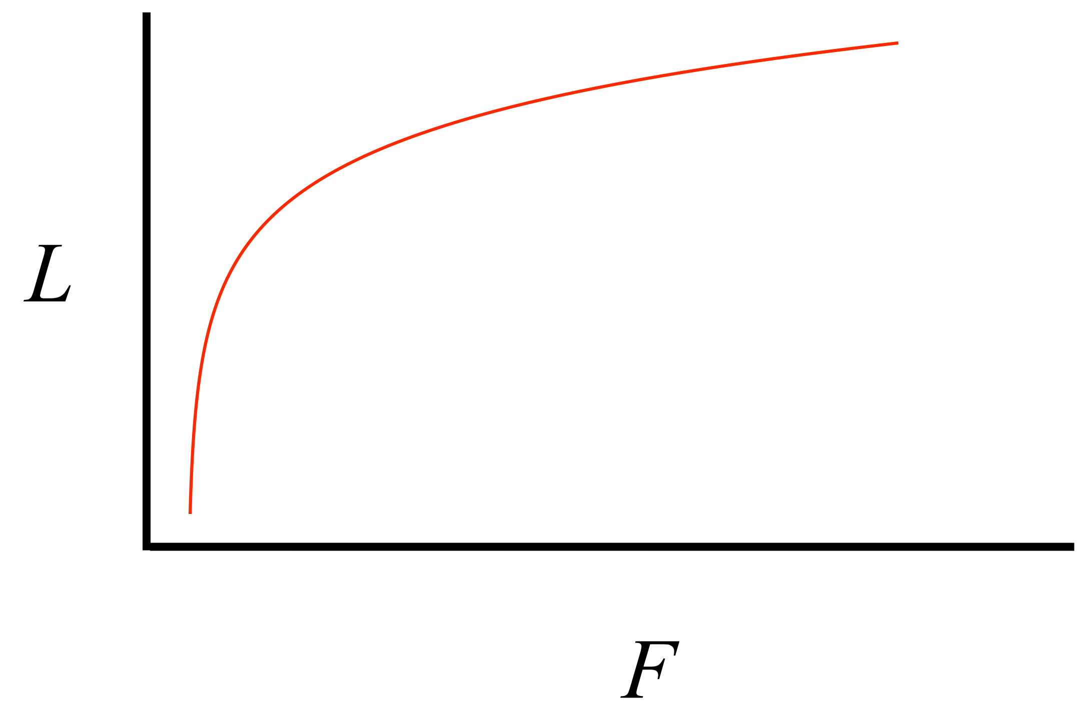
$$L = 10.4 \ln F + D$$



Living on the Forbes curve

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E(F, L)$$

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



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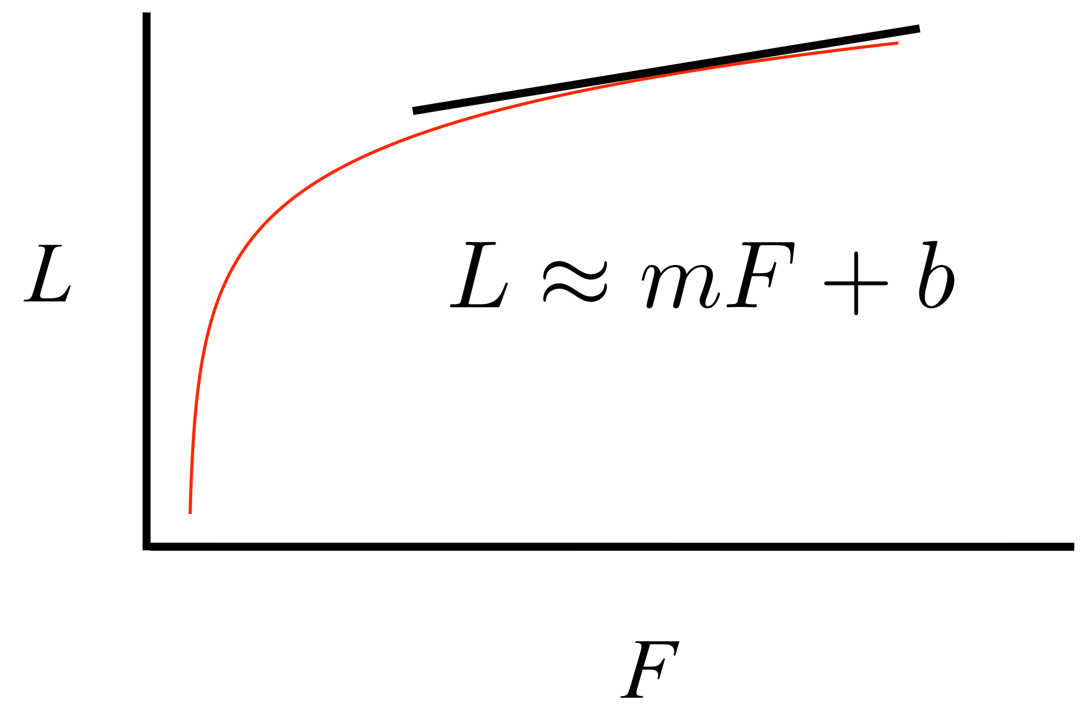
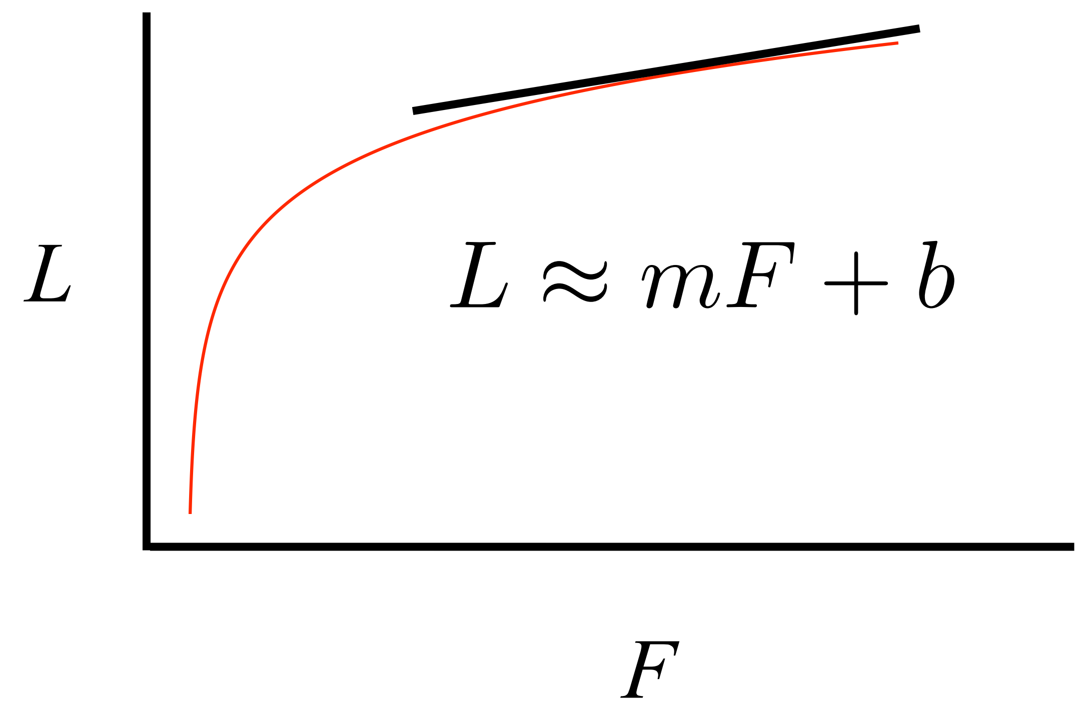


Living on the Forbes curve

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E(F, L)$$

$$F = M - L$$

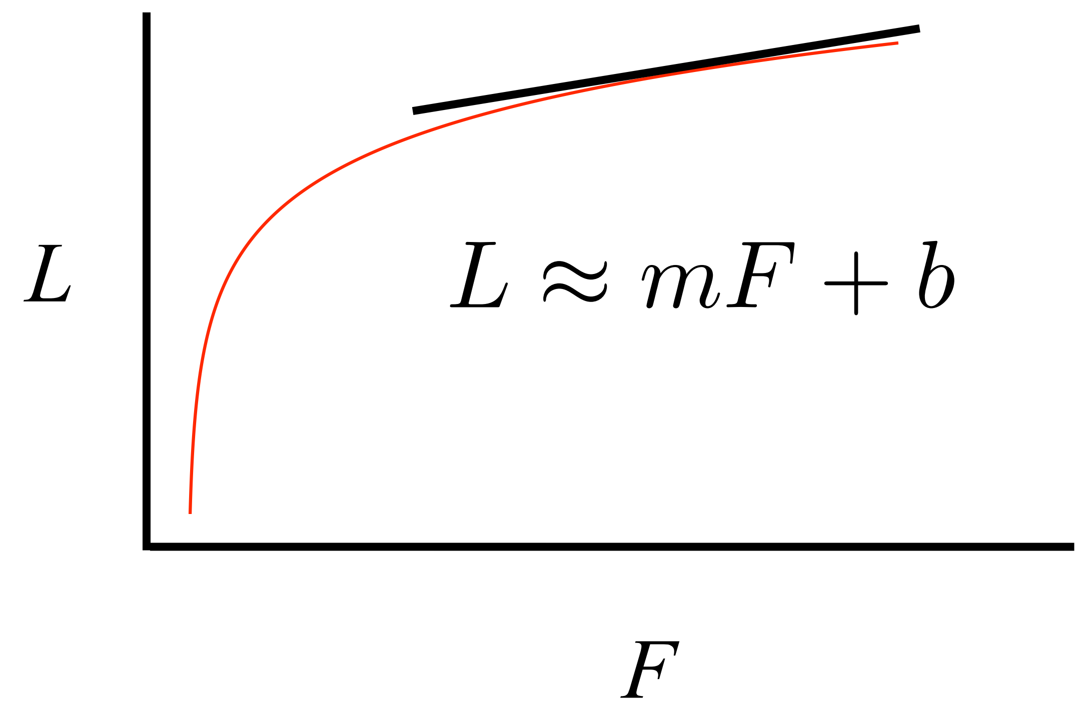
$$L = 10.4 \ln F + D$$



Living on the Forbes curve

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

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E(F, L)$$



$$F = M - L$$

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

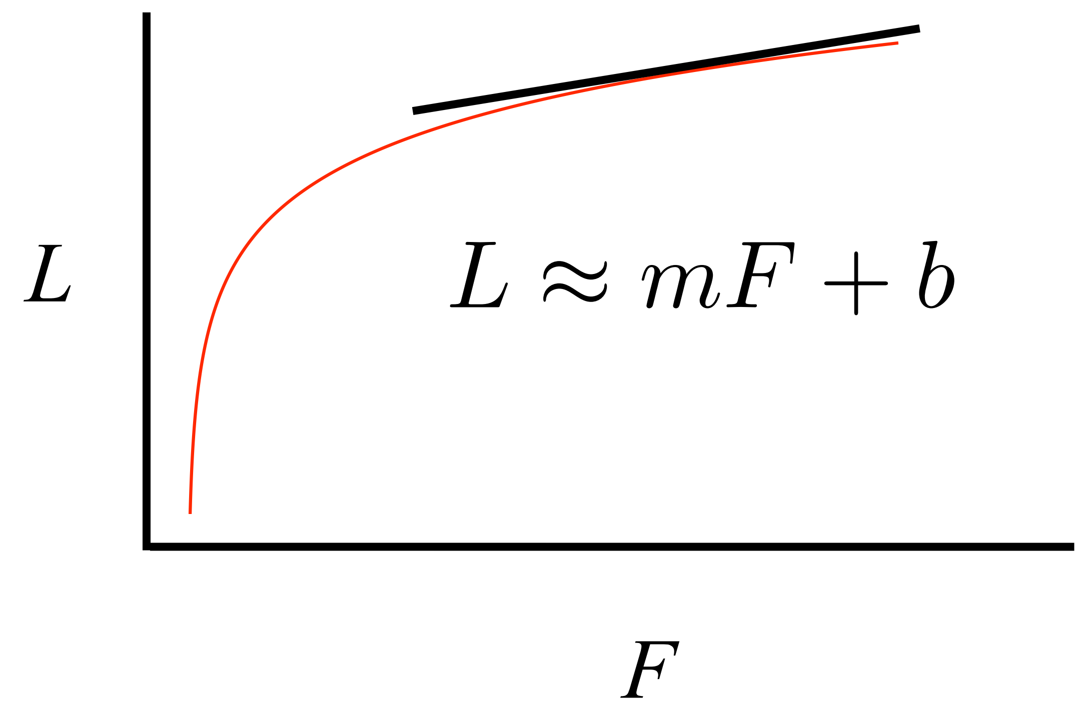
Living on the Forbes curve

$$\rho_L \frac{dL}{dt} + \rho_F \frac{dF}{dt} = I - E(F, L)$$

$$F = M - L$$

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

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



One dimensional model

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

One dimensional model

$$\rho = \rho(F) \qquad \rho'(F) > 0$$

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

One dimensional model

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

$$\rho = \rho(F) \qquad \rho'(F) > 0$$

$$\epsilon = \epsilon(F) \qquad \epsilon'(F) < 0$$

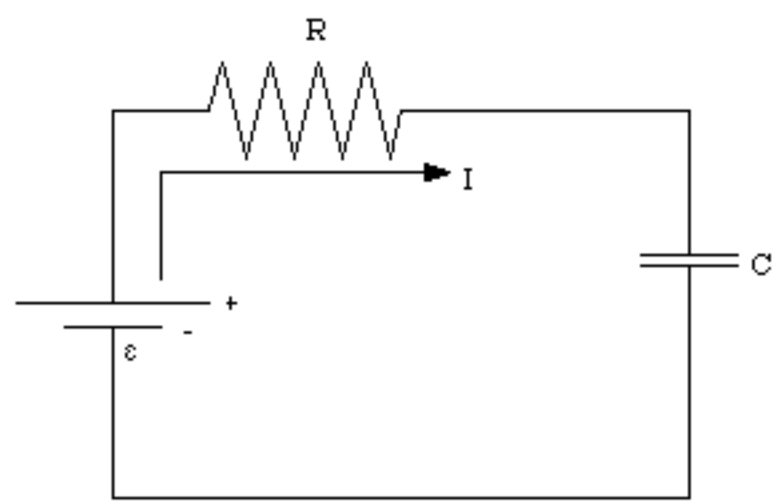
One dimensional model

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

$$\rho = \rho(F) \qquad \rho'(F) > 0$$

$$\epsilon = \epsilon(F) \qquad \epsilon'(F) < 0$$

Leaky integrator



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

Steady state

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

Steady state

$$\rho \frac{dM}{dt} = I - \epsilon M - b = 0 \qquad M = (I - b)/\epsilon$$

Steady state

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

$$M = (I - b)/\epsilon$$

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

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ε ~ 0.1 MJ/kg/day*

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ε ~ 0.1 MJ/kg/day*

1 cal = 4.2 J
kcal = Calorie

Steady state

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

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~ 22 kcal/kg/day

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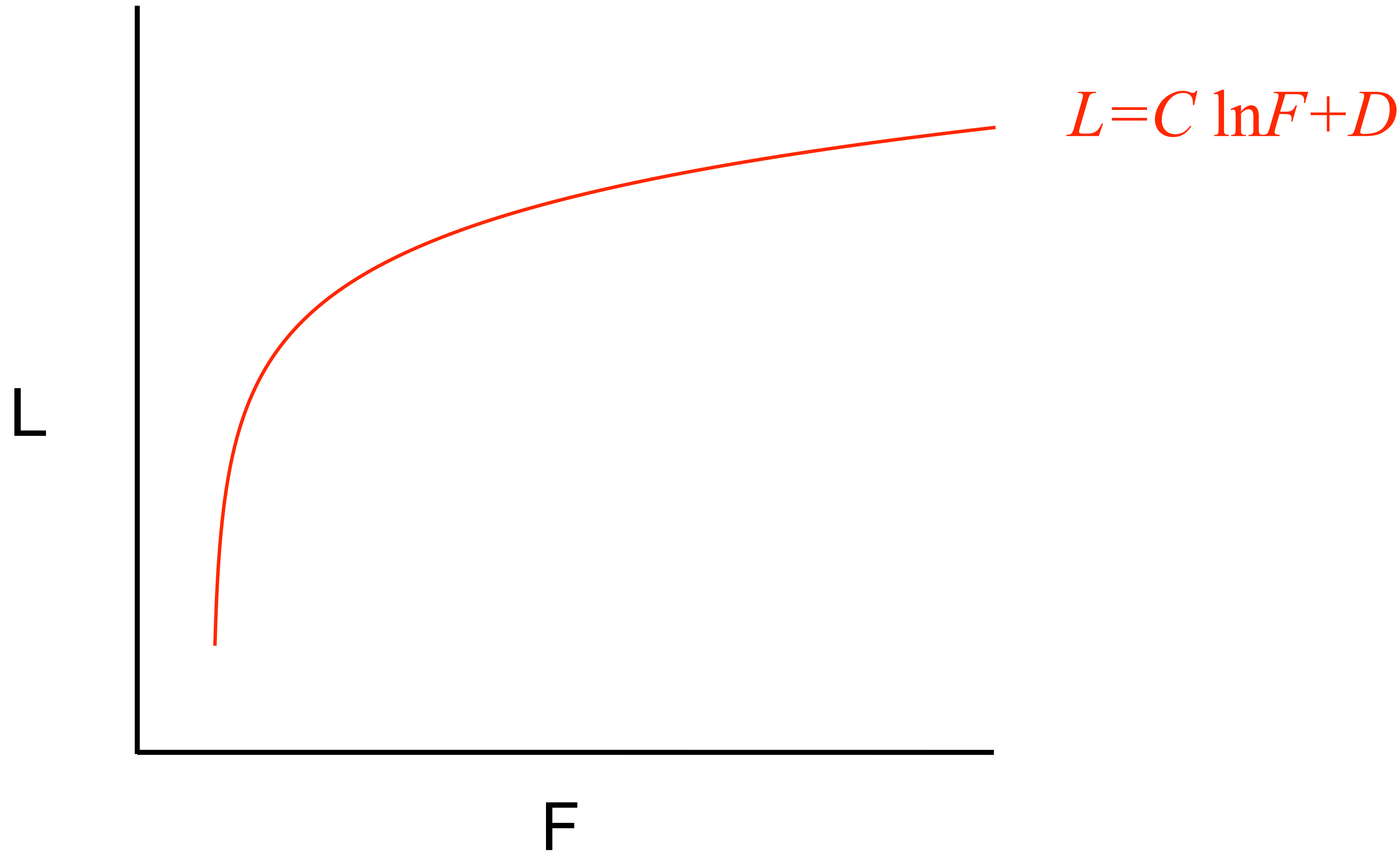
~ 22 kcal/kg/day

1 cal = 4.2 J kcal = Calorie

10 Calories a day = 1 pound

Weight gain increases with weight



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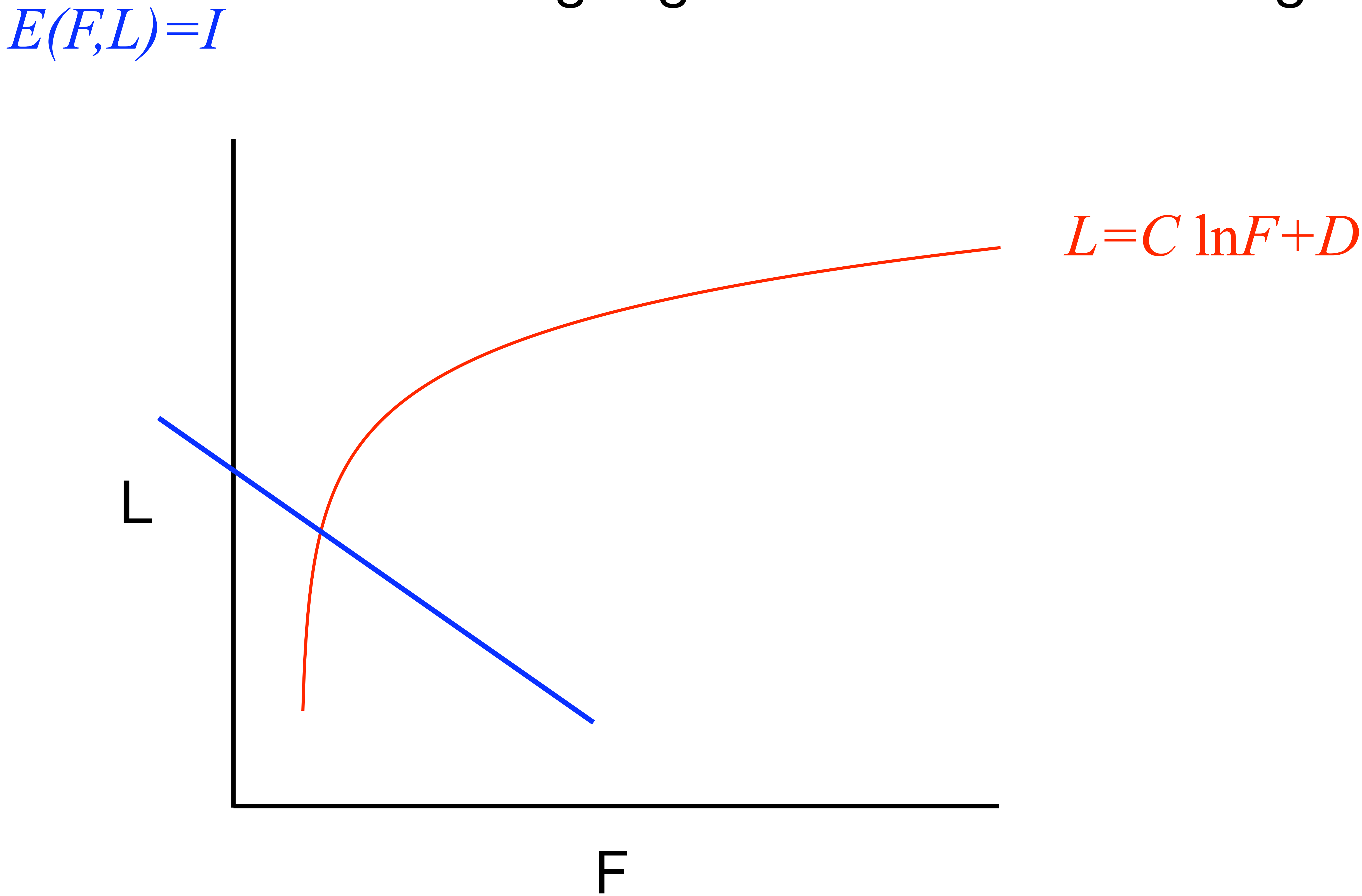
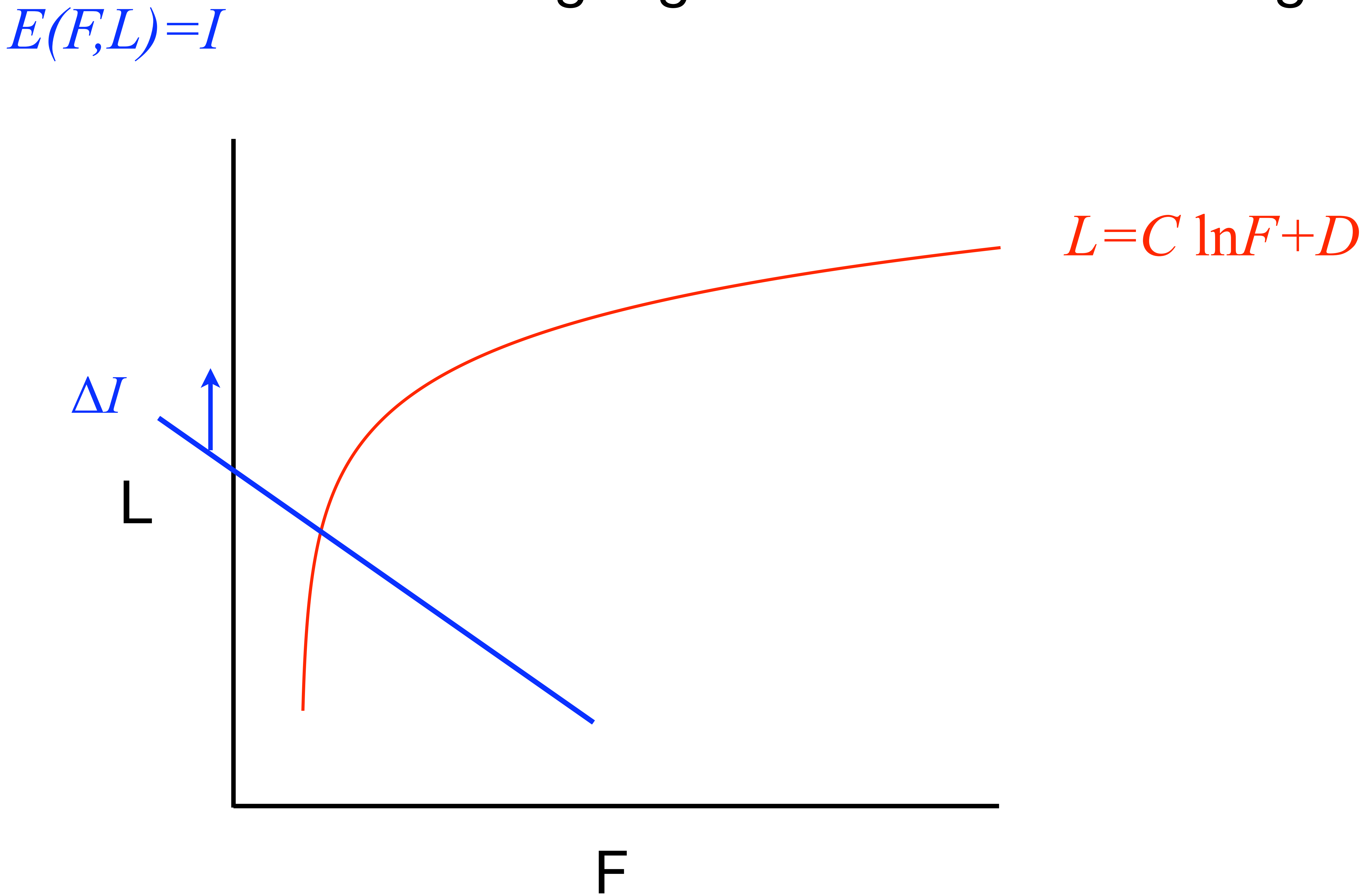
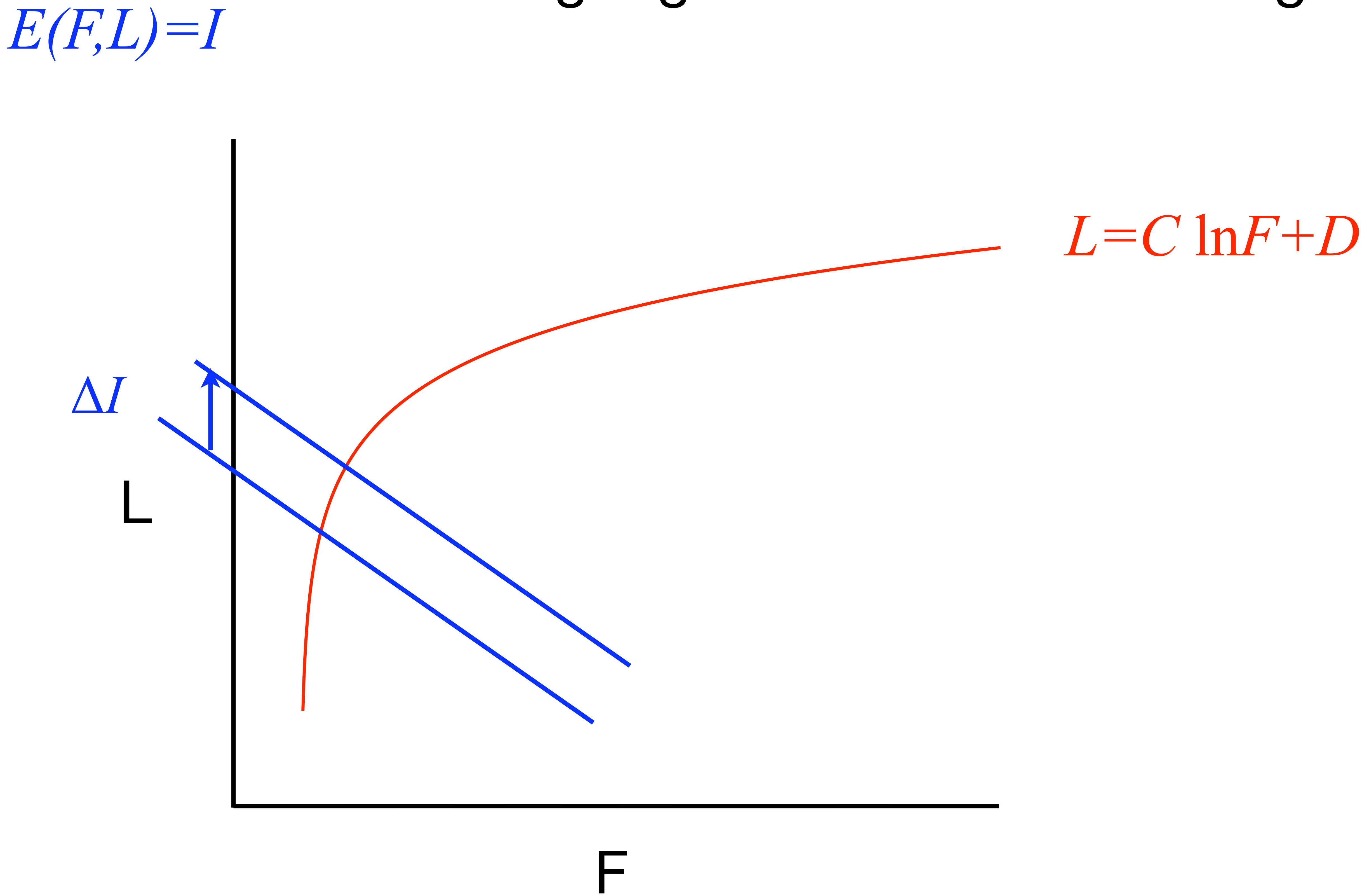


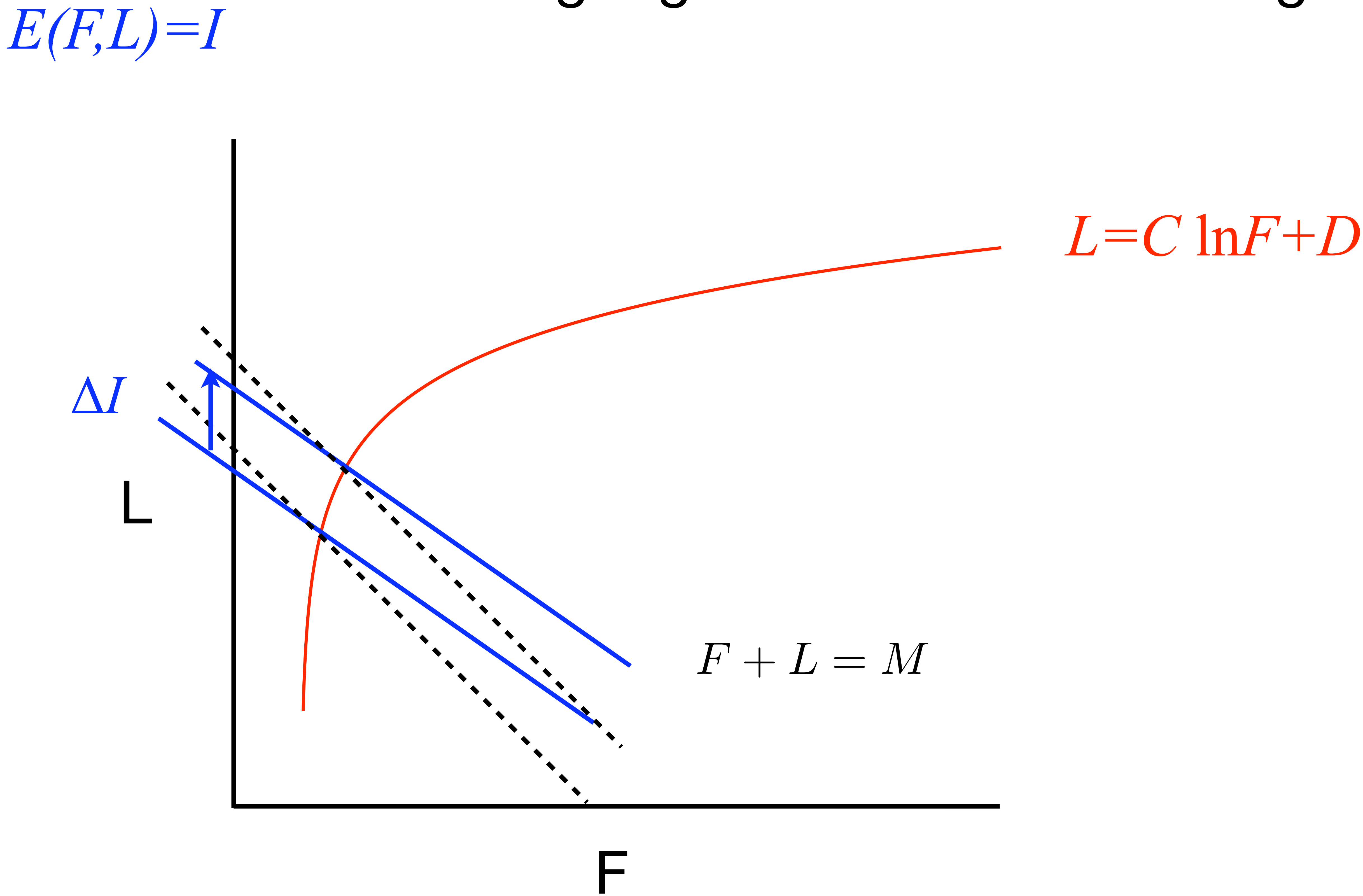
Weight gain increases with weight



Weight gain increases with weight

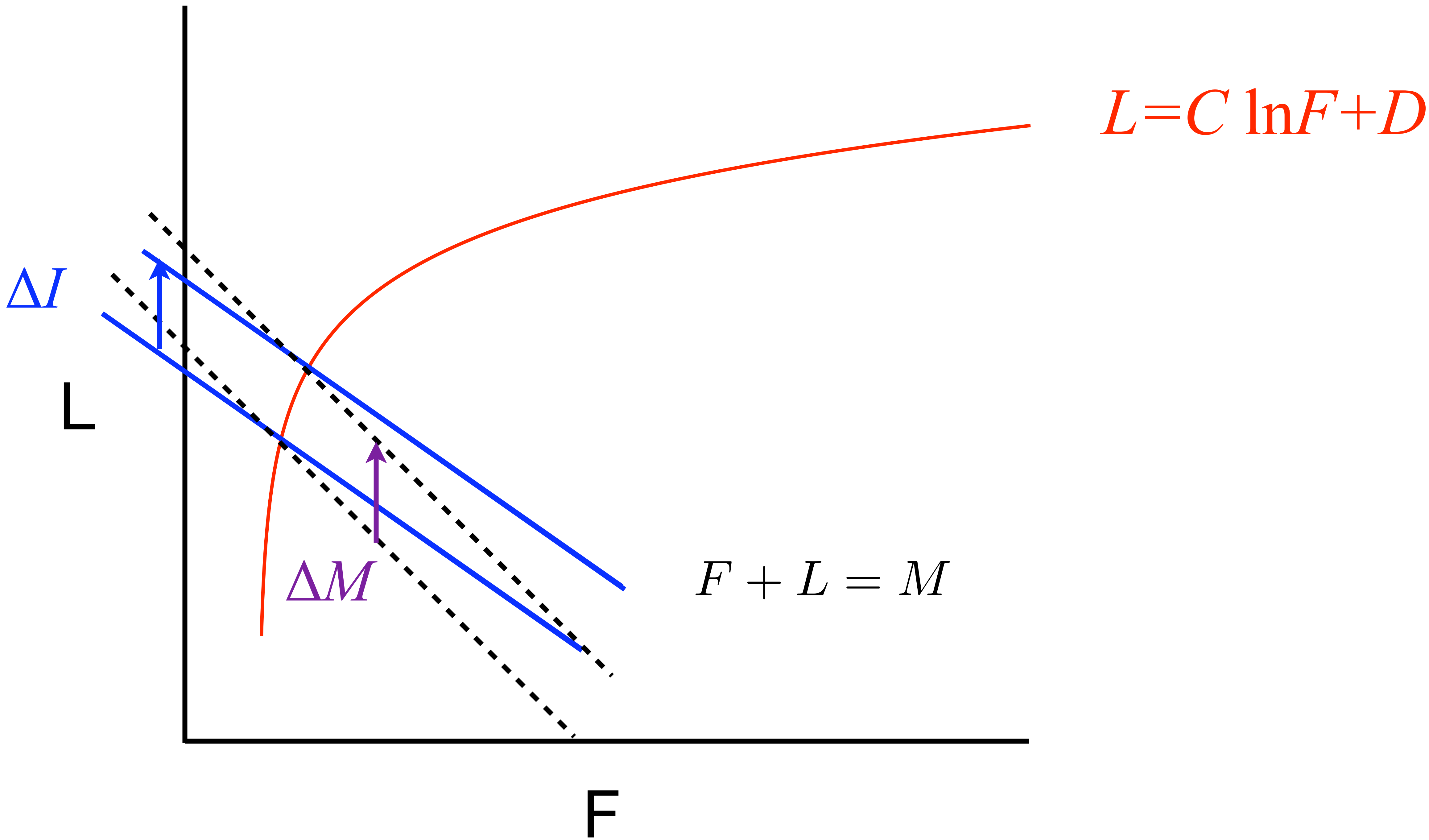


Weight gain increases with weight

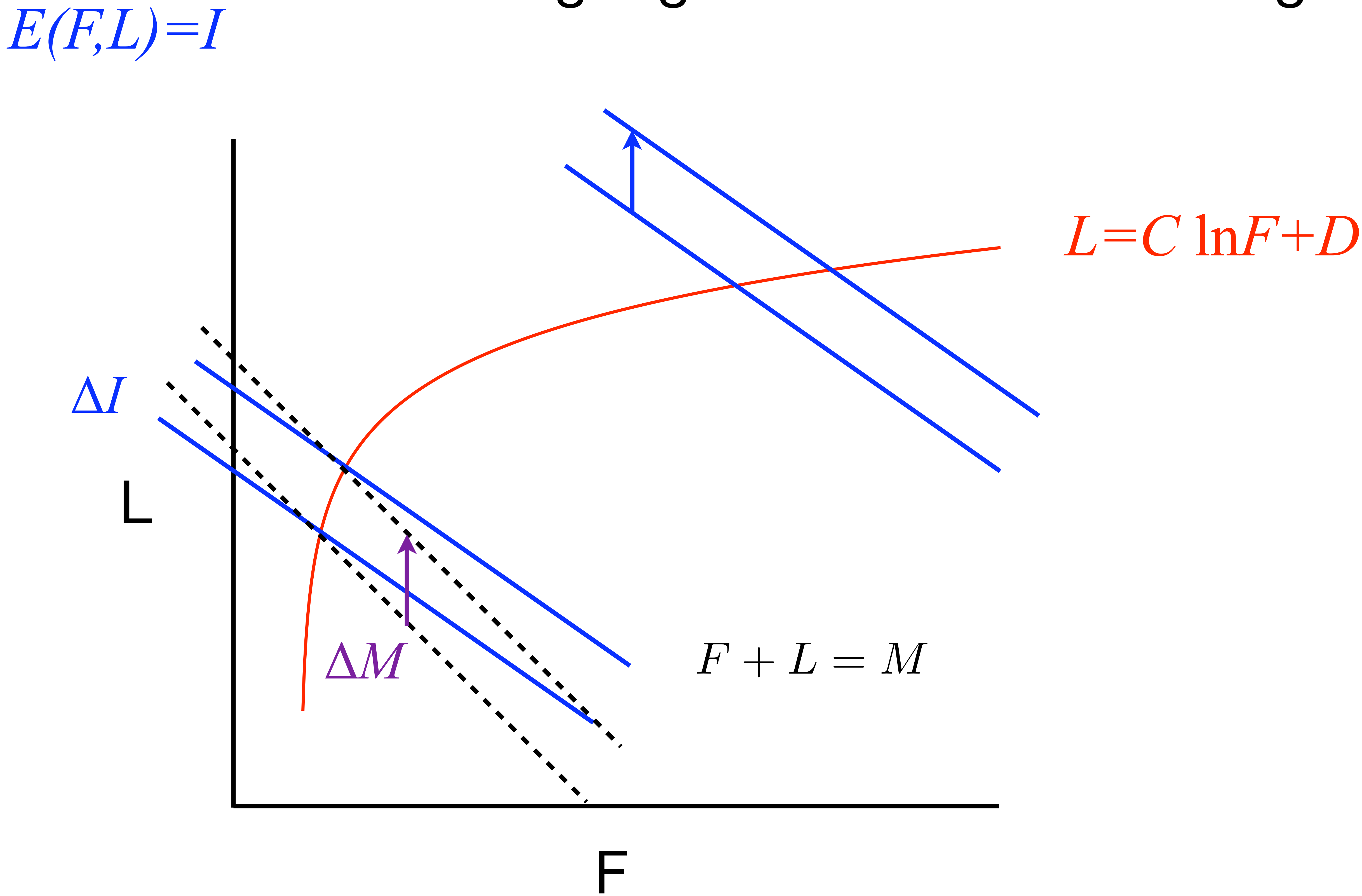


Weight gain increases with weight

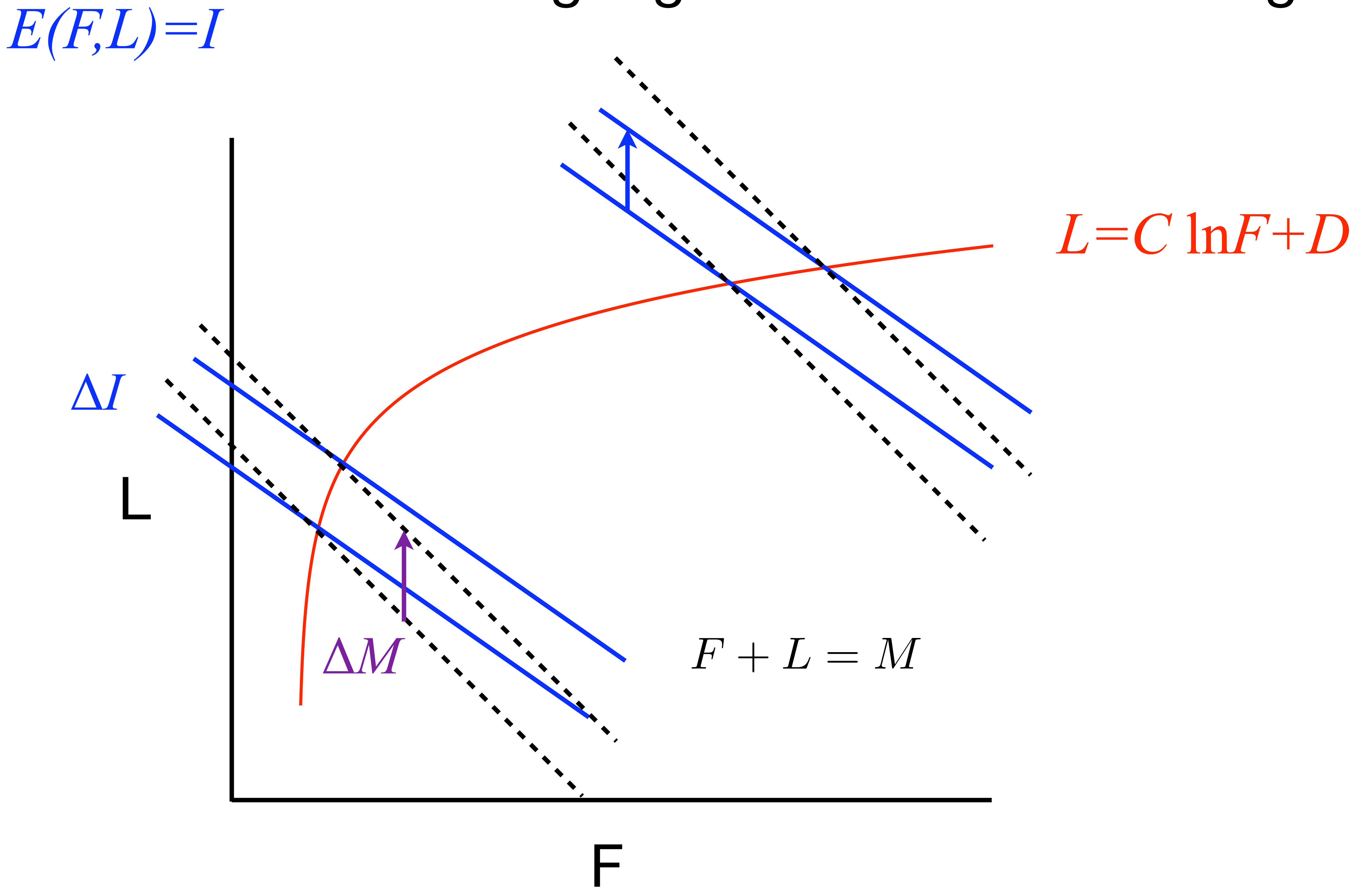
$E(F,L)=I$



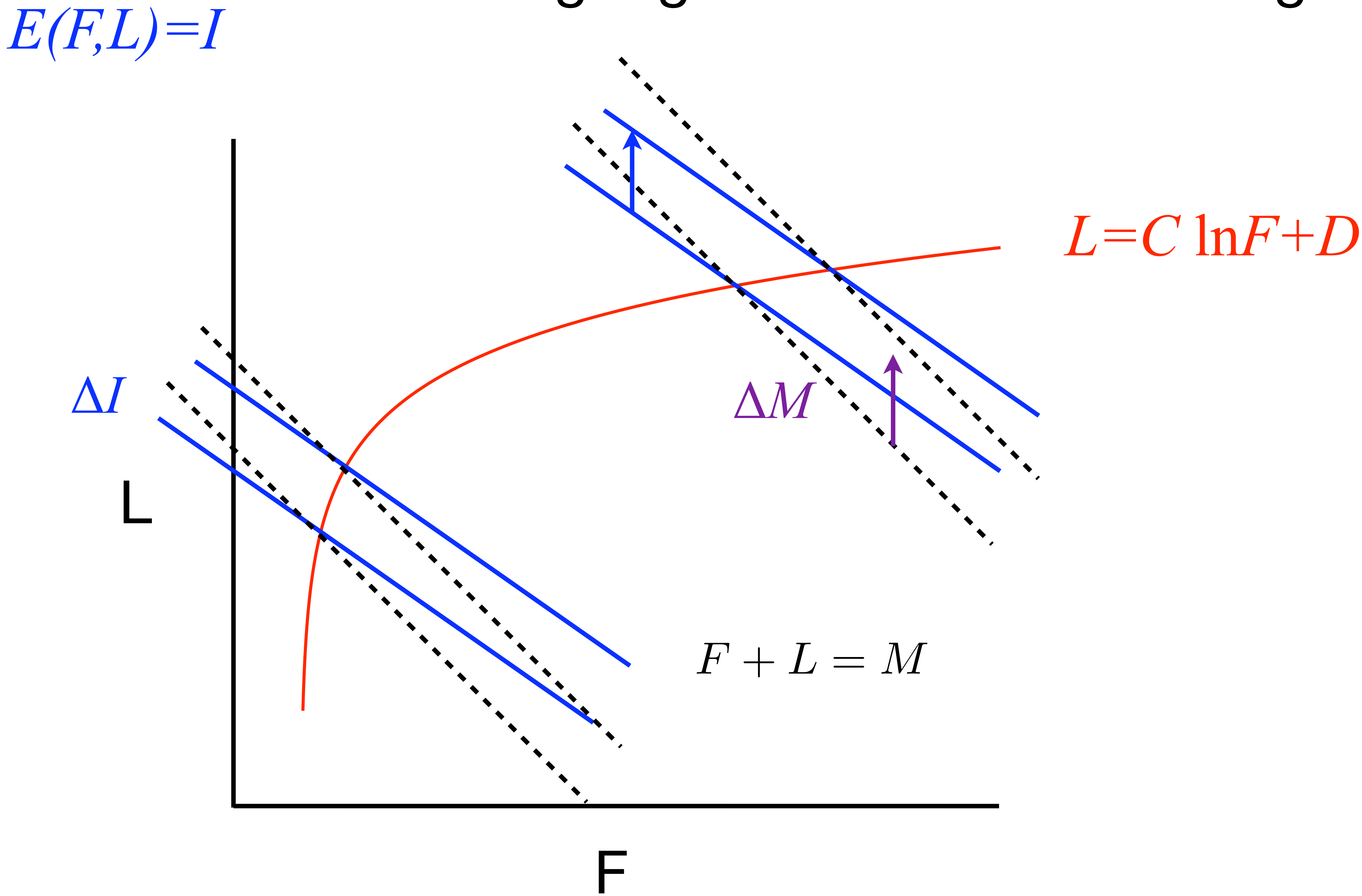
Weight gain increases with weight



Weight gain increases with weight



Weight gain increases with weight



Time Constant

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

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

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

Time Constant

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

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

$\rho \sim 7700$ kcal/kg, $\varepsilon \sim 22$ kcal/day, $\tau \sim 1$ year

τ increases with weight, decreases with activity

Myth: 3500 Calories is a pound

Myth: 3500 Calories is a pound

ρ ~ 7700 kcal/kg ~ 3500 kcal/lb

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ρ ~ 7700 kcal/kg ~ 3500 kcal/lb

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

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$$\rho \frac{dM}{dt} = I - \epsilon M - b \quad \simeq 0$$ in steady state

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Go on diet $I \to I - \Delta I$

Myth: 3500 Calories is a pound

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$$\rho \frac{dM}{dt} = I - \epsilon M - b \quad \simeq 0$$ in steady state

Go on diet $I \rightarrow I - \Delta I$

Assume no leak

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$$\rho \frac{dM}{dt} = I - \epsilon M - b \quad \simeq 0$$ in steady state

Go on diet $I \to I - \Delta I$

Assume no leak $\rho \frac{dM}{dt} \simeq -\Delta I \quad \Rightarrow \quad \Delta M = -\frac{\Delta I \Delta t}{\rho}$

Myth: 3500 Calories is a pound

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$$\rho \frac{dM}{dt} = I - \epsilon M - b \quad \simeq 0$$ in steady state

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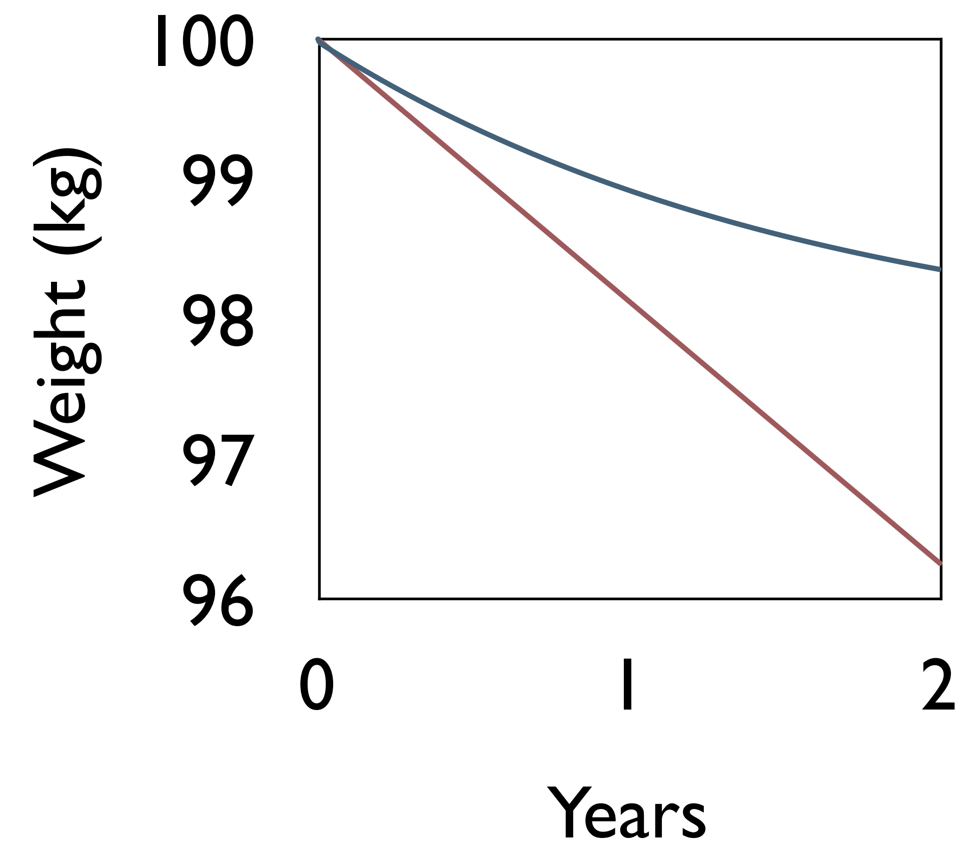

Go on diet $I \to I - \Delta I$

Assume no leak $\rho \frac{dM}{dt} \simeq -\Delta I \quad \Rightarrow \quad \Delta M = -\frac{\Delta I \Delta t}{\rho}$

Intake Paradox

"There is no stranger phenomenon than the maintenance of a constant body weight under marked variation in bodily activity and food consumption." Eugene Dubois, 1927.

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3500 kcal = 1 lb

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3500 kcal = 1 lb

Eat one million kcal/year

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~~3500 kcal = 1 lb Eat one million kcal/year~~

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1 kg ~ 22 kcal/day

Intake Paradox

"There is no stranger phenomenon than the maintenance of a constant body weight under marked variation in bodily activity and food consumption." Eugene Dubois, 1927.

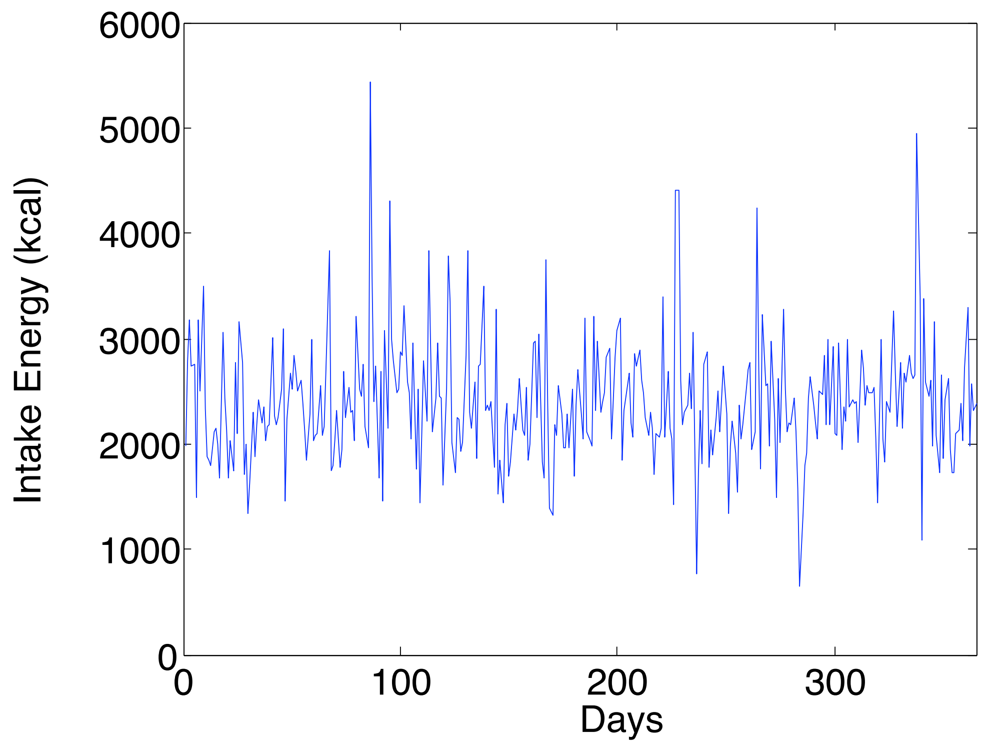
~~3500 kcal = 1 lb~~ ~~Eat one million kcal/year~~

1 kg ~ 22 kcal/day

~220 kcal

Intake fluctuations

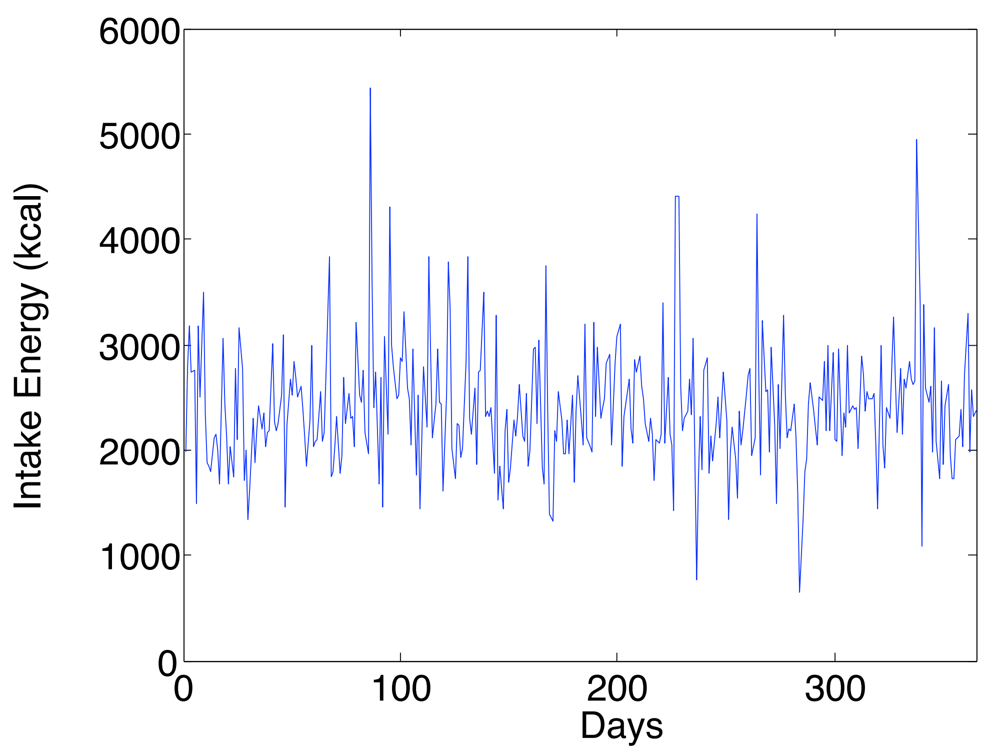
Beltsville one year intake study (courtesy of W. Rumpler)

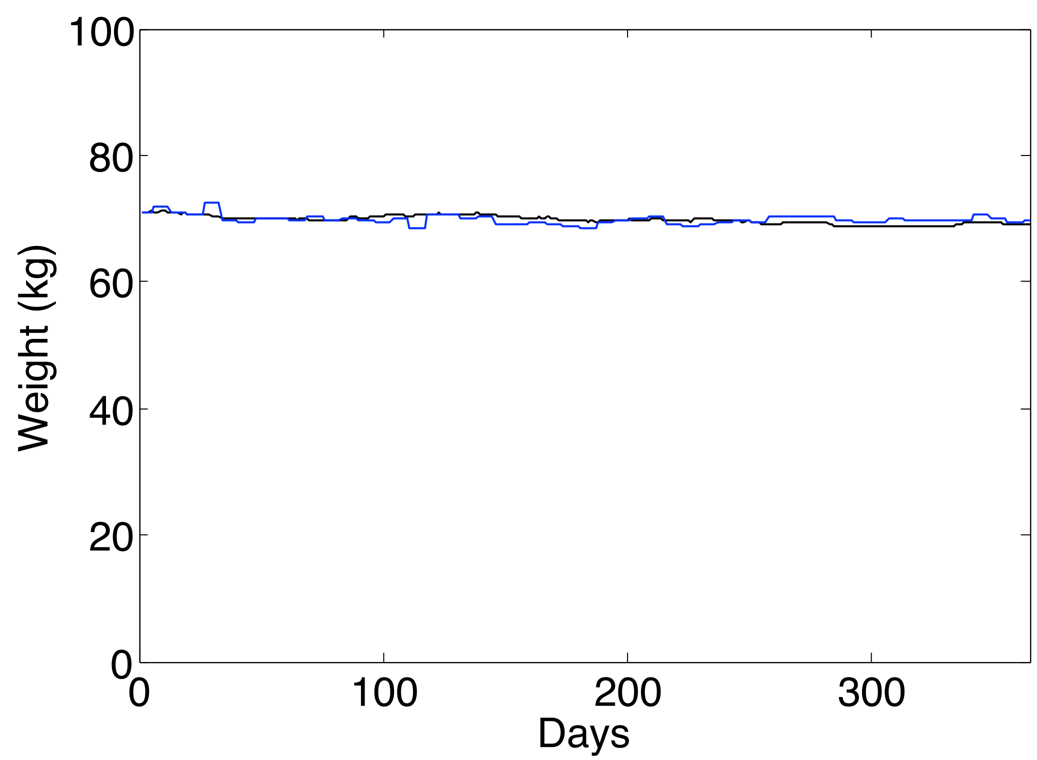


$CV \sim 24\%$

Intake fluctuations

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





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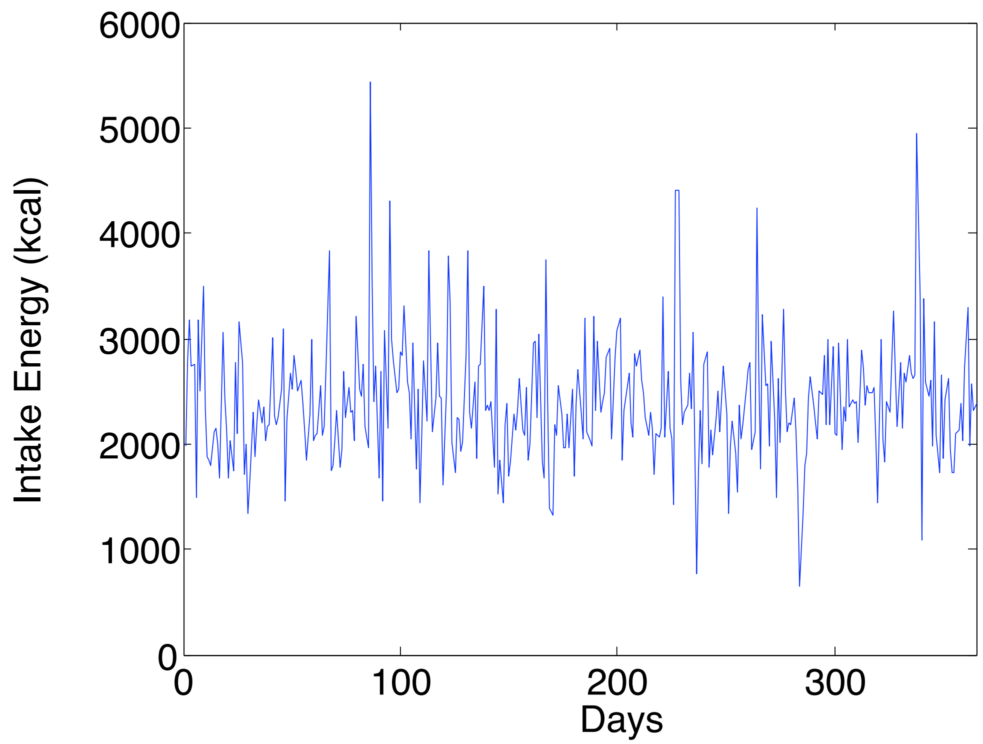
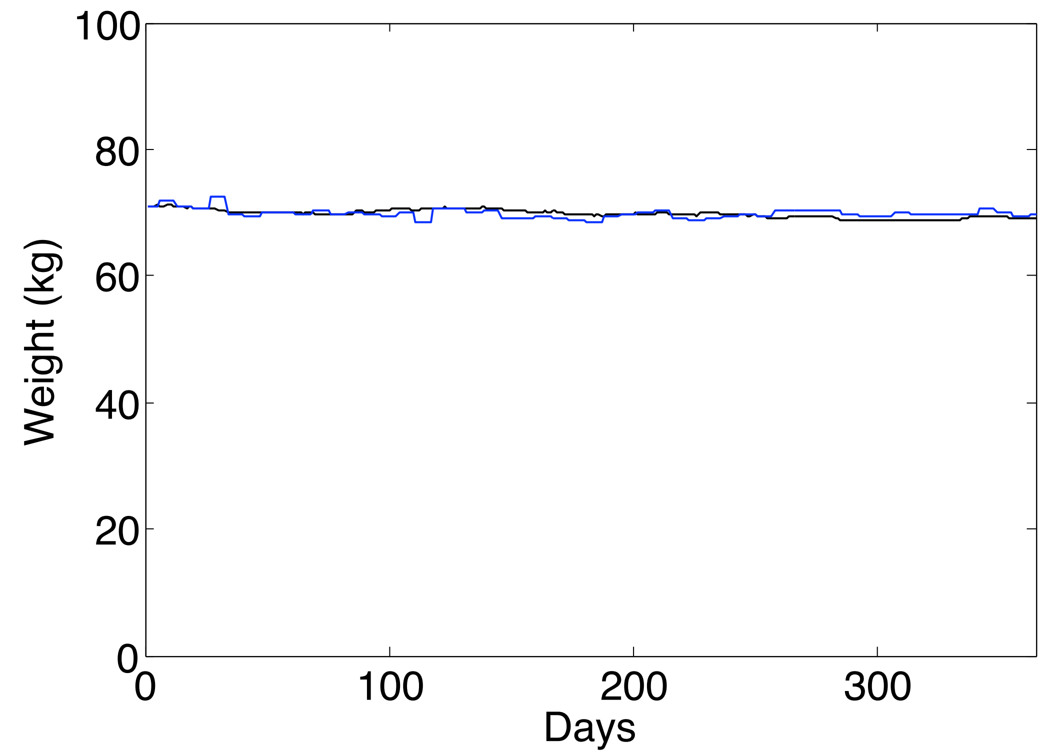


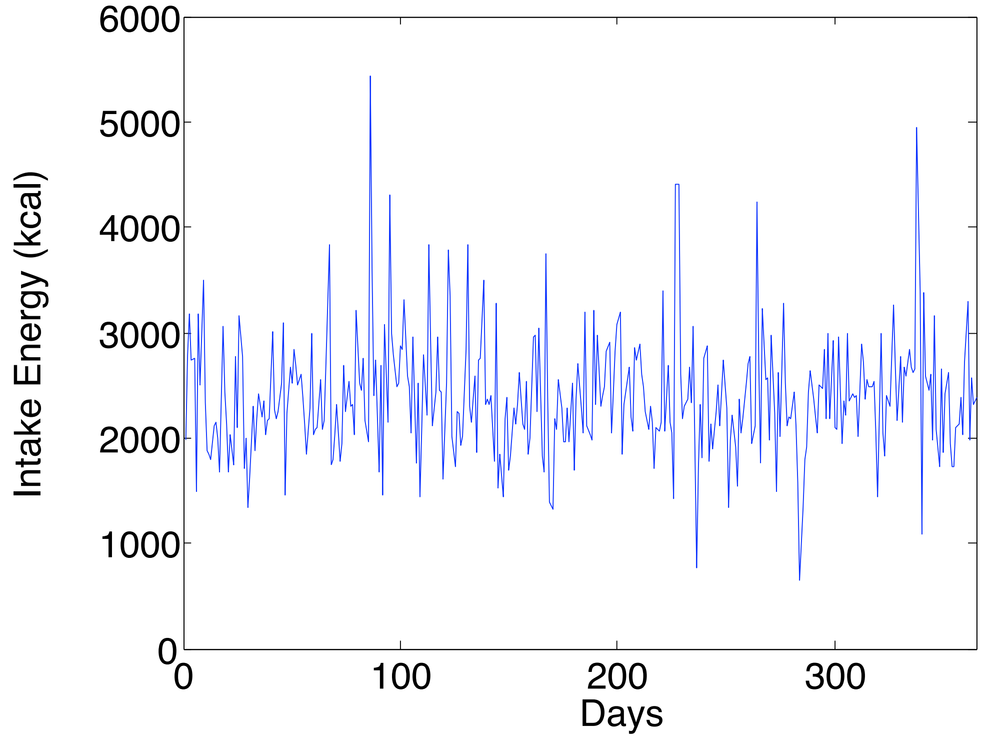


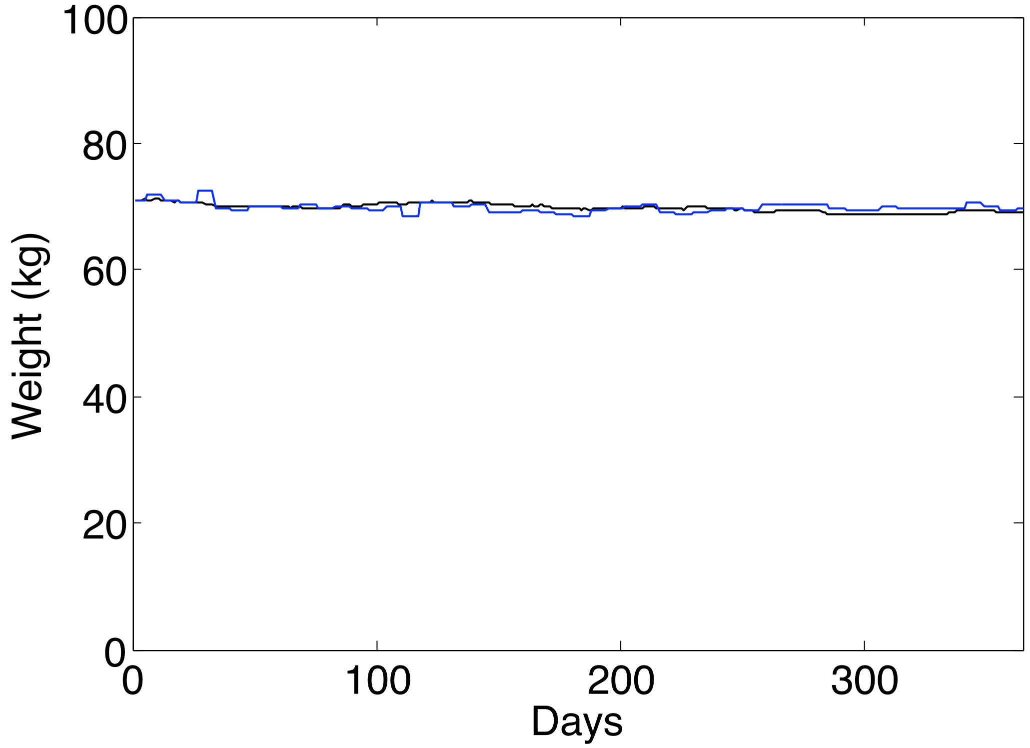
$CV \sim 24\%$

$CV \sim 1\%$

Intake fluctuations

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

Noisy intake

$$I(t) = \bar{I} + \eta(t) \qquad \langle \eta(t)\eta(t') \rangle = \sigma^2 \delta(t - t')$$

Time varying intake

Noisy intake

$$I(t) = \bar{I} + \eta(t) \qquad \langle \eta(t)\eta(t') \rangle = \sigma^2 \delta(t - t')$$

Ornstein-Uhlenbeck process

Time varying intake

Noisy intake

$$I(t) = \bar{I} + \eta(t) \qquad \langle \eta(t)\eta(t') \rangle = \sigma^2 \delta(t - t')$$

Ornstein-Uhlenbeck process

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

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Ornstein-Uhlenbeck process

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

CV(I) is $\frac{\sigma\sqrt{\mathrm{day}}}{\bar{I}}$ find *CV(M)*

Weight variance

$$\mathrm{Var}(M) = \frac{\sigma^2}{2\tau\epsilon^2}$$

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

Weight variance $\mathrm{Var}(M) = \frac{\sigma^2}{2\tau\epsilon^2}$

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

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For $\sqrt{2\tau} \sim 30, \bar{I} \sim 2500, b \sim 600$ $\quad CV(M) \sim CV(I)/20$

Weight variance $\mathrm{Var}(M) = \dfrac{\sigma^2}{2\tau\epsilon^2}$

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

For $\sqrt{2\tau} \sim 30, \bar{I} \sim 2500, b \sim 600$ $CV(M) \sim CV(I)/20$

No paradox because of long time constant

Intake and activity fluctuations

$$\rho \frac{dM}{dt} = \bar{I} - b - (\epsilon + \eta_a(t))M + \eta_I(t)$$

Intake and activity fluctuations

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$$dM = \frac{1}{\rho}(\bar{I} - b - \epsilon M)dt + \frac{1}{\rho}\sqrt{\sigma_I^2 - 2c\sigma_I\sigma_a + \sigma_a^2 M^2}dW$$

Intake and activity fluctuations

$$\rho \frac{dM}{dt} = \bar{I} - b - (\epsilon + \eta_a(t))M + \eta_I(t)$$

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$$\mathrm{Var}(M) = \frac{\frac{\sigma_I^2}{2\epsilon\rho} + \frac{\sigma_a^2(I-b)^2}{2\epsilon^3\rho^3} - \frac{c\sigma_I\sigma_a(I-b)}{2\epsilon^2\rho^2}}{1 - \frac{\sigma_a^2}{2\epsilon^3\rho^2}}$$

Intake and activity fluctuations

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Intake and activity fluctuations

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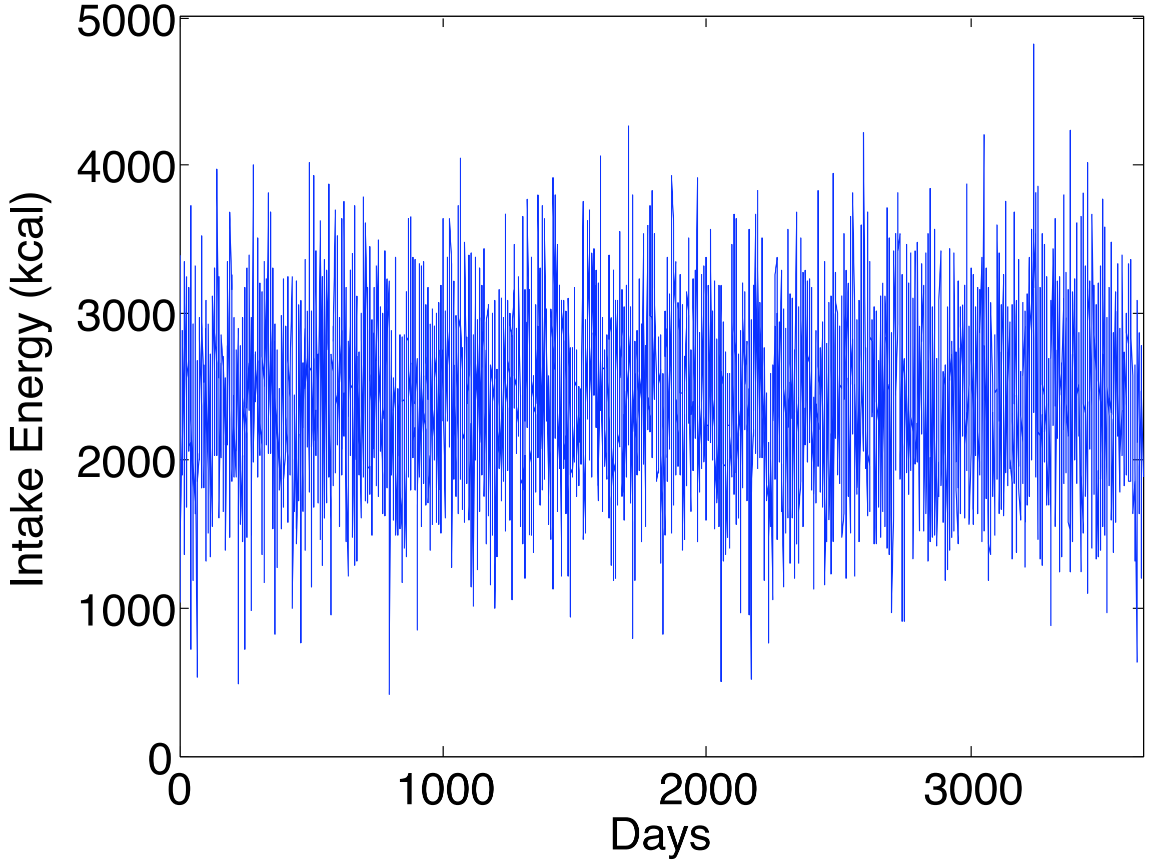
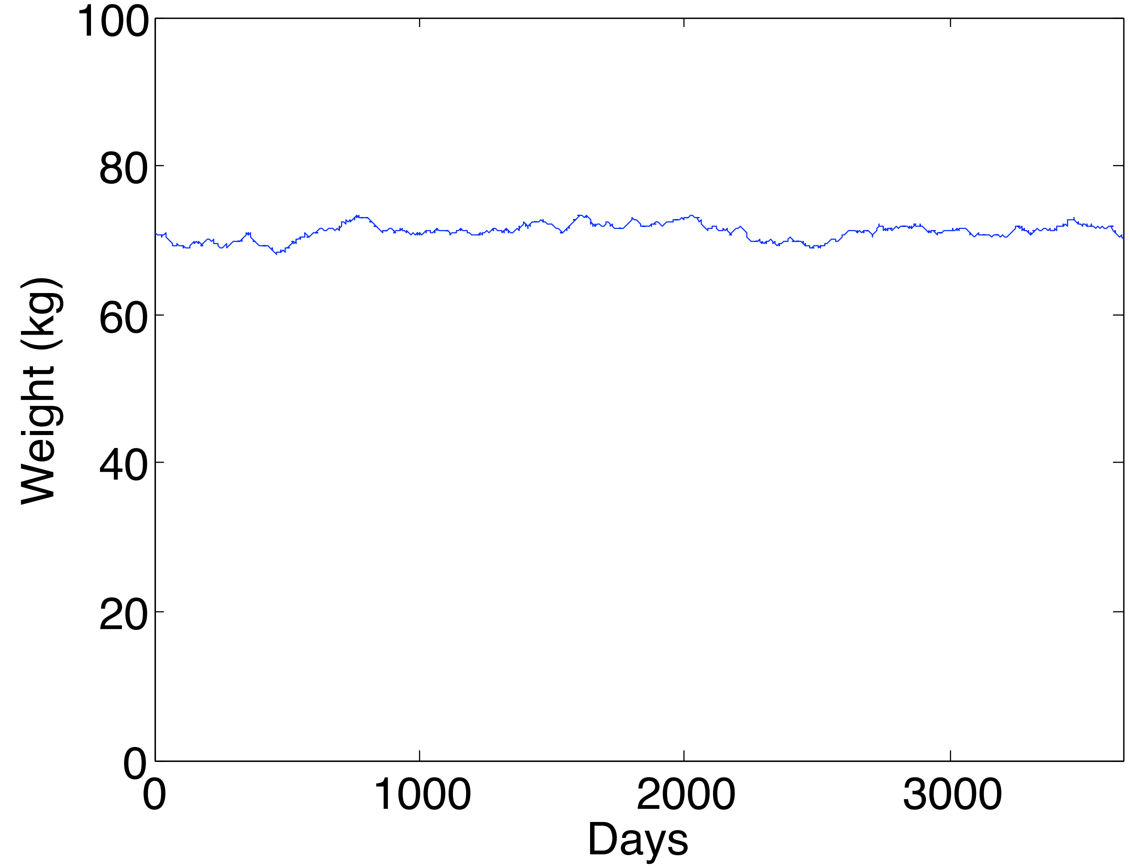
Simulated data 10 years

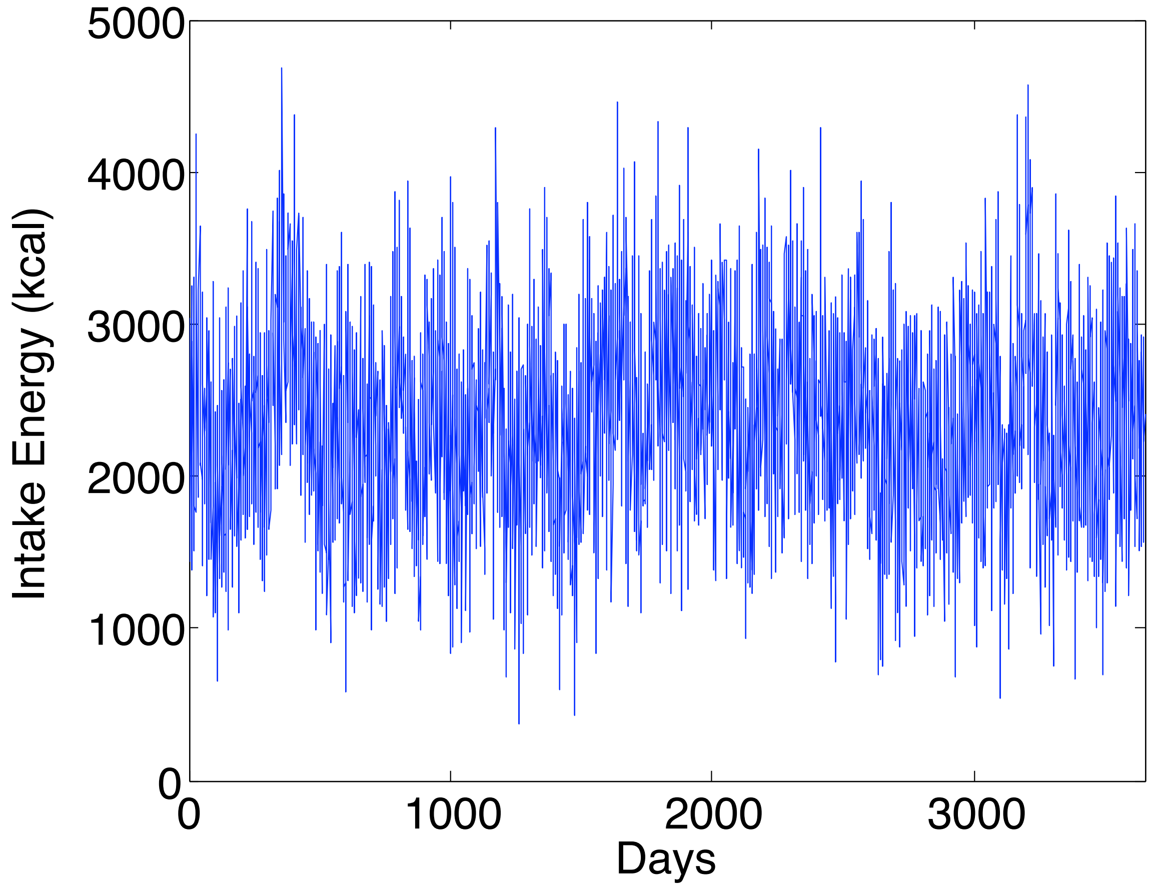


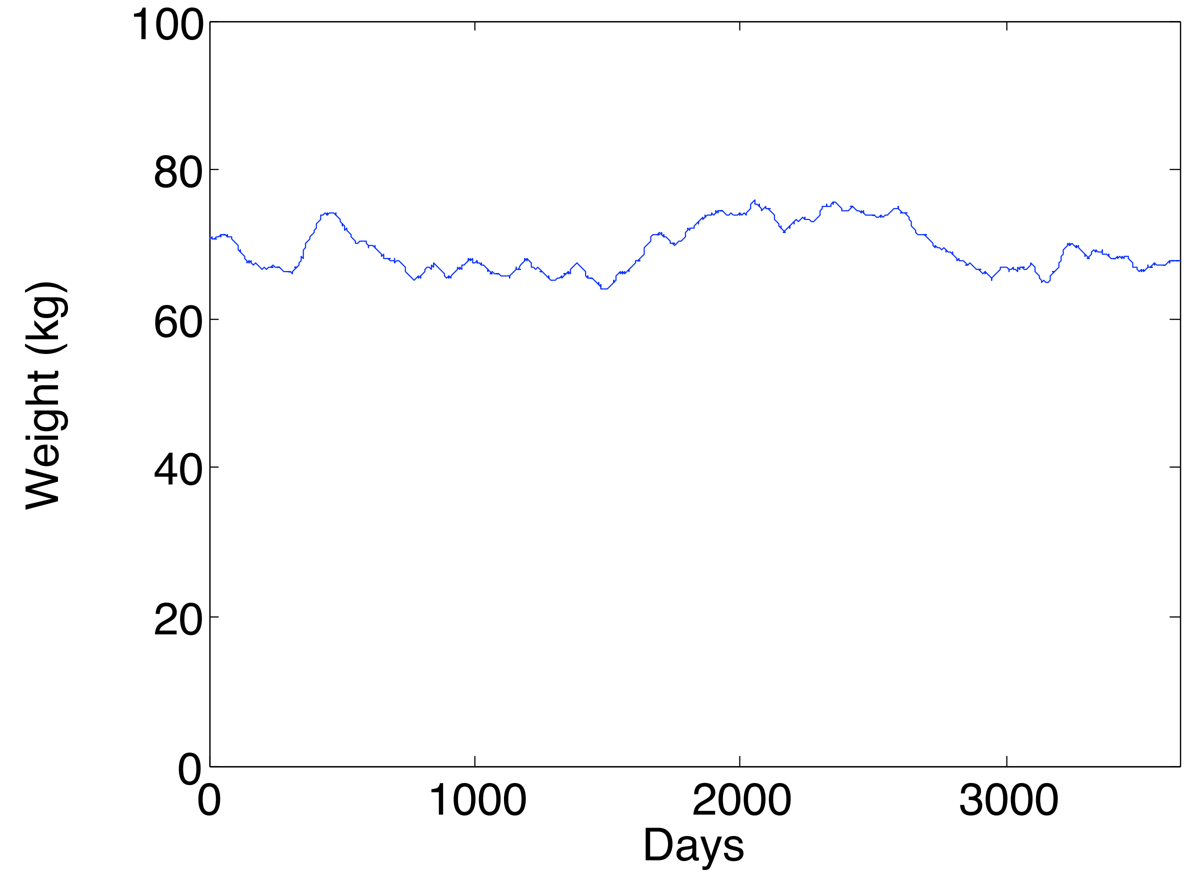


CV ~ *23%*

CV ~ *2%*

Correlations increase fluctuations

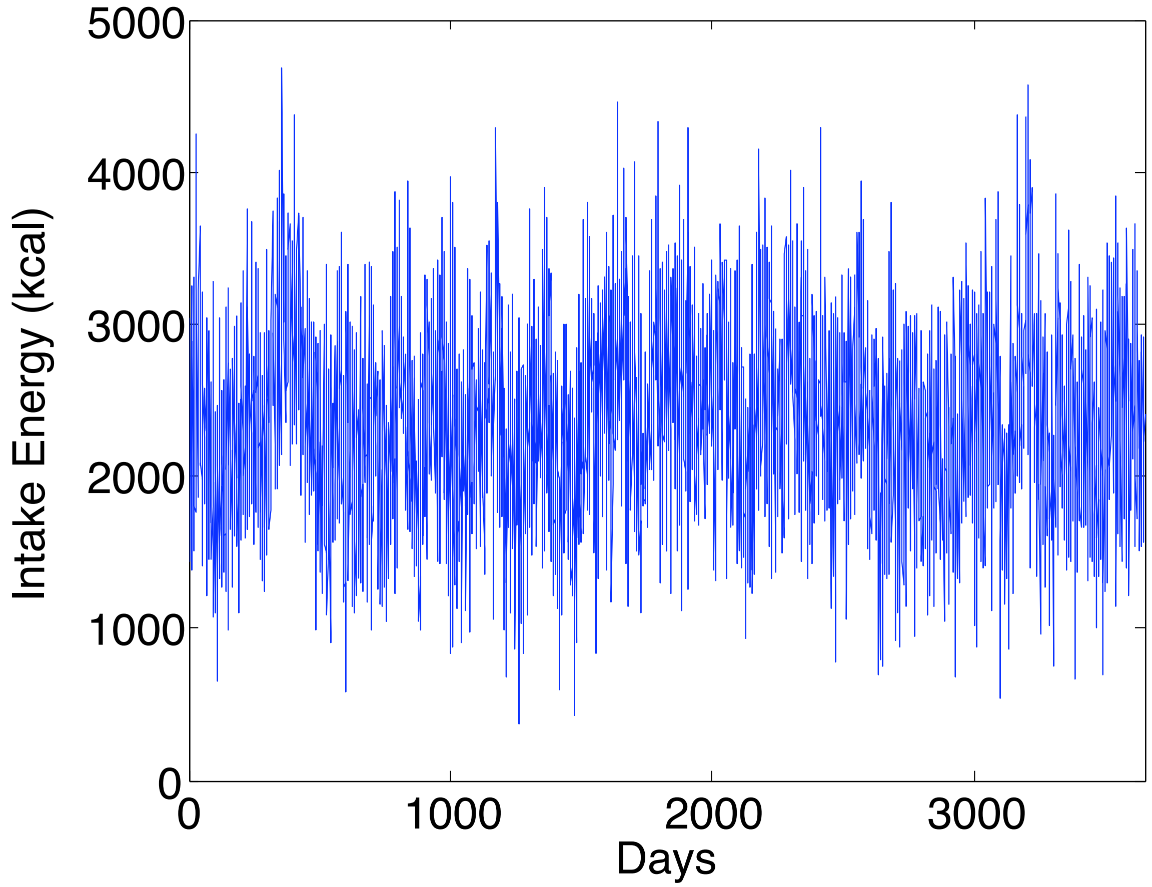


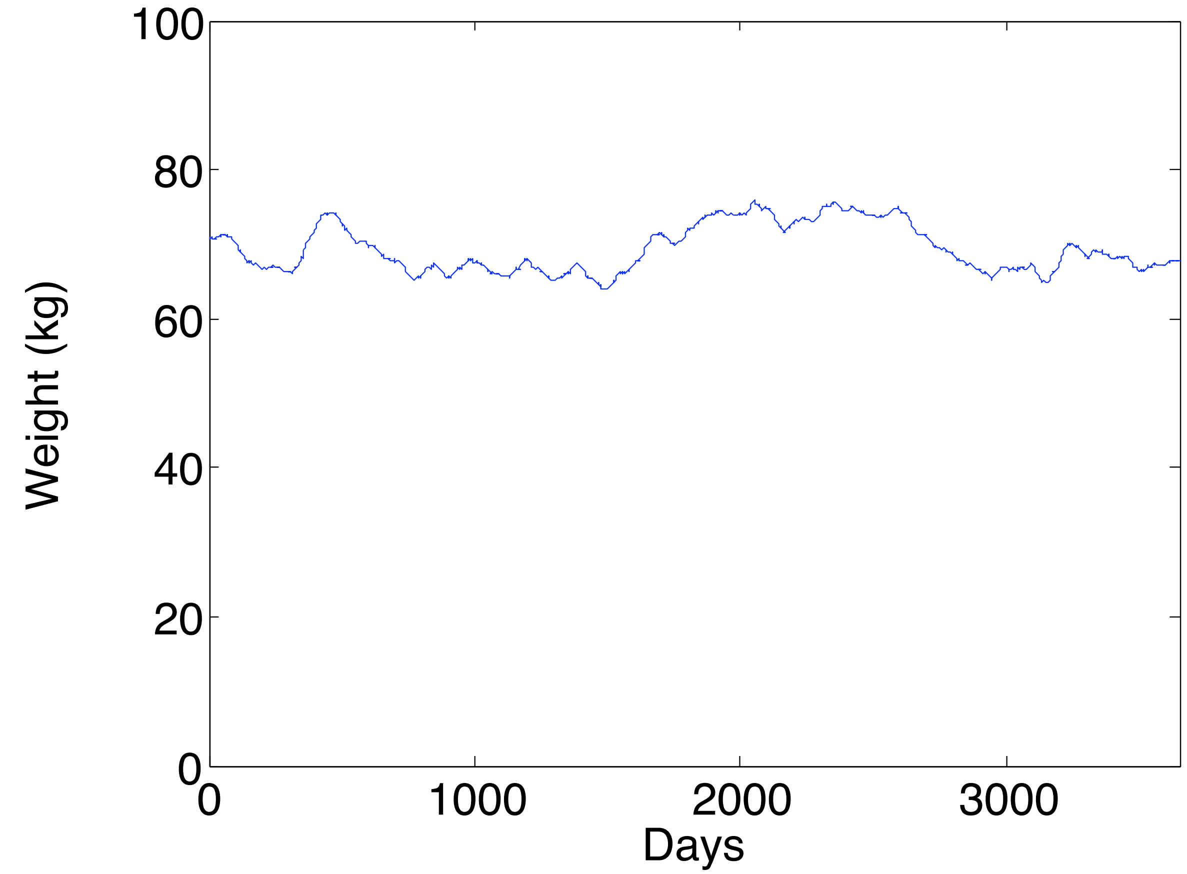


CV ~ *26%*

CV ~ *5%*

Correlations increase fluctuations





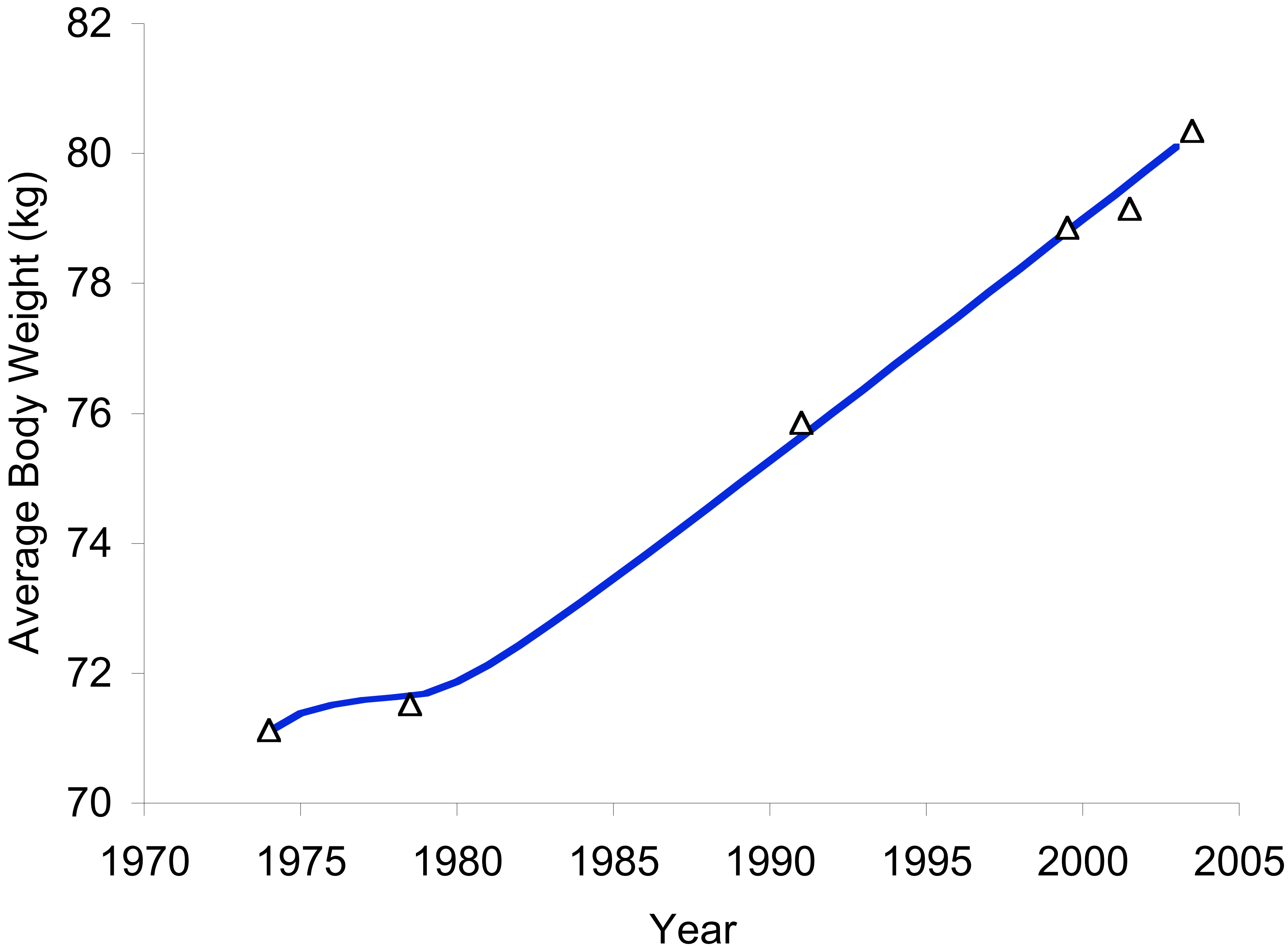
CV ~ *26%*

CV ~ *5%*

Longer correlations ⇒ higher BMI

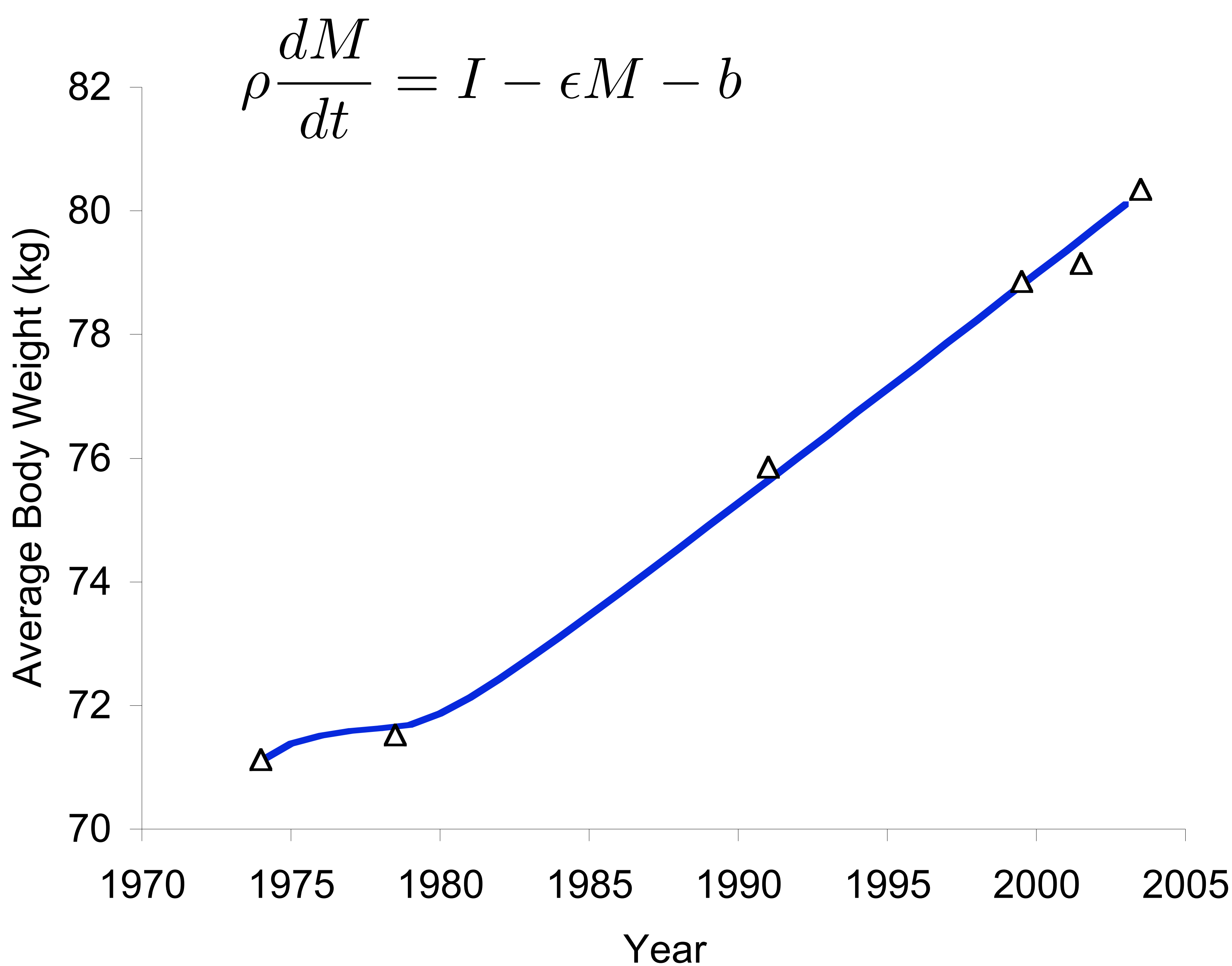
Periwal and Chow, AJP:EM, 291:929-36 (2006)

Mean US body weight



Data from National Health and Nutrition Examination Survey (NHANES)

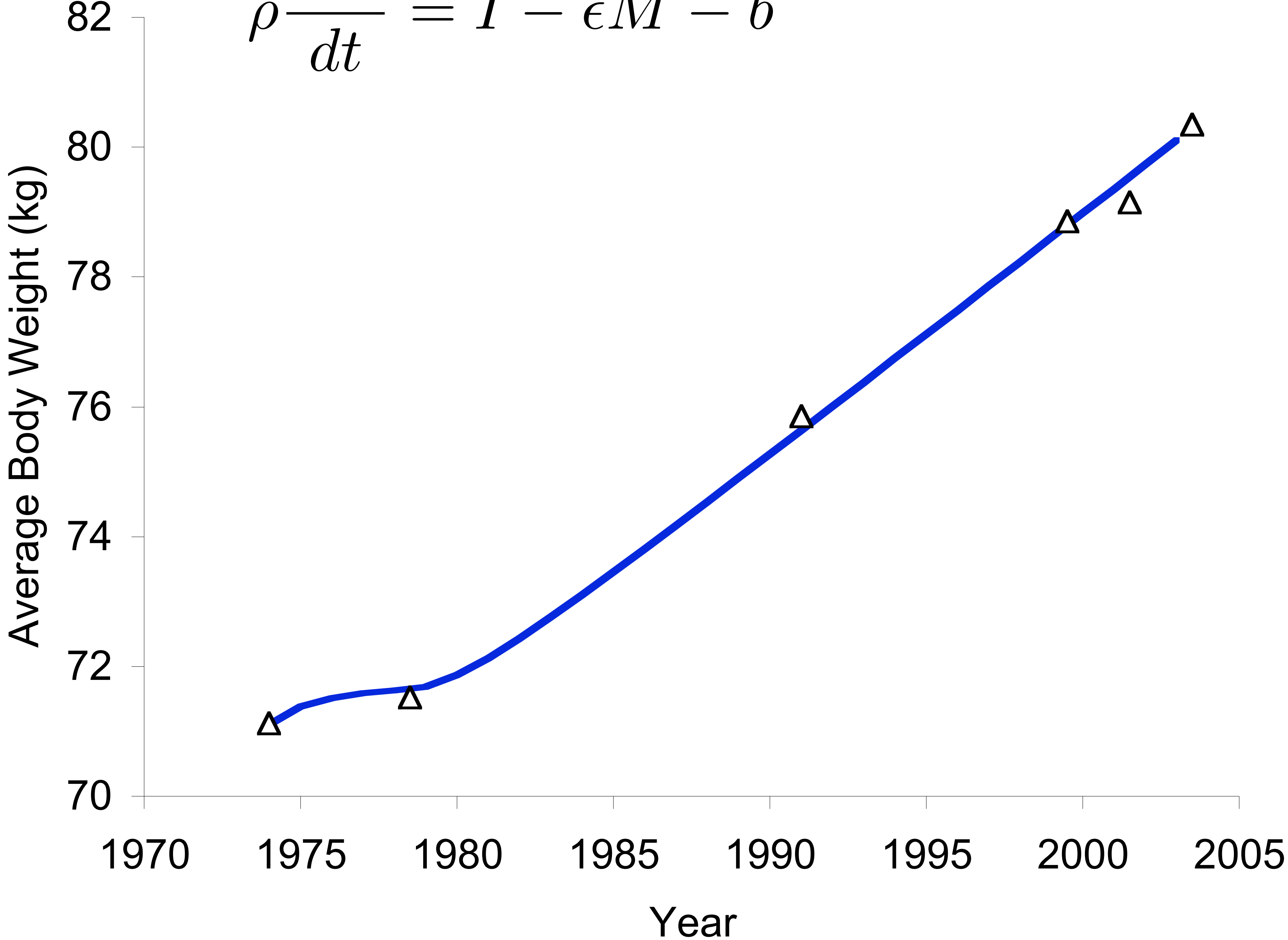
Mean US body weight



Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight

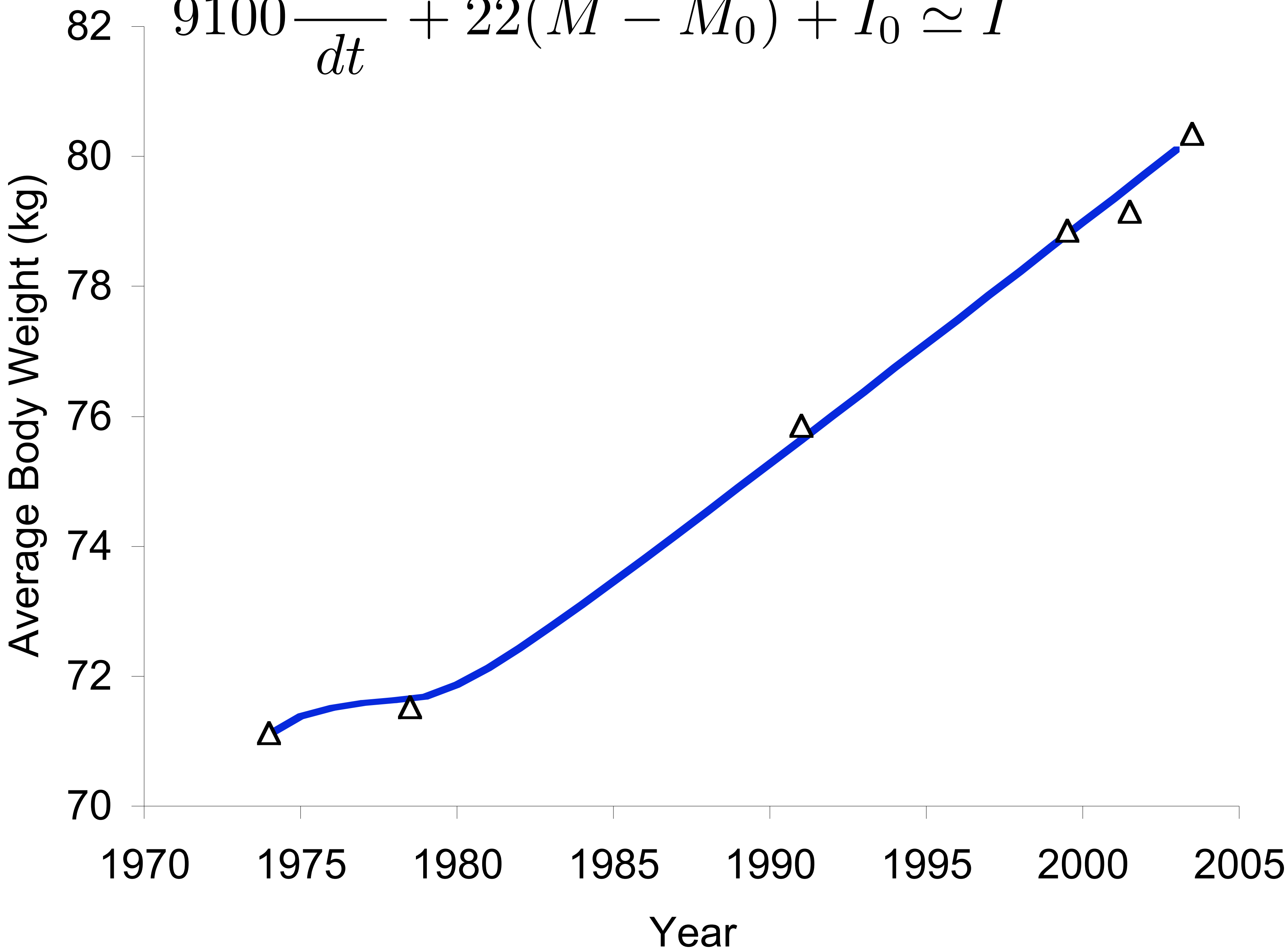
$$\rho \overline{\frac{dM}{dt}} = \overline{I} - \overline{\epsilon M} - b$$



Data from National Health and Nutrition Examination Survey (NHANES)

Mean US body weight

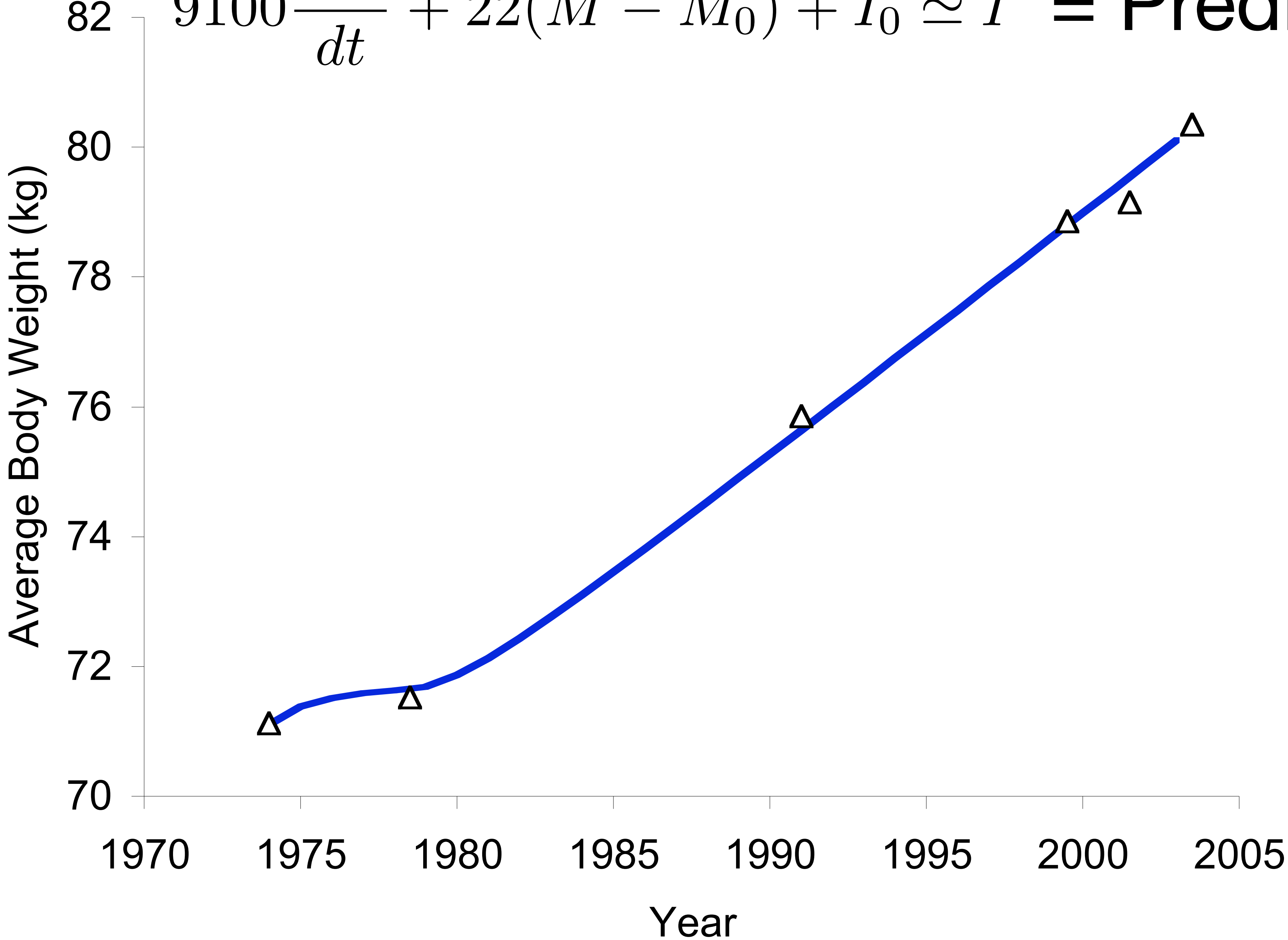
$$9100\frac{d\overline{M}}{dt} + 22(\overline{M} - M_0) + I_0 \simeq \overline{I}$$



Data from National Health and Nutrition Examination Survey (NHANES)

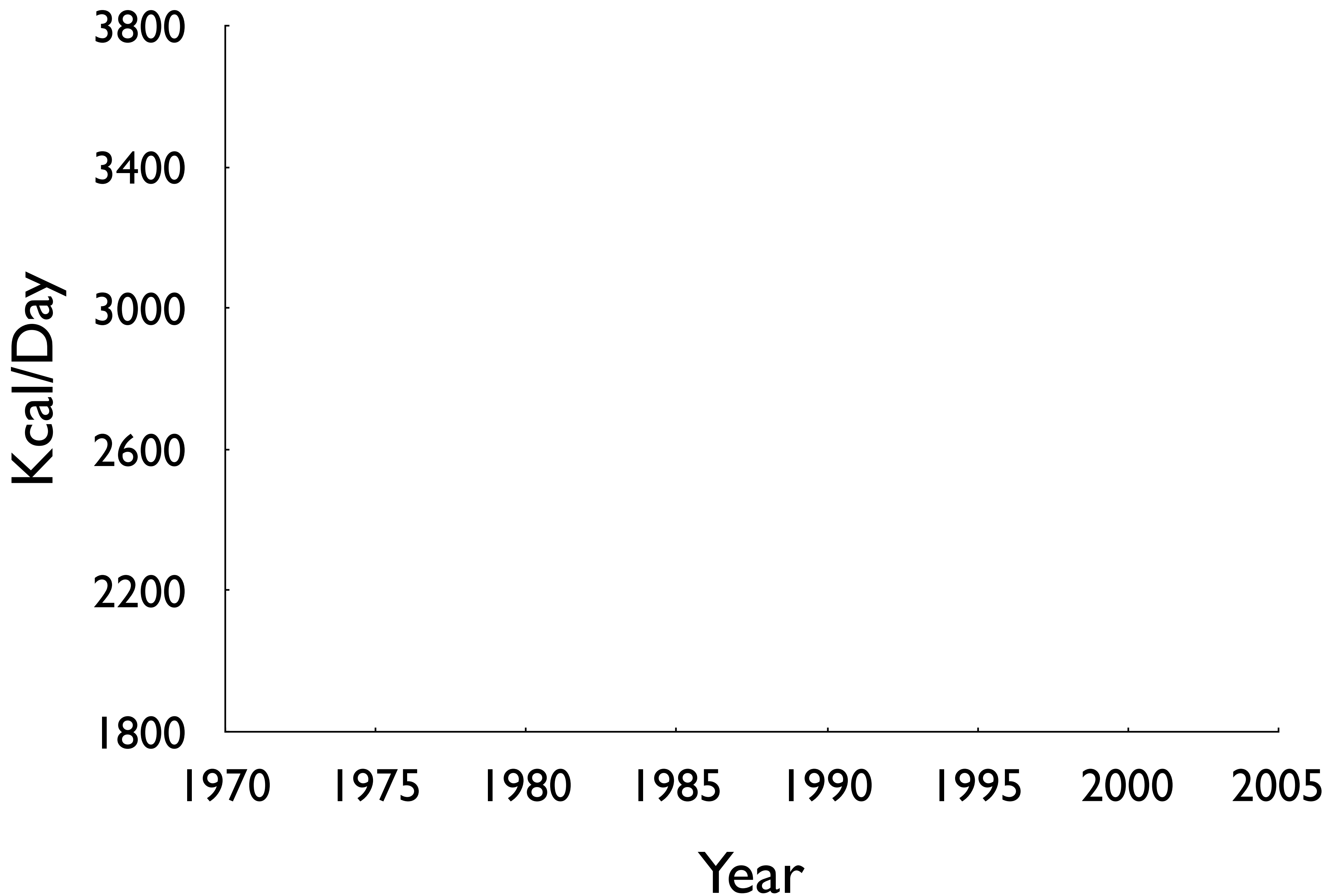
Mean US body weight

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

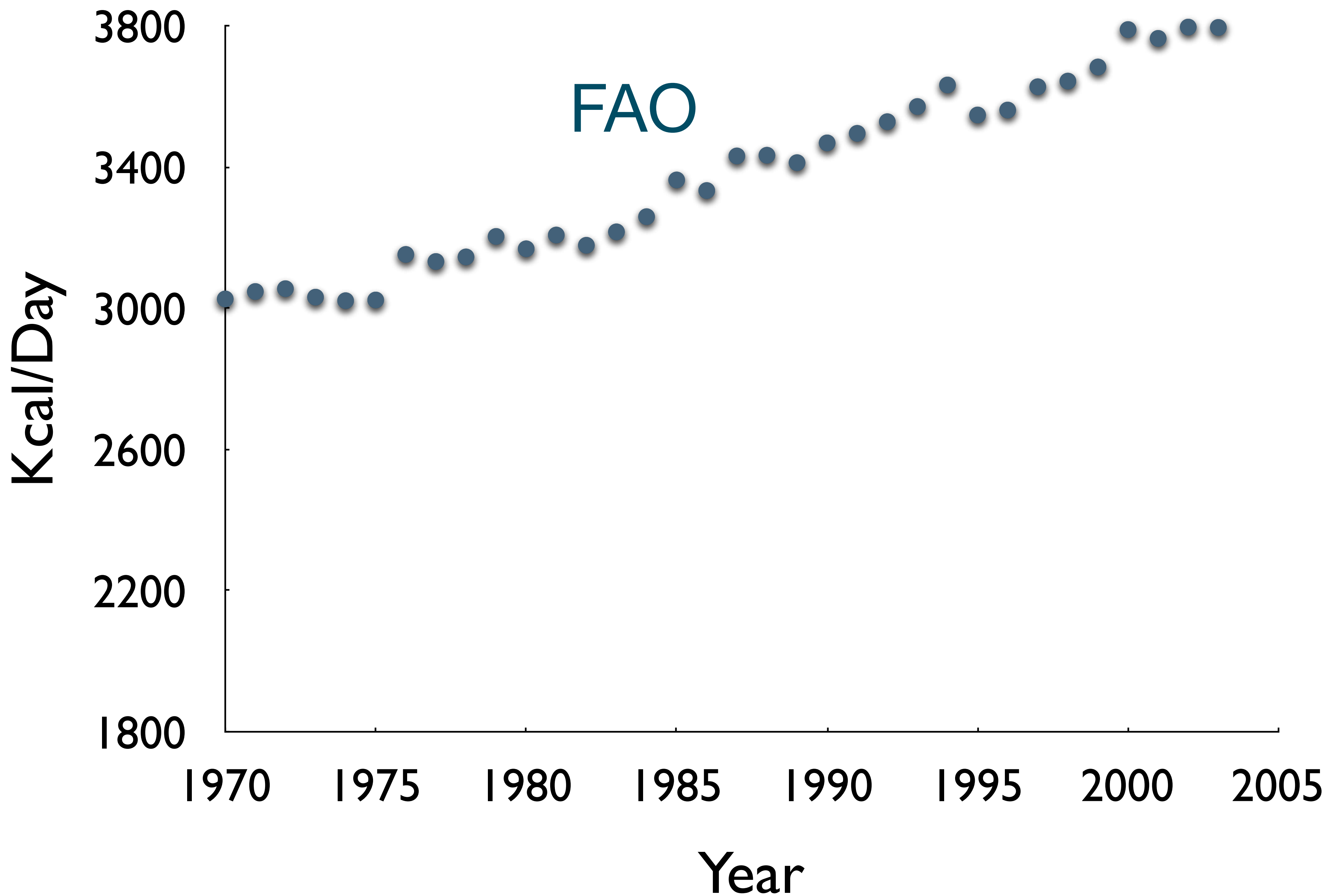


Data from National Health and Nutrition Examination Survey (NHANES)

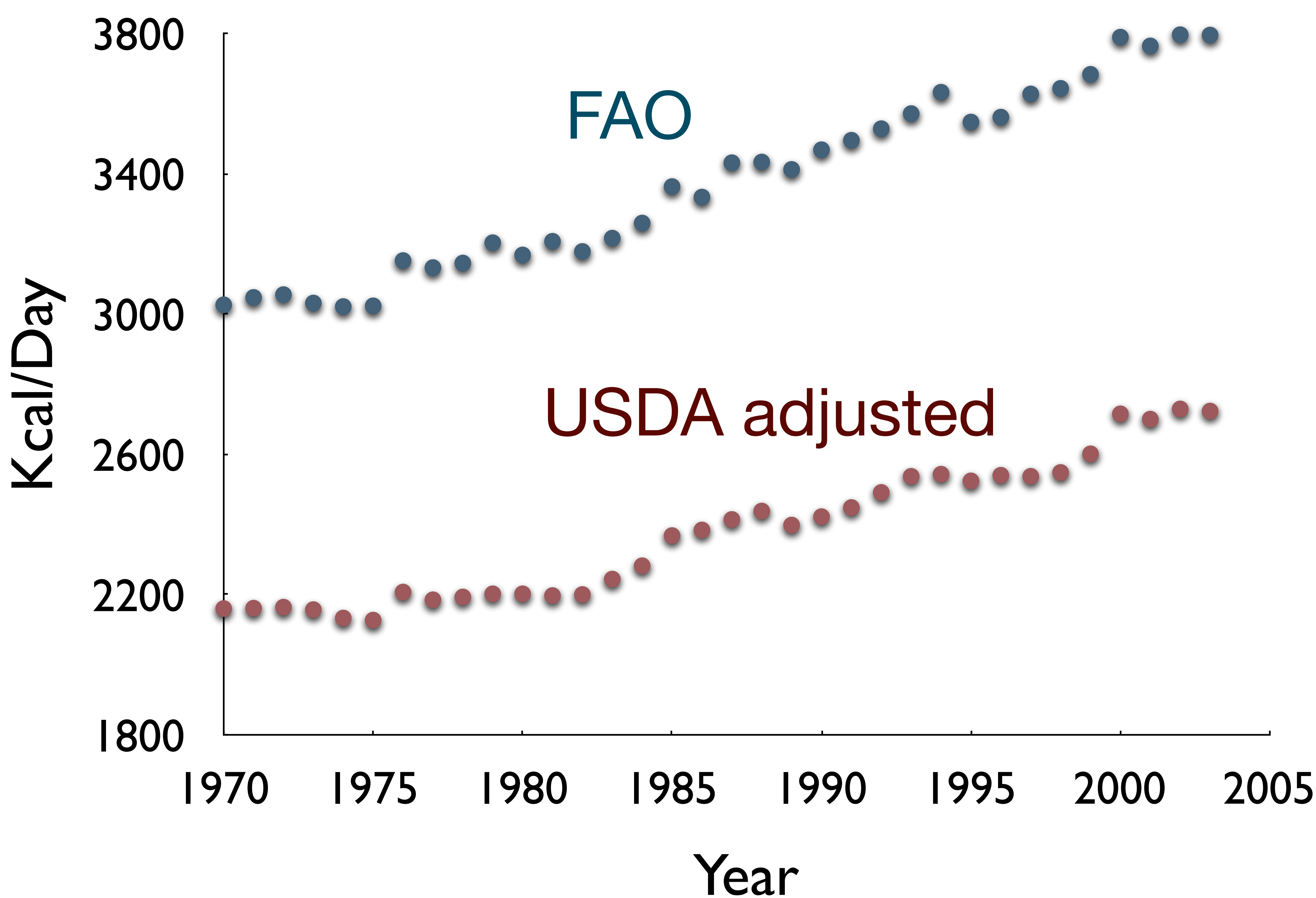
Hall, Guo, Dore, Chow. *PLoS One* (2009)



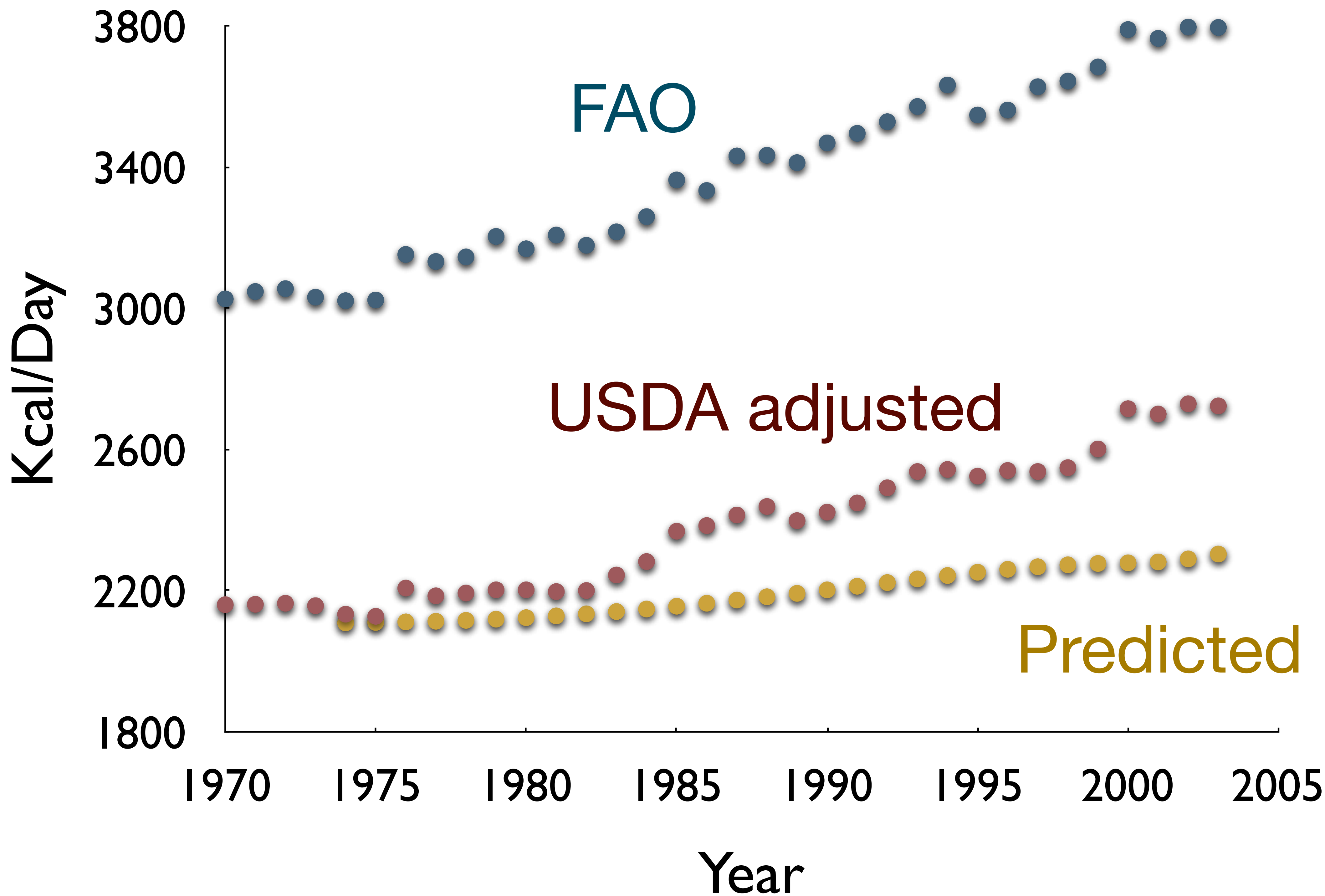
Hall, Guo, Dore, Chow. *PLoS One* (2009)



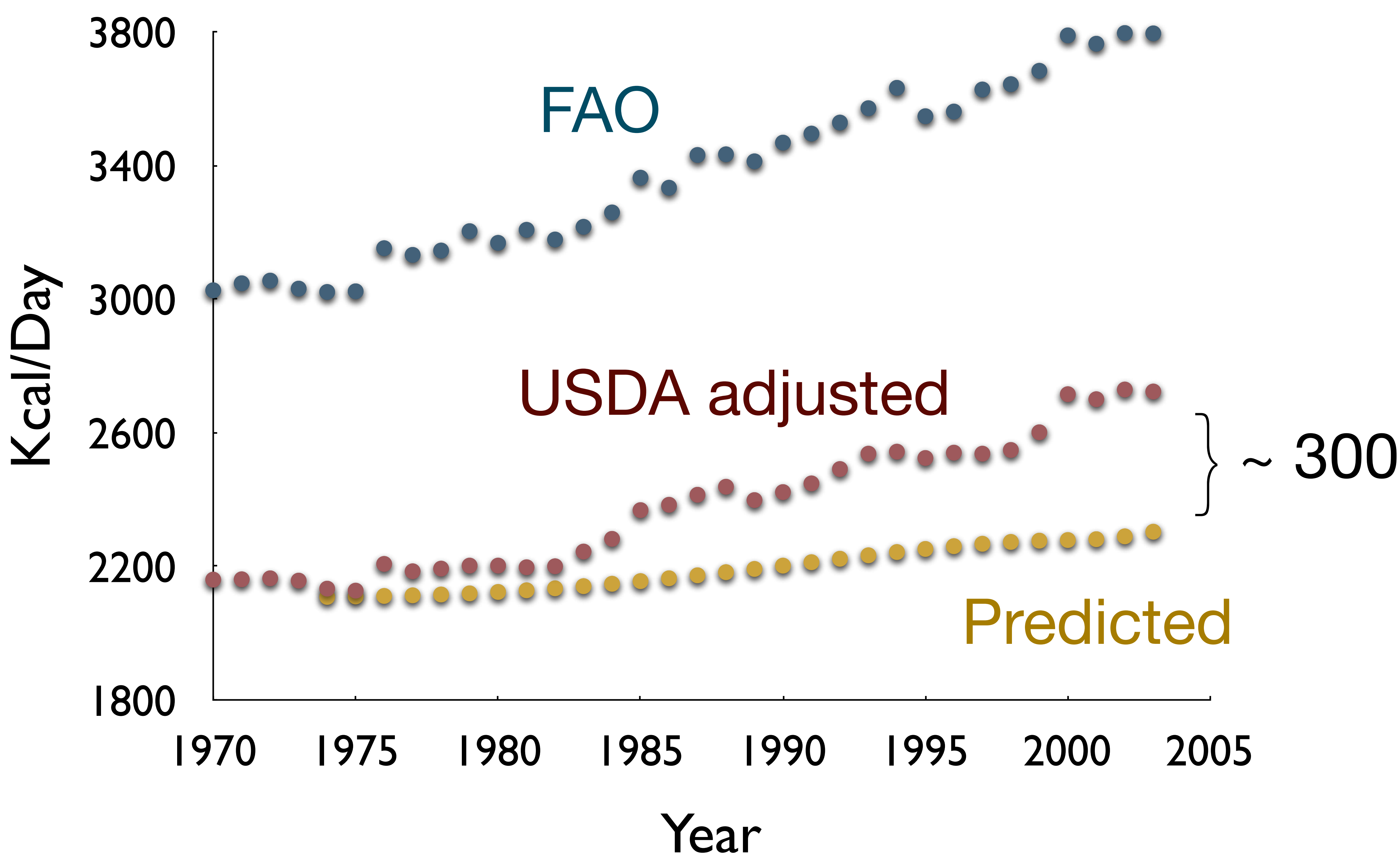
Hall, Guo, Dore, Chow. *PLoS One* (2009)



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

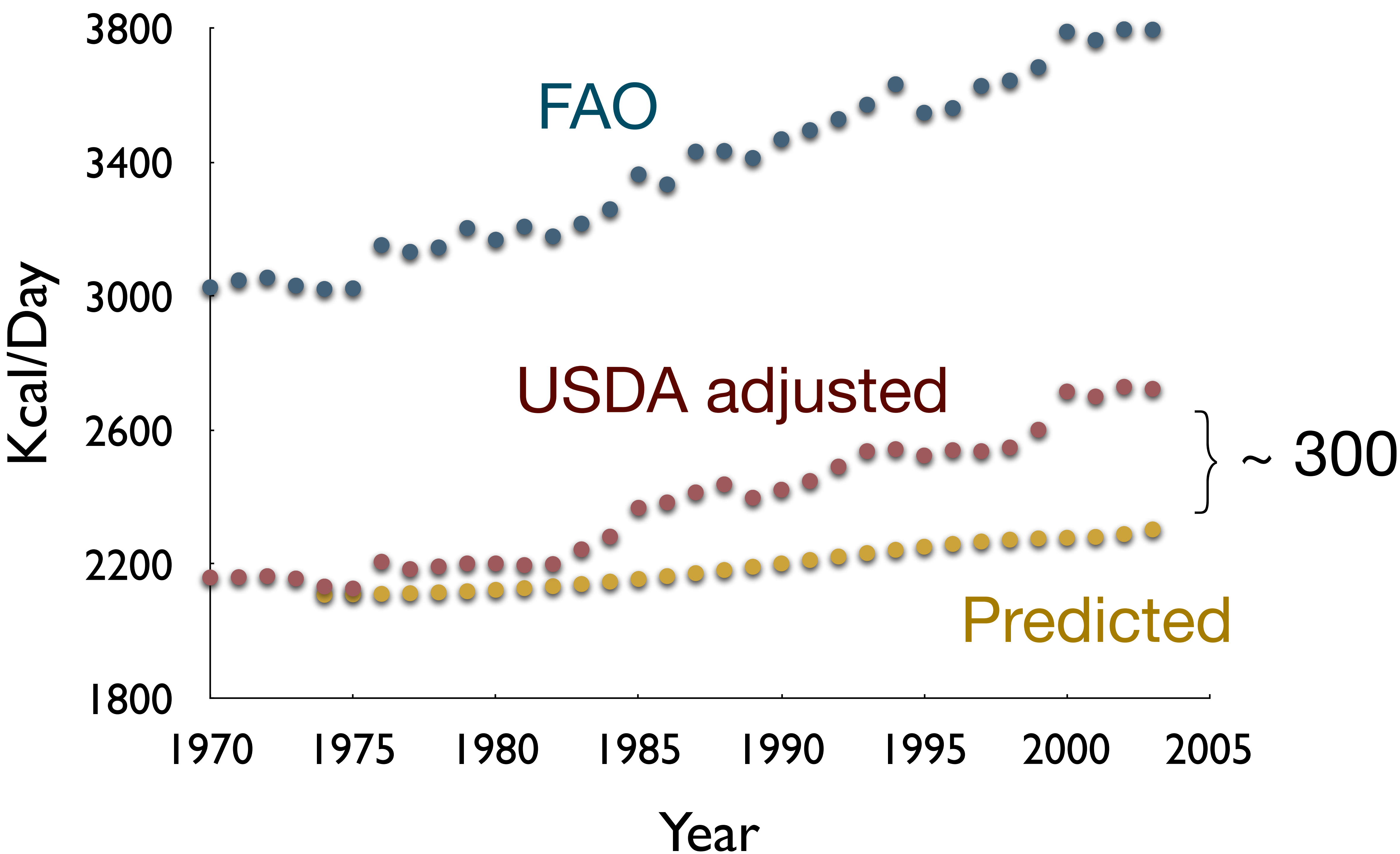


Hall, Guo, Dore, Chow. *PLoS One* (2009)



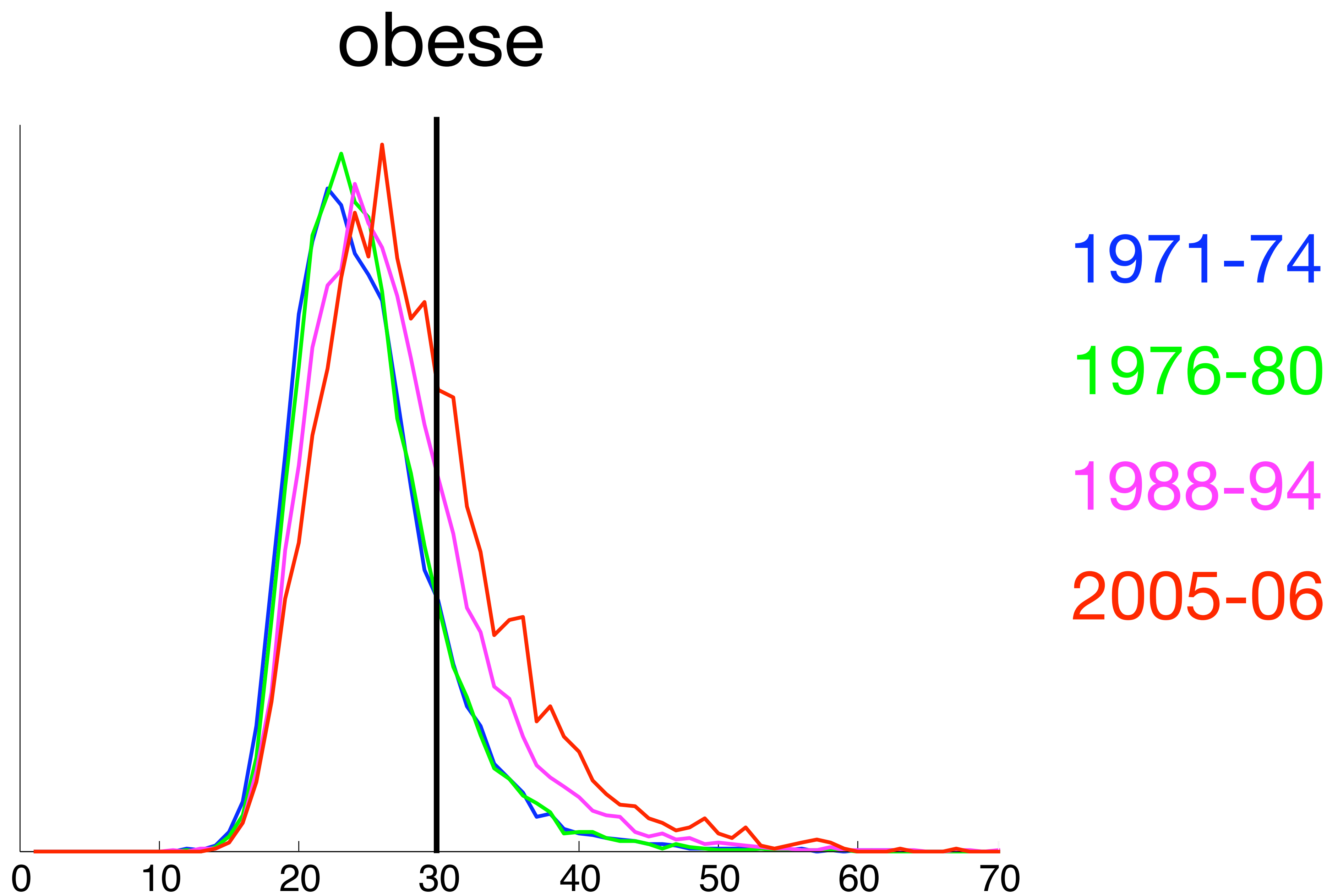
Hall, Guo, Dore, Chow. *PLoS One* (2009)

Excess food more than explains obesity epidemic



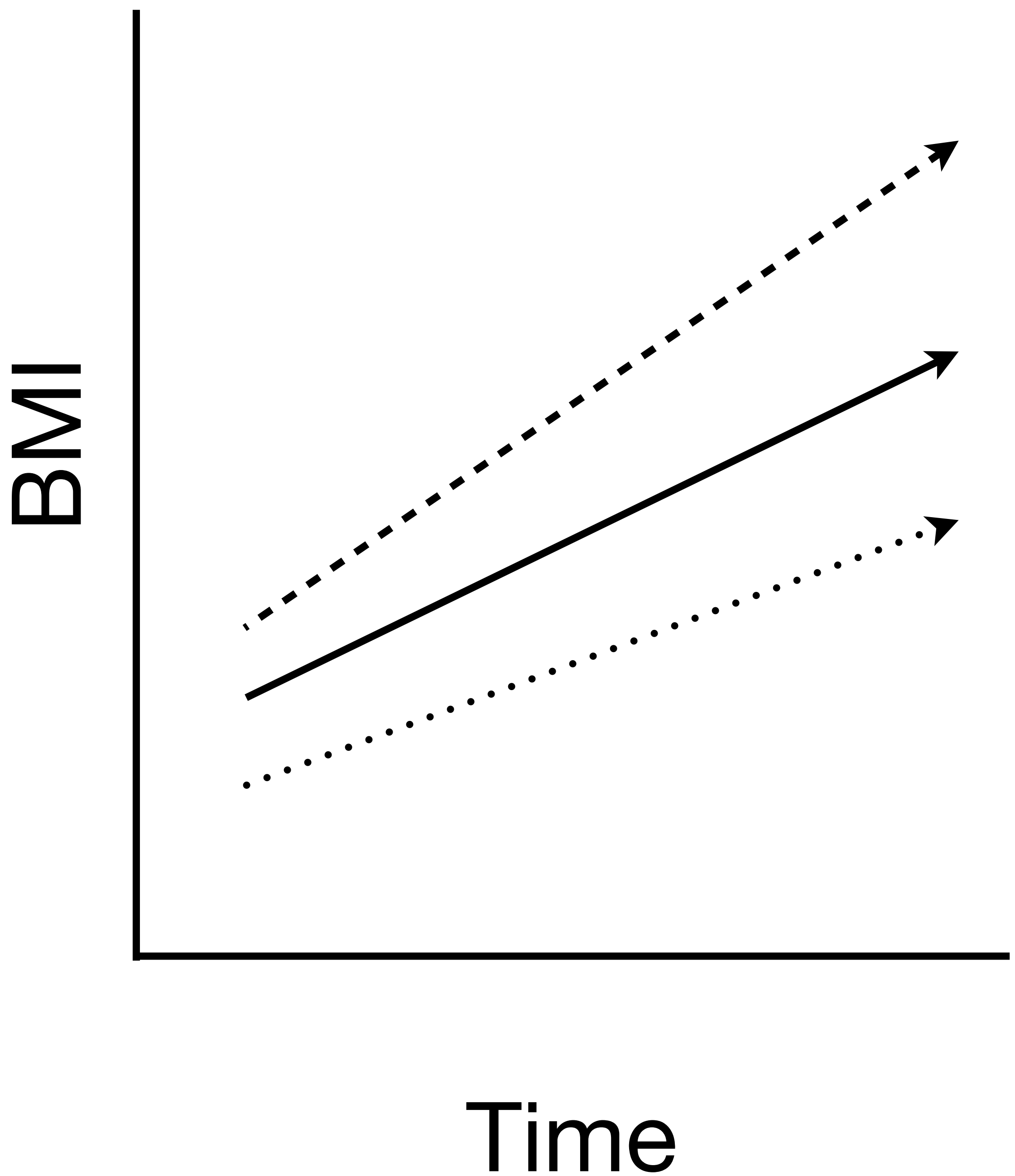
Hall, Guo, Dore, Chow. *PLoS One* (2009)

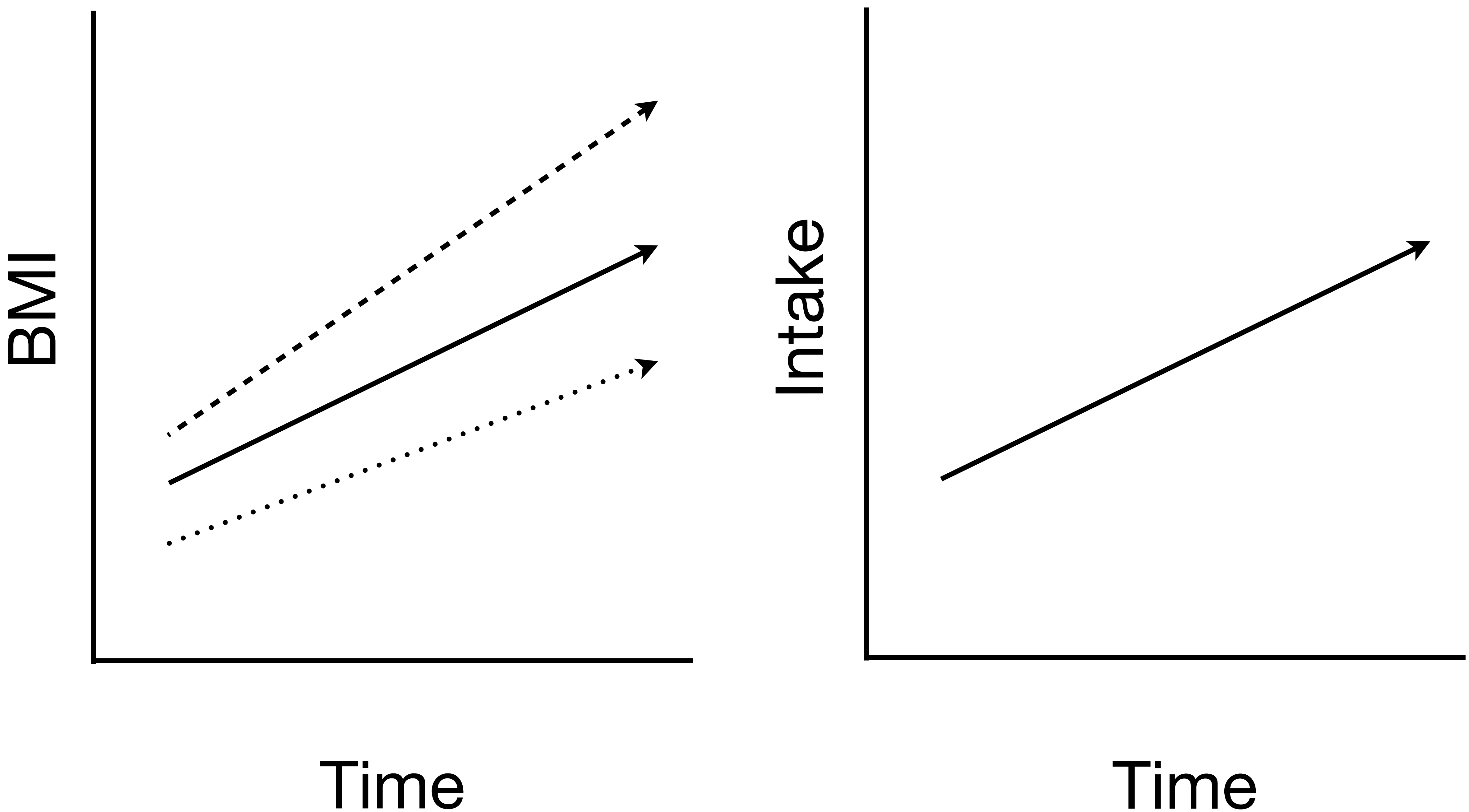
BMI distribution

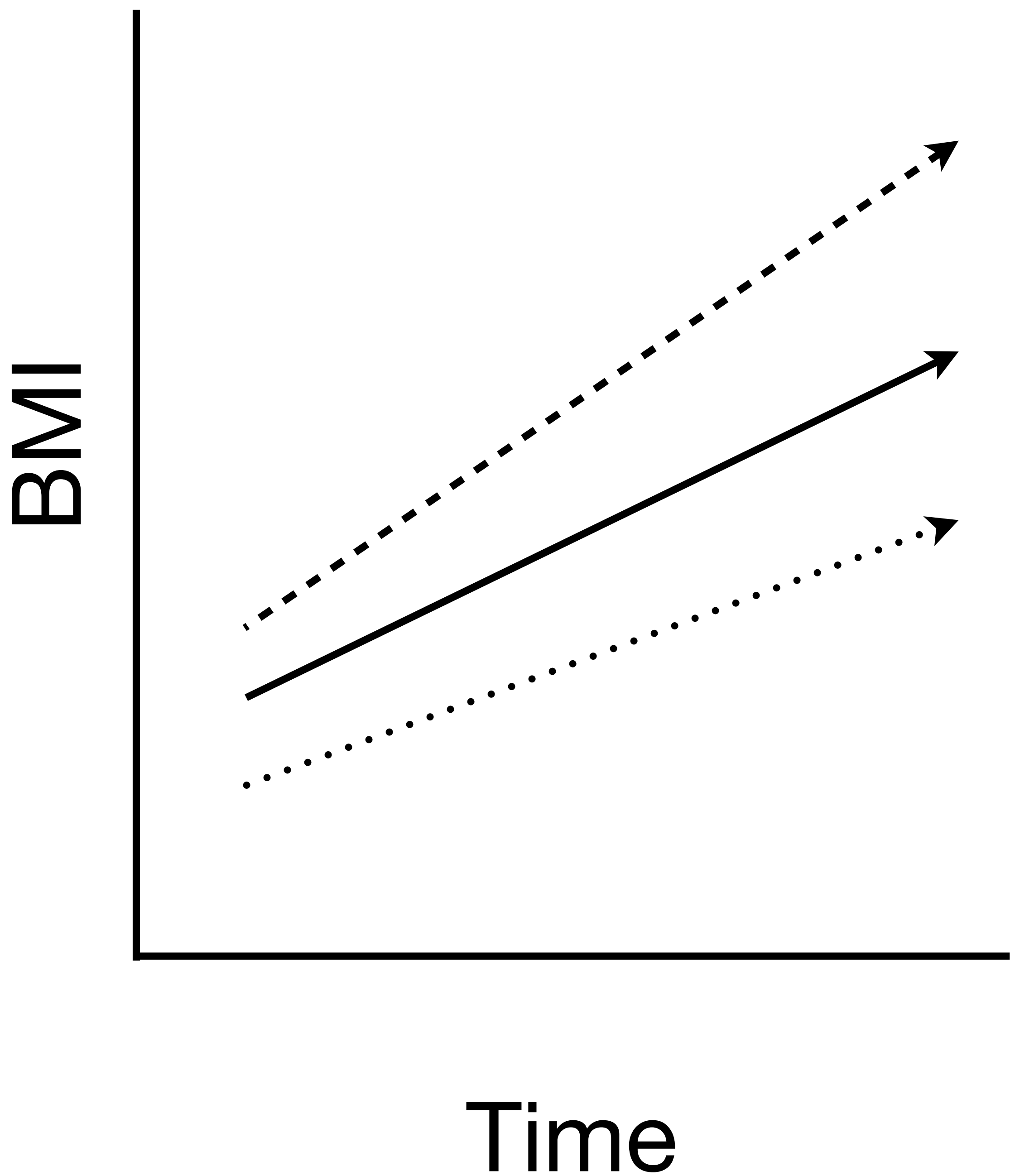


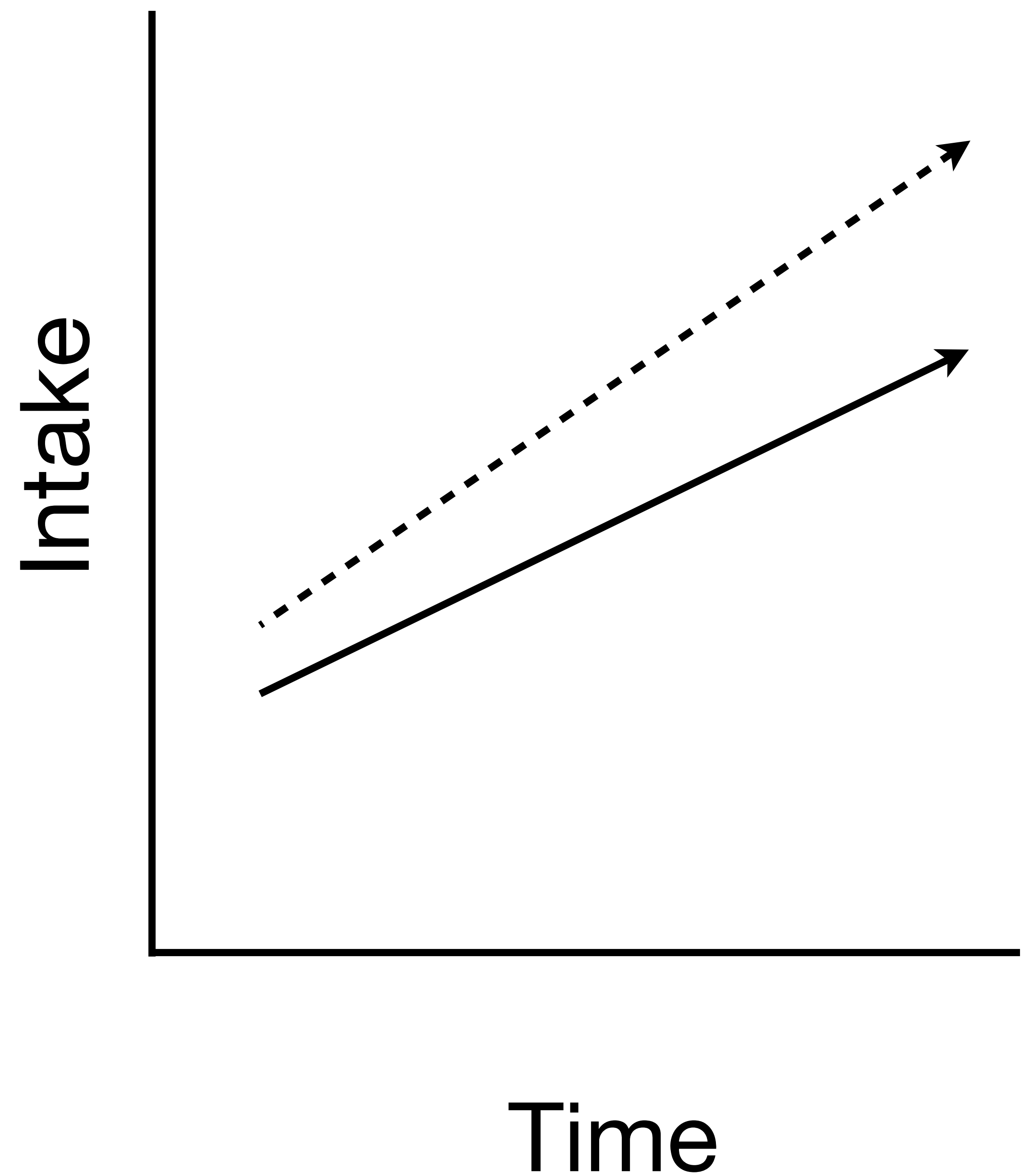
BMI = weight / height^2

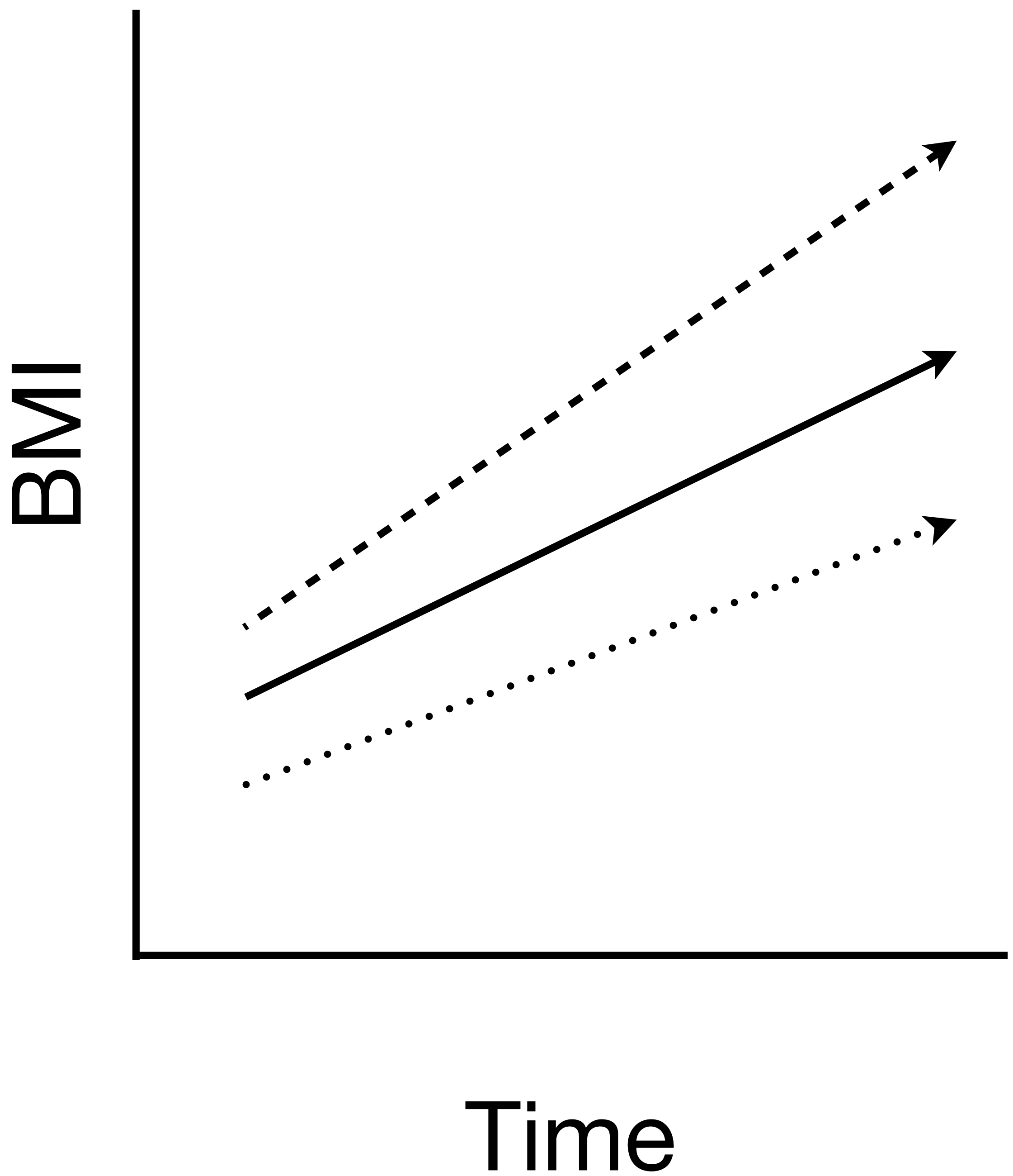
NHANES data

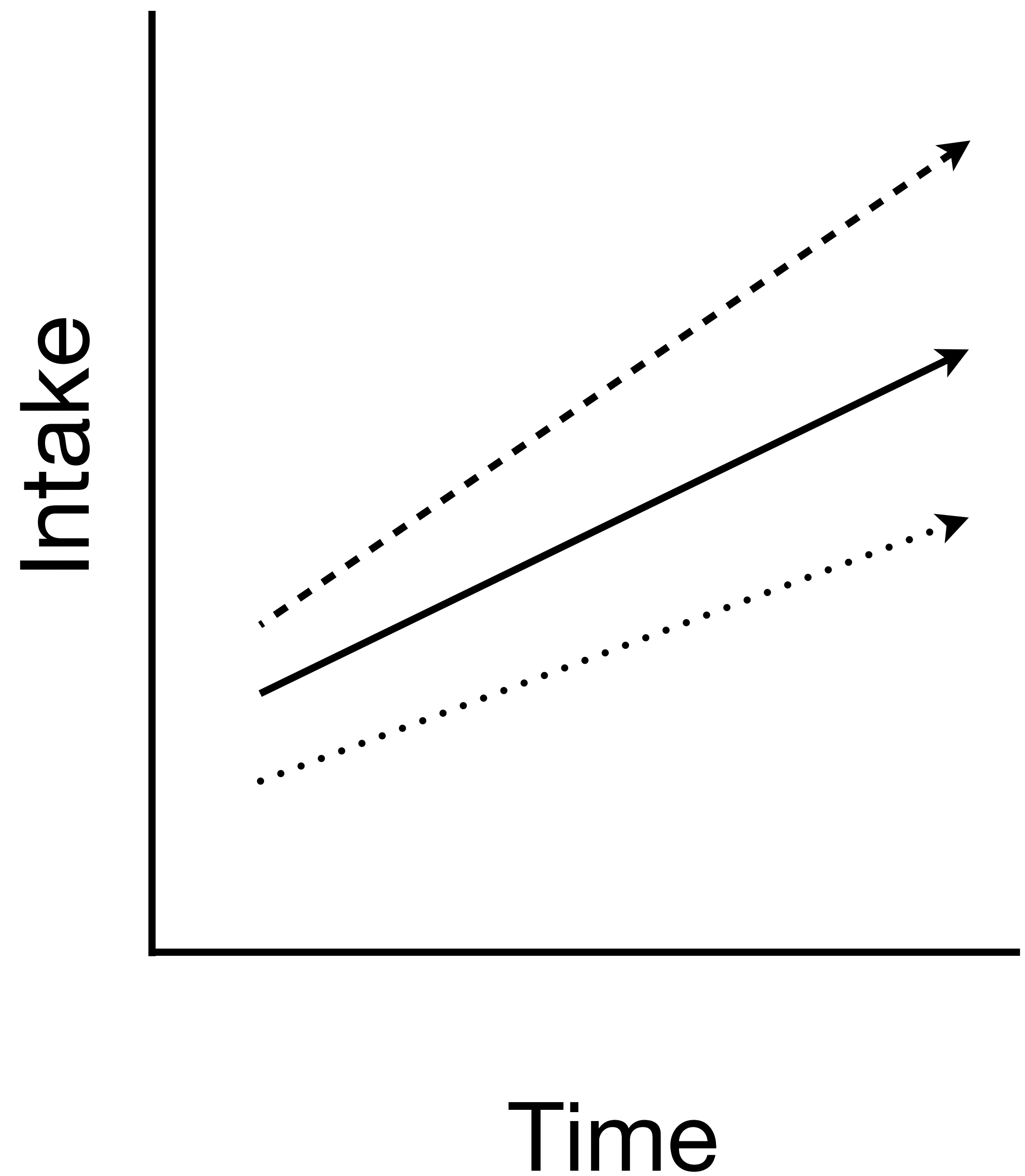

BMI
Time


BMI
Time
Intake
Time

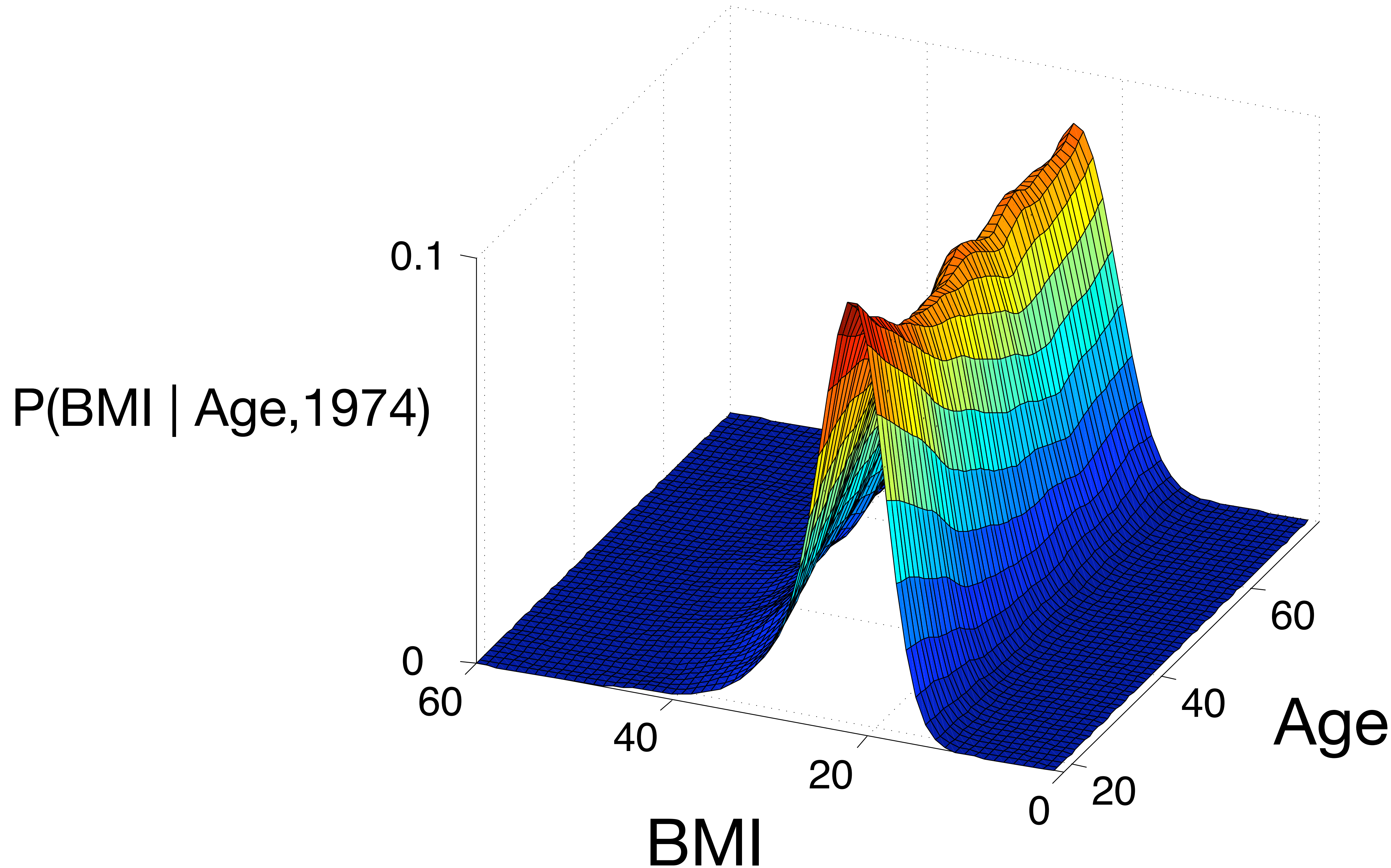

BMI
Time


Intake
Time

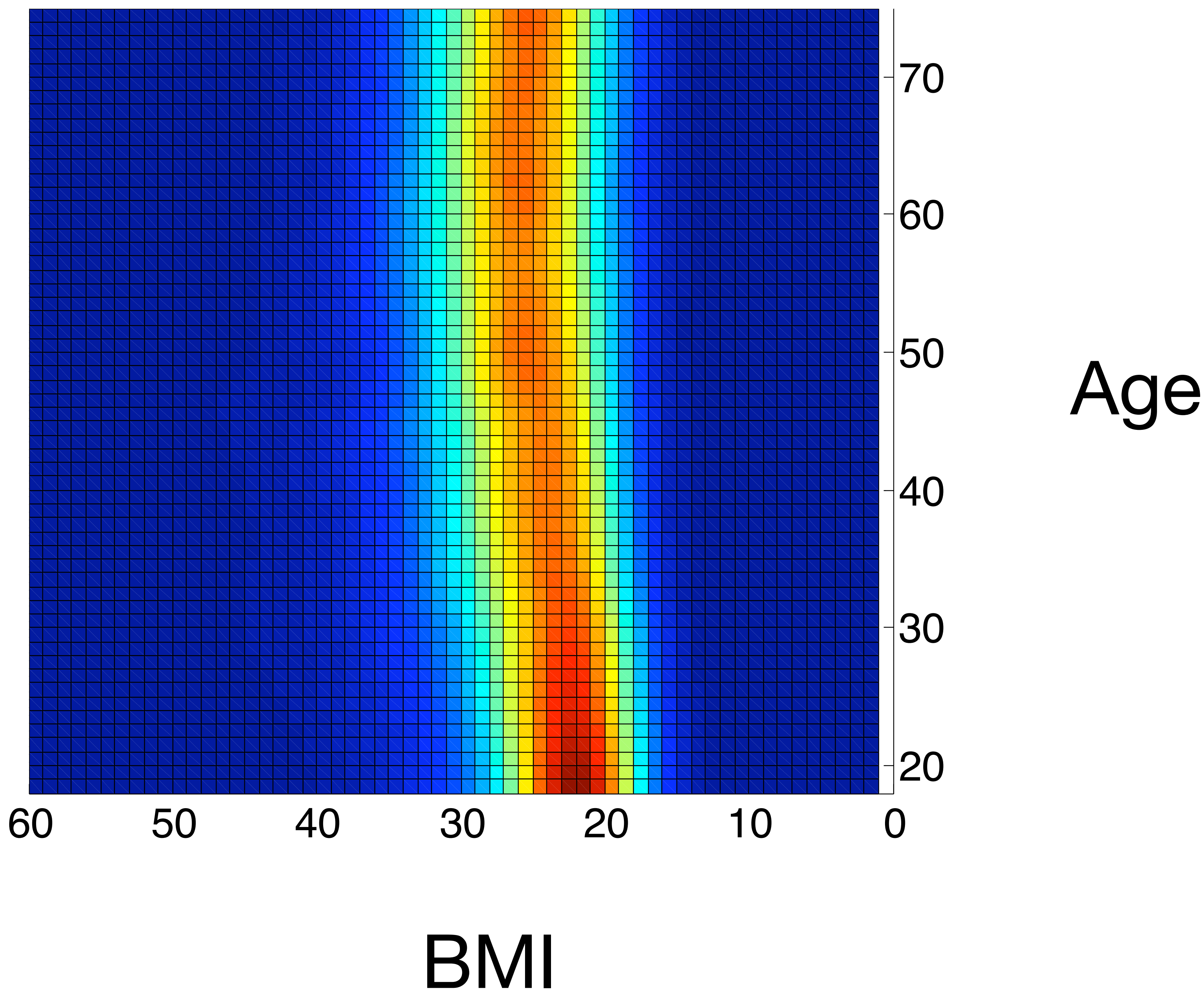

BMI
Time


Intake
Time

BMI distribution 1974

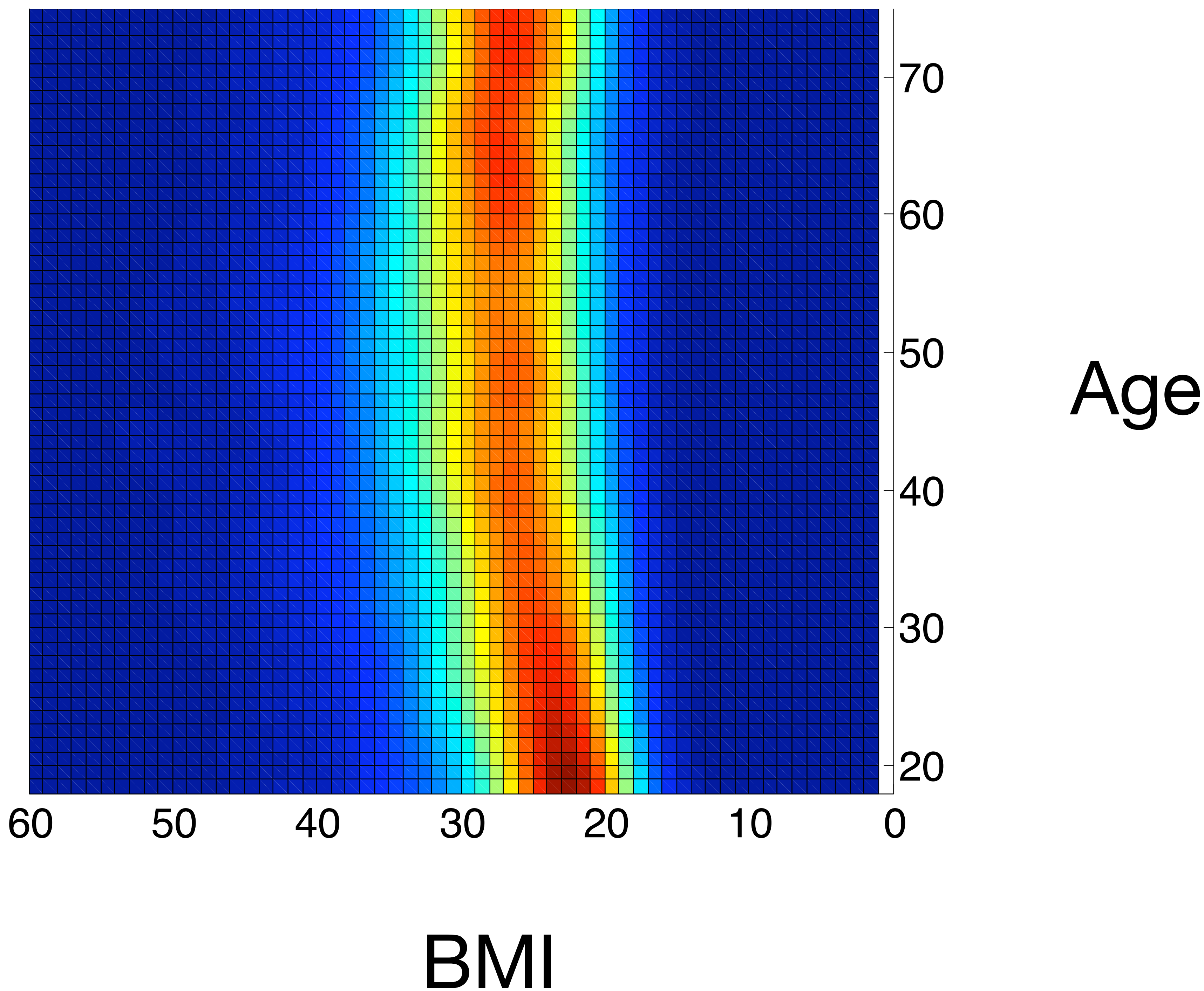


BMI distribution 1974

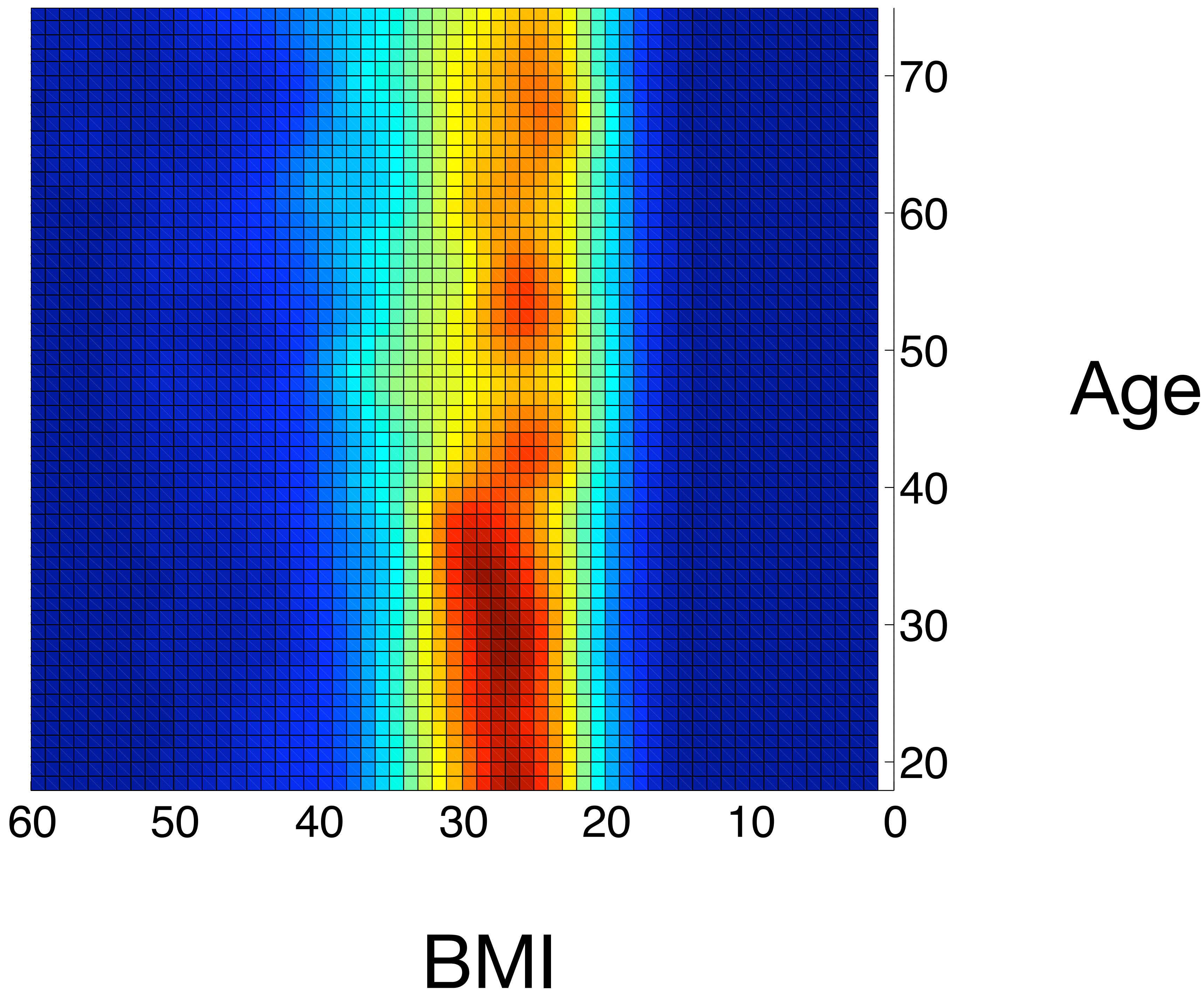


Monday, July 12, 2010

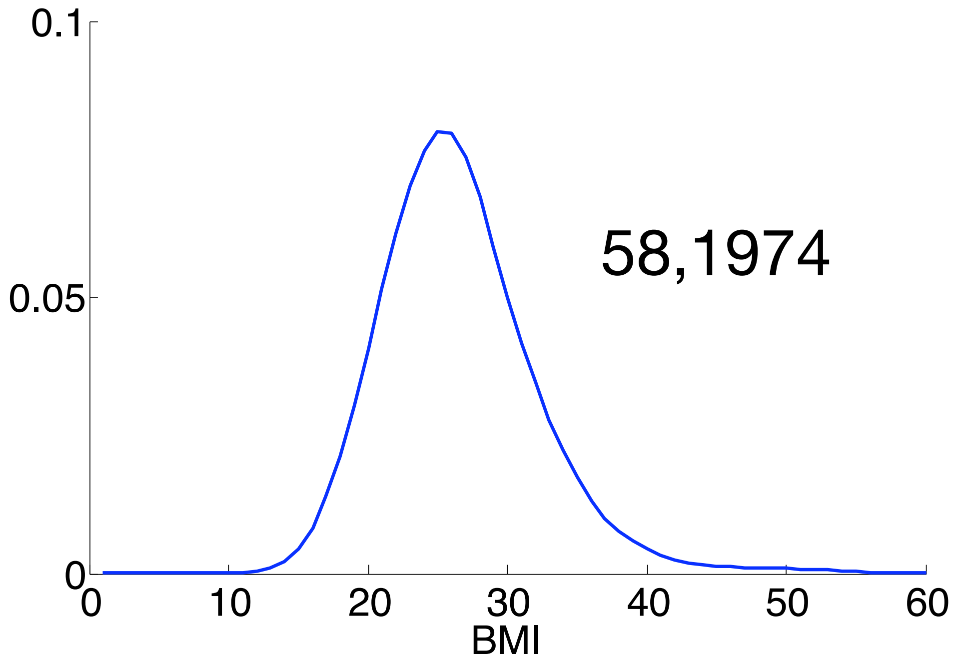
BMI distribution 1992



BMI distribution 2005

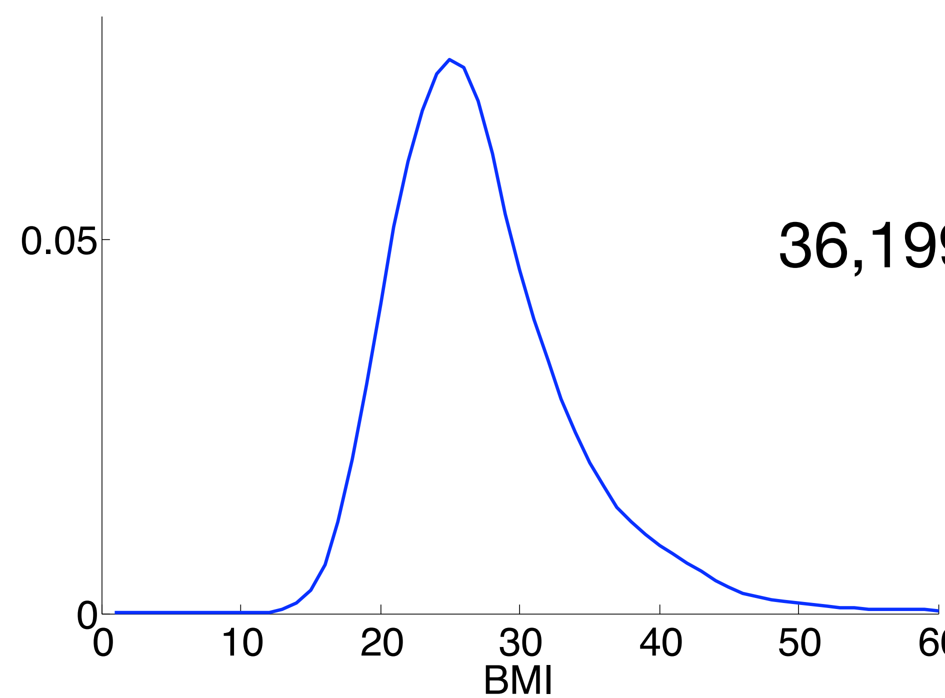


BMI map

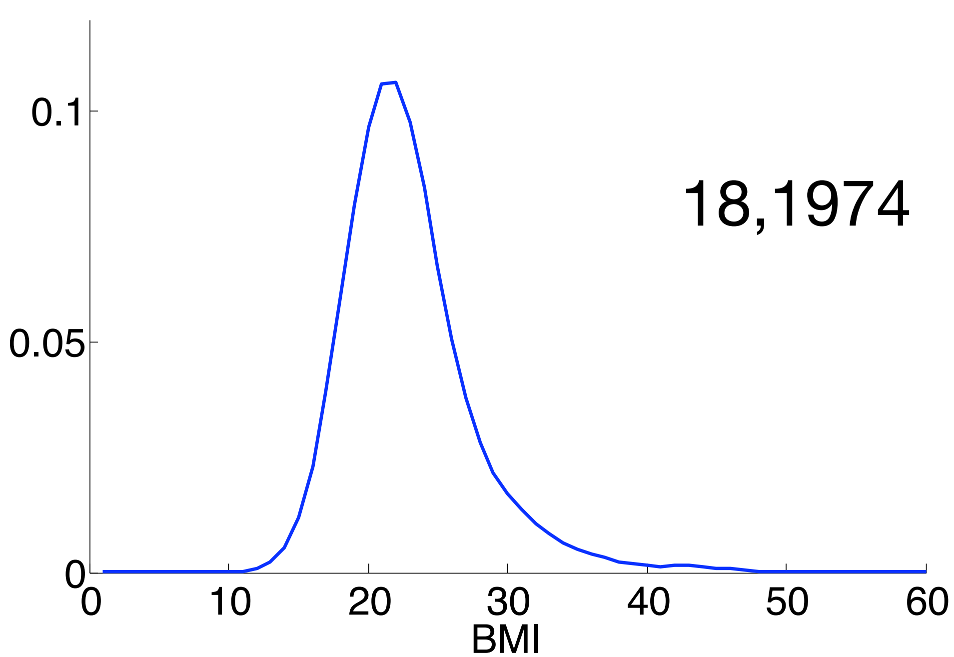


58,1974

$$g : \mathbb{R}^3 \rightarrow \mathbb{R}$$

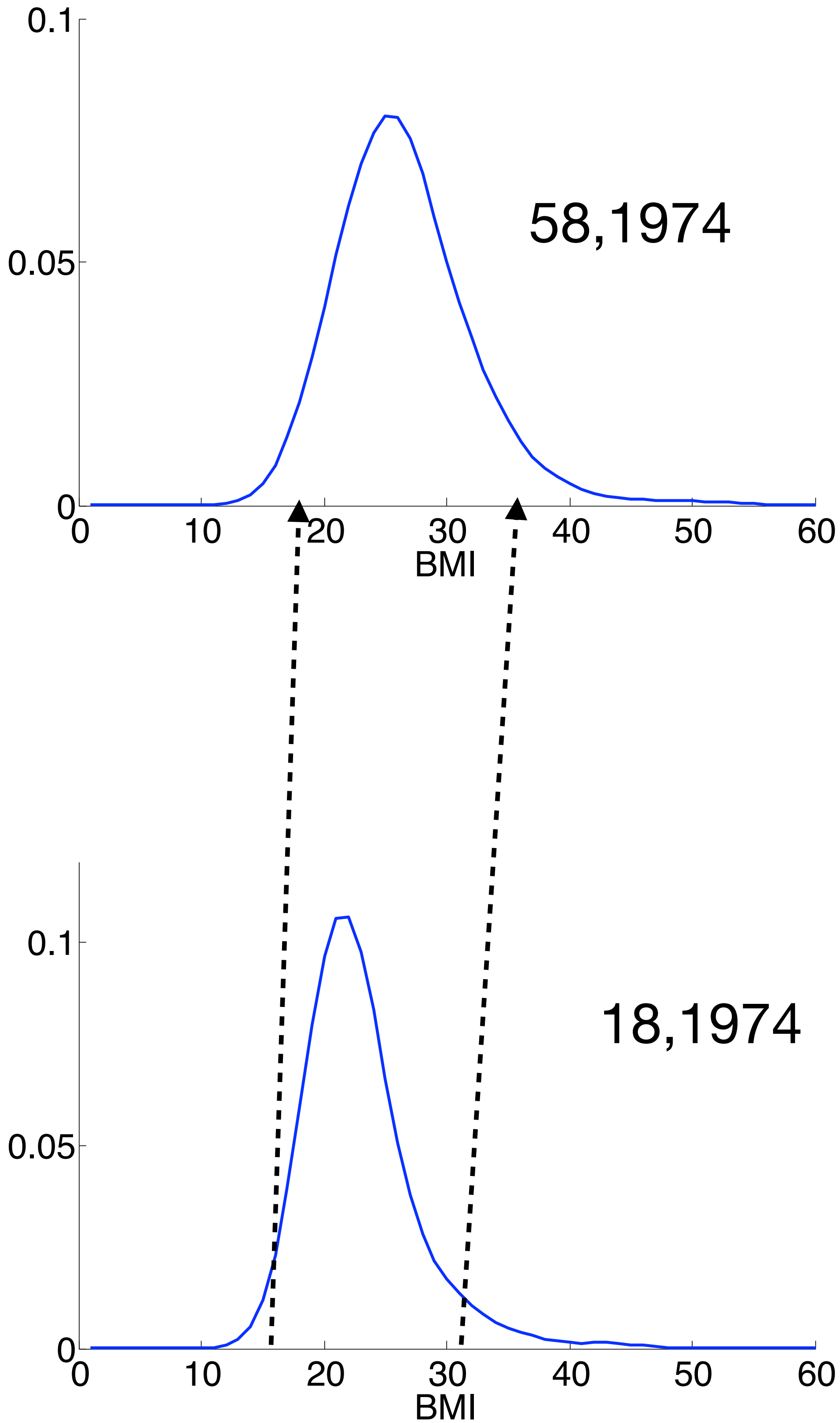


36,1992

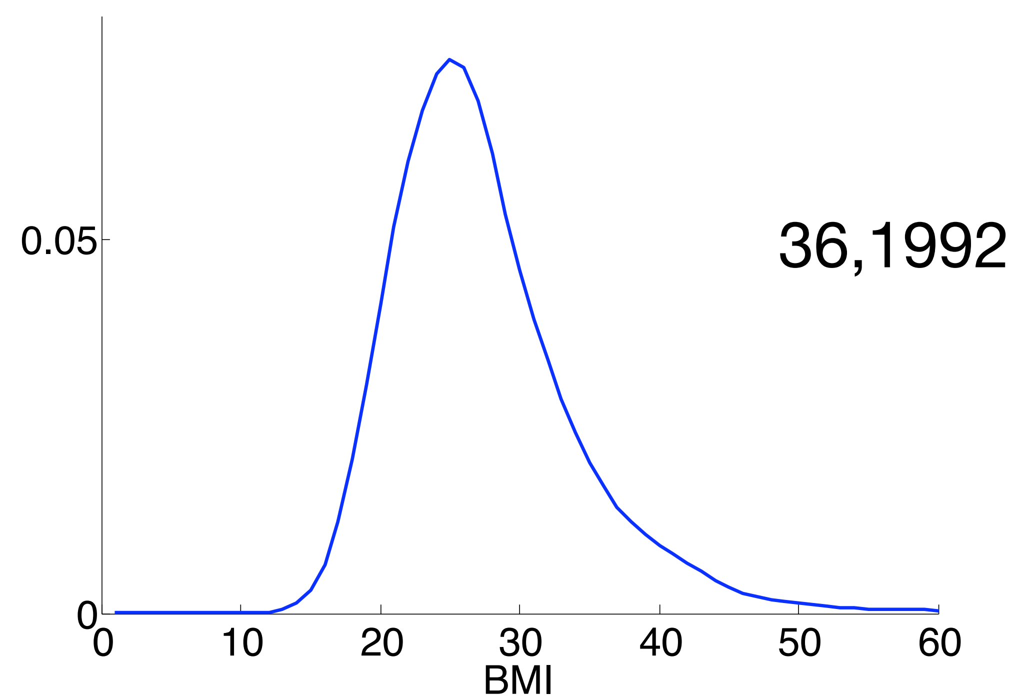


18,1974

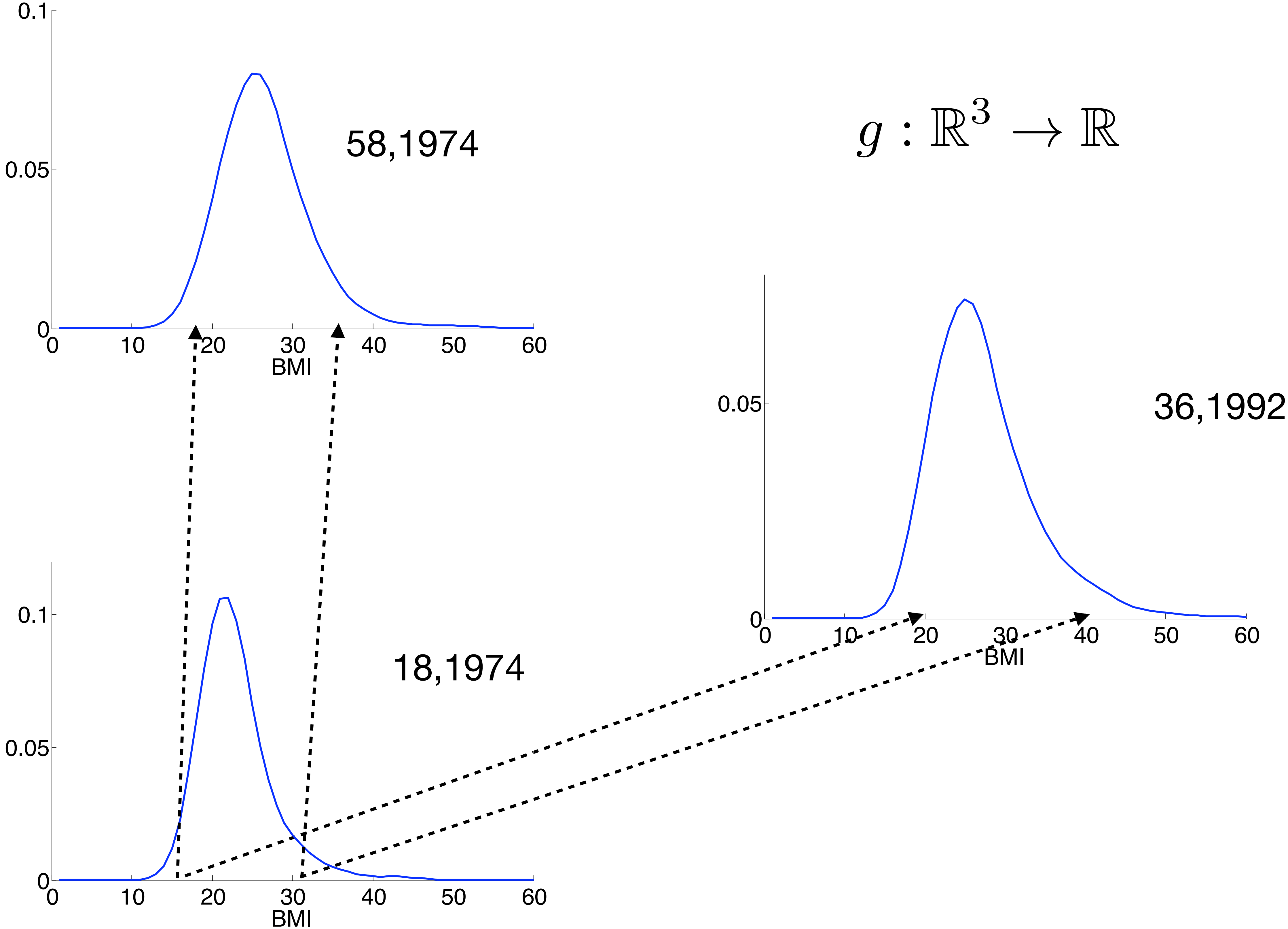
BMI map



$$g : \mathbb{R}^3 \rightarrow \mathbb{R}$$



BMI map


58,1974
$g : \mathbb{R}^3 \to \mathbb{R}$
36,1992
18,1974
BMI
0.1
0.05
0
0
10
20
30
40
50
60

BMI map

$$B(A, Y) = g(B(0,0), A, Y)$$

B = BMI

A = Age -18

Y = Year -1974

BMI map

$$B(A, Y) = g(B(0,0), A, Y)$$

B = BMI
A = Age -18
Y = Year -1974

- Use Bayesian Model Comparison, e.g. MS50

BMI map

B = BMI

A = Age -18

Y = Year -1974

$$B(A,Y) = g(B(0,0),A,Y)$$

- Use Bayesian Model Comparison, e.g. MS50

$$\chi^2 = \sum_{A,Y}\left(P[g(B,A,Y)|A,Y]\frac{dg}{dB} - P[B|0,0]\right)^2$$

BMI map

B = BMI
A = Age -18
Y = Year -1974

$$B(A,Y) = g(B(0,0),A,Y)$$

- Use Bayesian Model Comparison, e.g. MS50

$$\chi^2 = \sum_{A,Y} \left(P[g(B,A,Y)|A,Y]\frac{dg}{dB} - P[B|0,0] \right)^2$$

Does Forbes law explain distribution change?

BMI map

B = BMI
A = Age -18
Y = Year -1974

$$B(A,Y) = g(B(0,0),A,Y)$$

- Use Bayesian Model Comparison, e.g. MS50

$$\chi^2 = \sum_{A,Y} \left(P[g(B,A,Y)|A,Y] \frac{dg}{dB} - P[B|0,0] \right)^2$$

Does Forbes law explain distribution change?

$$\frac{P(\text{Not Forbes}^*|\text{NHANES})}{P(\text{Forbes}|\text{NHANES})} \simeq 1.6$$

Best model

Best model

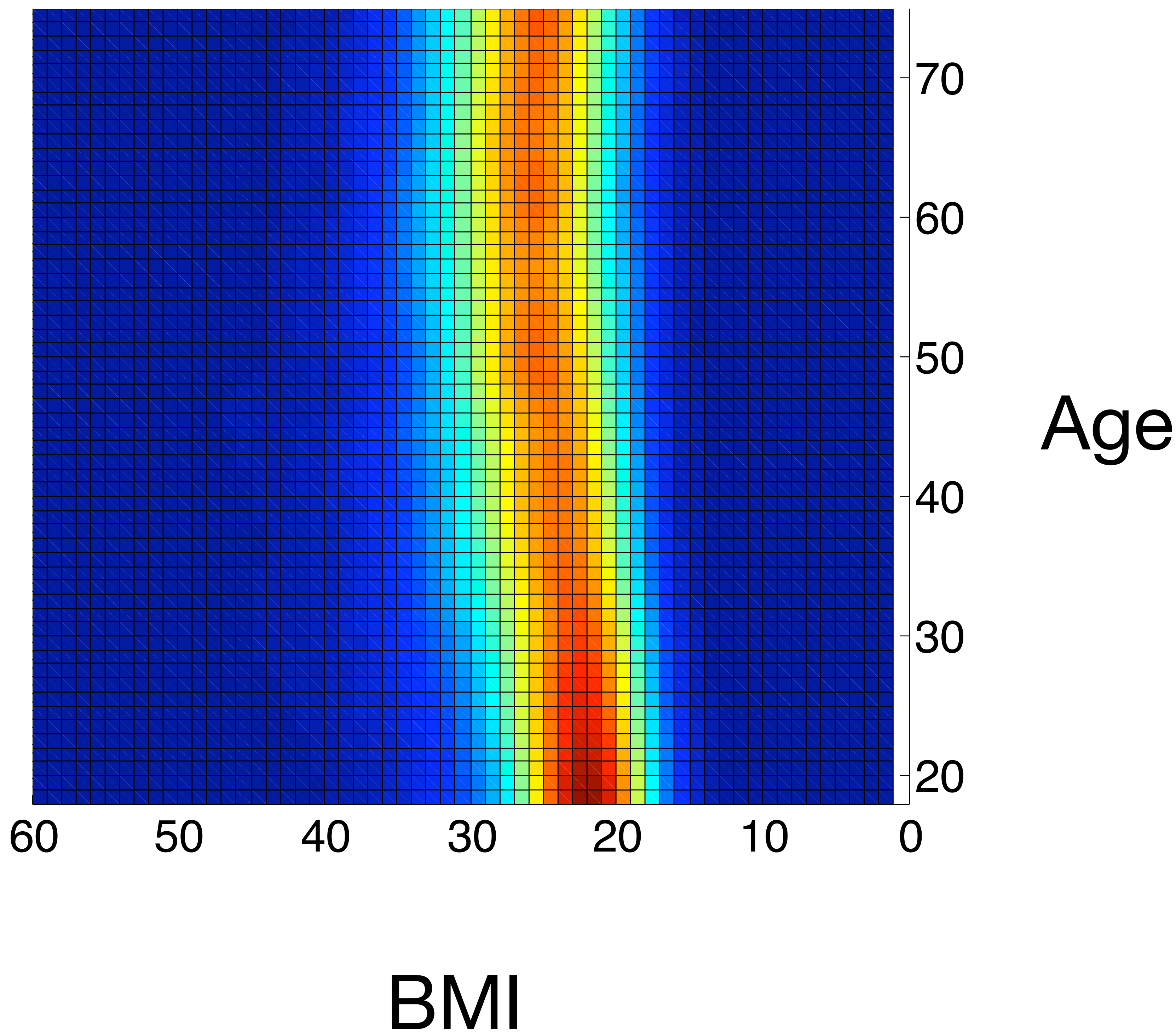
$$B(A,Y) = B(0,0)(1 + 0.0049A + 0.015Y) - 0.038A - 0.20Y$$

Best model

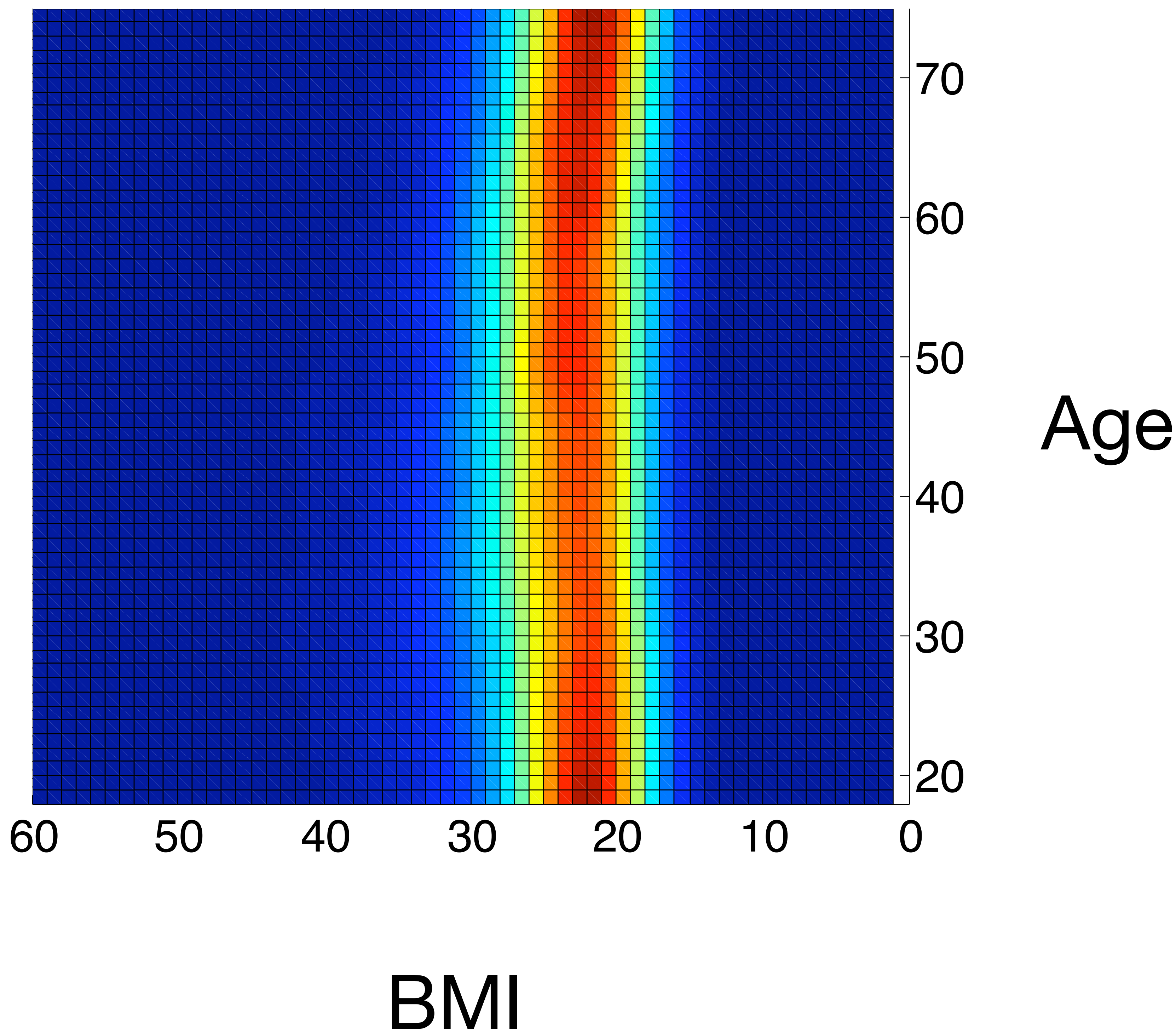
$$B(A,Y) = B(0,0)(1 + 0.0049A + 0.015Y) - 0.038A - 0.20Y$$

$$B(A_2,Y_2) = (B(A_1,Y_1) + 0.038A_1 + 0.2Y_1)\frac{1 + 0.0049A_2 + 0.015Y_2}{1 + 0.0049A_1 + 0.015Y_1} - 0.038A_2 - 0.2Y_2$$

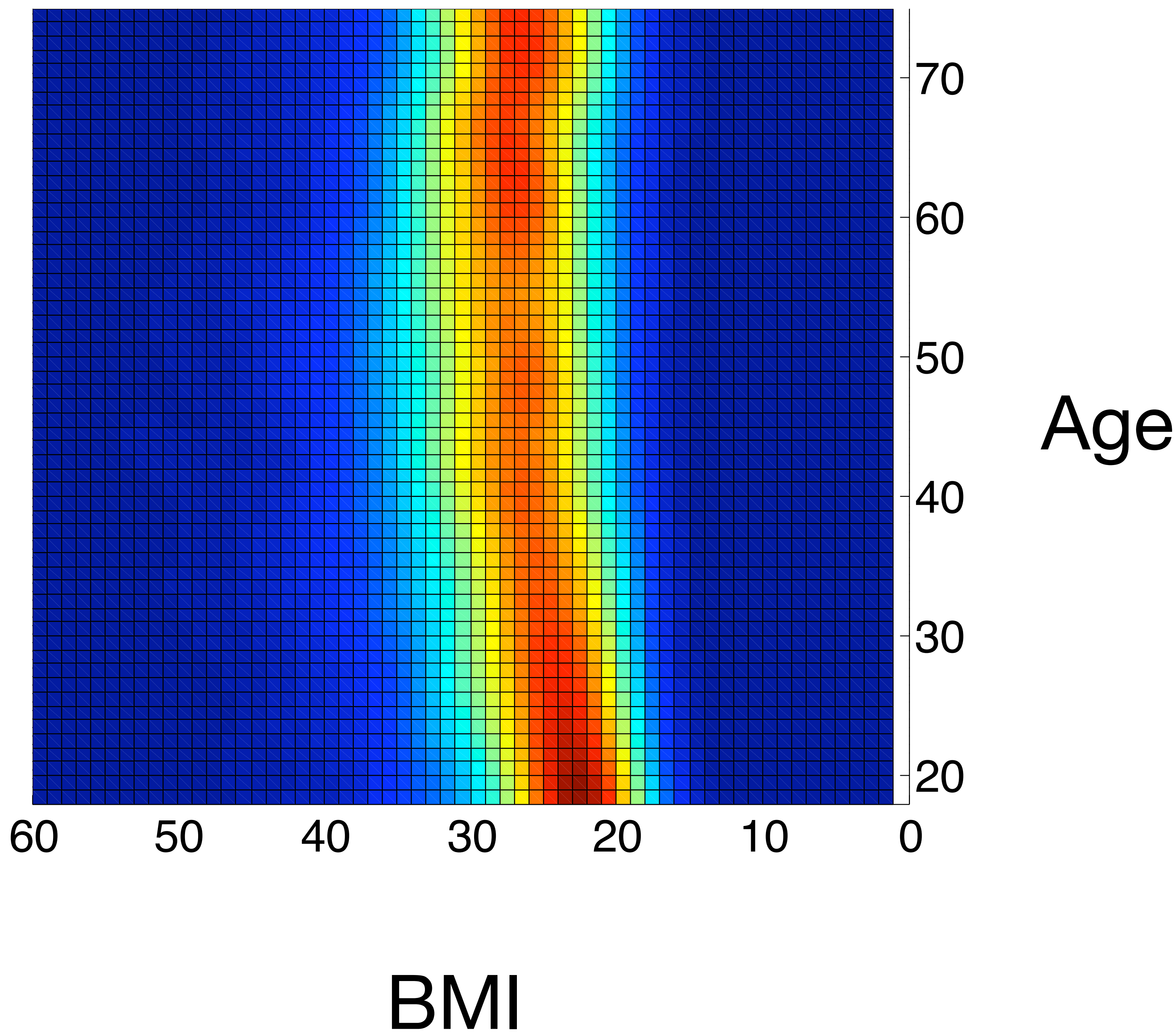
1974



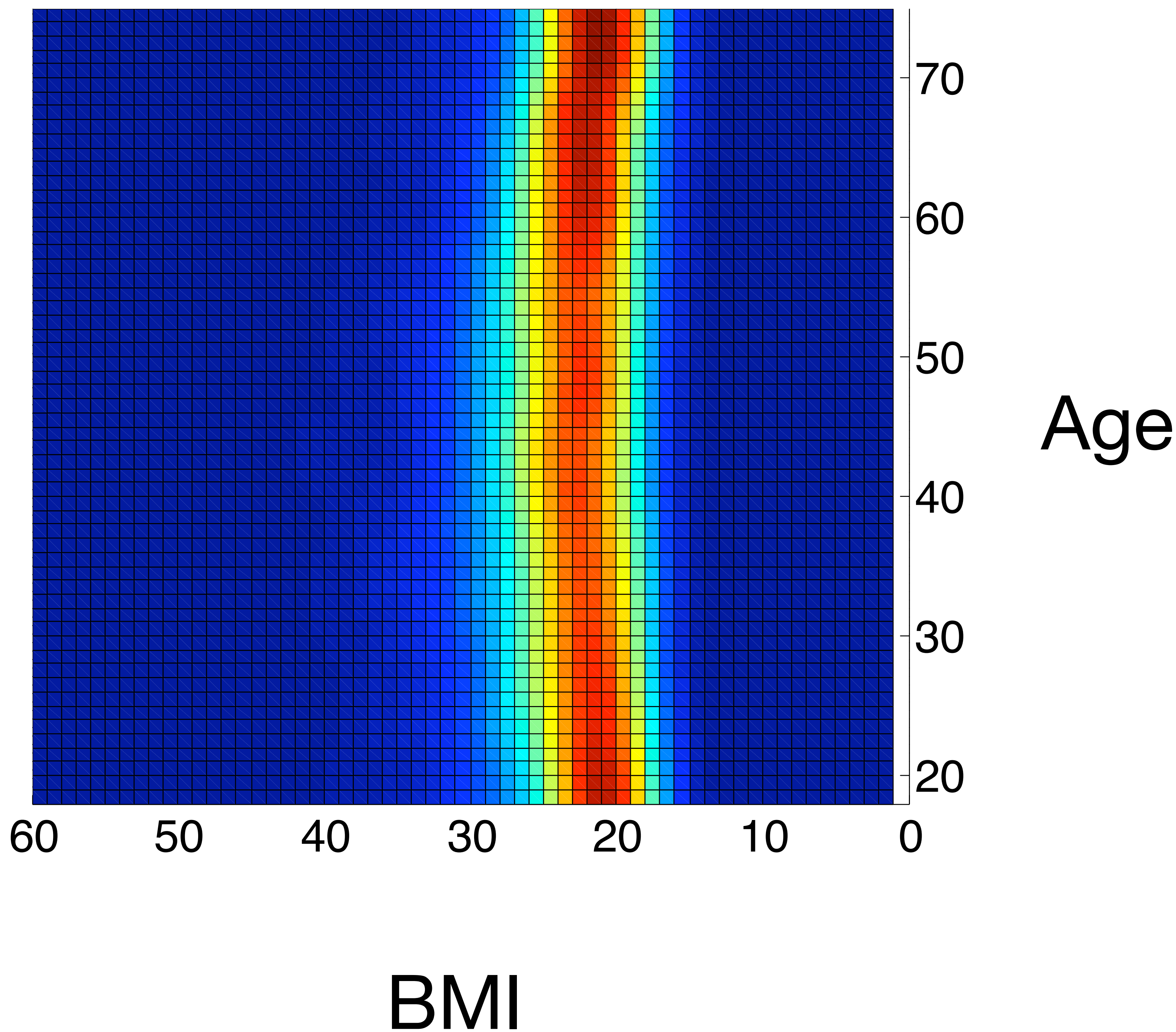
Transformed 1974



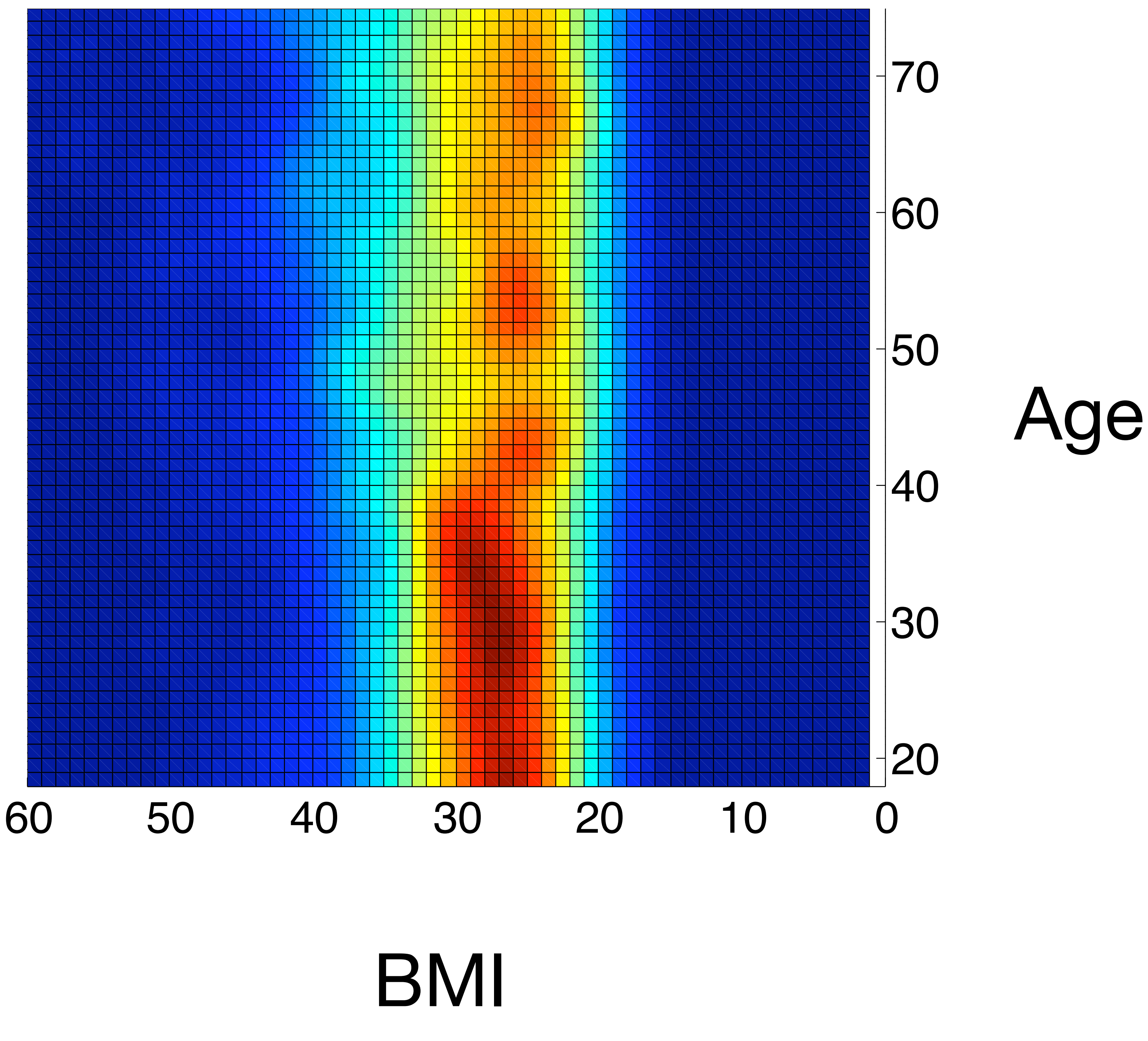
1985



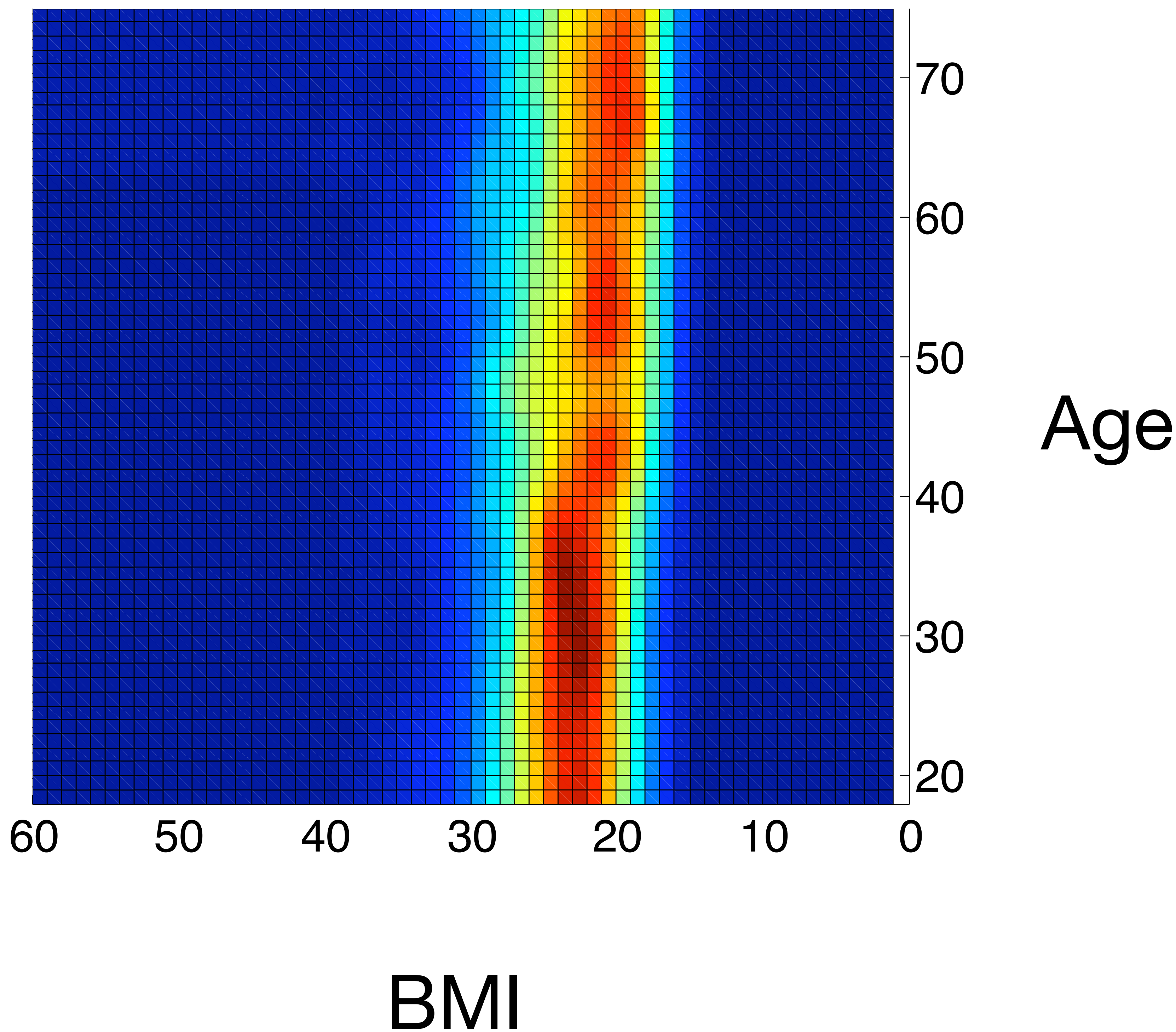
Transformed 1985

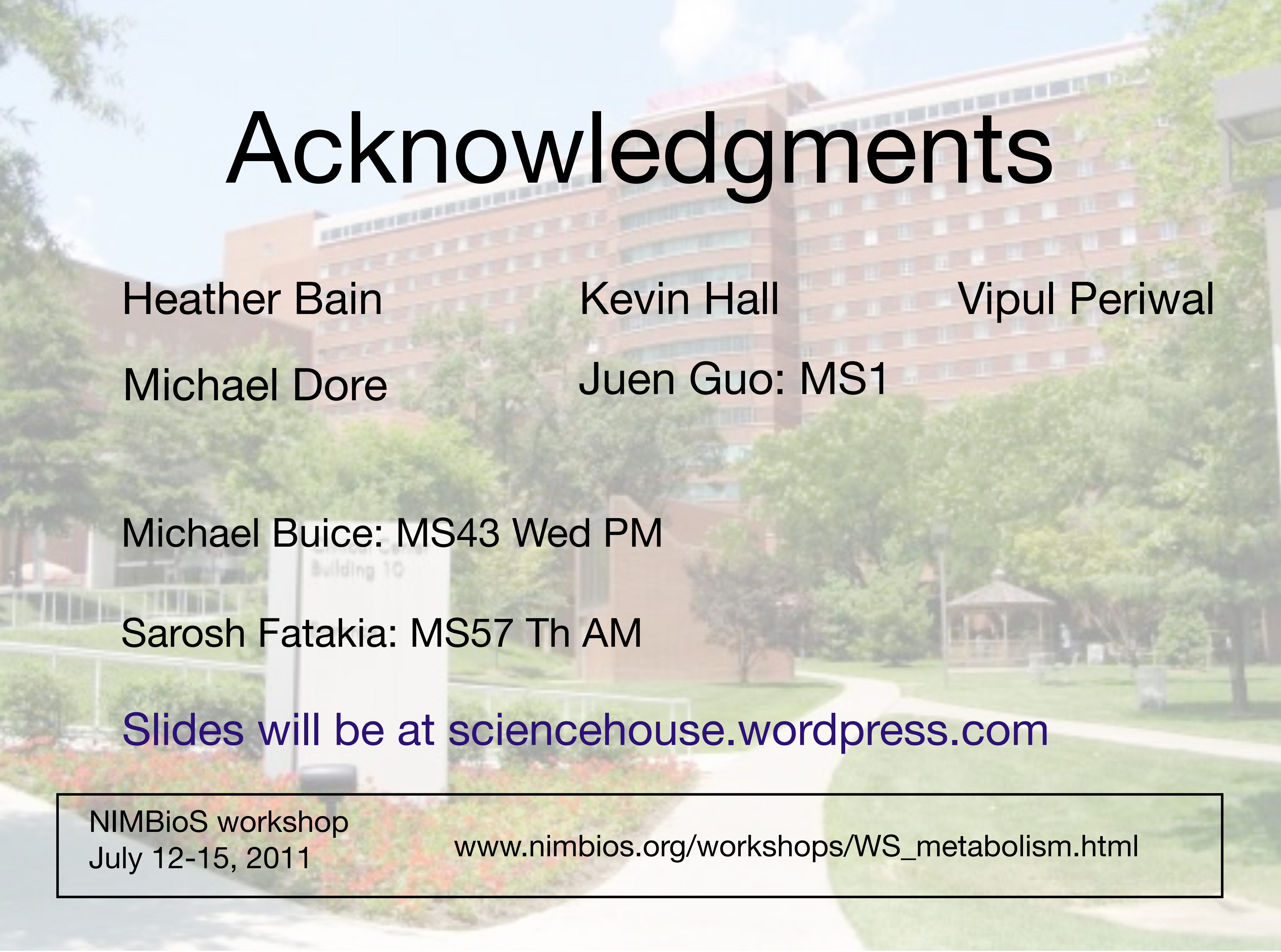


2005



Transformed 2005





Acknowledgments

Heather Bain

Kevin Hall

Vipul Periwal

Michael Dore

Juen Guo: MS1

Michael Buice: MS43 Wed PM

Sarosh Fatakia: MS57 Th AM

Slides will be at sciencehouse.wordpress.com

NIMBioS workshop
July 12-15, 2011

www.nimbios.org/workshops/WS_metabolism.html