



Glucose and Insulin Responses Modeling

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Introduction: Objectives

- To model the glucose and insulin response
- To evaluate influence on the extreme condition on body glucose level
 - **Reduced or No insulin production**
 - **Reduced or No Liver function**
 - **Reduced or No Kidney function**
 - **Different insulin delivery methods**
- **Basic model: www.Aida.org**

Introduction: Model

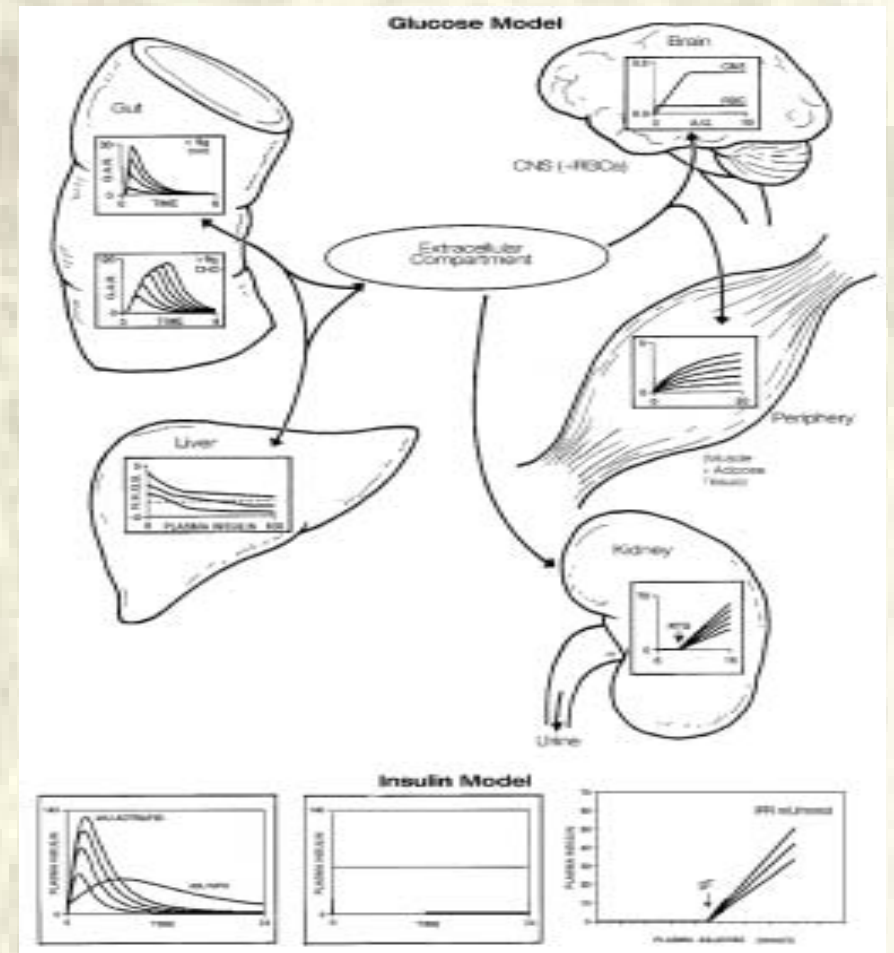
- Single glucose pool
 - **One compartment model**
- Glucose enters via:
 - **Gut absorption,**
 - **Hepatic glucose production,**
- Glucose is removed:
 - **insulin independent glucose utilization**
 - **insulin dependent glucose utilization,**
 - **excretion of glucose by the kidney,**

G_{in}
 $NHGB$

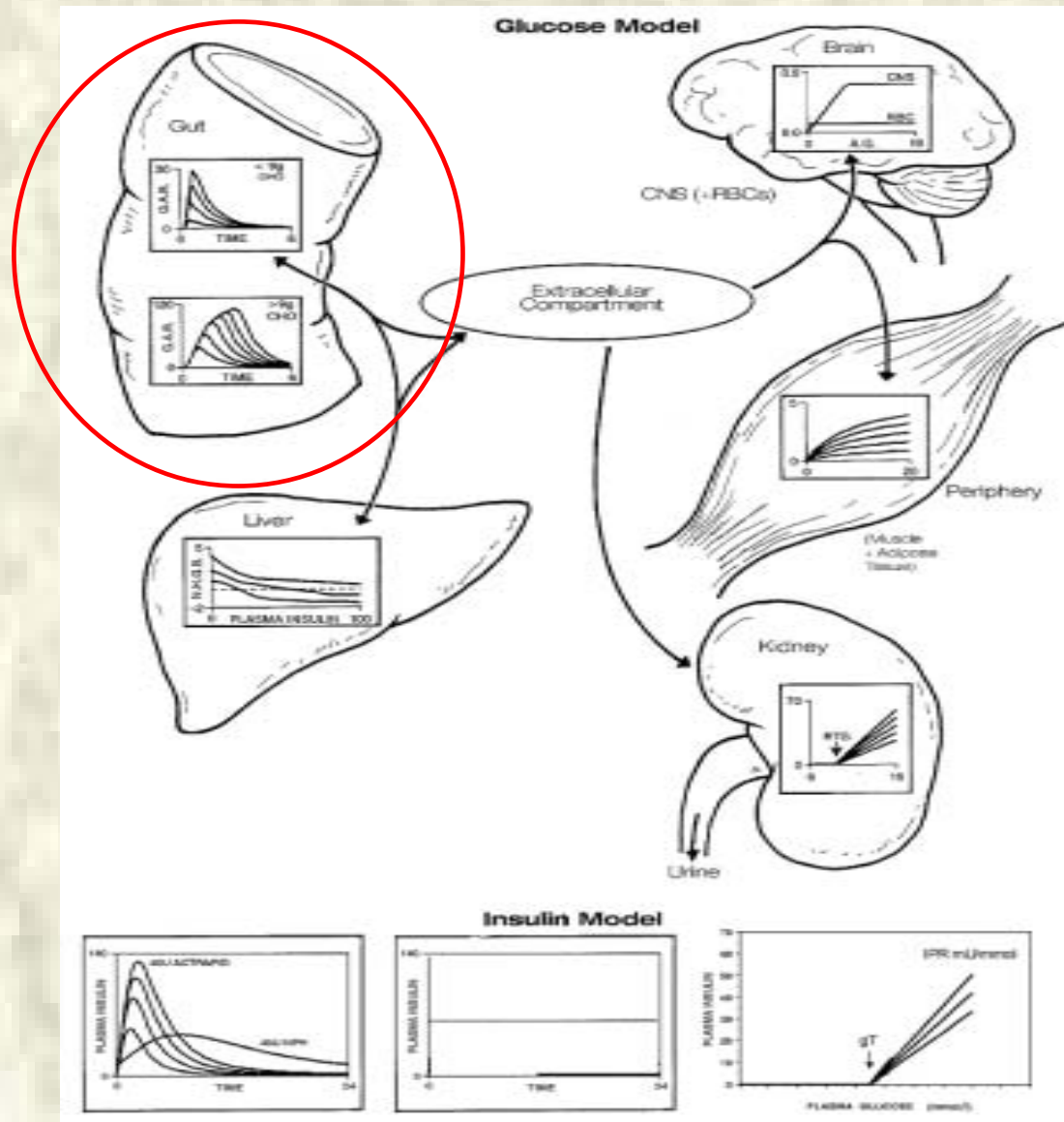
ρG_{out}

G_{ren}

$$\frac{dG}{dt} = \frac{G_{in} + NHGB - G_{out} - G_{ren}}{V_g}$$

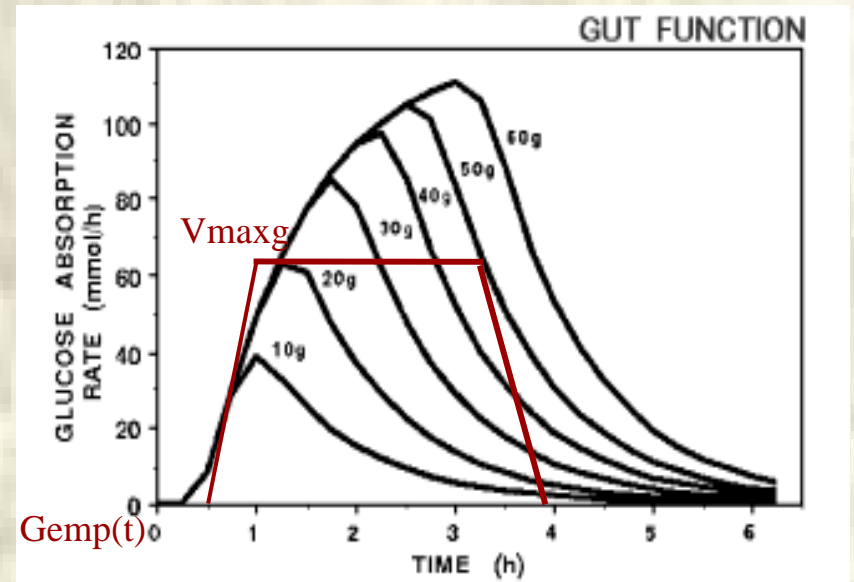


Model: Gut



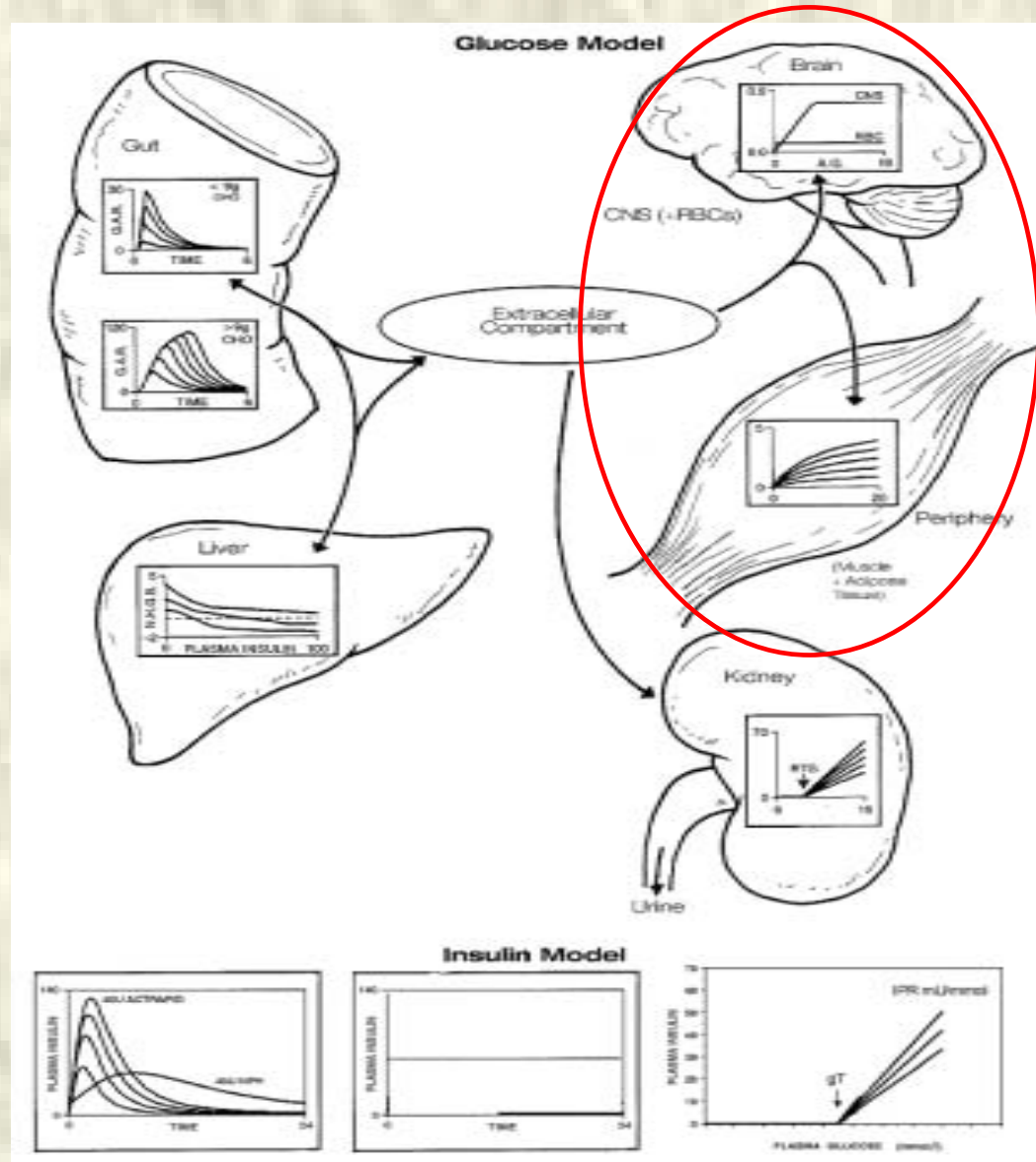
Model: Gut

- One compartment model with constant glucose supply



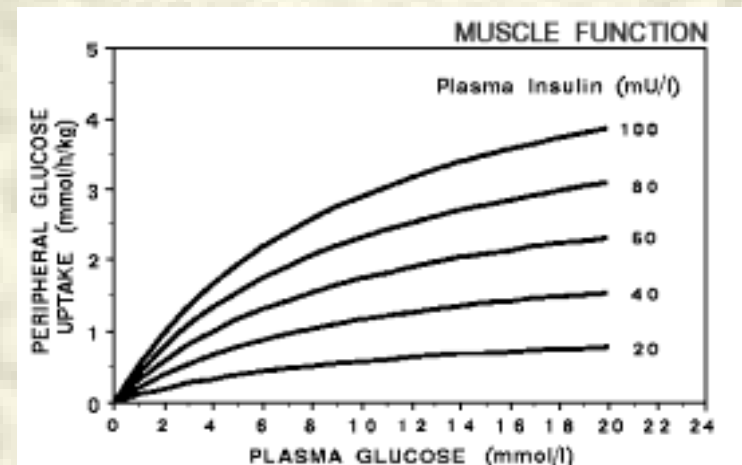
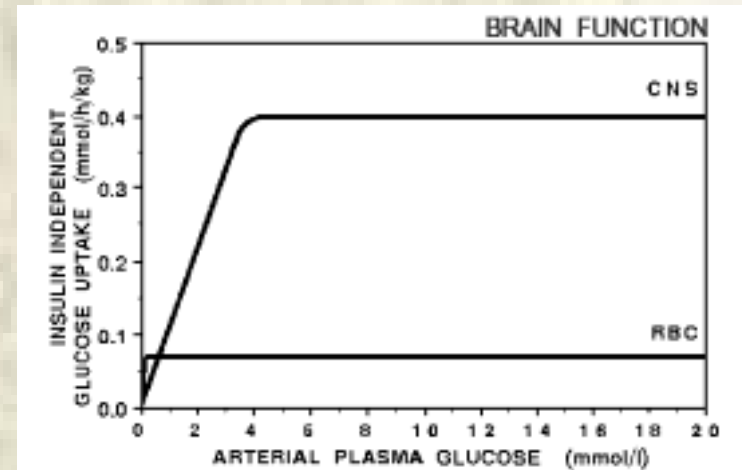
$$\frac{dG(t)_{gut}}{dt} = G(t)_{empt} - k_{gabs} G(t)_{gut}$$

Model: Utilization

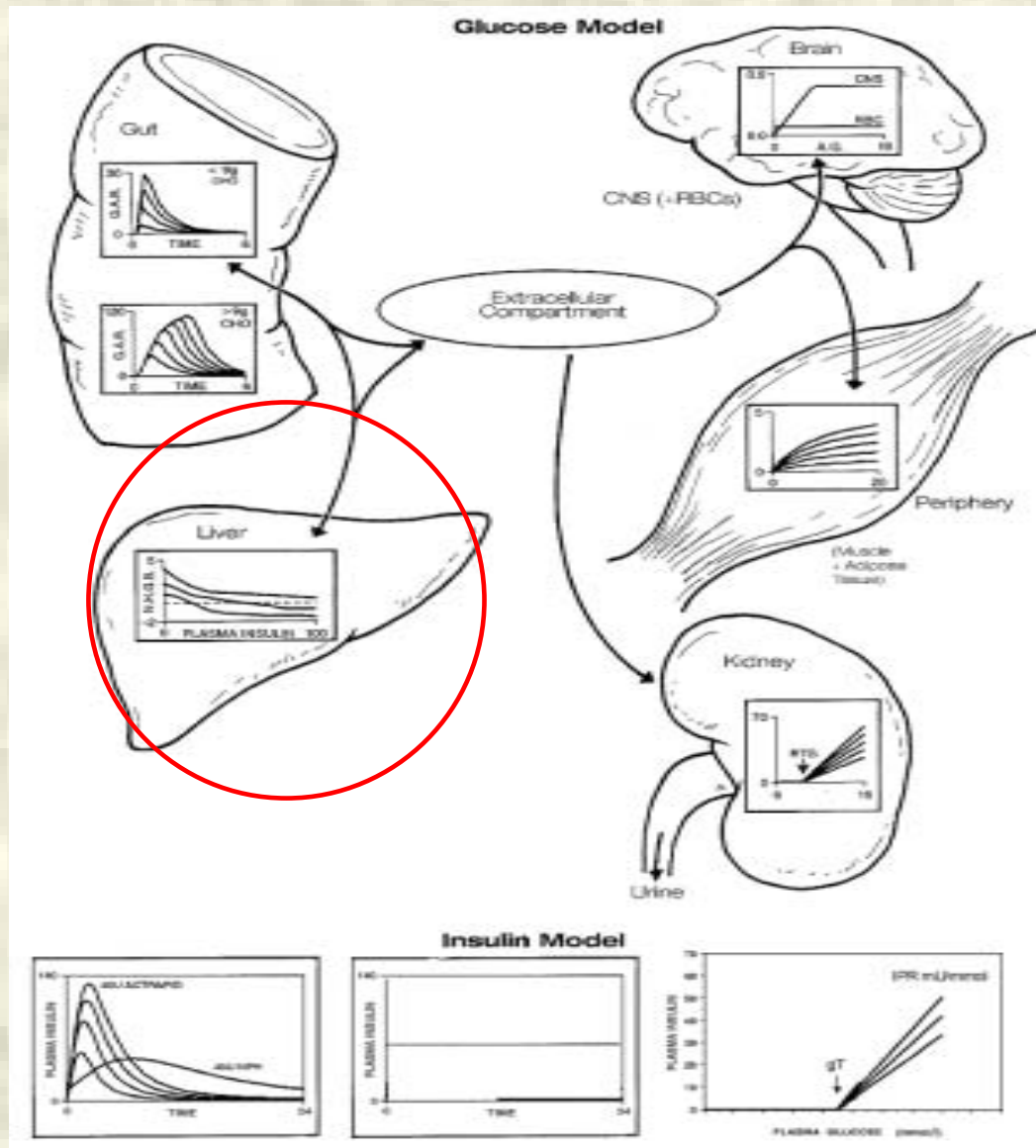


Model: Utilization

- Insulin-independent
 - red blood cells (RBCs)
 - the central nervous system (CNS),
- Insulin dependent
 - the liver
 - periphery

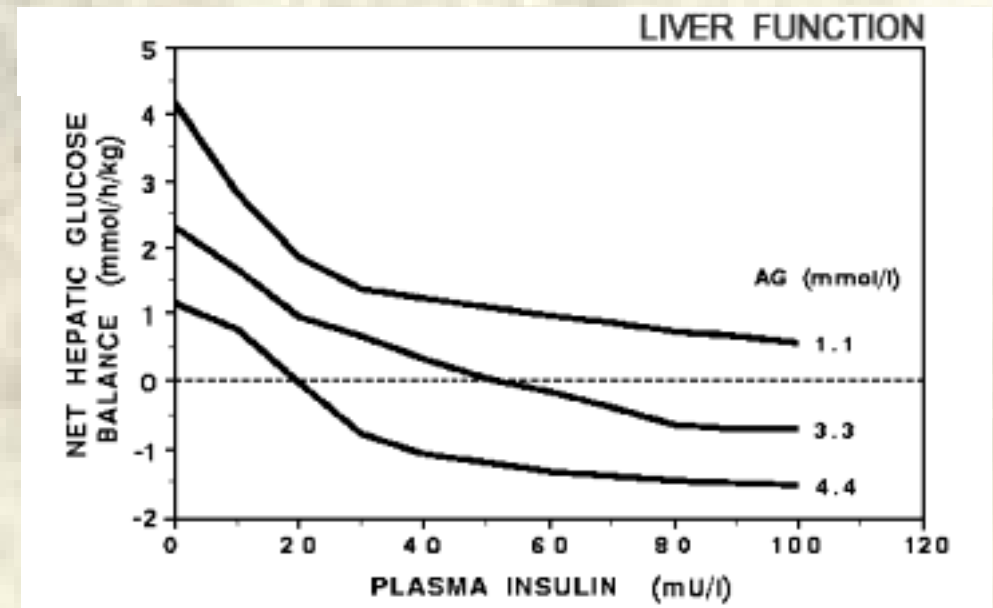


Model: Liver

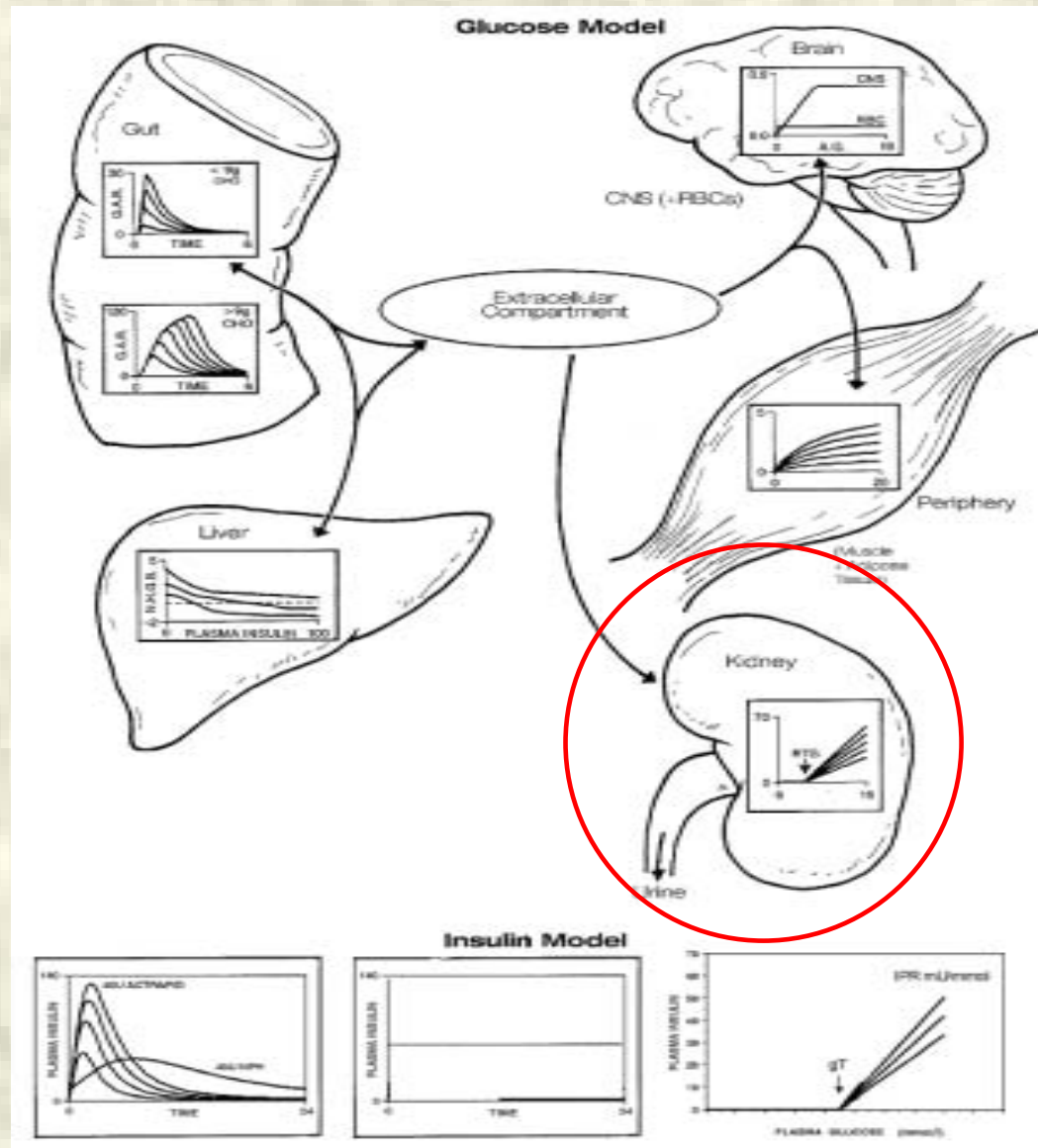


Model: Liver

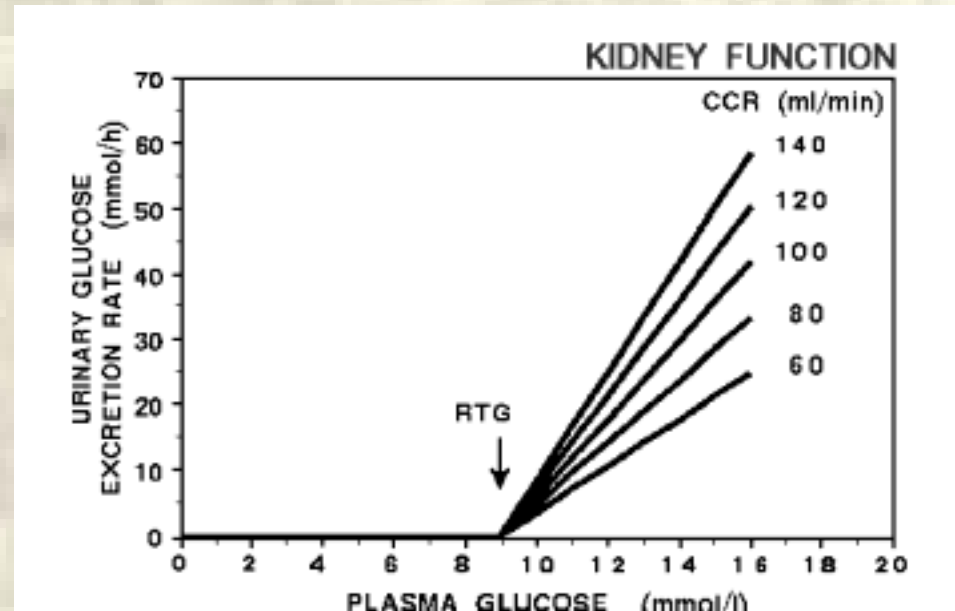
- Hepatic glucose balance
 - liver glucose production (+)
 - liver glucose utilization (-)
- Function of the
 - plasma insulin level
 - arterial glucose concentration
 - finite capacity of the liver



Model: Kidney

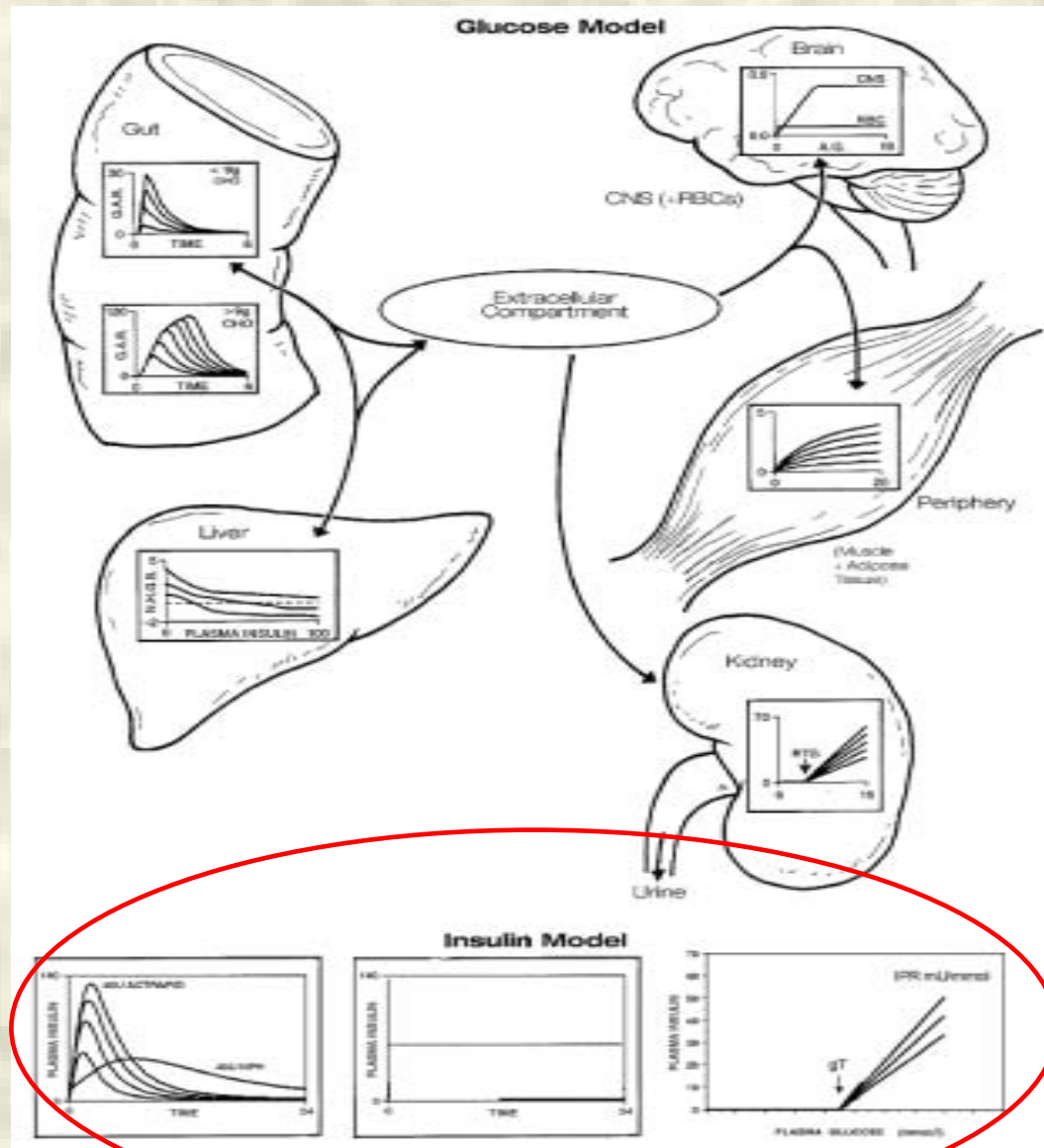


Model: Kidney



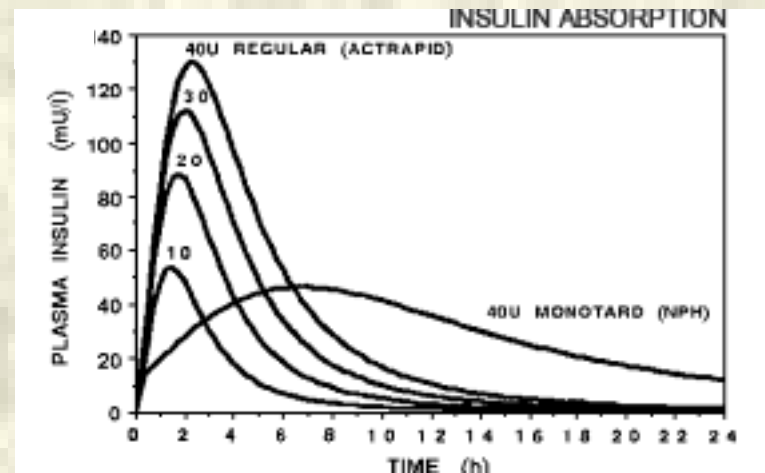
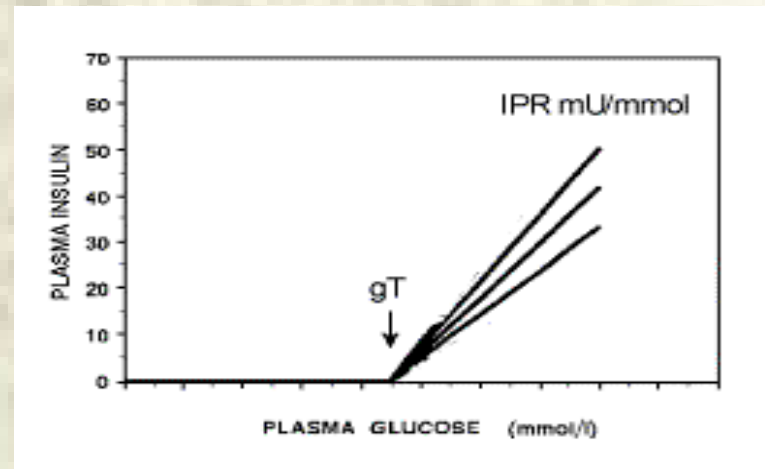
- Excretion from the blood to urine
 - renal threshold (RTG)
 - creatinine clearance rate (CCR)

Model: Insulin Input



Model: Insulin Input

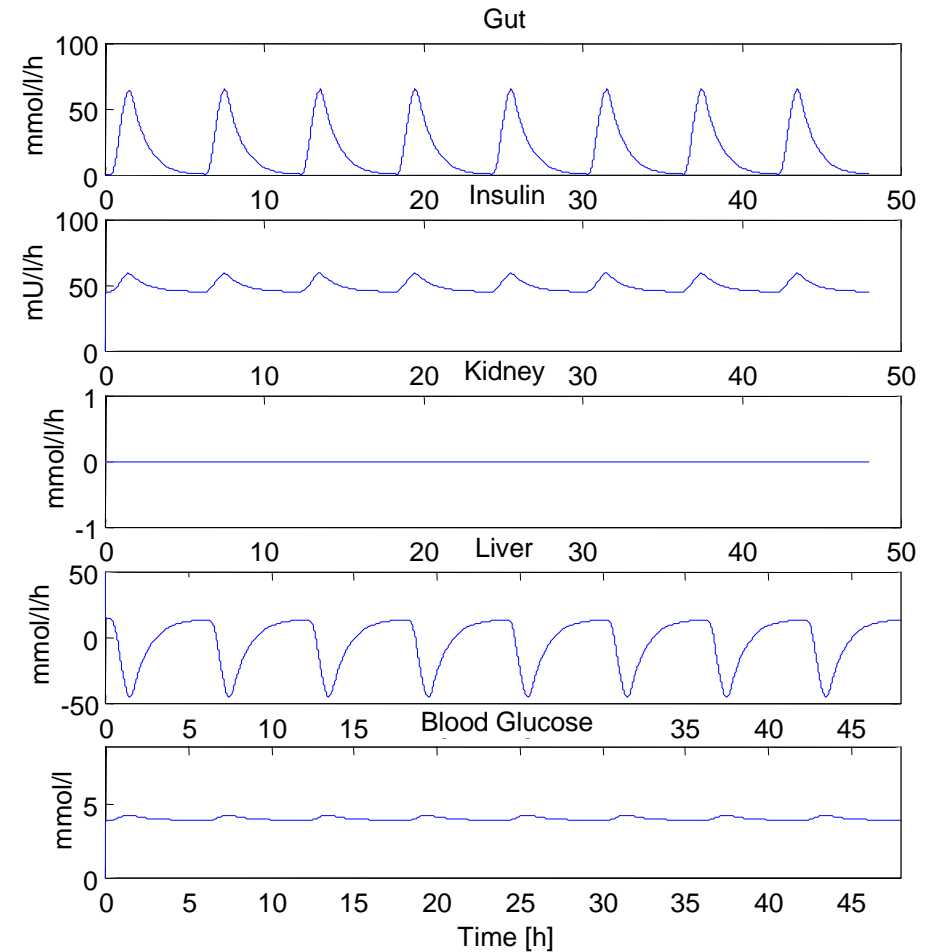
- Insulin input models:
 - **Healthy patient**
 - glucose threshold (gT)
 - insulin production rate (IPR)
 - **Injection of insulin**
 - one compartment method with delay
 - **Insulin pump with constant drip**



Results: Normal Subject

• Healthy patient

- Input : 20g/6h
- Liver buffer :100g- CH initial 50g
- CH from gut : 160.0g
- CH to peripheral: 138.4g
- CH to liver : 21.6g
- excreted : 0.0g
- delivered insulin: 2374mU

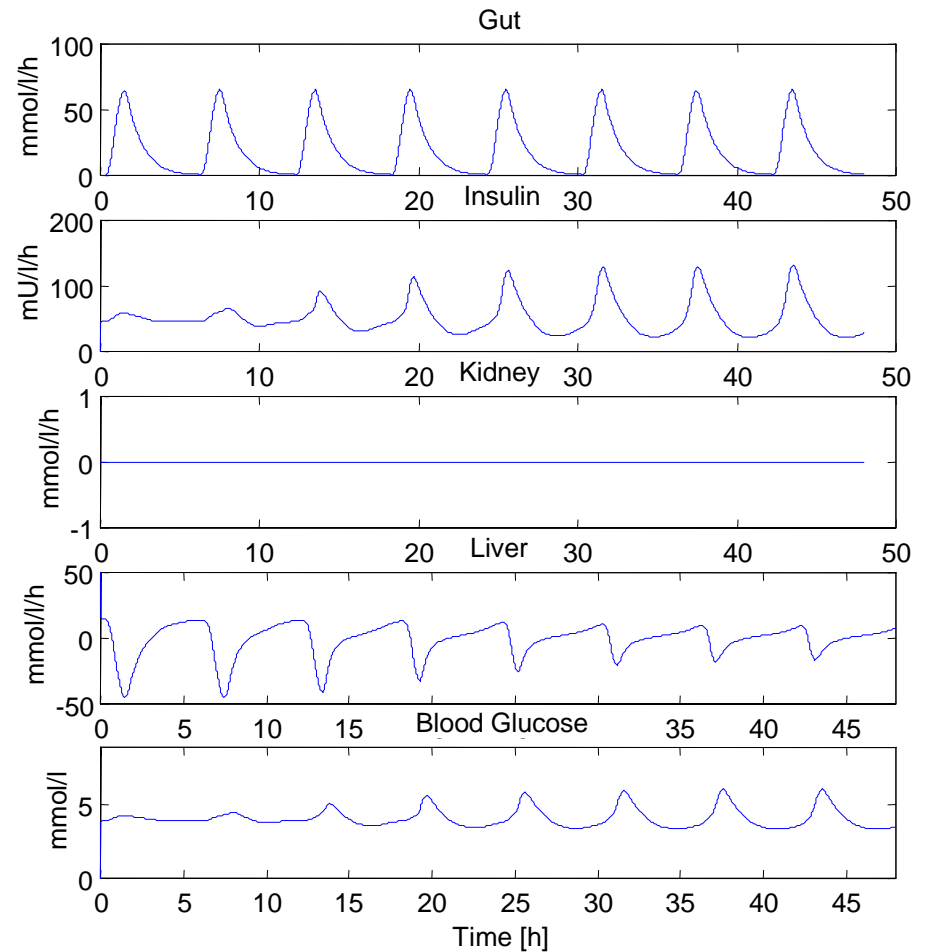


Results: Normal Subject

- Effect of finite liver capacity

- Input : 20g/6h
- Liver buffer :15g-CH initial 7.5
- CH from gut : 160.0g
- CH to peripheral:150.0g
- CH to liver : 10.0g
- excreted : 0.0g
- delivered insulin: 2452mU

- Note: Liver get full

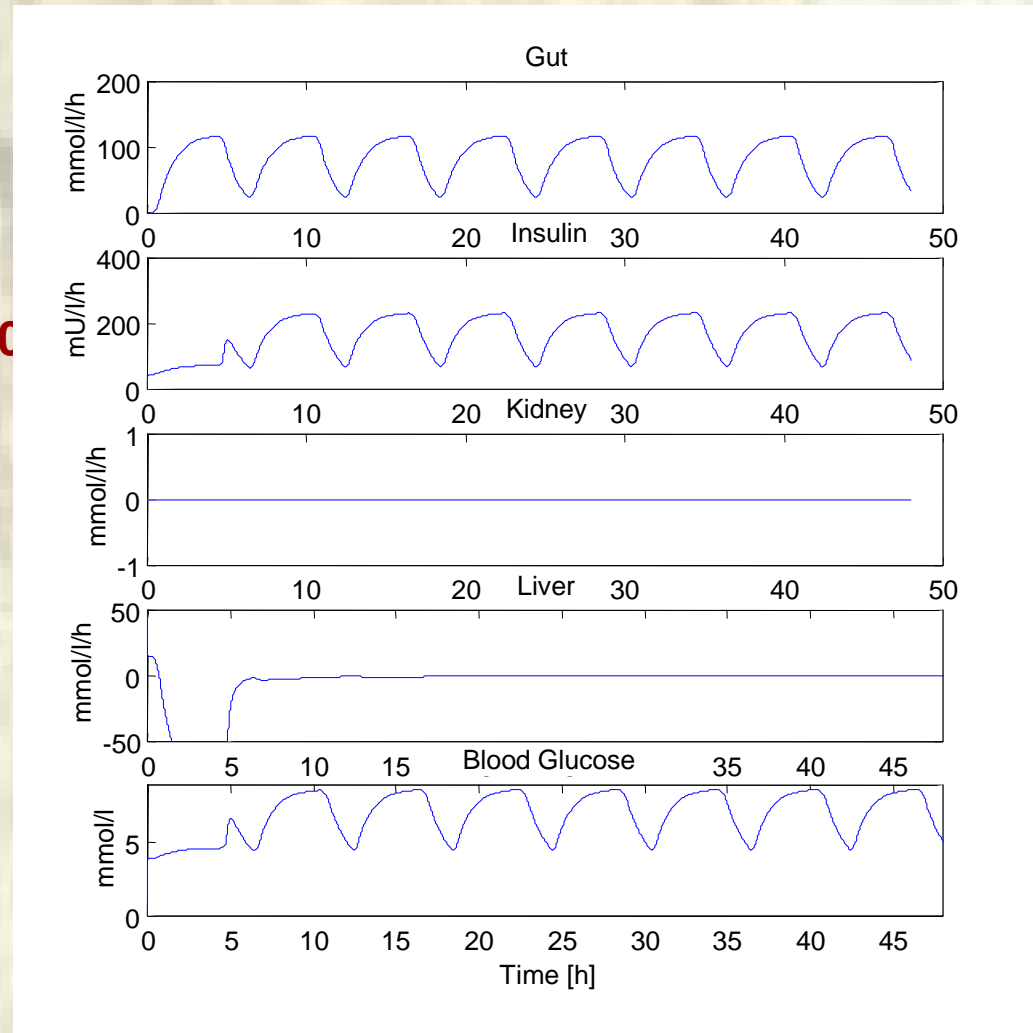


Results: Normal Subject

- Effect of finite liver capacity

- Input : 90g/6h
- Liver buffer :100g-CH initial 50
- CH from gut : 720.0g
- CH to peripheral:659.3g
- CH to liver : 60.6g
- excreted : 0.0g
- delivered insulin: 7839mU

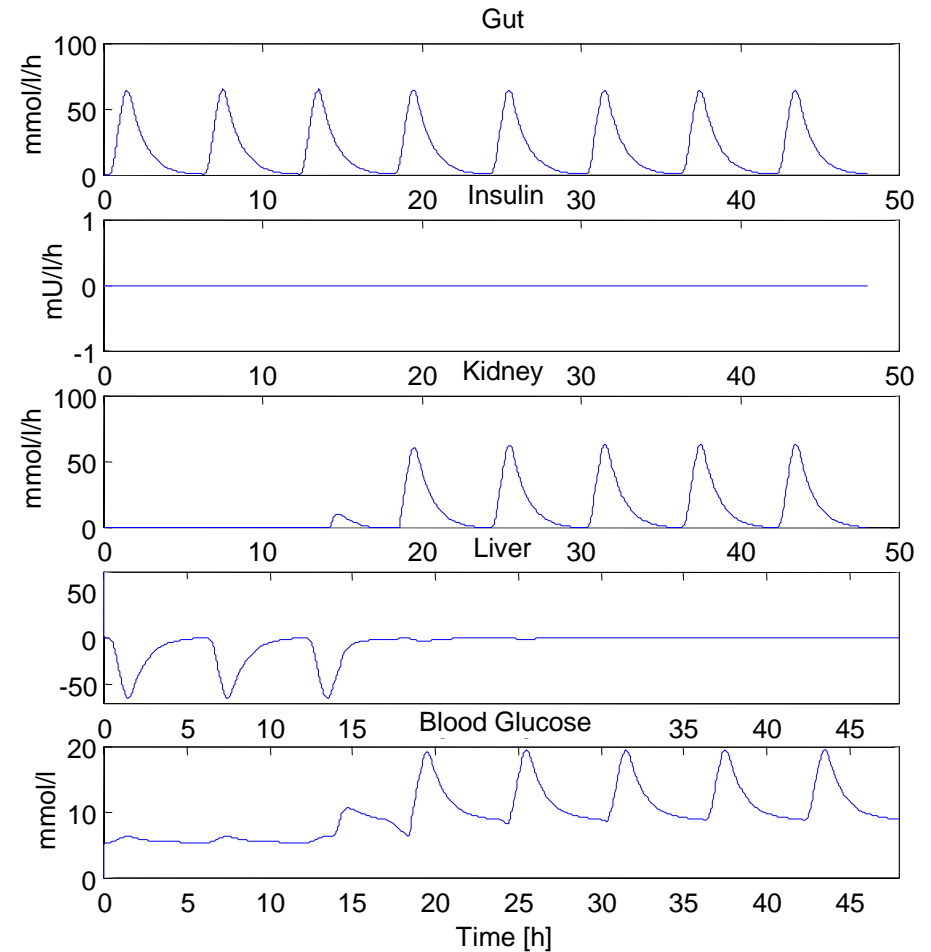
- Note: Liver get full



Results: No Insulin production

- Input : 20g/6h
- Liver buffer :100g-CH initial 50g
- CH from gut : 160.0g
- CH to peripheral: 6.7g
- CH to liver : 57.6g
- excreted : 95.4g
- delivered insulin: 0.0mU

**Note : Kidney excretion occur.
Liver full.**

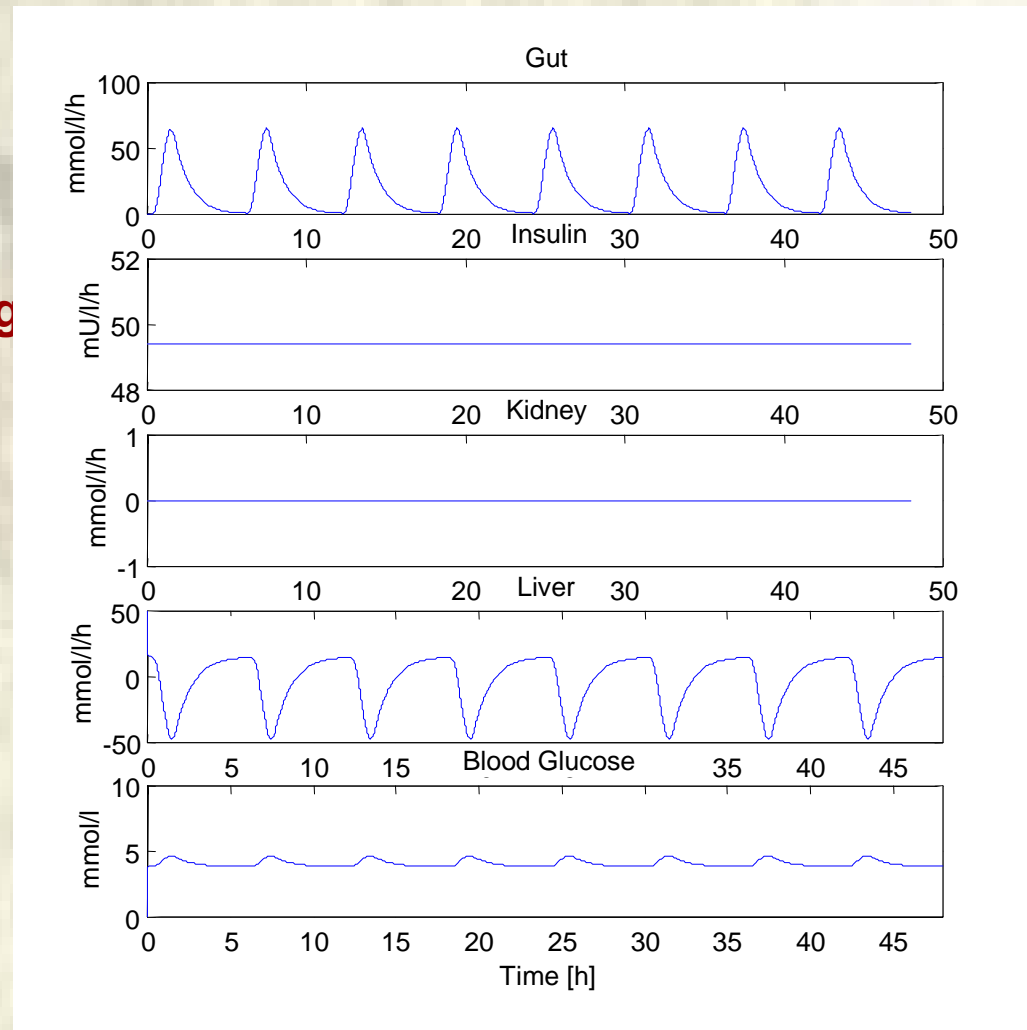


Results: No Insulin production

•Constant drip 49.4mU/h

- Input : 20g/6h
- Liver buffer :100g-CH initial 50g
- CH from gut : 160.0g
- CH to peripheral:137.9g
- CH to liver : 22.6g
- excreted : 0.0g
- delivered insulin: 2371mU

Note : Look Normal :)

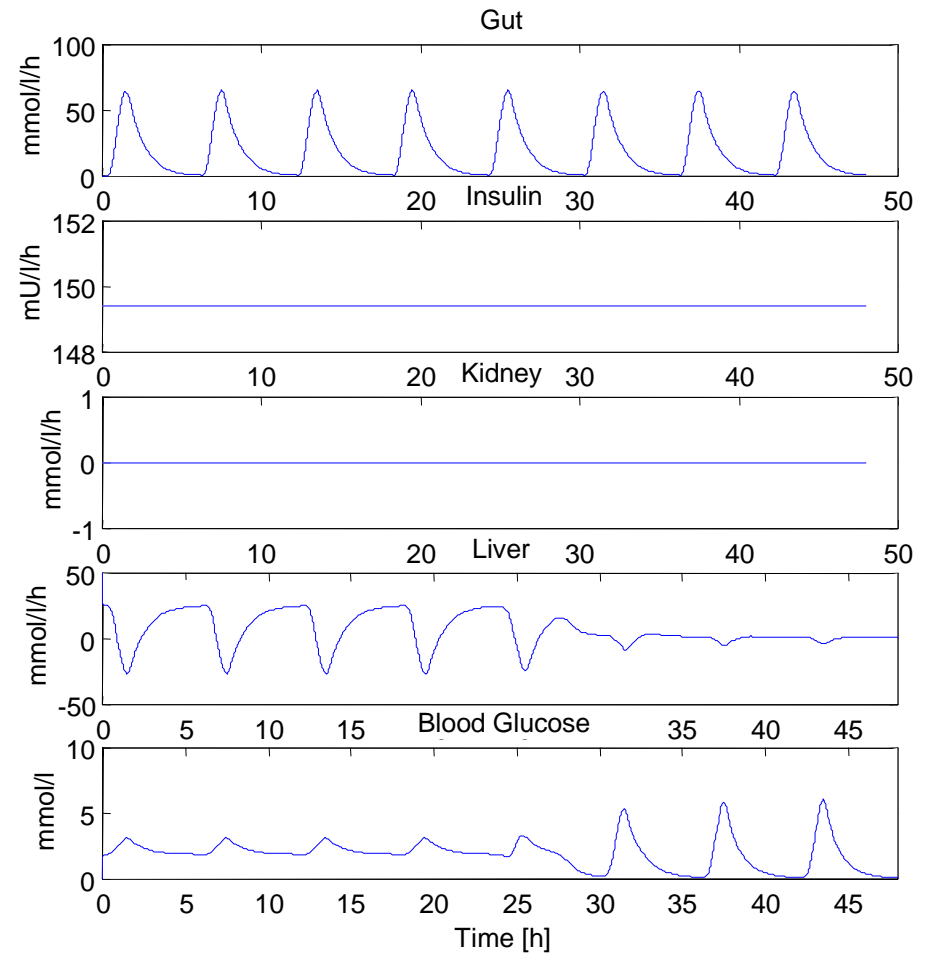


Results: No Insulin production

•Constant drip 149.4mU/h

- Input : 20g/6h
- Liver buffer :100g-CH initial 50g
- CH from gut : 160.0g
- CH to peripheral: 214.9g
- CH to liver : -54.3g
- excreted : 0.0g
- delivered insulin: 7171mU

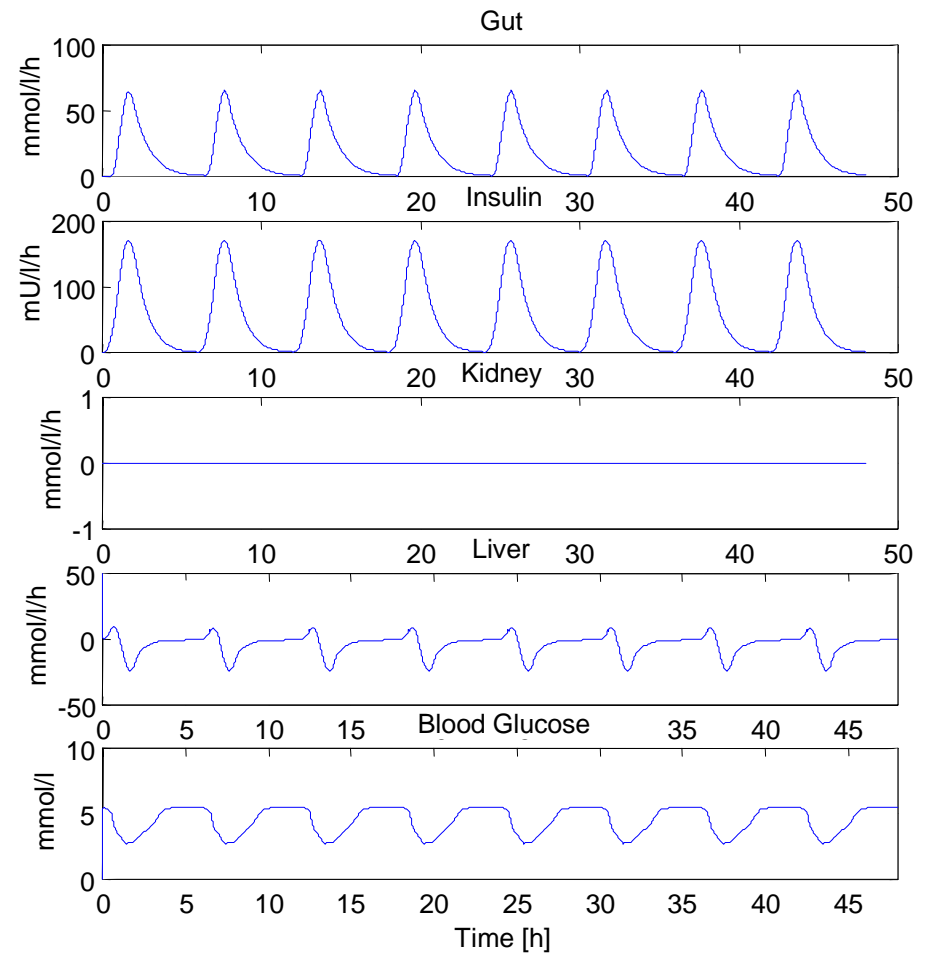
Note : ouch!!



Results: No Insulin production

- **Injection : 40U/6h 20 min before meal**

- **Input : 20g/6h**
- **Liver buffer :100g-CH initial 50g**
- **CH from gut : 160.0g**
- **CH to peripheral:126.7g**
- **CH to liver : 32.9g**
- **excreted : 0.0g**
- **delivered insulin: 2503mU**

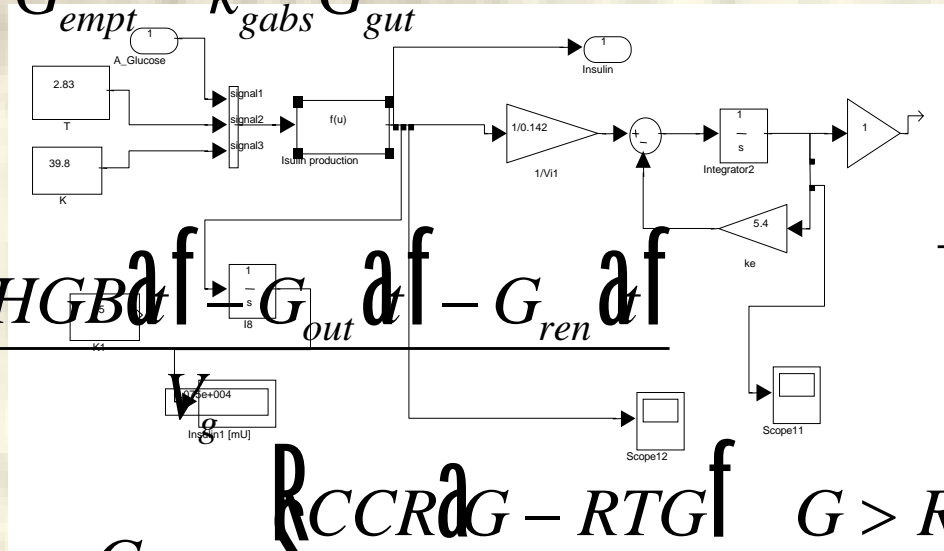


Questions

$$\frac{dI}{dt} = k_1 I_a - k_2 I$$

$$I = \begin{cases} \frac{RIPR}{gT} G - gT & G > gT \\ 0 & \text{elsewhere} \end{cases}$$

$$\frac{dG_{gut}}{dt} = G_{empt} - k_{gabs} G_{gut}$$



$$\frac{dG}{dt} = \frac{G_{in} + NHGB - G_{out} - G_{ren}}{V_i}$$

$$\frac{dI_a}{dt} = \frac{I_{abs}}{V_i} - k_e I_a$$

$$G_{ren} = \begin{cases} \frac{RCCR}{RTG} G - RTG & G > RTG \\ 0 & \text{elsewhere} \end{cases}$$

$$G_{out}; G, I = \frac{G_{bc} \cdot S_F \cdot I + G_I K_m + G_x}{G_x K_m + G}$$

