



Technische  
Universität  
Braunschweig



**BRICS**

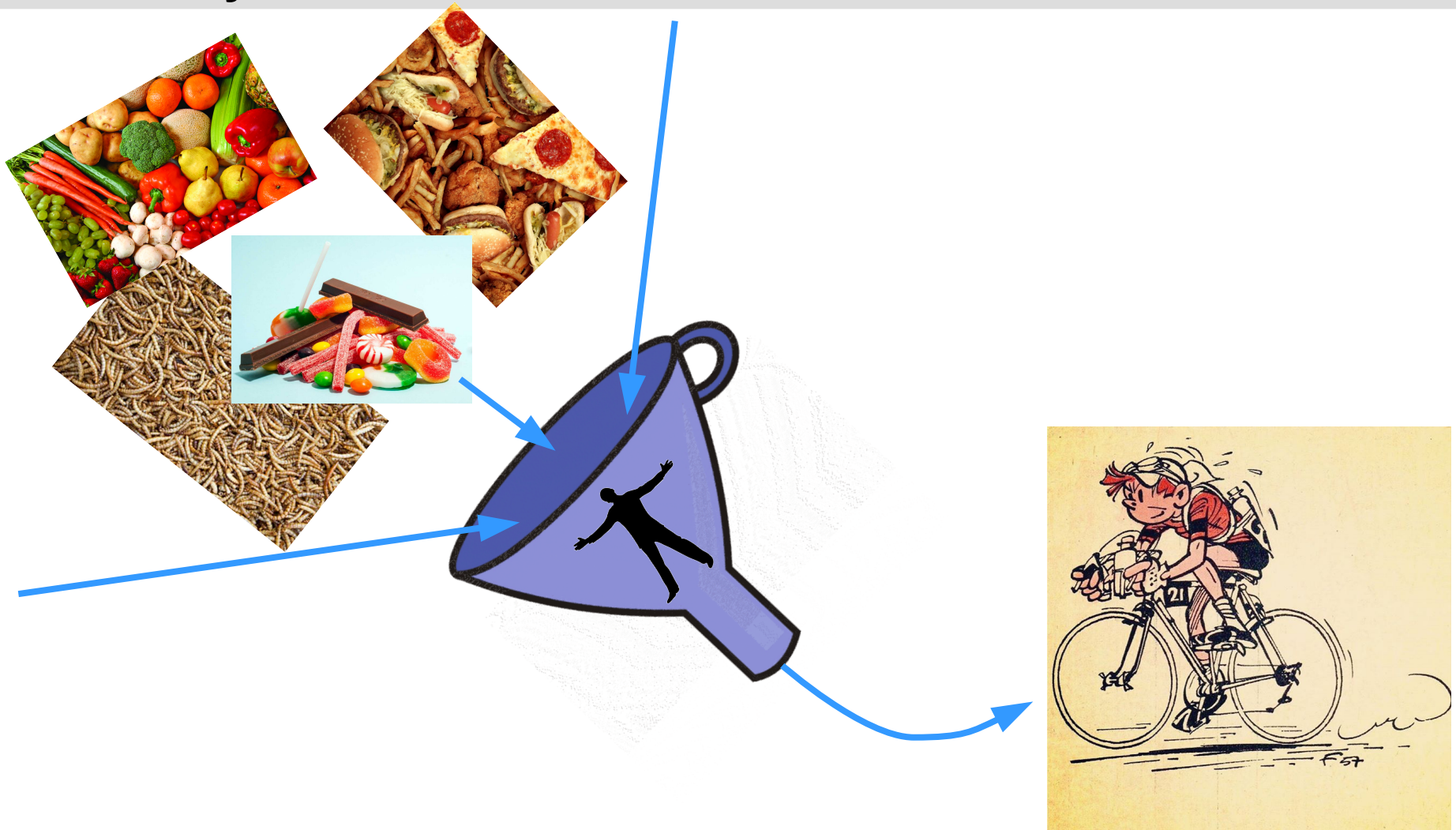
Braunschweig Integrated Centre  
of Systems Biology



# Systems Approaches for Defining the Dietary Landscape

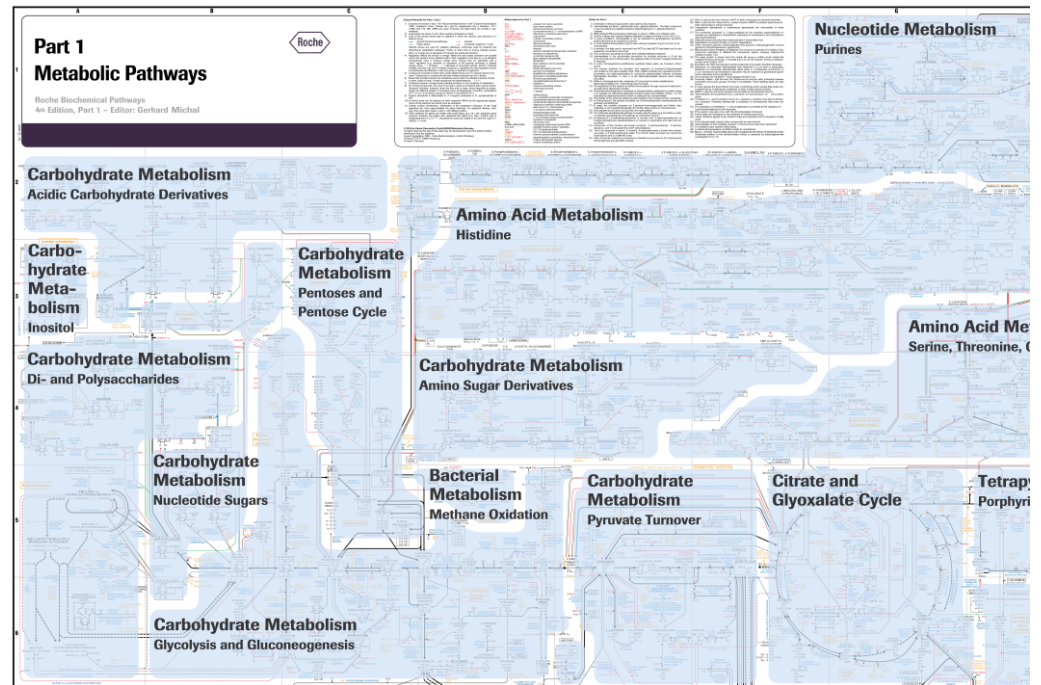
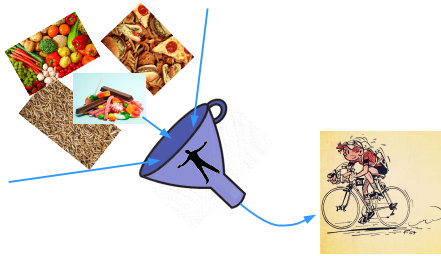
[karsten.hiller@tu-braunschweig.de](mailto:karsten.hiller@tu-braunschweig.de)

# Diversity of diet



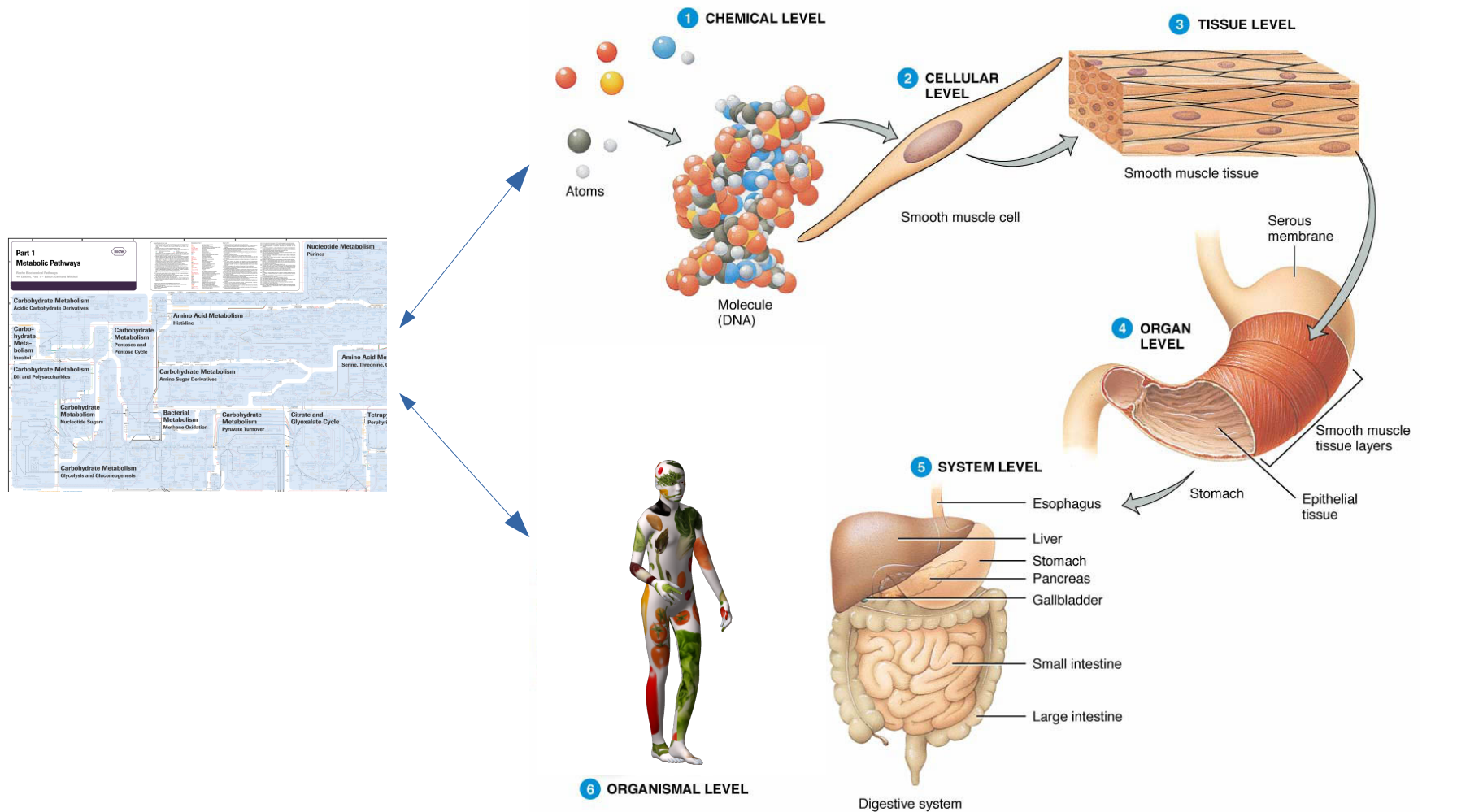


# Metabolic network ensures homeostasis...



Michal, M. & Schomburg, D. (2012). *Biochemical Pathways. An Atlas of Biochemistry and Molecular Biology (Second Edition)*. Hoboken, NJ: John Wiley & Sons.

# ...and integrates activities of specialized organs and tissues

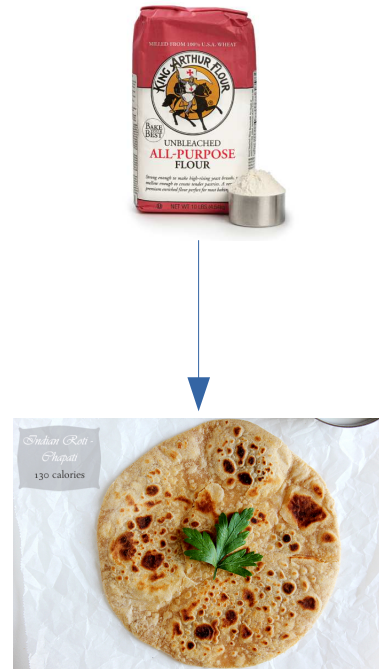


<http://anatomyandphysiologyi.com/ap-levels-of-structural-organization/>

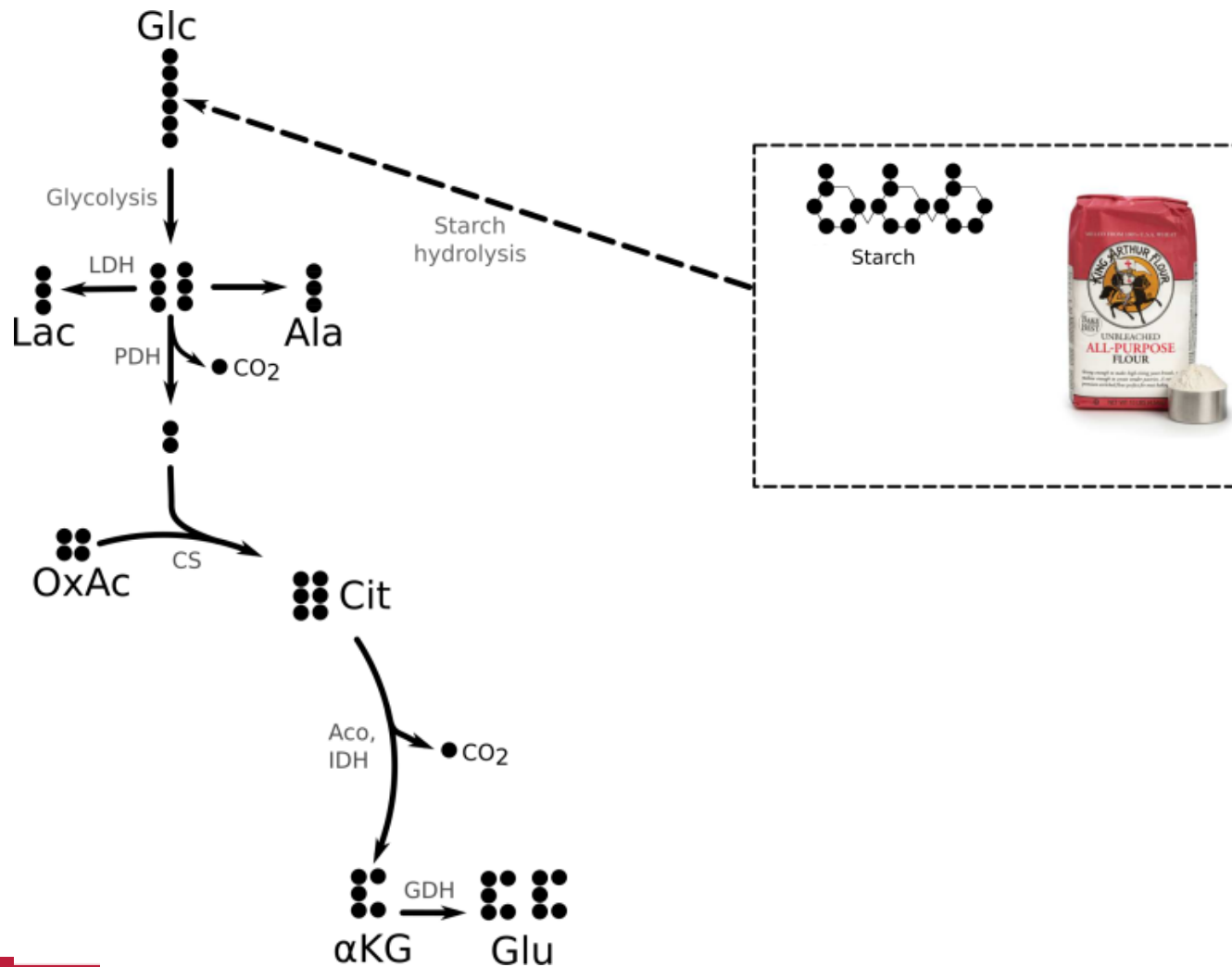


## Defining the dietary landscape

...fate of wheat flour in human metabolism

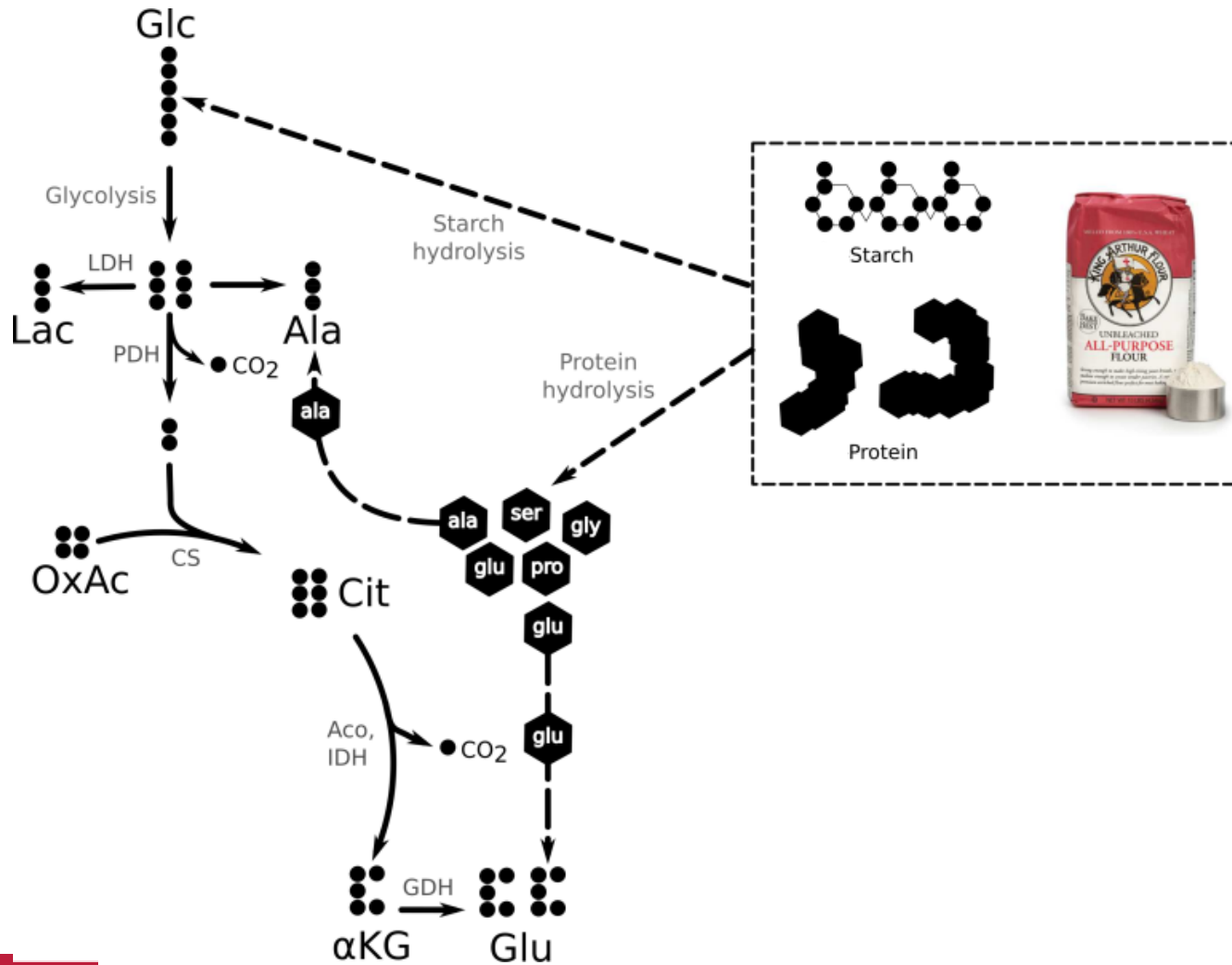


# Catabolism of wheat starch

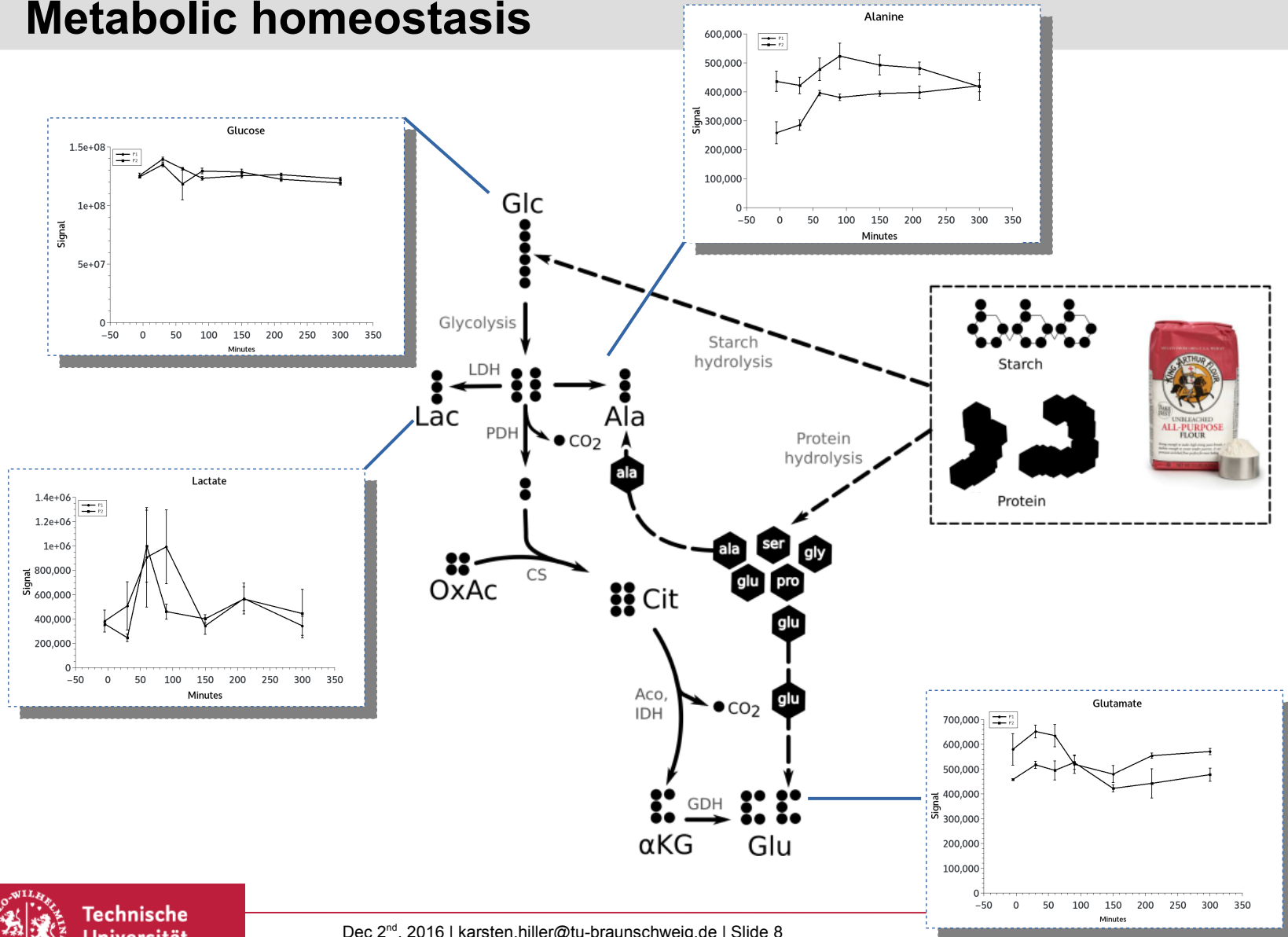




# Catabolism of wheat starch

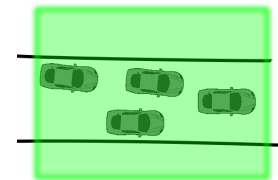
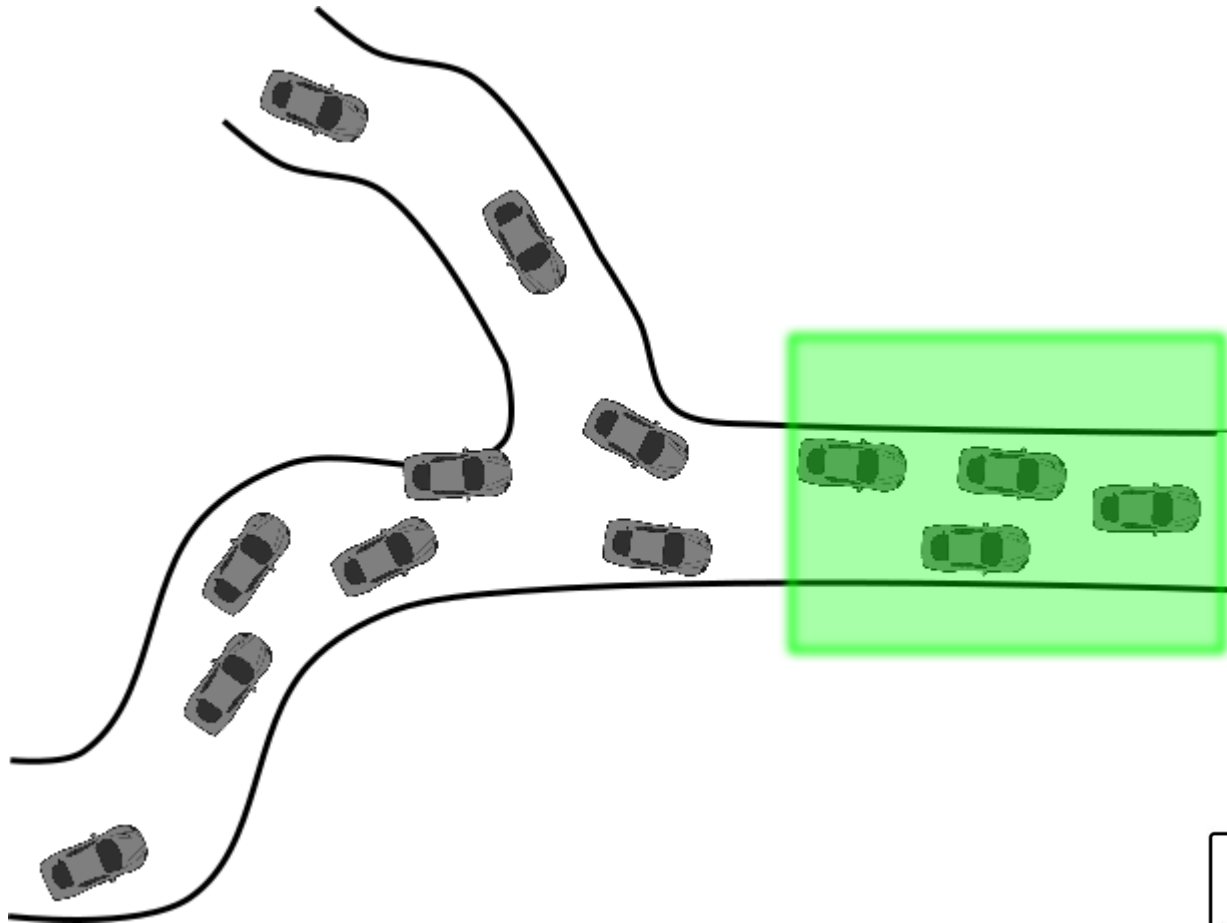


# Metabolic homeostasis

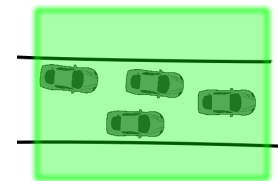
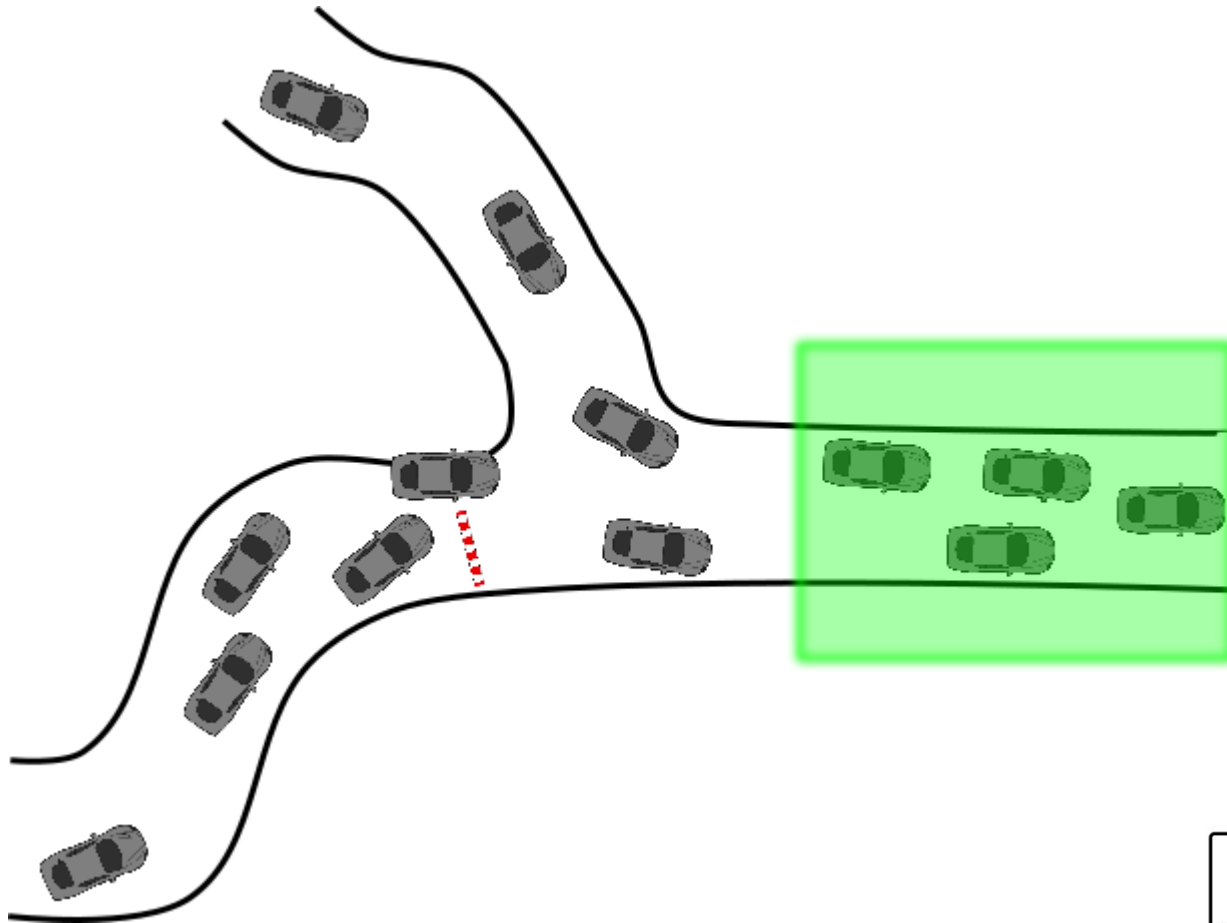




# Metabolic fluxes (turn-over rates)

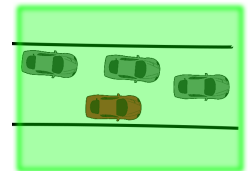
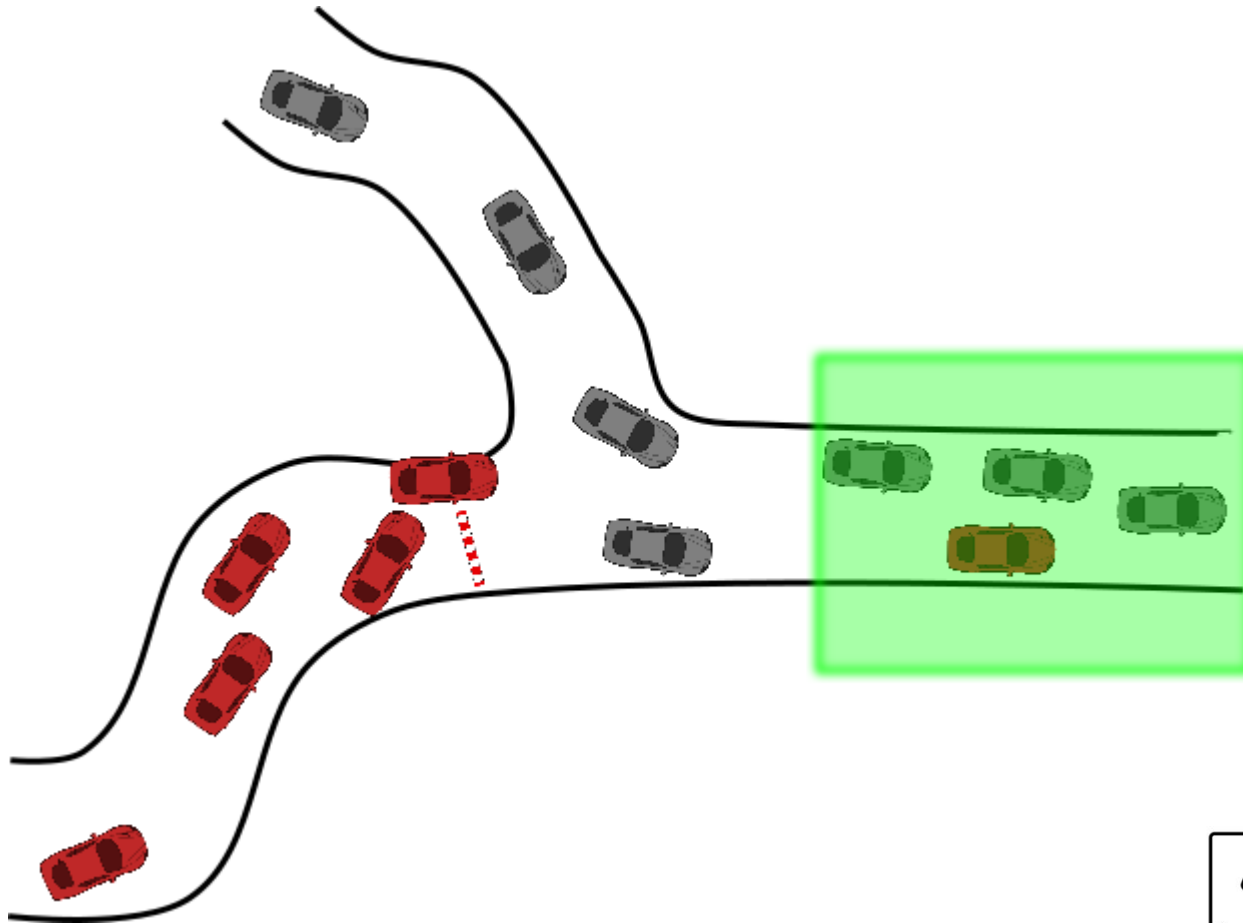


# Metabolic fluxes (turn-over rates)

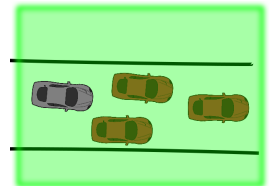
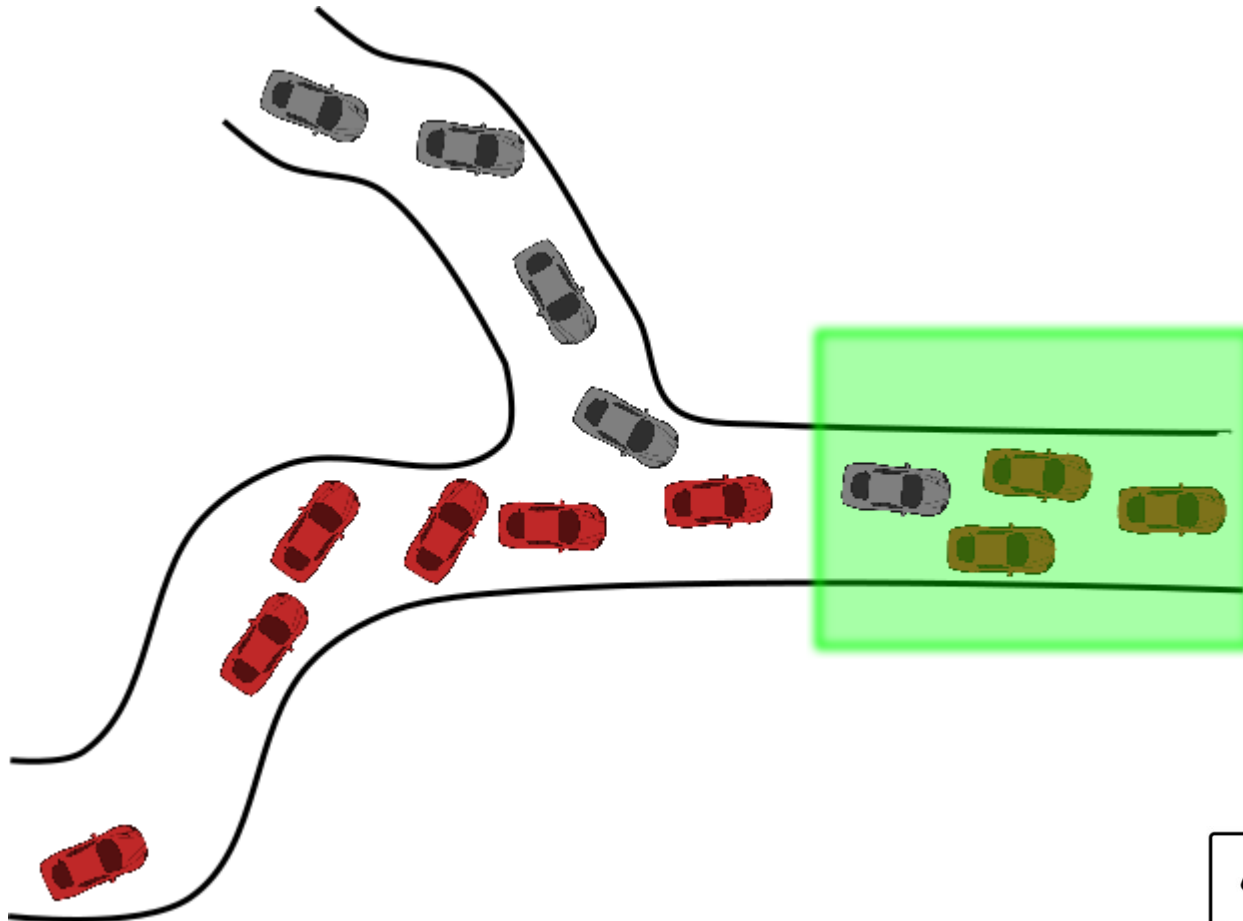




# Metabolic fluxes (turn-over rates)



# Metabolic fluxes (turn-over rates)



# Postprandial plasma metabolome

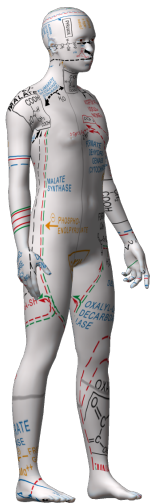


98%

$^{13}\text{CO}_2$



2%



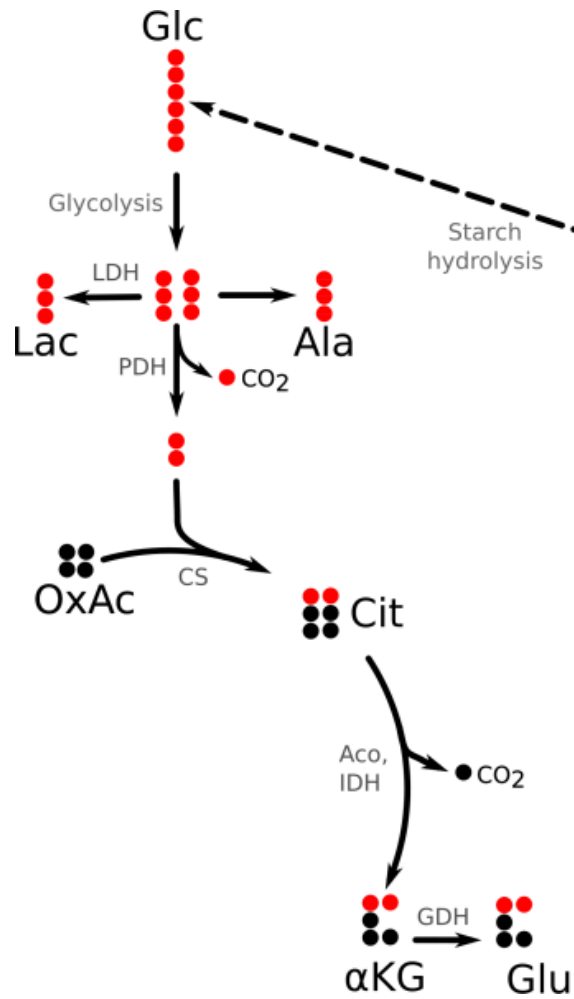
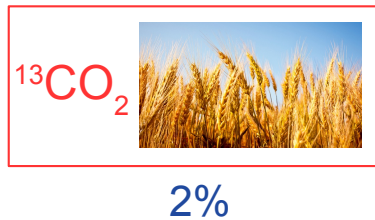
Dr Doris Jacobs  
Unilever R&D,  
Vlaardingen,  
The Netherlands



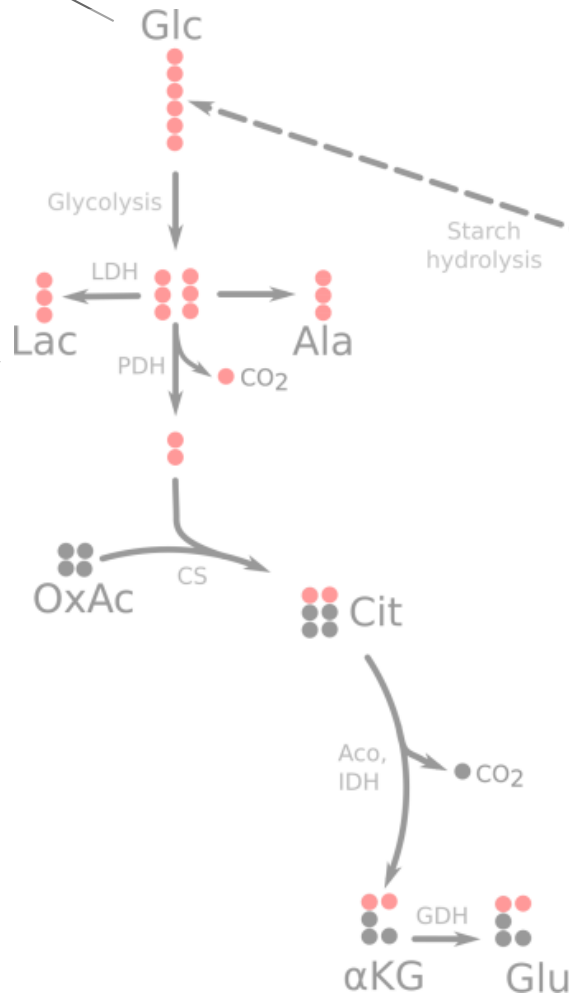
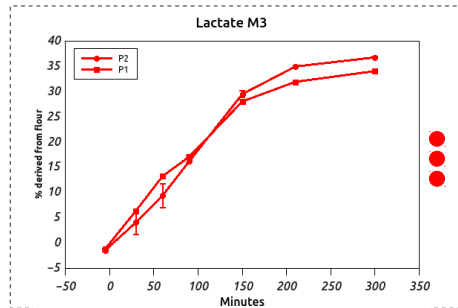
*The Postprandial Glucose Response is not a good reflection of the actual rate of Glucose Release from a Starchy Food; An exploratory Study using Dual Stable Isotope Technique, H.P.F. Peters, H.M. Boers, C. Eelderink, T.H. van Dijk, H. Hiemstra, A.R. Hoogenraad, D.J. Mela, M.G. Priebe*



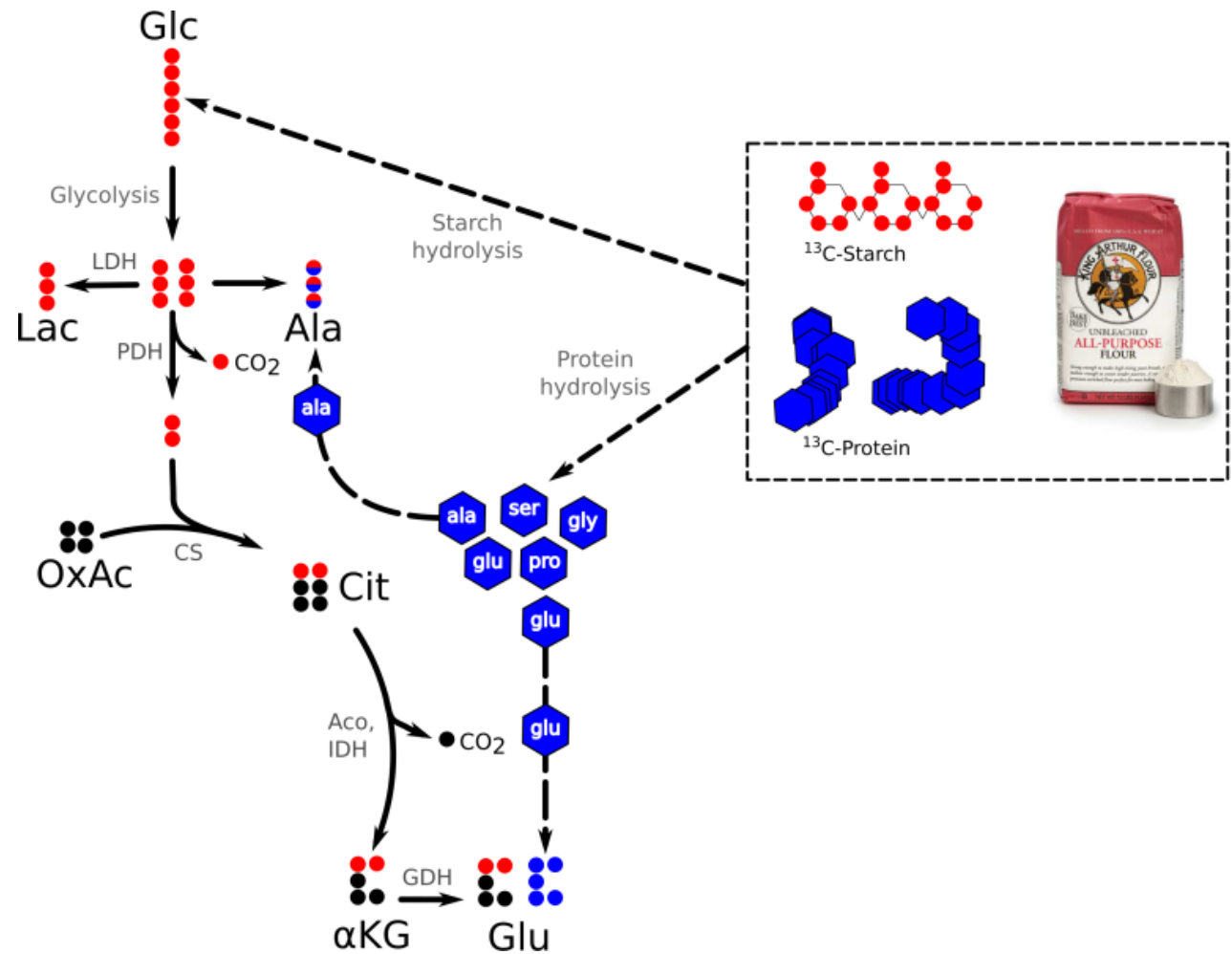
# $^{13}\text{C}$ labeling reveals metabolic activity



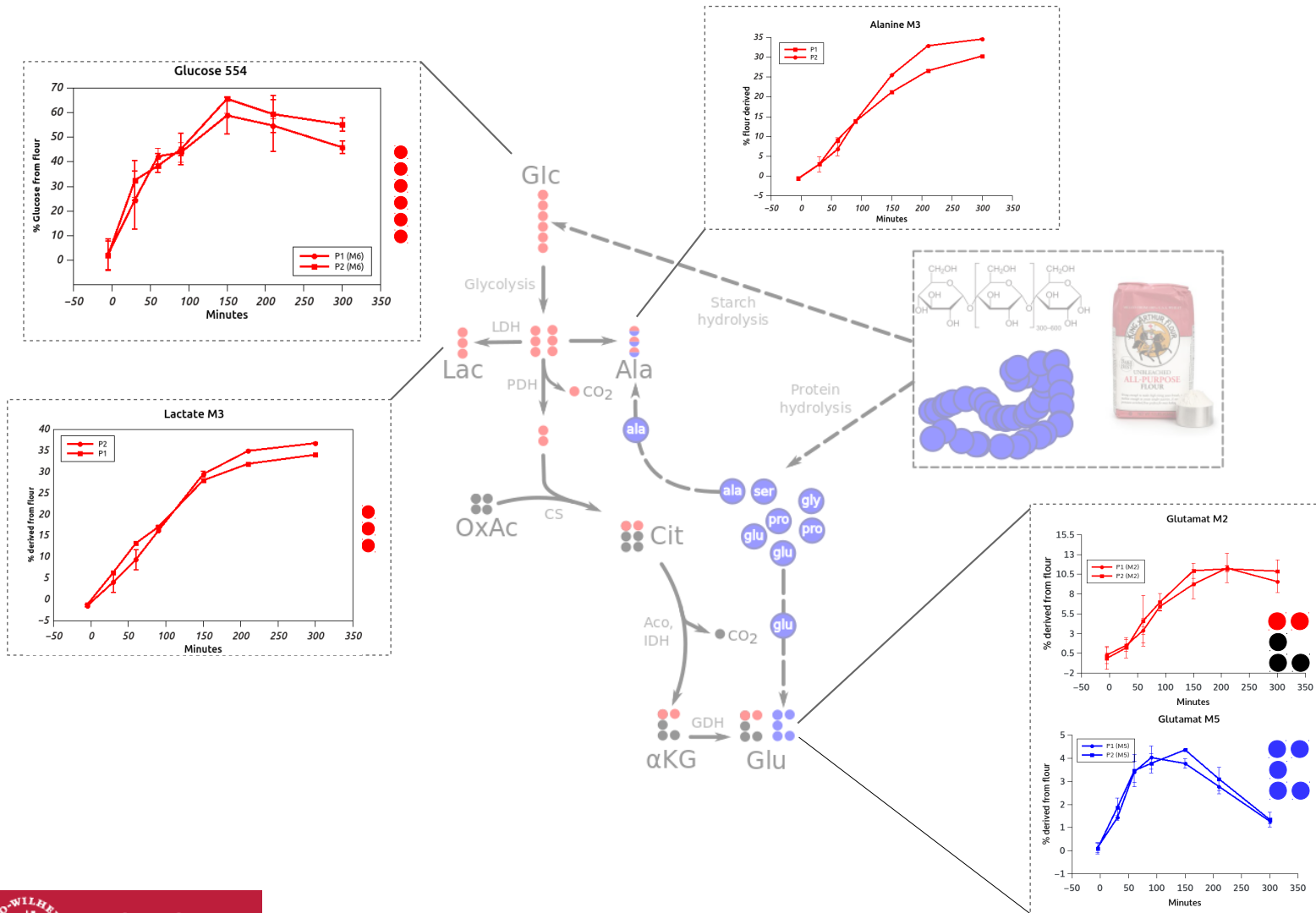
# Looking under the surface: $^{13}\text{C}$ labeling reveals metabolic activity



# Metabolism of wheat protein generates specific mass isotopomers

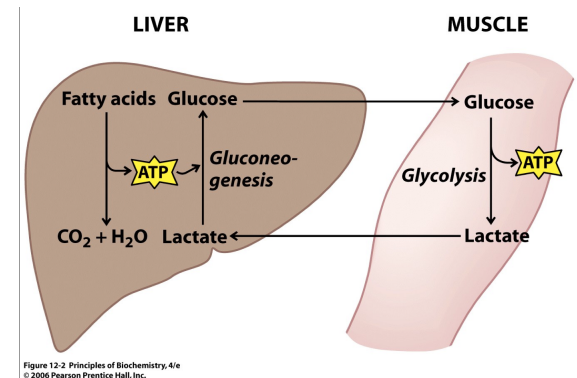


# Looking under the surface: $^{13}\text{C}$ labeling reveals metabolic activity

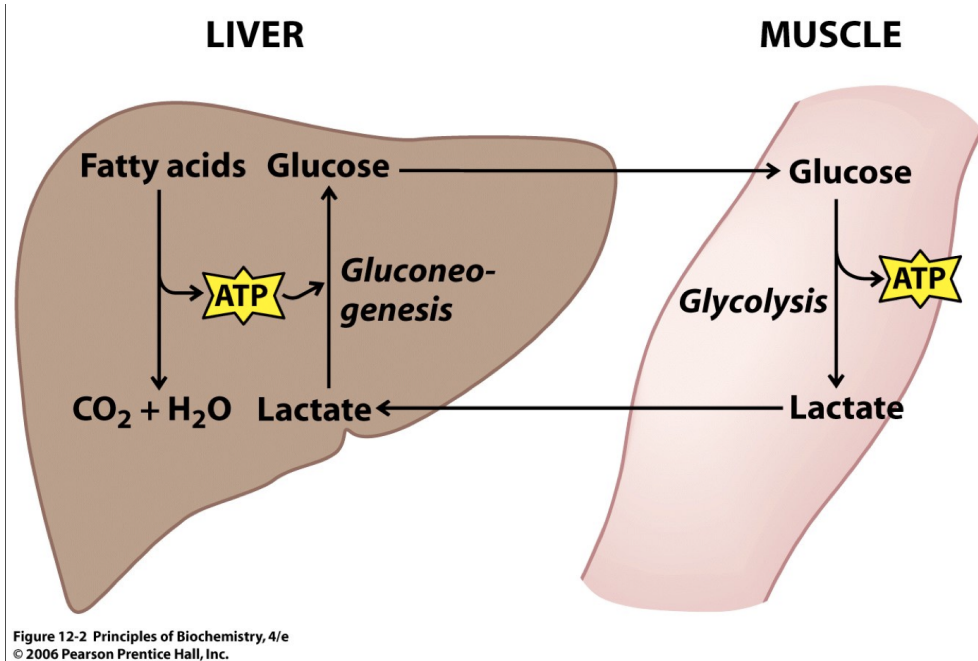


## “Small systems” biology:

Quantitative Cori cycle fluxes through  
stable-isotope labeling  
and ODE modeling



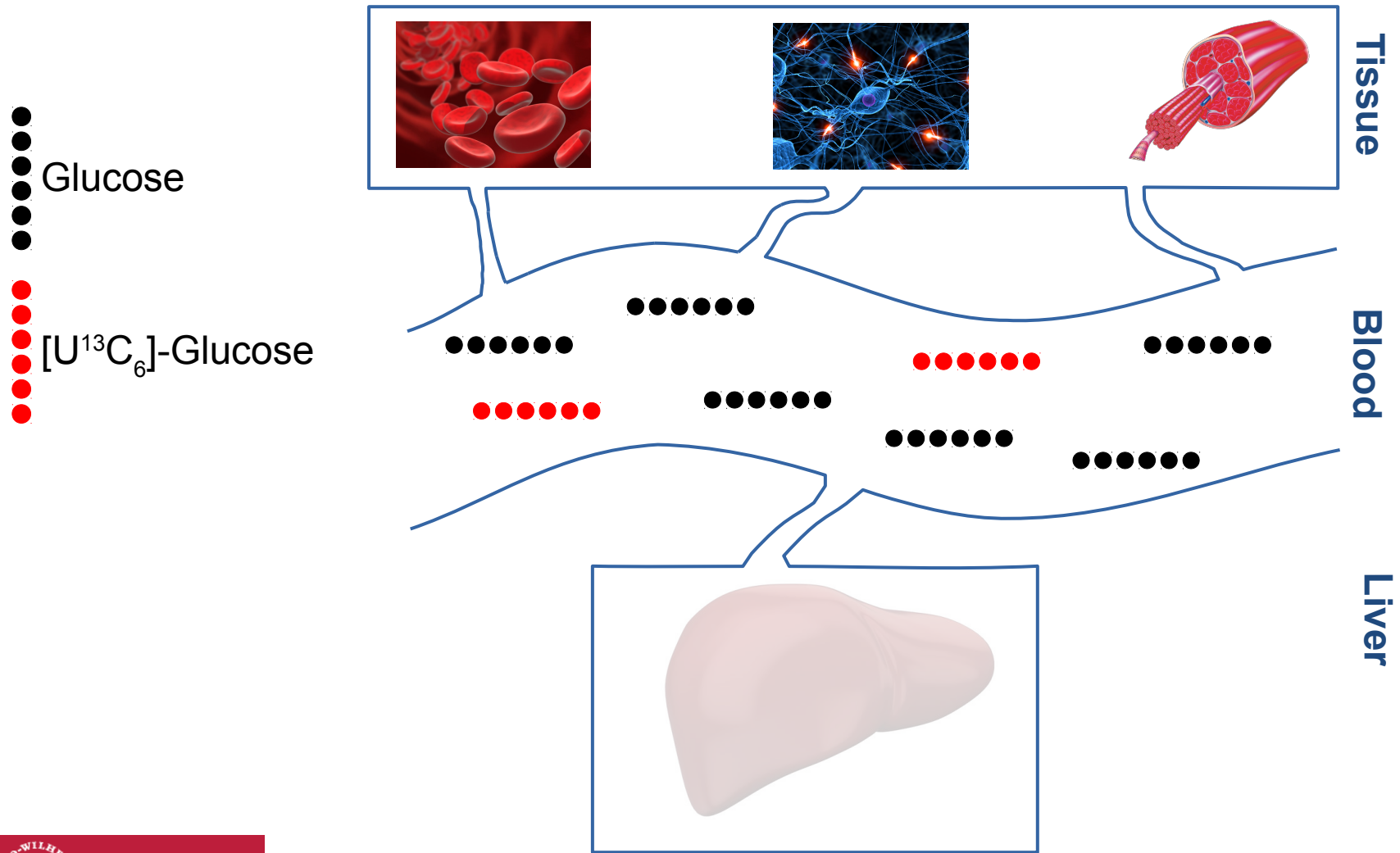
# Cori cycle



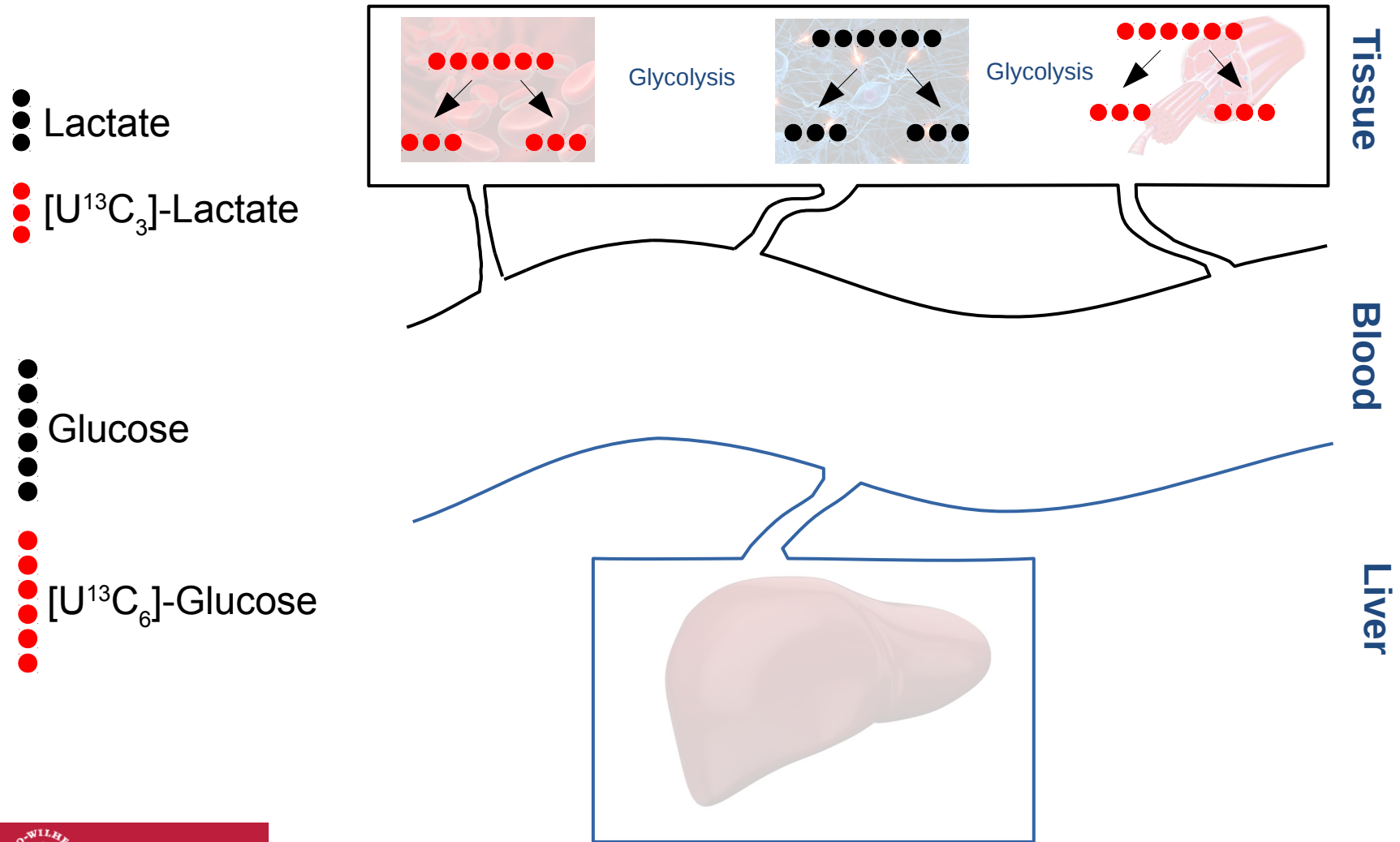
Courtesy Bernard Becker Medical Library,  
Washington University School of Medicine



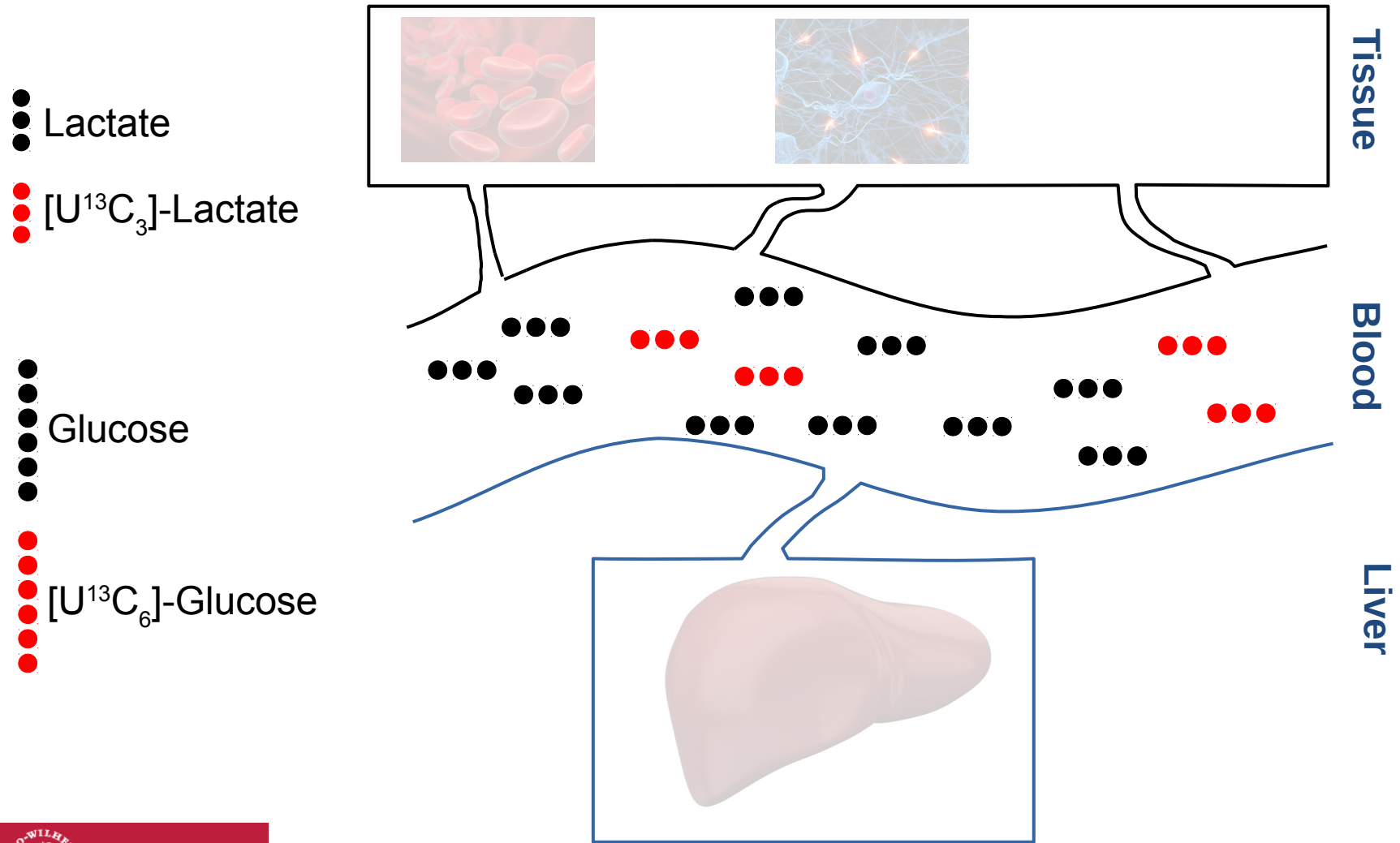
# Stable-isotope labeling to determine glucose turnover and Cori cycle activity



# Stable-isotope labeling to determine glucose turnover and Cori cycle activity



# Stable-isotope labeling to determine glucose turnover and Cori cycle activity



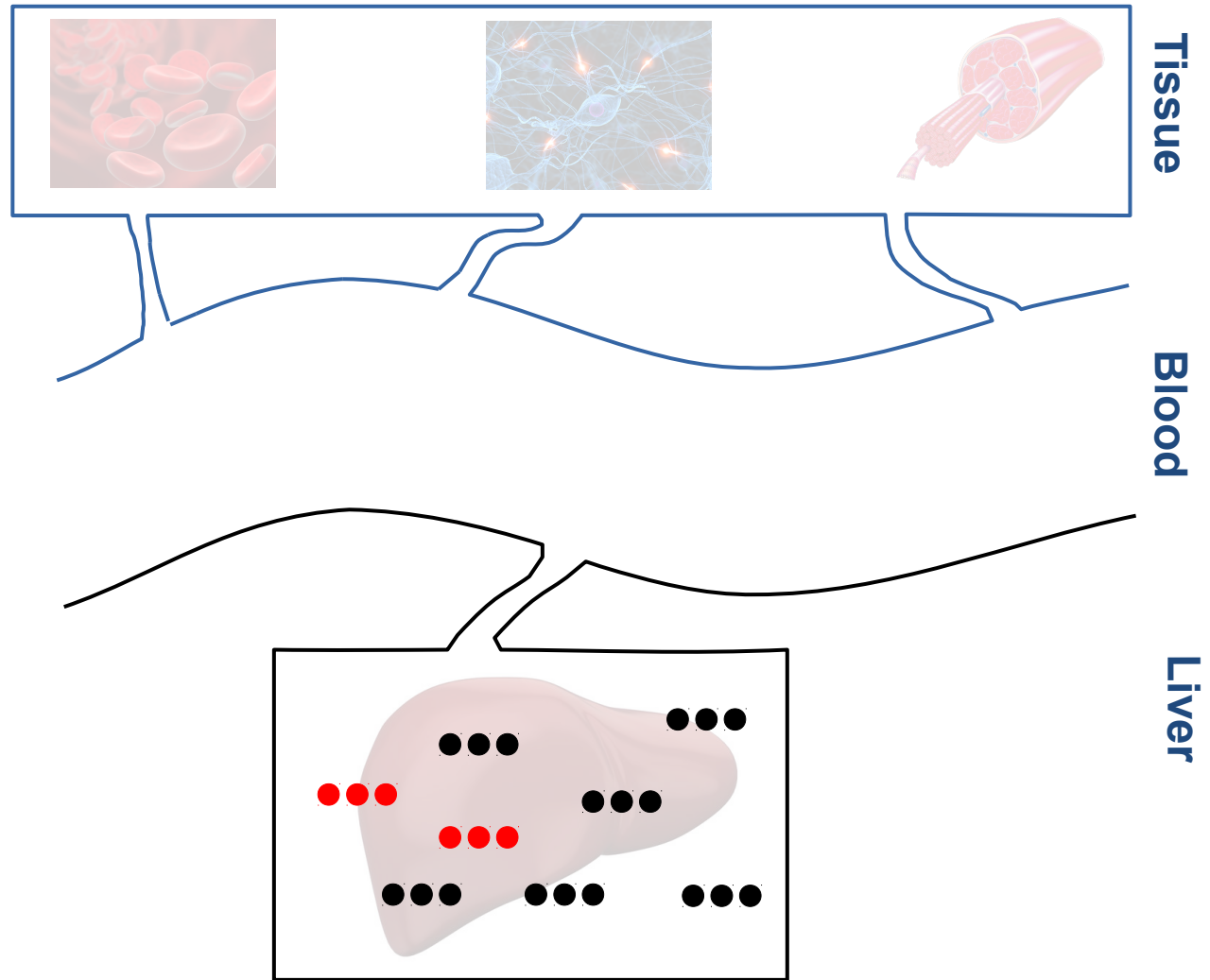
# Stable-isotope labeling to determine glucose turnover and Cori cycle activity

●●● Lactate

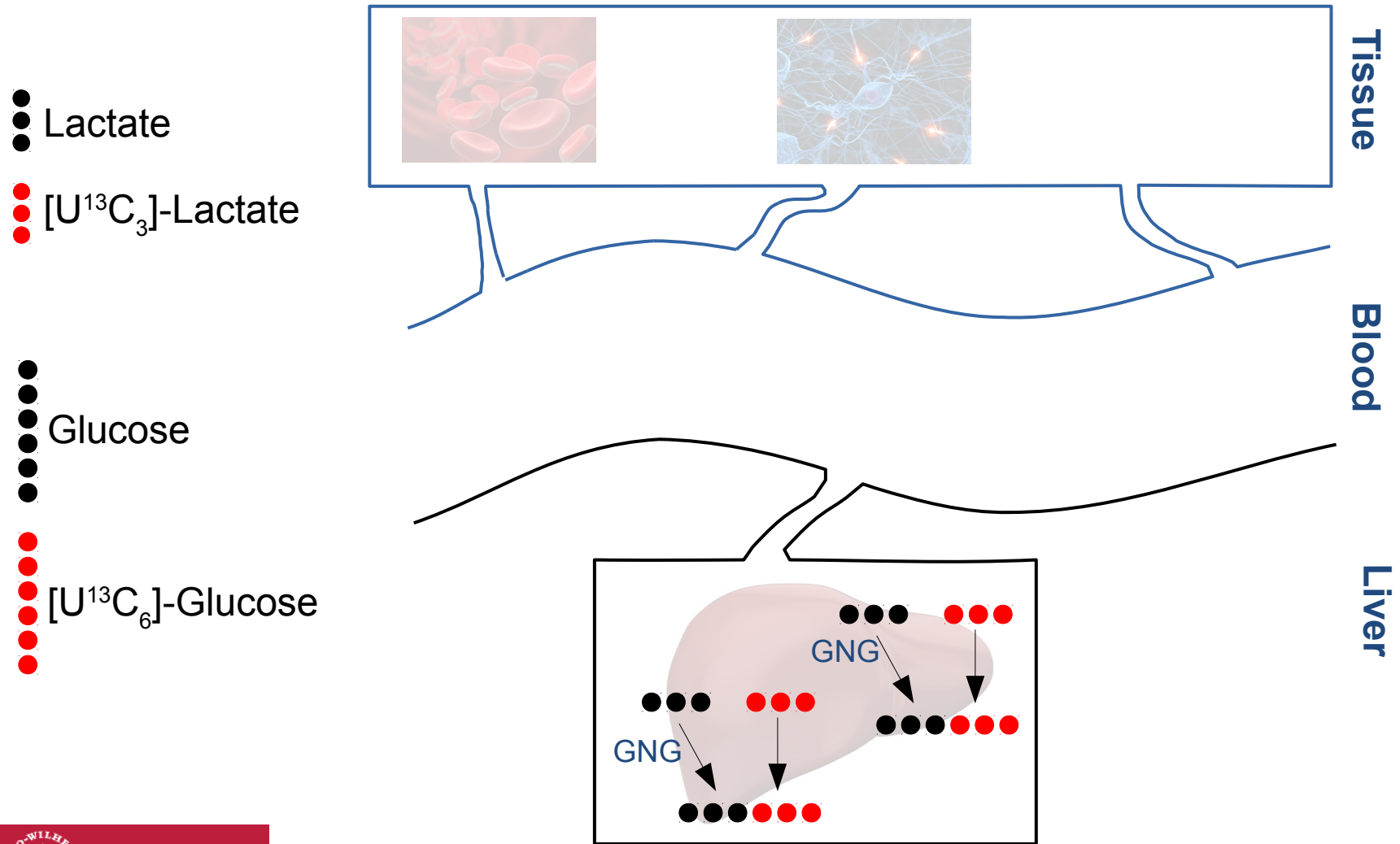
●●● [U<sup>13</sup>C<sub>3</sub>]-Lactate

●●●●●● Glucose

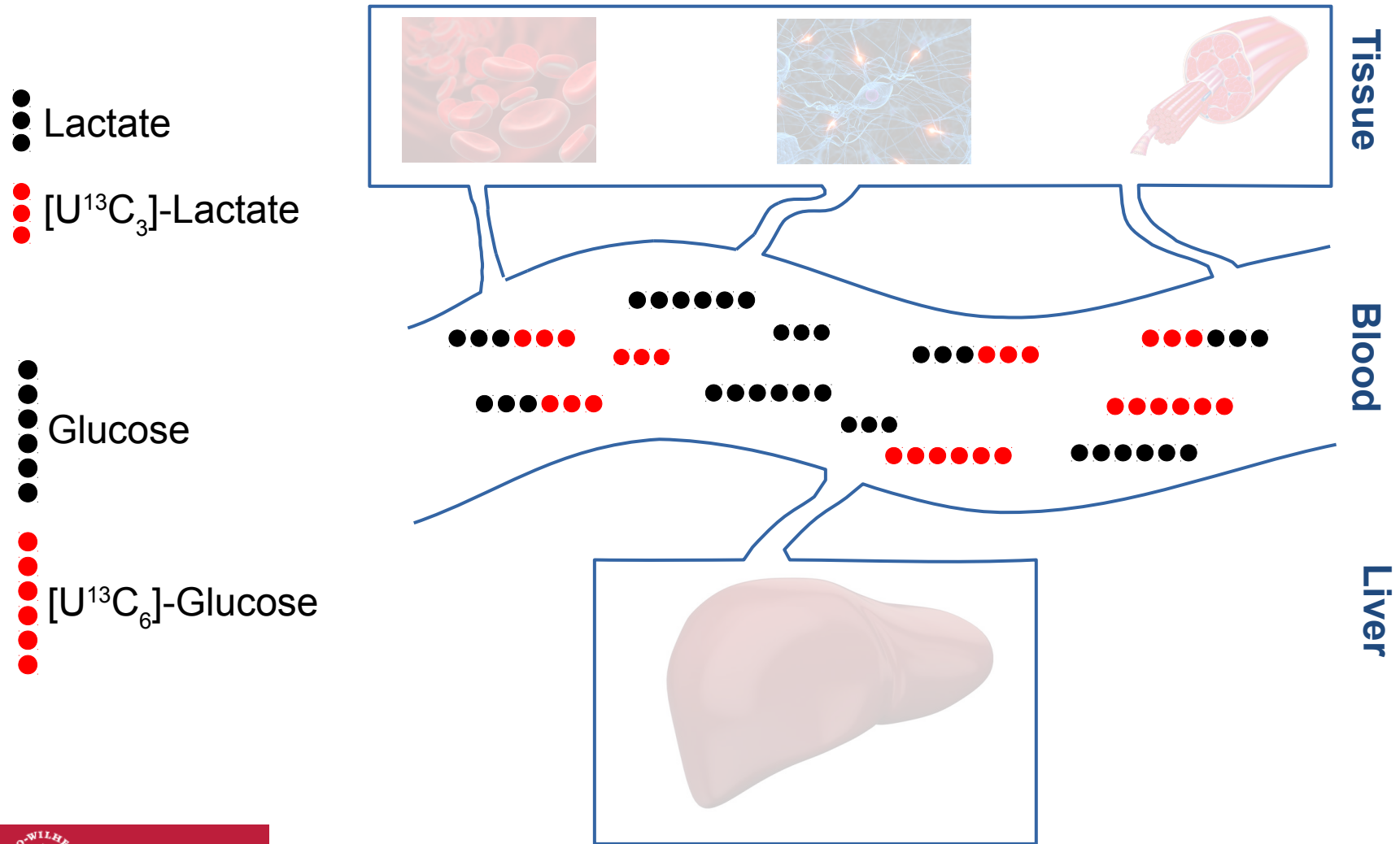
●●●●●● [U<sup>13</sup>C<sub>6</sub>]-Glucose



# Stable-isotope labeling to determine glucose turnover and Cori cycle activity

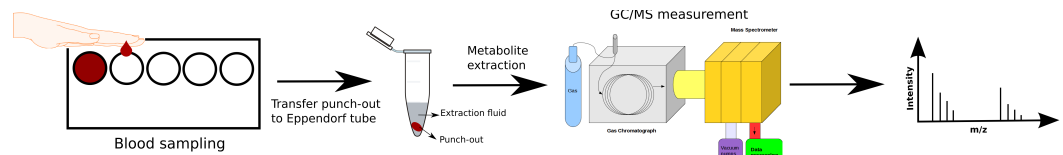
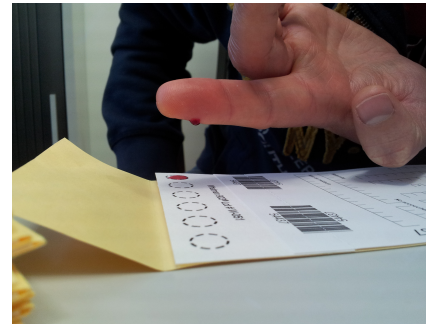
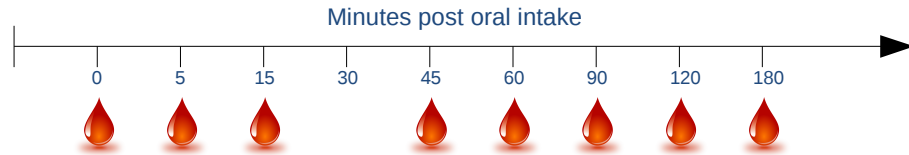
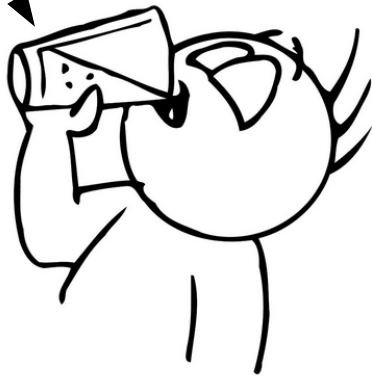
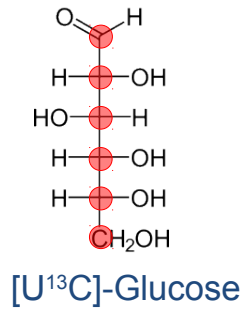


# Stable-isotope labeling to determine glucose turnover and Cori cycle activity

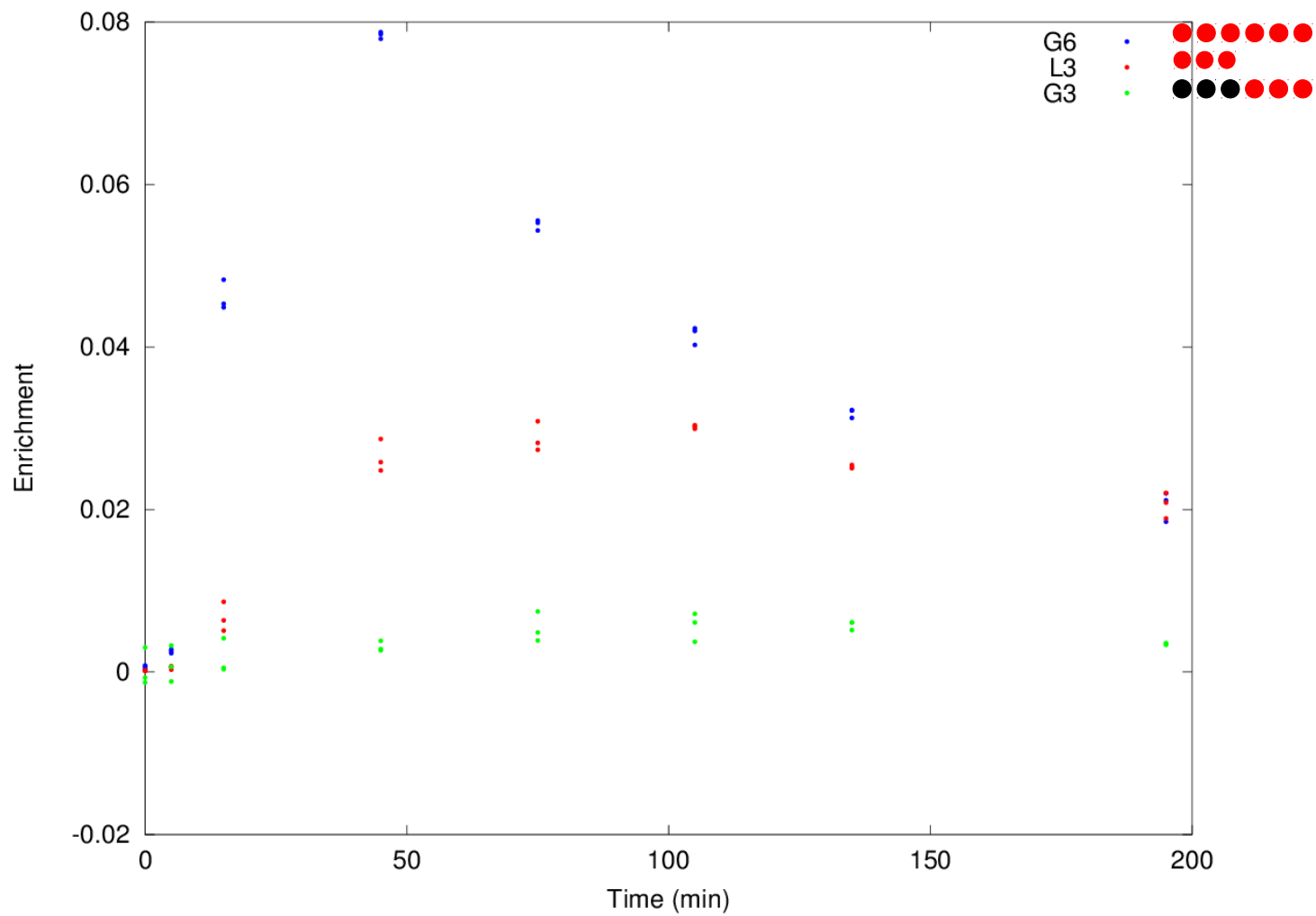




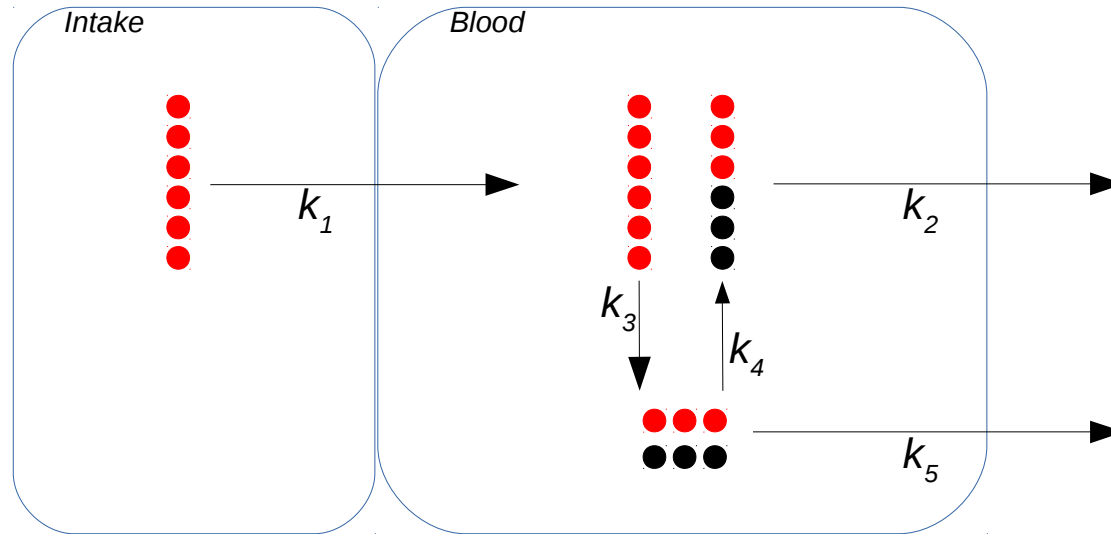
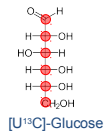
# Stable-isotope labeling in vivo



# Stable-isotope labeling to determine Cori cycle activity



# Differential equation system to model Cori cycle



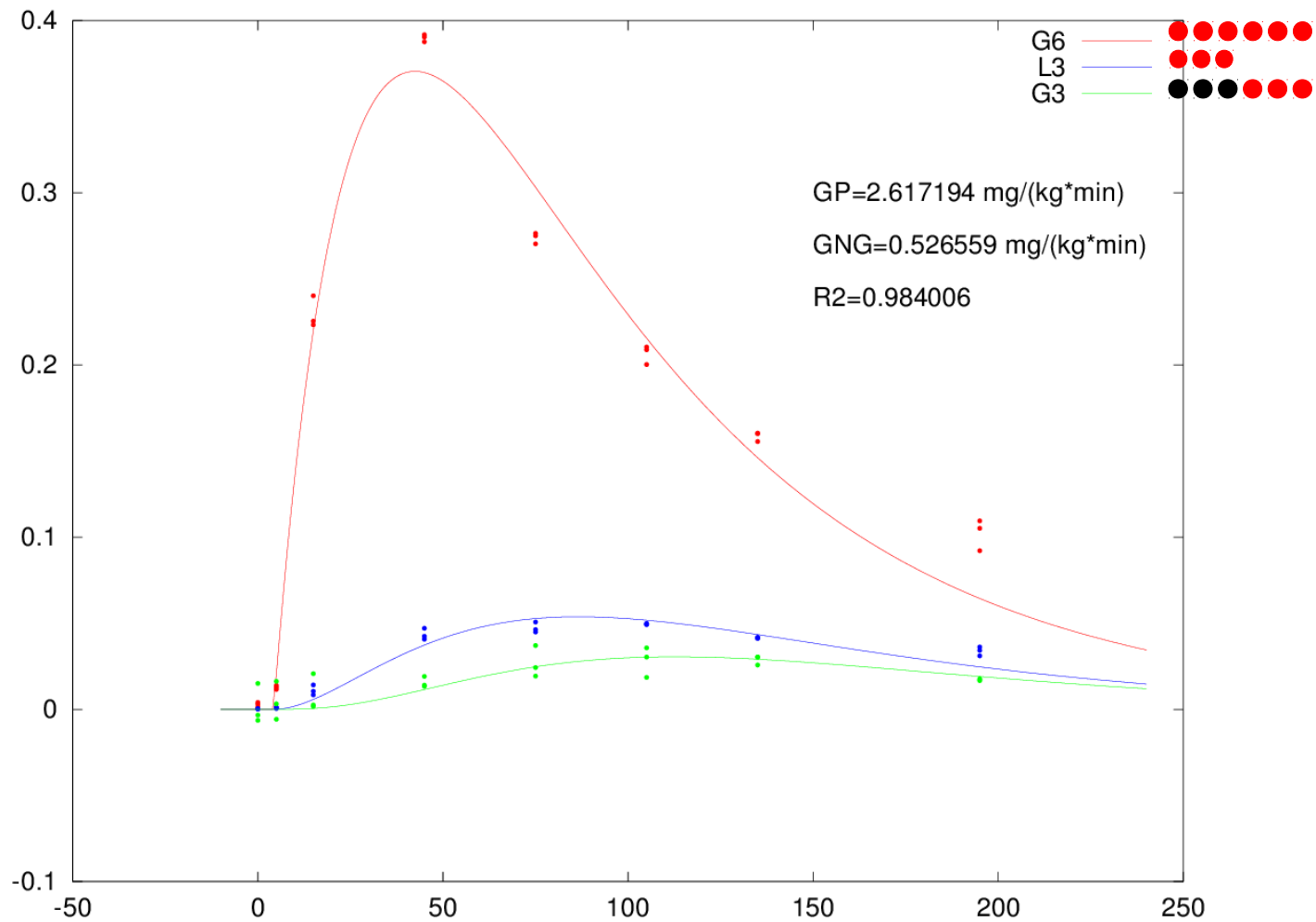
$$\frac{dG 6_i}{dt} = -k_1 \cdot G 6_i(t)$$

$$\frac{dG 6_b}{dt} = k_1 \cdot G 6_i(t) - k_2 \cdot G 6_b(t) - k_3 \cdot G 6_b(t)$$

$$\frac{dL 3}{dt} = k_3 \cdot G 6_b(t) - k_4 \cdot L 3(t) - k_5 \cdot L 3(t)$$

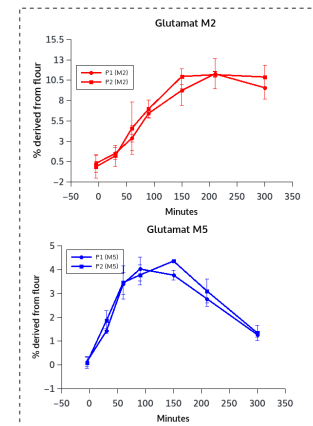
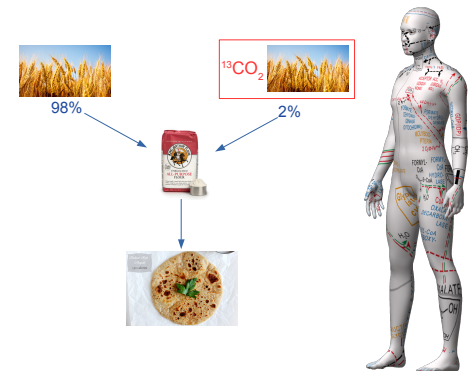
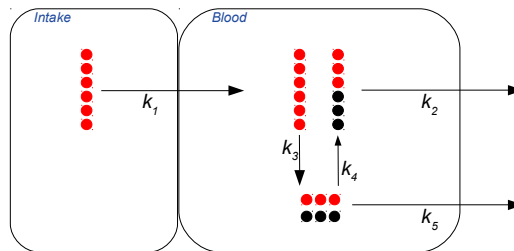
$$\frac{dG 3}{dt} = k_4 \cdot L 3(t) - k_2 \cdot G 3(t) - k_3 \cdot G 3(t)$$

# Stable-isotope labeling to determine Cori cycle activity



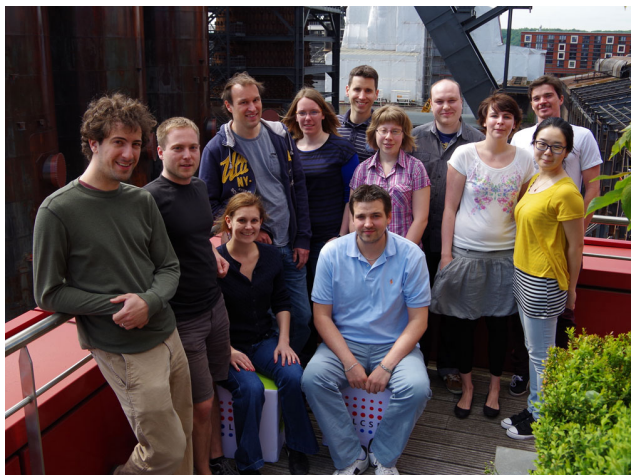
# Conclusions

- Small and robust metabolic models in combination with stable-isotope labeling can provide quantitative insights into otherwise not accessible mechanisms
- $^{13}\text{C}$  labeling of food enables profiling of nutrient utilization and opens up windows for systems based approaches in nutrition



# Thank you for your attention!

## Metabolomics Group at LCSB



- Jean-Pierre Trezzi
- Lisa Krämer
- Christian Jäger
- Jochen Schneider
- Alex Skupin



## Unilever R&D

Vlaardingen, The Netherlands



Dr Doris Jacobs

## Molecular Nutrition Unit at Technische Universität München



Prof Hannelore Daniel

## Medical Translational Research at LCSB

- Prof Jochen Schneider



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