



# Influence of Dietary Changes on the Dynamics of $^{13}\text{C}/^{12}\text{C}$ in Selected Urinary Steroids

Institute of Biochemistry, German Sport University  
Cologne

Ulrich Flenker, Carsten von Kuk, Frank Hülsemann,  
Vassilios Gougoulidis, Ute Güntner and Wilhelm Schänzer



## Background

### Endogenous Steroids in Doping Control

$^{13}\text{C}/^{12}\text{C}$ -Difference of 3 ‰ between Target and Reference Compound indicates Presence of Synthetic Material

(WADA TD2004EAAS)

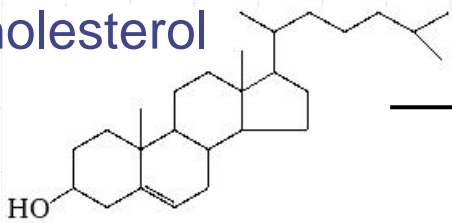
#### Assumptions:

1. Target and Reference Compounds isotopically equilibrated (Diet)
2. Metabolic Isotope Fractionation independent from physiological State

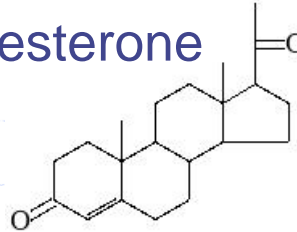


# Steroid Metabolism

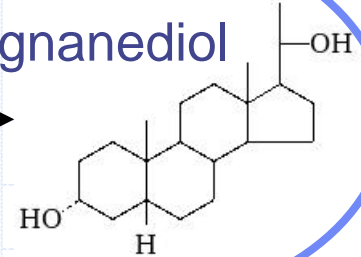
Cholesterol



Progesterone

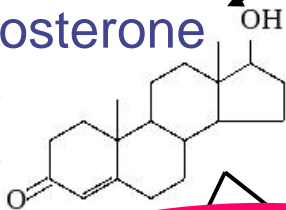


Pregnanediol



General Precursor (M/F),  
Gestagen, in Ovary (F)

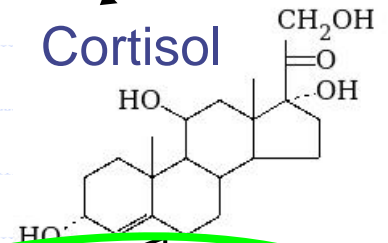
Testosterone



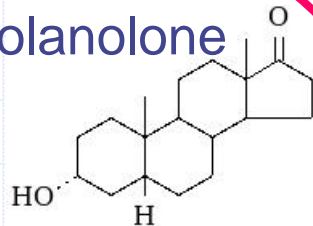
In Testes (M), in  
Adrenal Cortex(F)

In Adrenal  
Cortex (M/F)

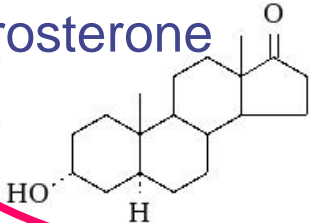
Cortisol



Etiocholanolone

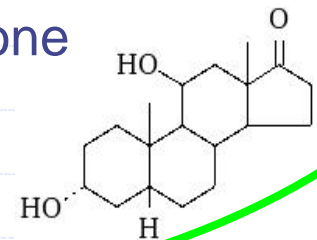
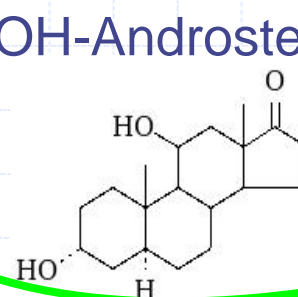


Androsterone



11OH-Etiocholanolone

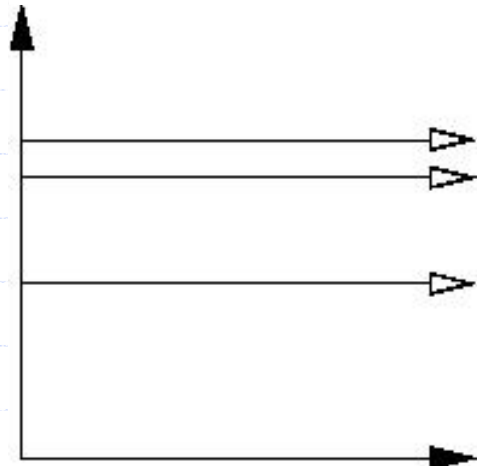
11OH-Androsterone



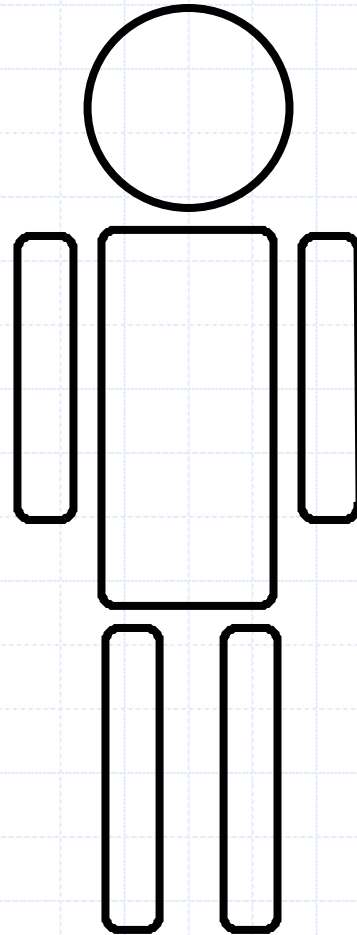


# Diet

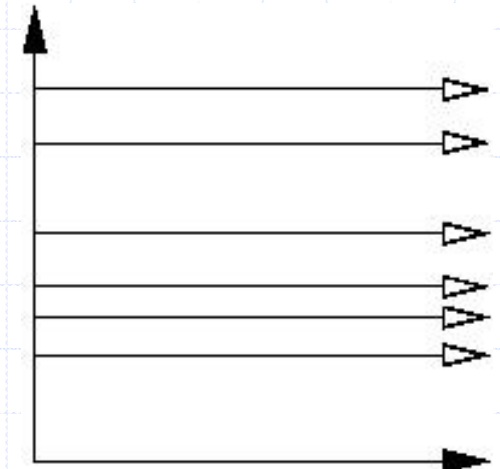
Isotope Ratio



Time

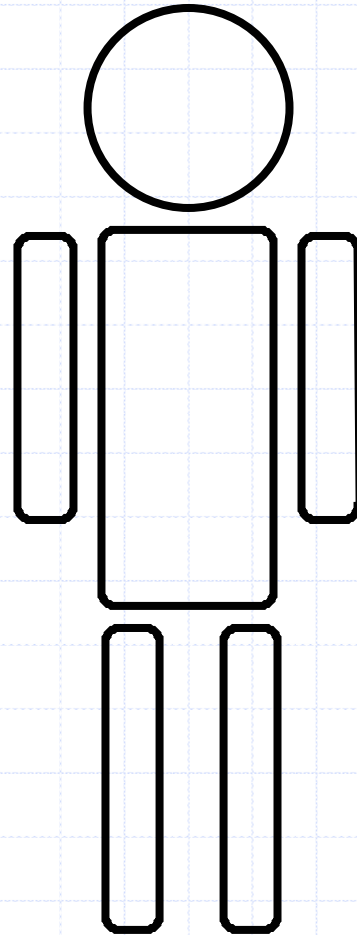


# „Metabolites“





Diet



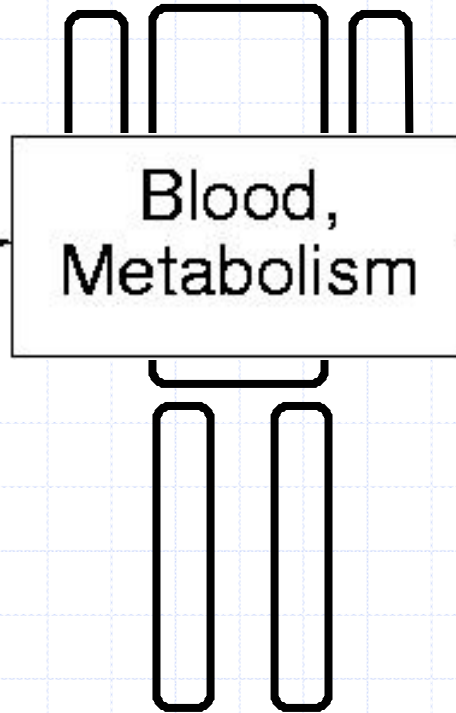
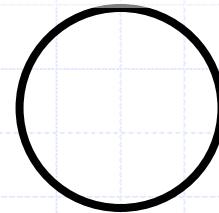
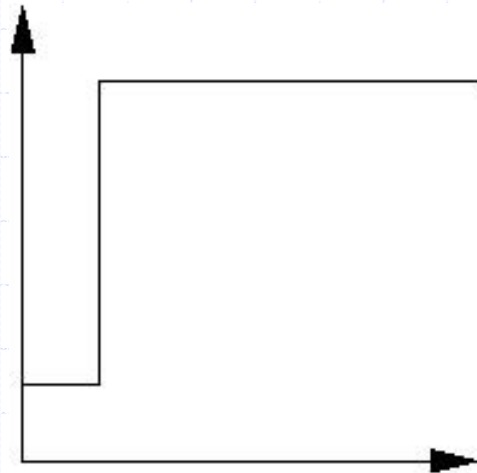
„Metabolites“



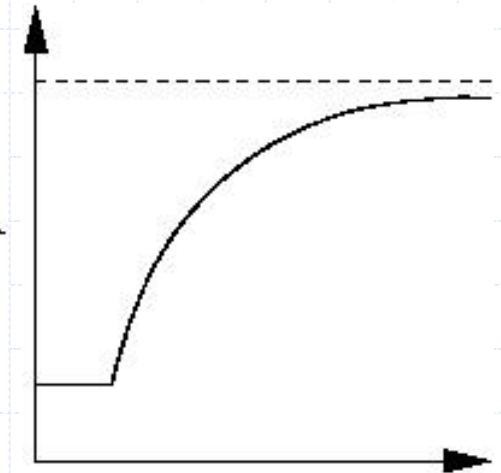


# Open One-Compartment Model

Diet

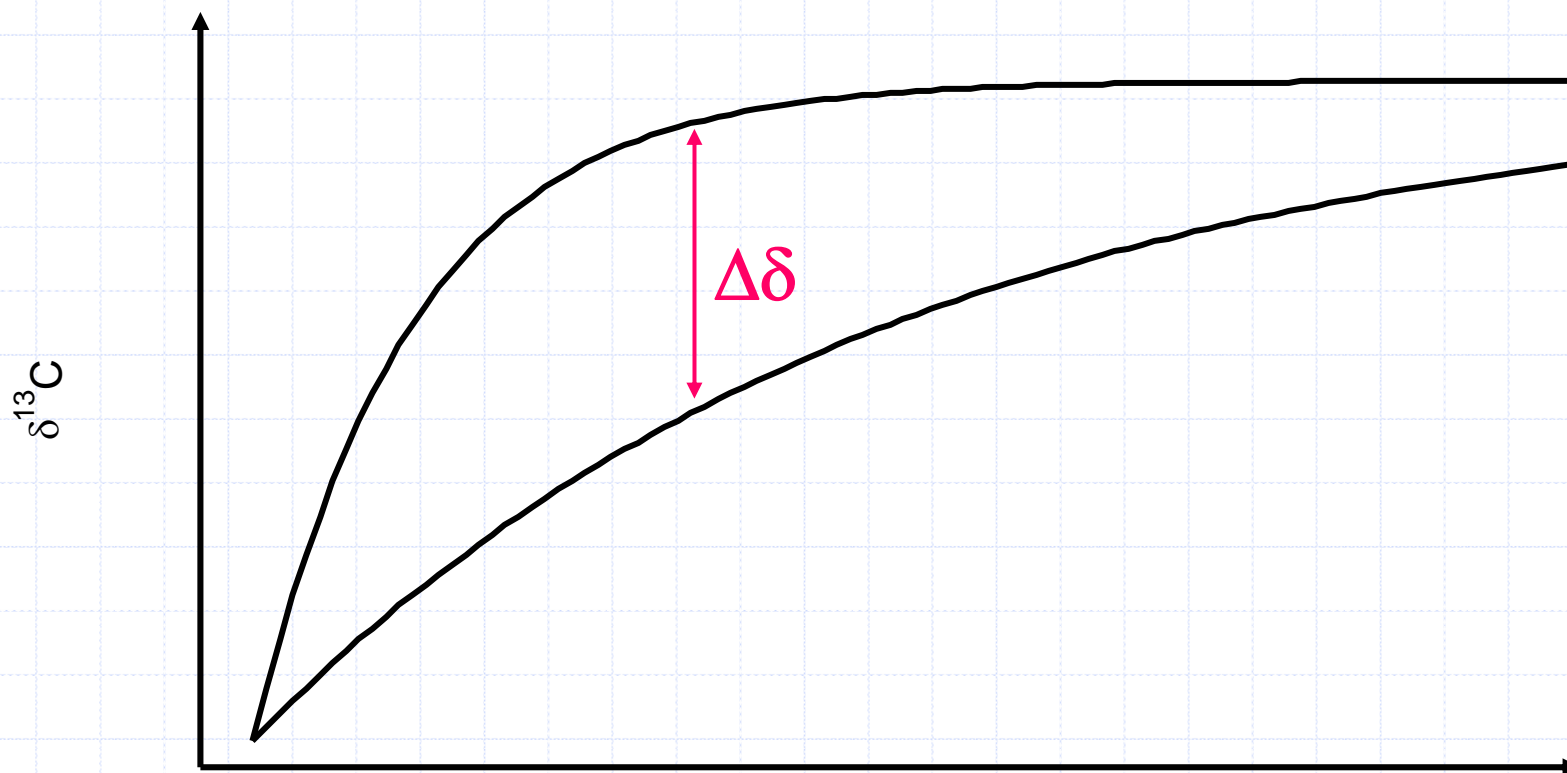


„Metabolites“





# Possible Influence of Different Exchange Rates





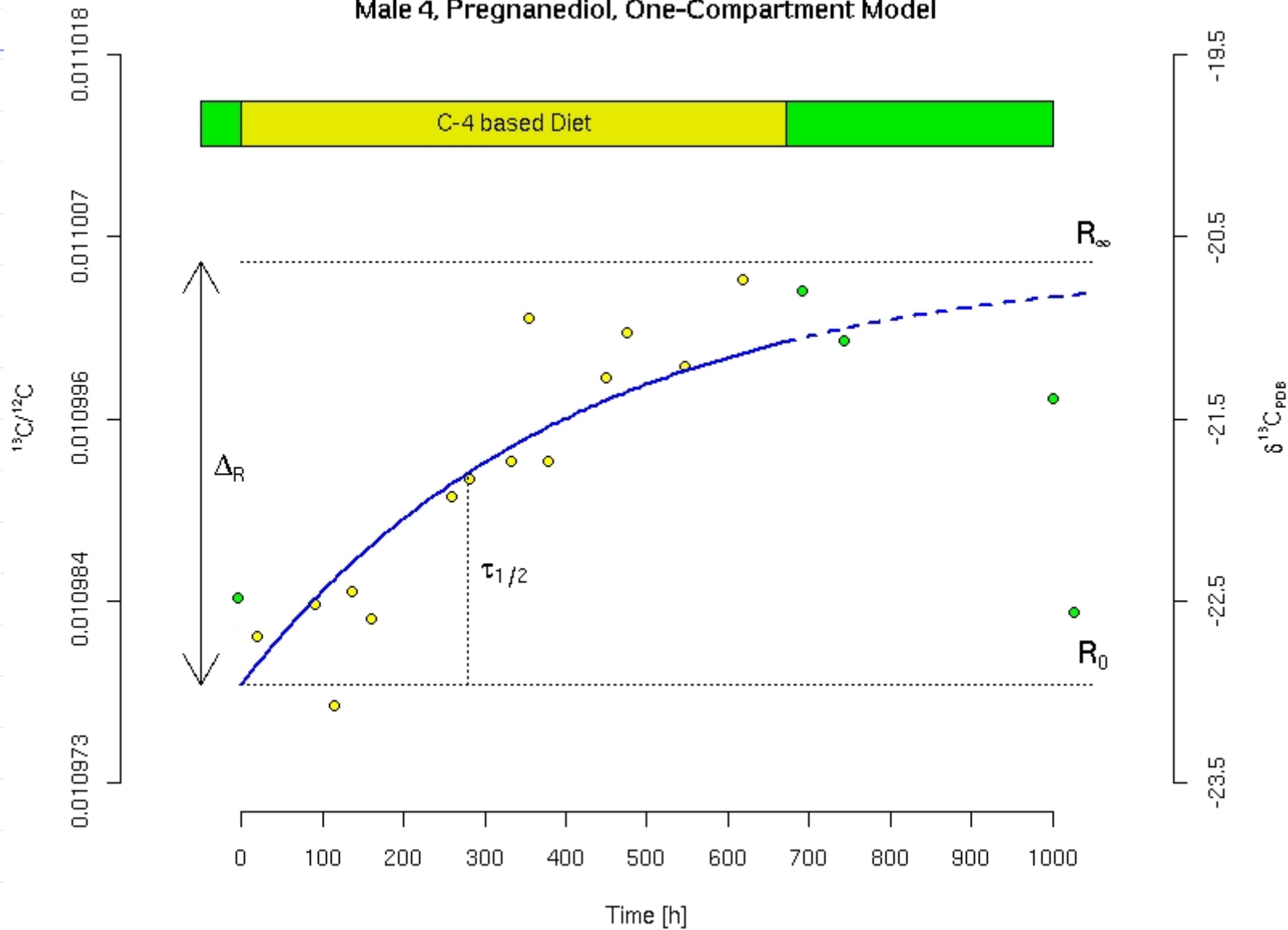
## Design of the Study

1. Subjects: 4 Males, 2 Females. Students and Members of the Institute.
2. Stimulus: Change to C-4 Plant dominated Diet for 28 Days (*Sorghum sp.*, *Zea mays*, ...). Diet free from Cholesterol!
3. Response:  $\delta^{13}\text{C}$  of selected urinary Steroids by GC/C/IRMS



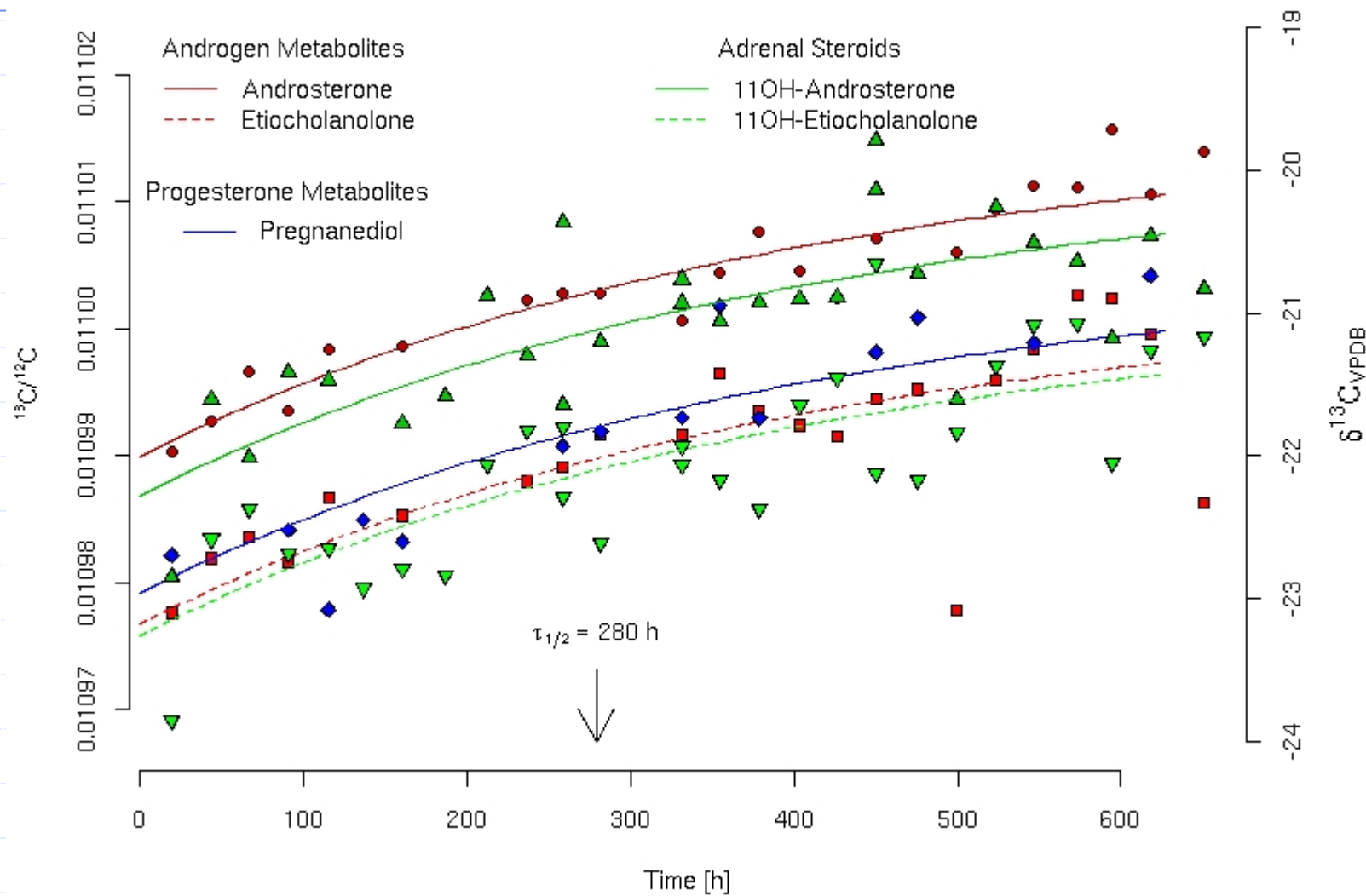


### Male 4, Pregnanediol, One-Compartment Model





### Male 4, One-Compartment Model



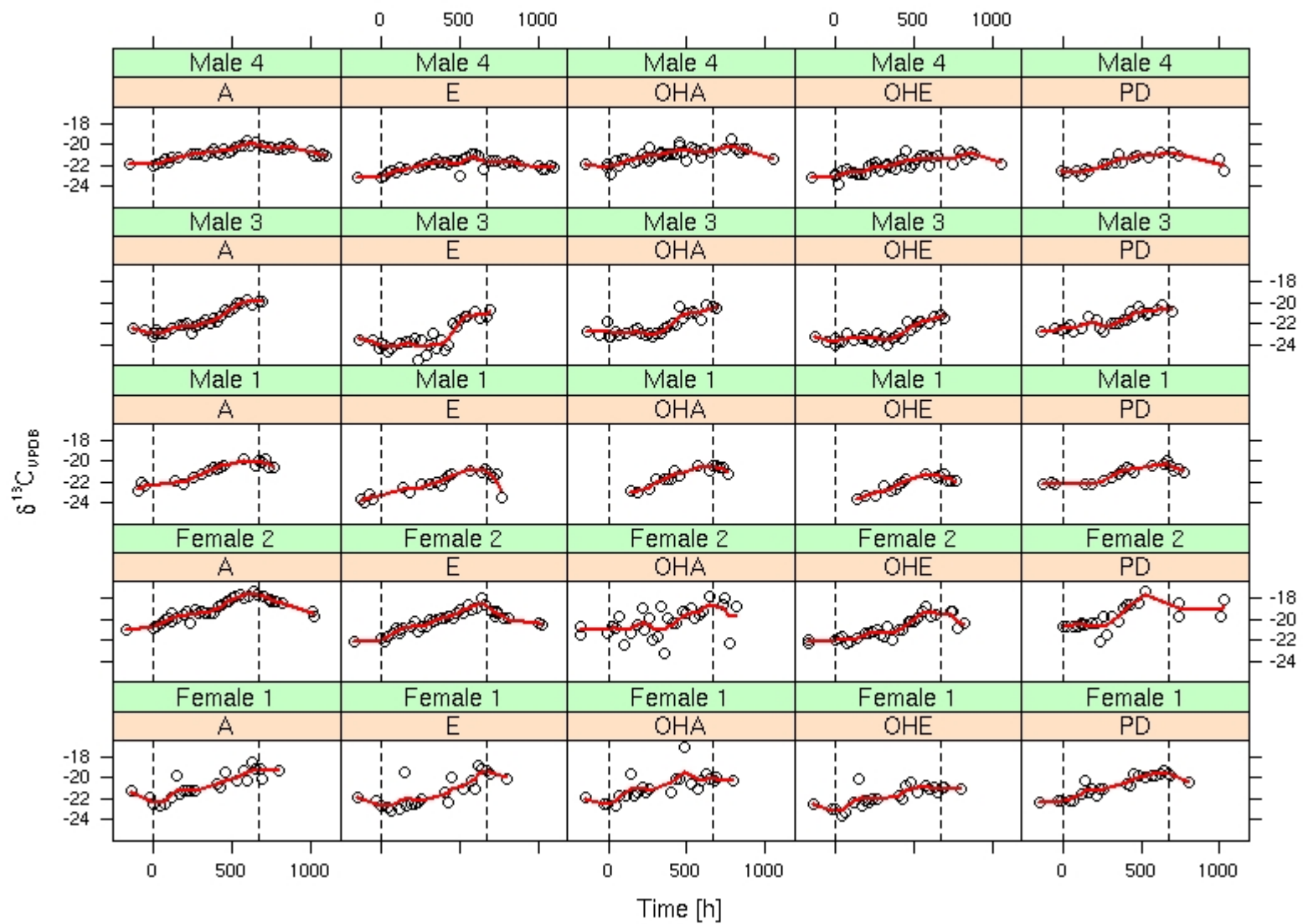


## Test Person #4, Male, 70 kg:

1. Identical Exchange Rates for all Steroids.
2. Identical Increase of  $\delta^{13}\text{C}$  for all Steroids.
3. Different Initial Values for different Steroids (Isotope Fractionation).
4. Different Asymptotes for different Steroids.



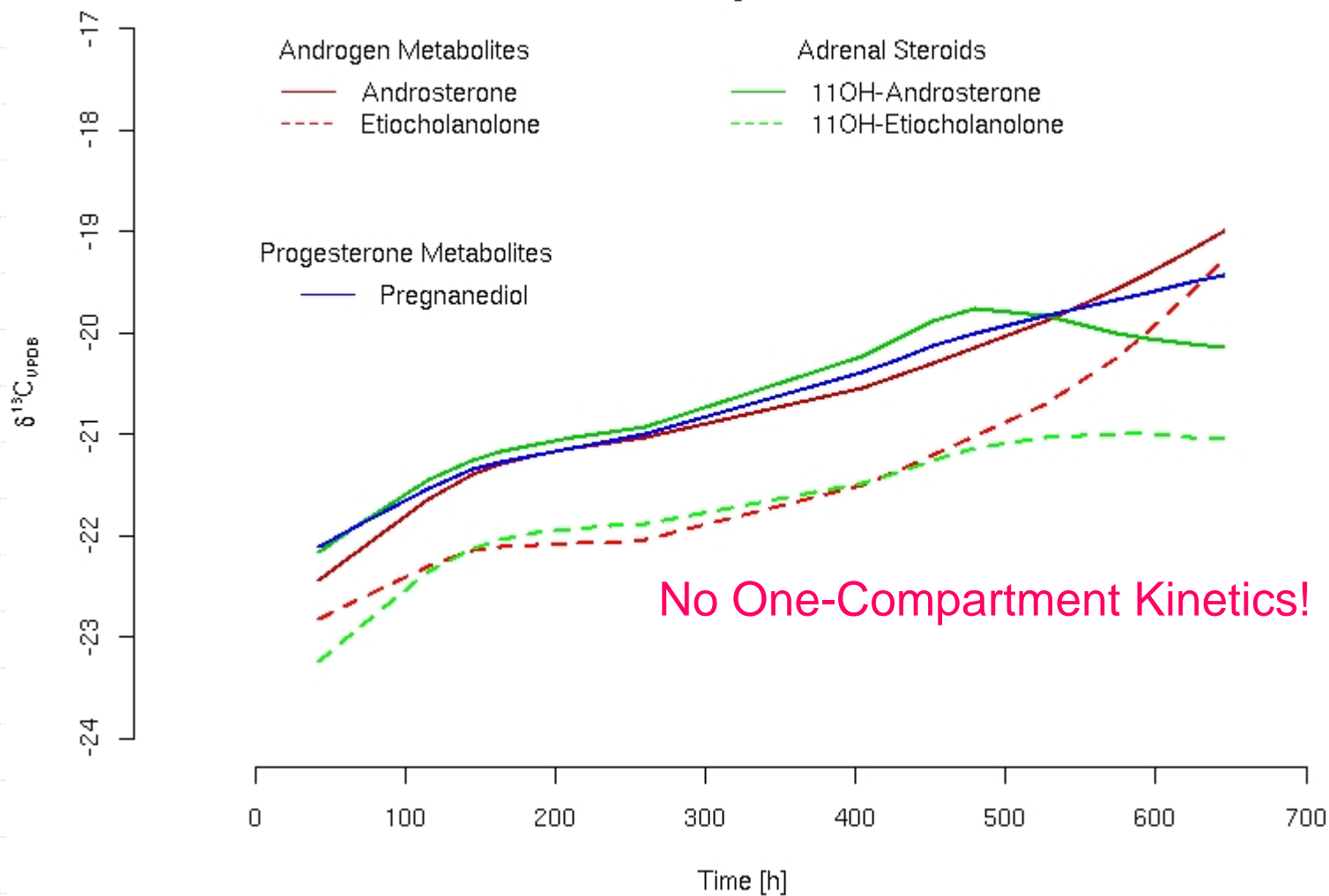
### Total Data, 3rd Order Smoothing Splines





### Female 1

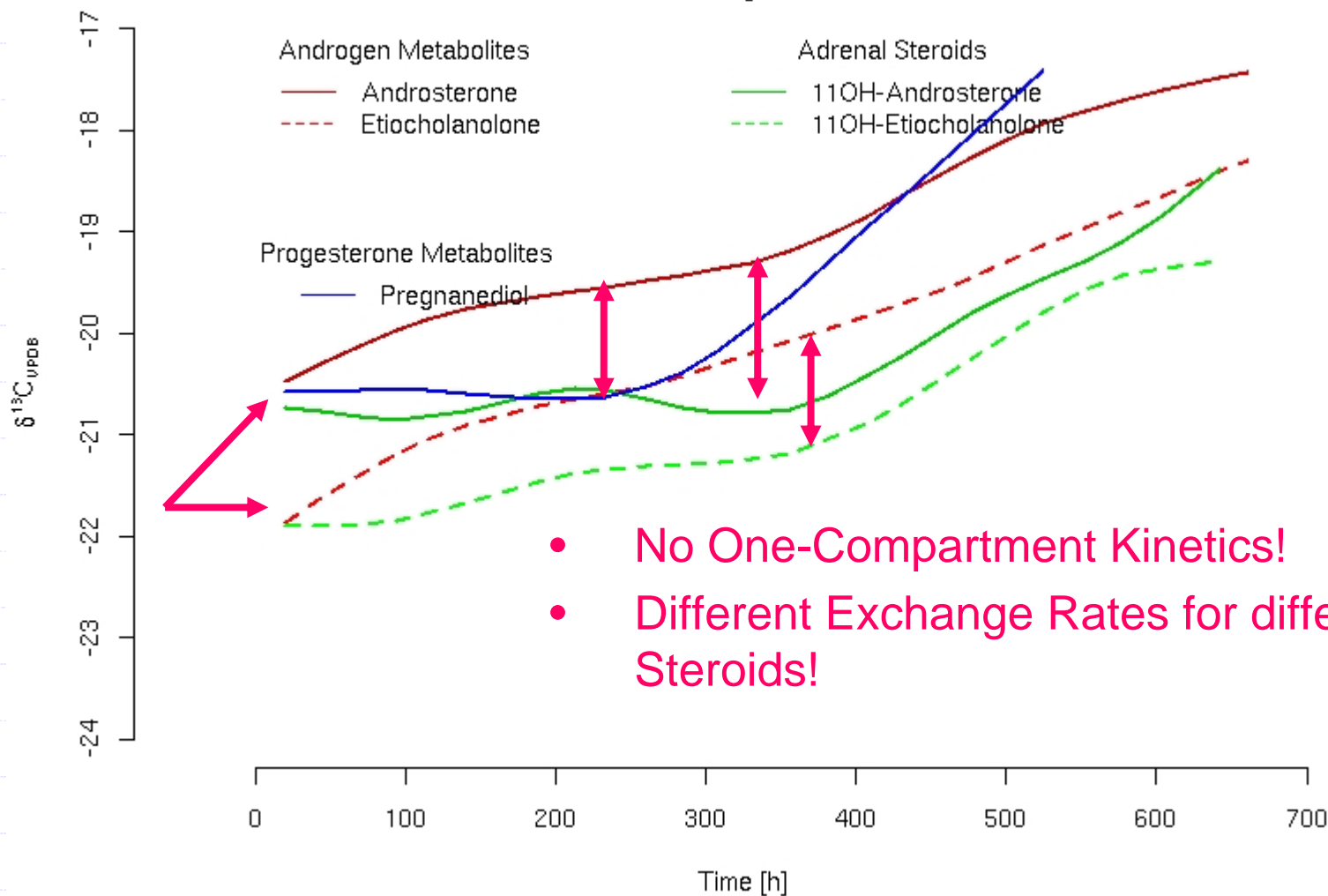
Mass 59.1 kg , 24.6 % Fat





## Female 2

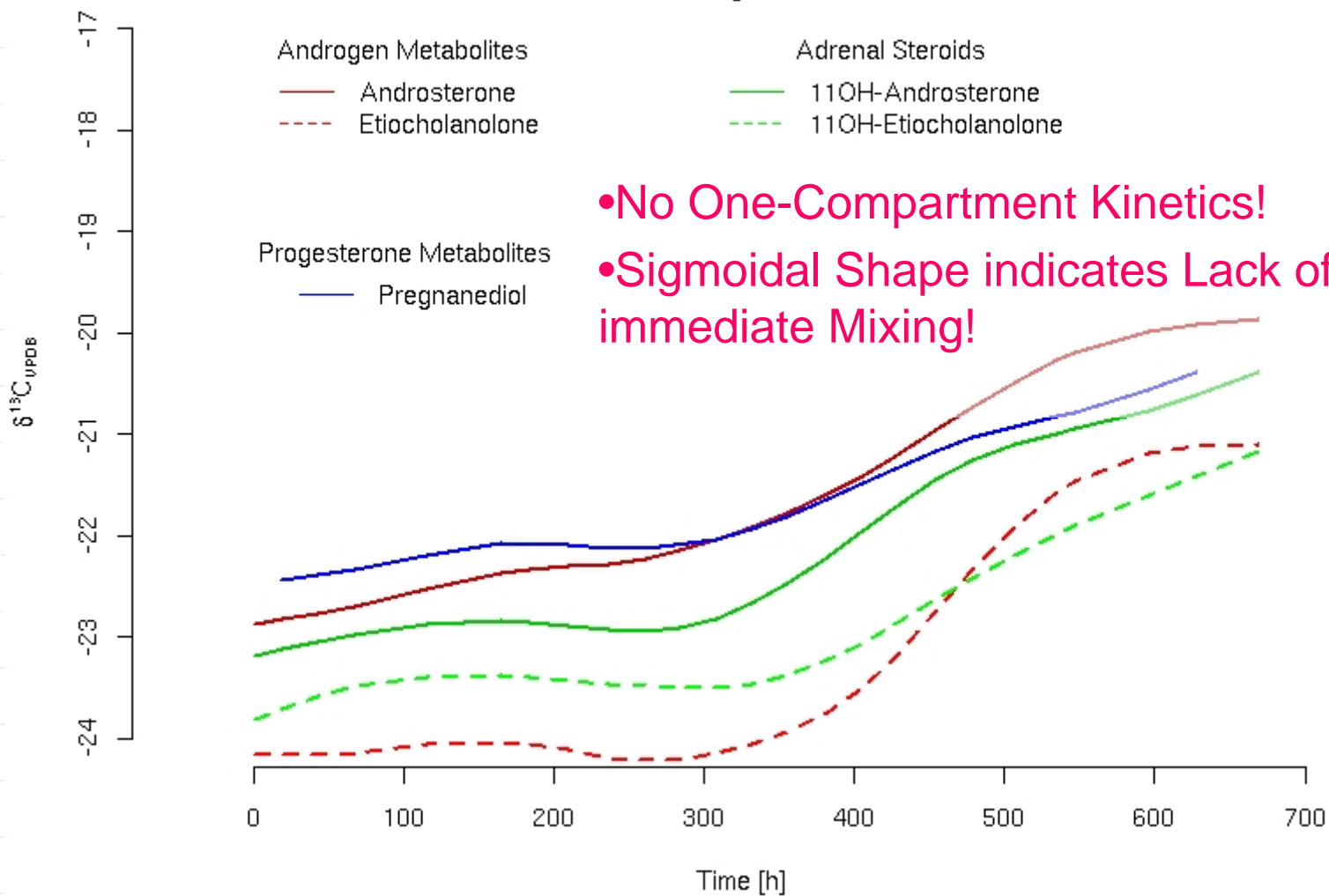
Mass 55.7 kg, 22 % Fat





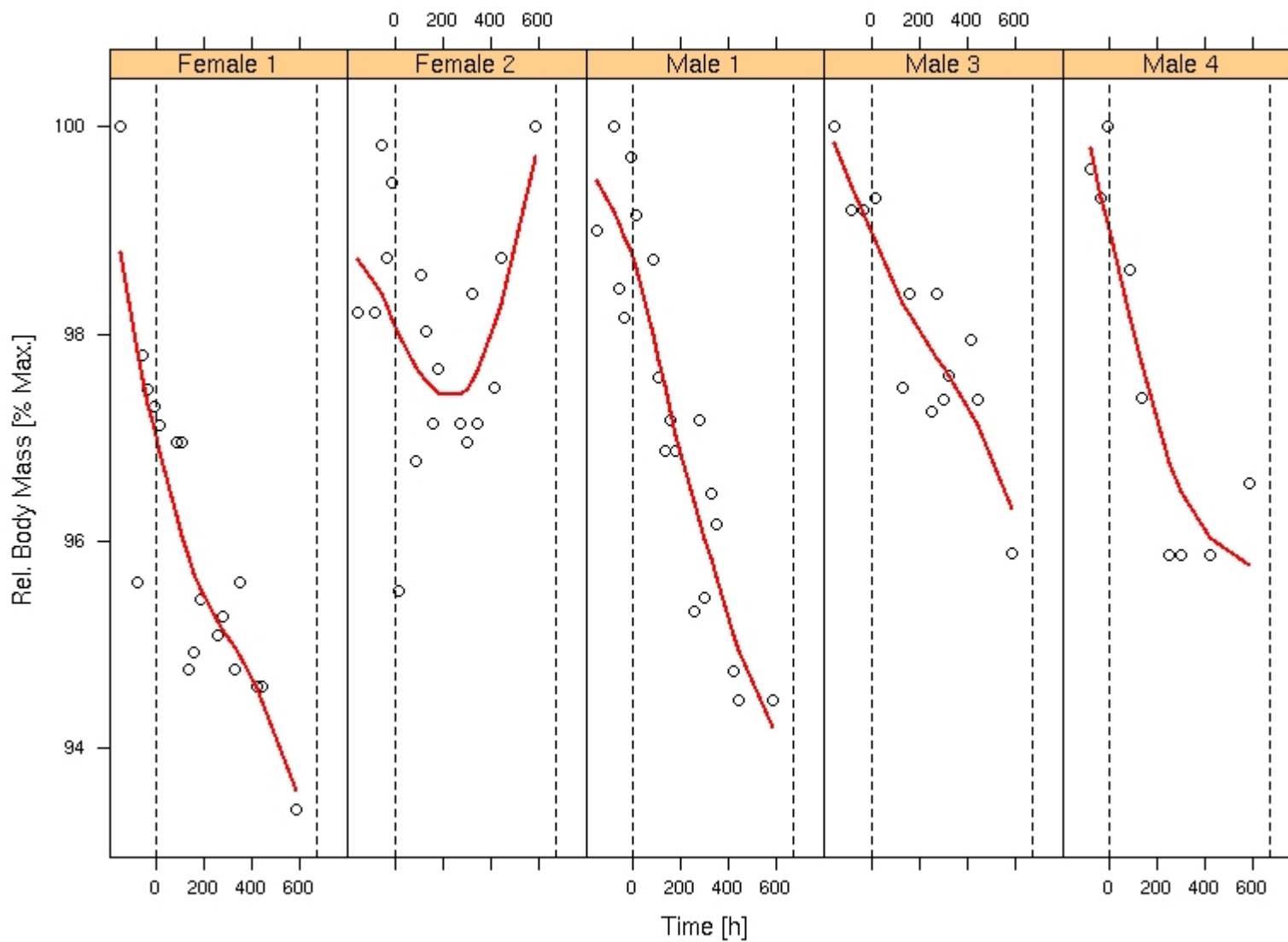
### Male 3

Mass 87.2 kg , 23.6 % Fat





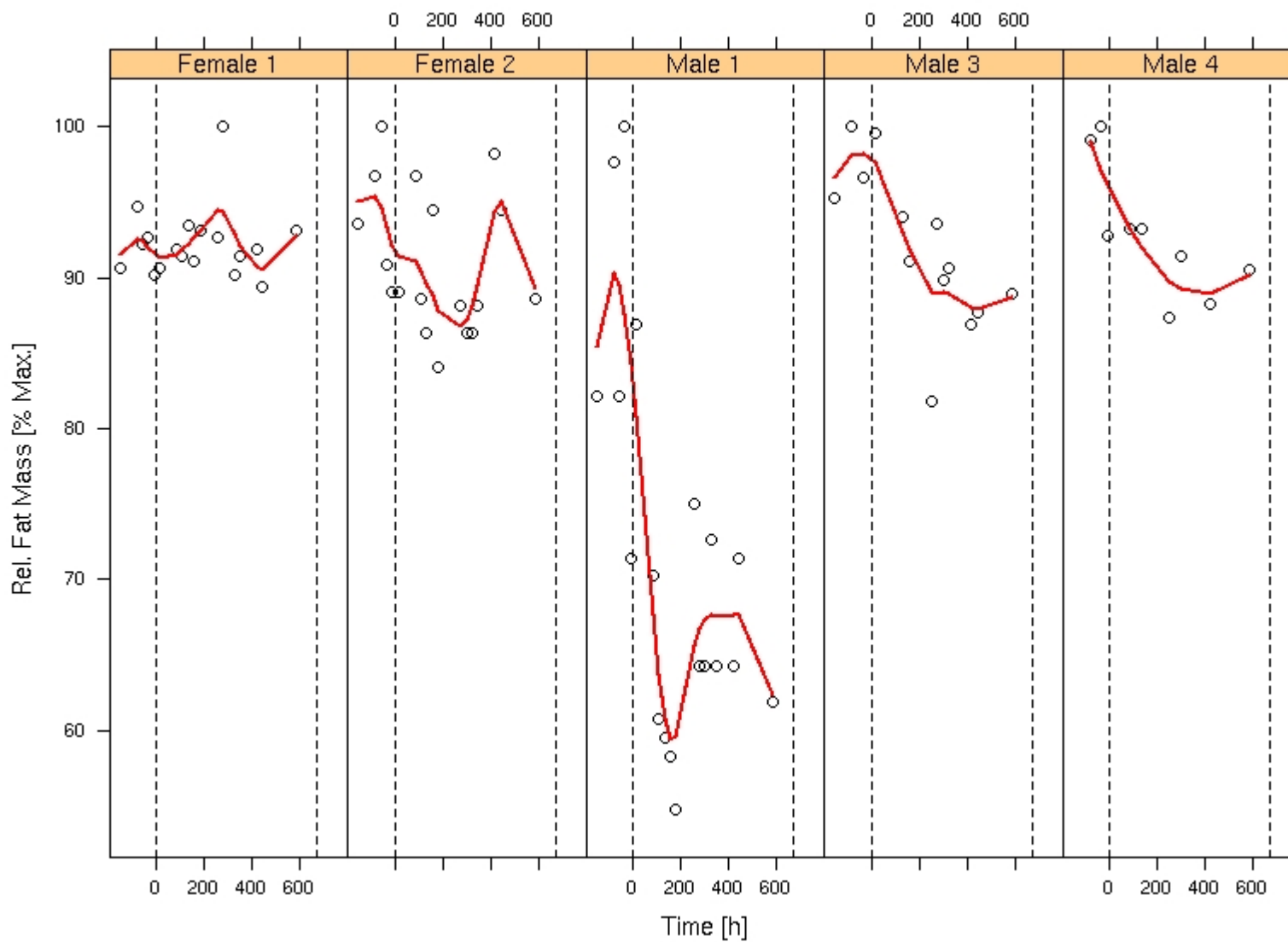
### Relative Change of Body Mass





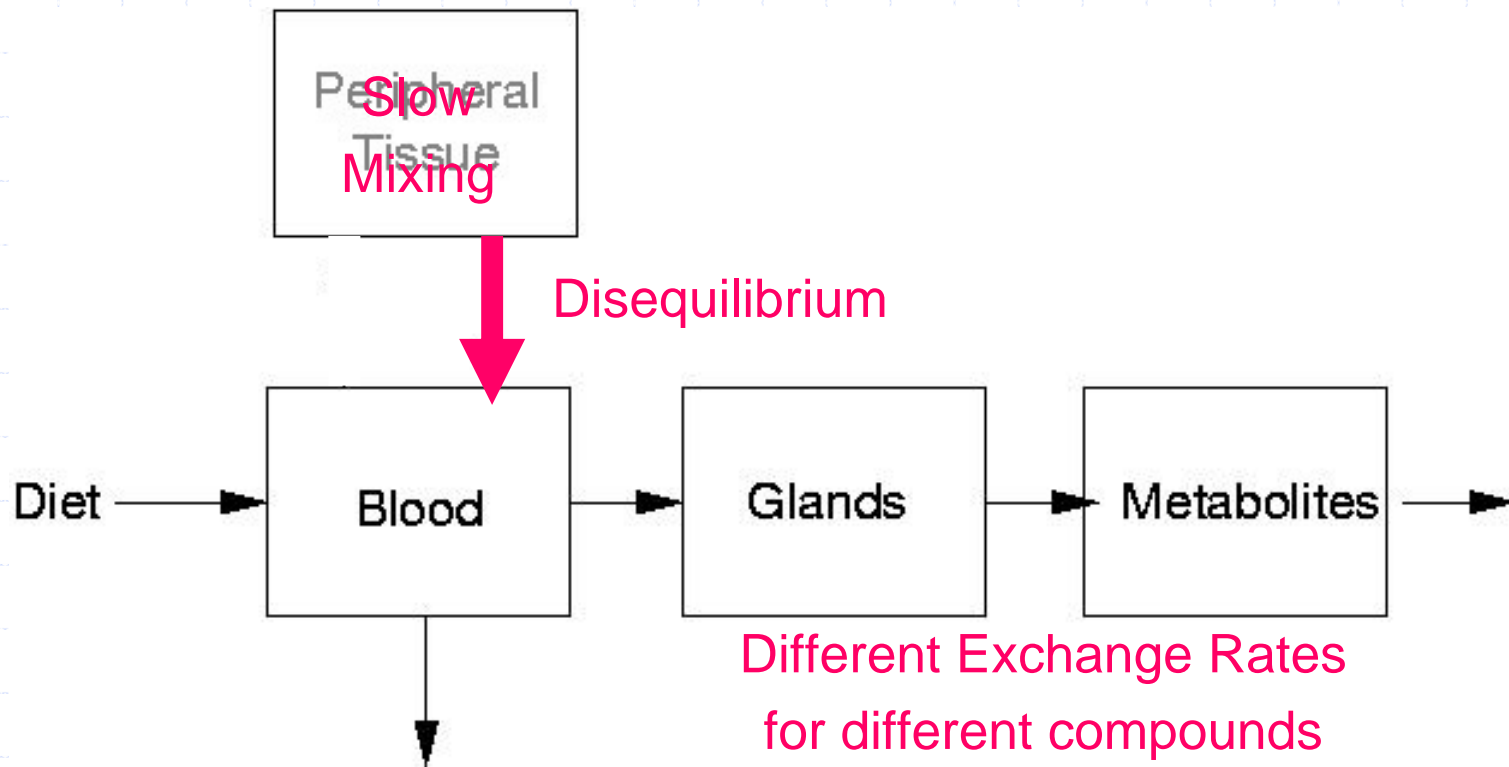


### Relative Change of Fat Mass





# Possible Multi-Compartment Model





## Conclusions

1. (At least some ) Dietary Carbon is immediately incorporated into *de novo* synthesized Steroid Hormones.
2. One-Compartment Models generally are inadequate in Steroid Metabolism.
3. Exchange Rates can be different for different Compounds.
4. (The 3 ‰-Criterion was not met however.)
5. Isotopic Fractionation is present in Steroid Metabolism.
6. C-4 Plant based Diet causes metabolic disequilibrium.



# Acknowledgements

