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UNIVERSITY OF ABERDEEN

HEINRICH HEINE UNIVERSITÄT DÜSSELDORF

CEPLAS
Cluster of Excellence on Plant Sciences

Polysaccharide Metabolism in silico: Conceptual Challenges and Approaches

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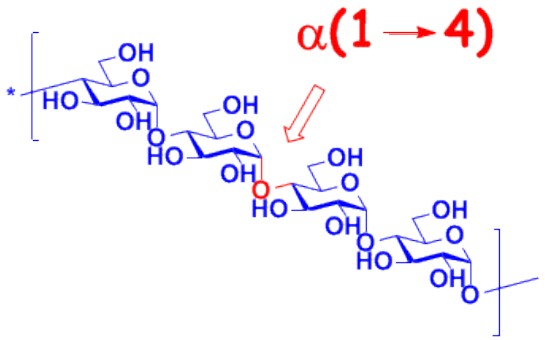
QTB Institut für Quantitative & Theoretische Biologie

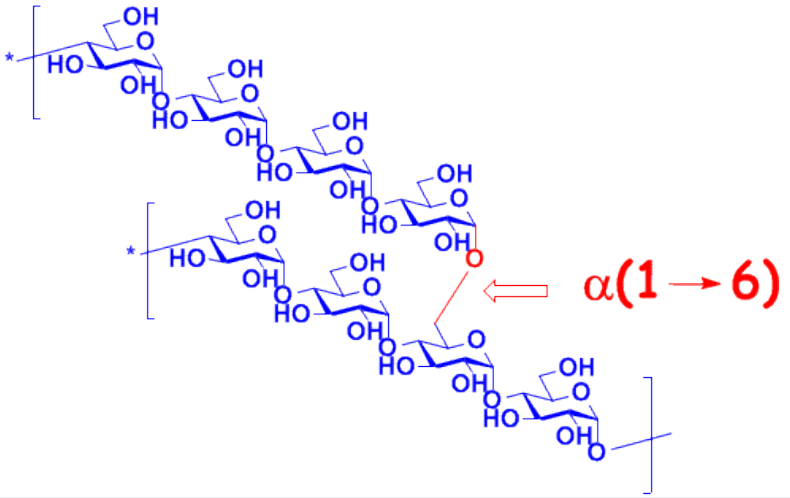
Edinburgh, 14.7.2016
Algal Polysaccharides Workshop

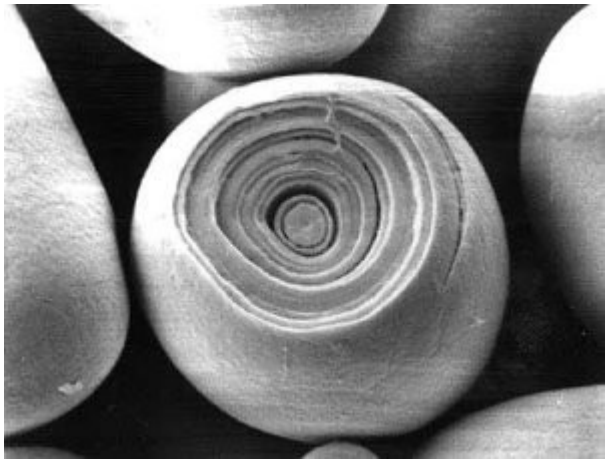
Starch

Amylose
(MW 32,000-113,000)

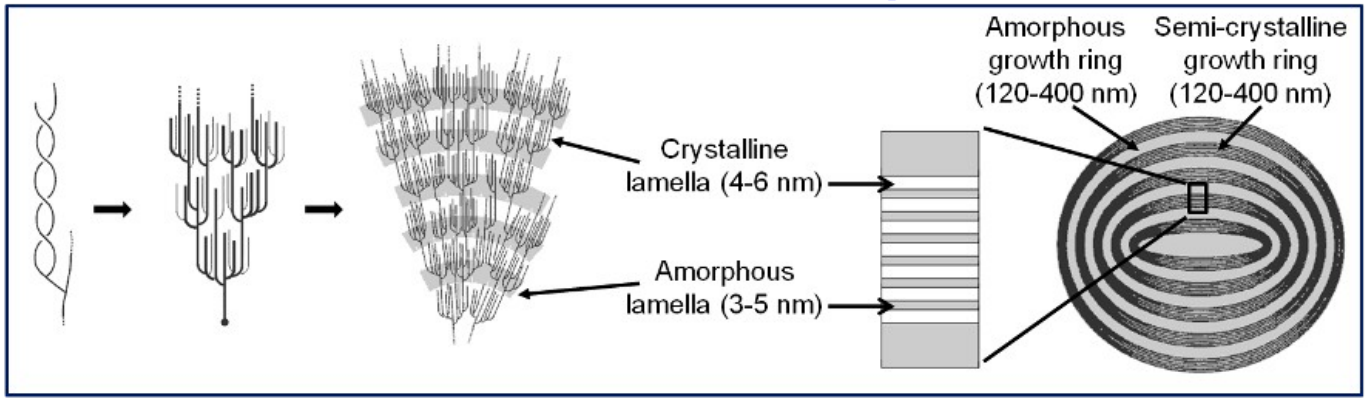


Amylopectin
(MW 10^7-10^9)





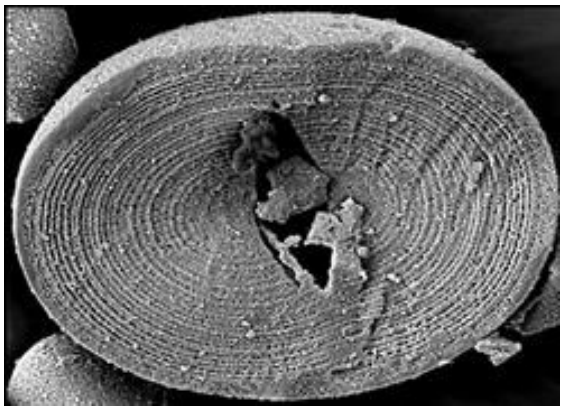
(ianhopkinson.org.uk)



(O'Neill and Field, 2015, Front Bioeng Biotechnol)

To understand the emergence of the complex structure of starch, we need to be able to model it!

Conceptual challenges



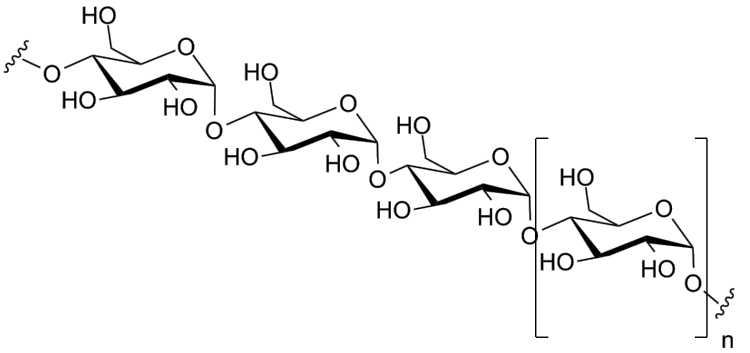
(szeeman-at-ethz.ch)

1

Biochemical reactions on surfaces

2

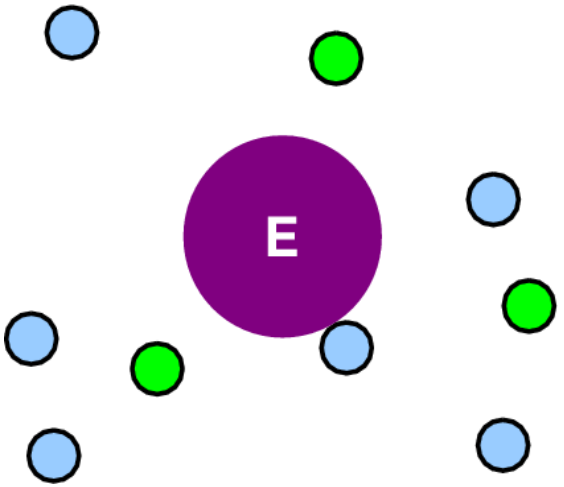
Biochemical reactions on polymers



(by glycoform, commons.wikimedia.org)

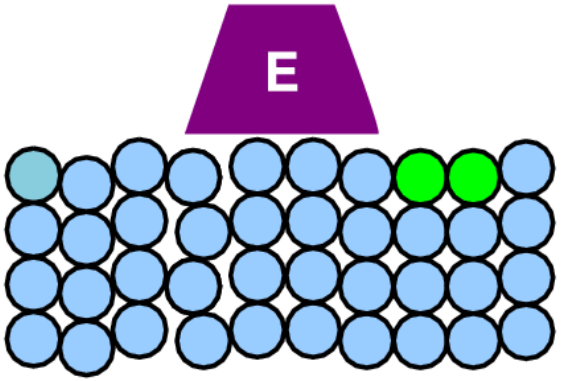
Challenge 1: surface-active enzymes

dissolved substrate



$$v = \frac{V_{max} S}{K_M + S}$$

aggregated substrate (with interfacial reaction space)

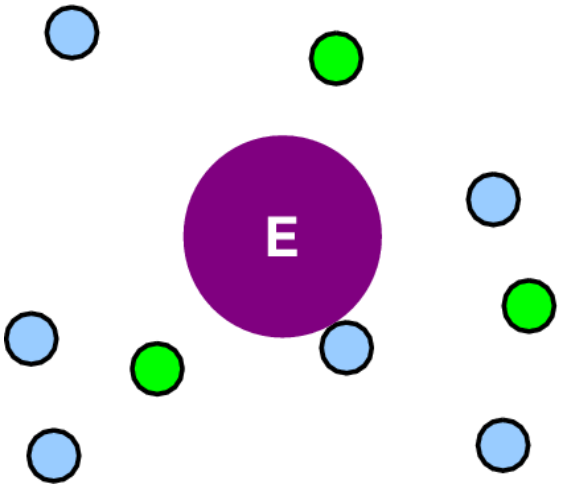


$$v = f(?)$$

Reaction space confined to 2D!

Rate laws for surfactive enzymes

dissolved substrate



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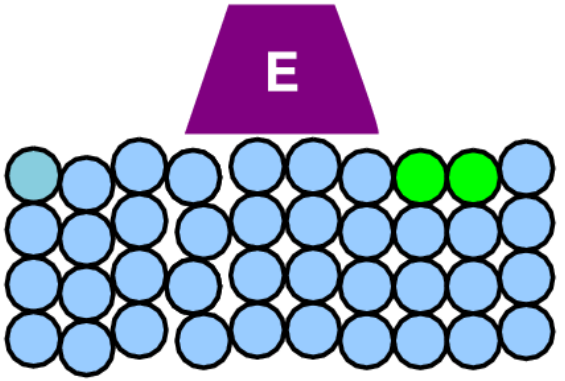


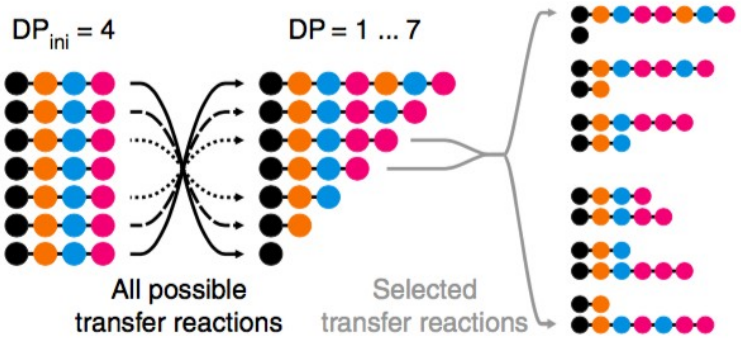
$$v = \frac{k_A a_s \Phi_{eq} [M][E_0](k_S \langle *S \rangle - k_P \langle *P \rangle)}{1 + k_A a_s \Phi_{eq} [M]\left(1 + \frac{\langle *S \rangle}{K_{mS}} + \frac{\langle *P \rangle}{K_{mP}}\right)} = \frac{V_M^{app} \frac{[M]}{K_{mM}^{app}}}{1 + \frac{[M]}{K_{mM}^{app}}}$$

Kartal and Ebenhöh (2013) FEBS Letters
(centenary issue commemorating Michaelis-Menten 'Kinetik der Invertinwirkung')

Challenge 2: polymer-active enzymes

How do you model enzymes catalysing an infinite number of reactions?

DPE1: $G_n + G_m \rightleftharpoons G_{n-q} + G_{m+q}$



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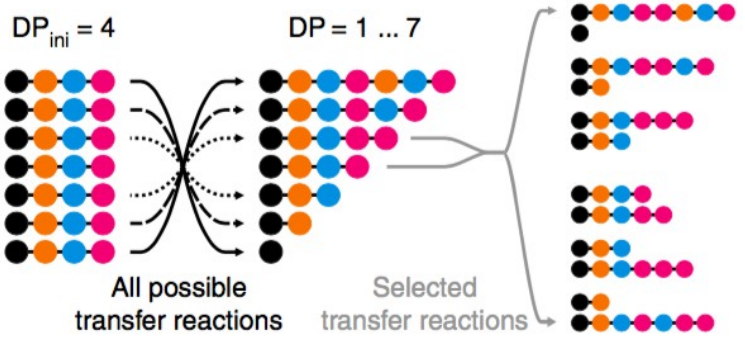
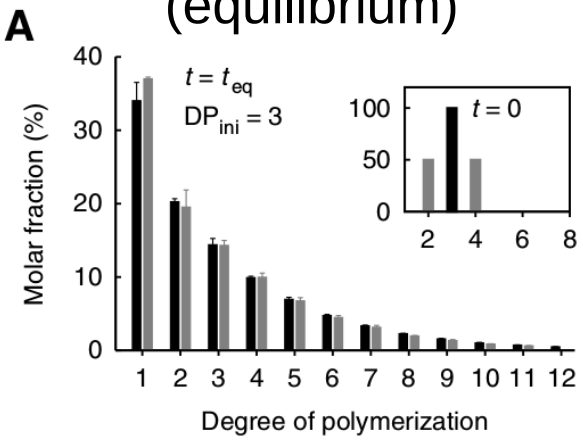
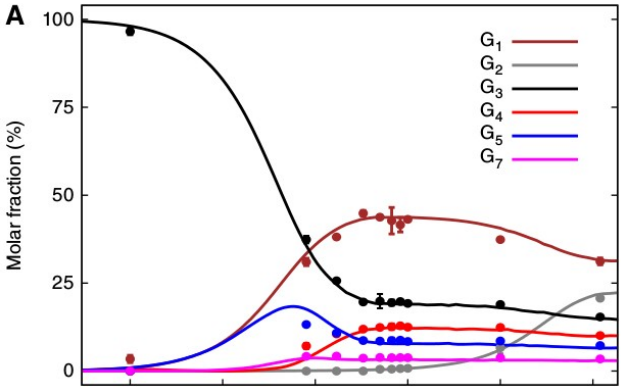


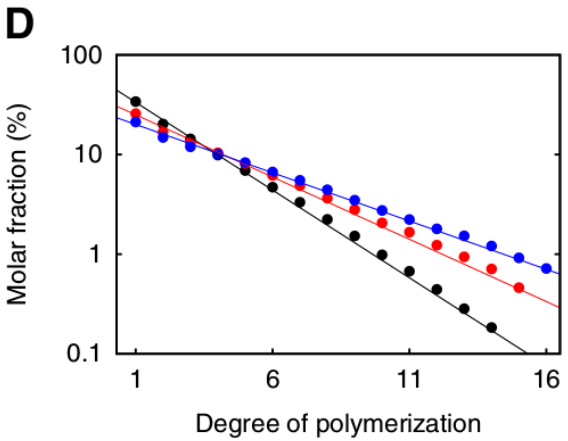
Solution

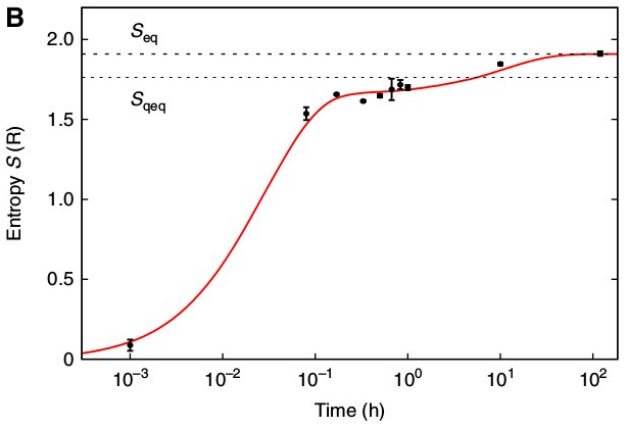
Statistical thermodynamics (equilibrium)

Stochastic simulations (dynamics)



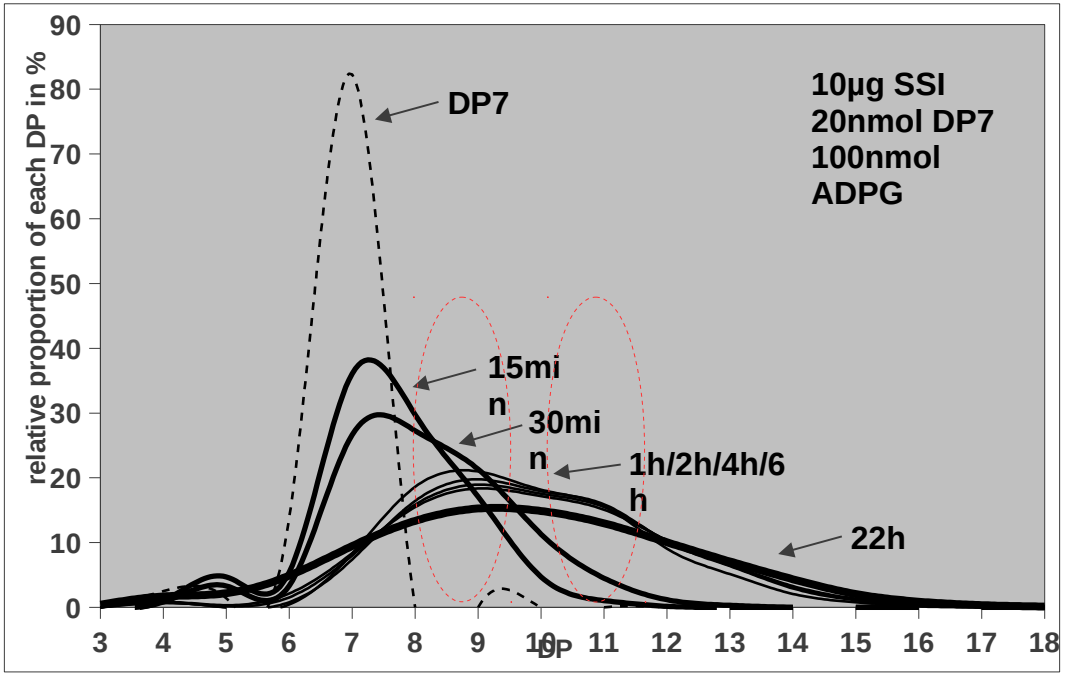






(Kartal et al, 2011, Mol Syst Biol)

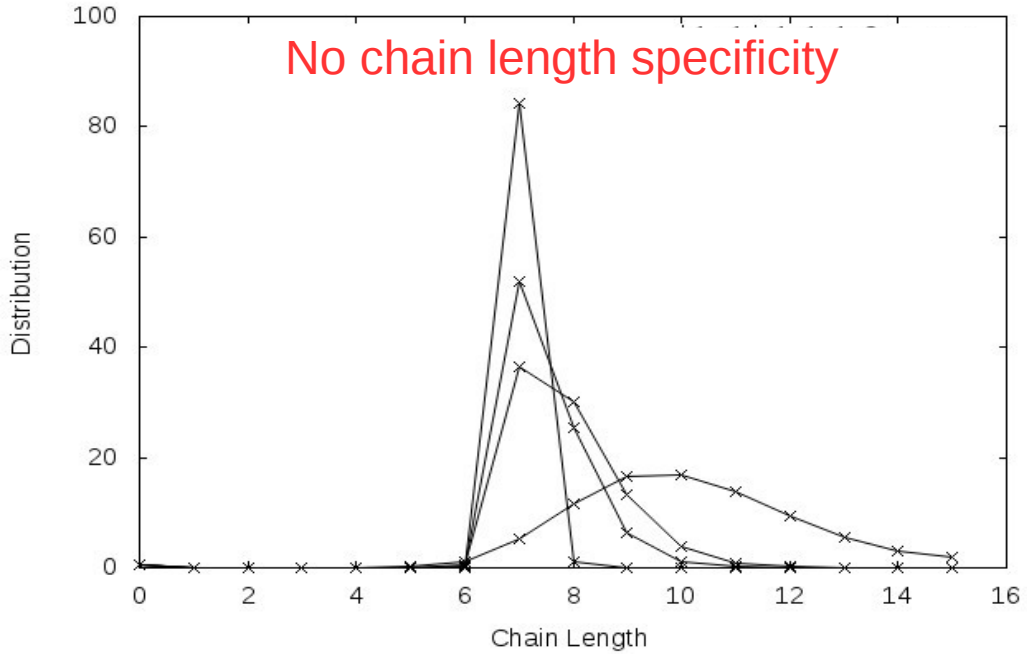
What can we learn from models?

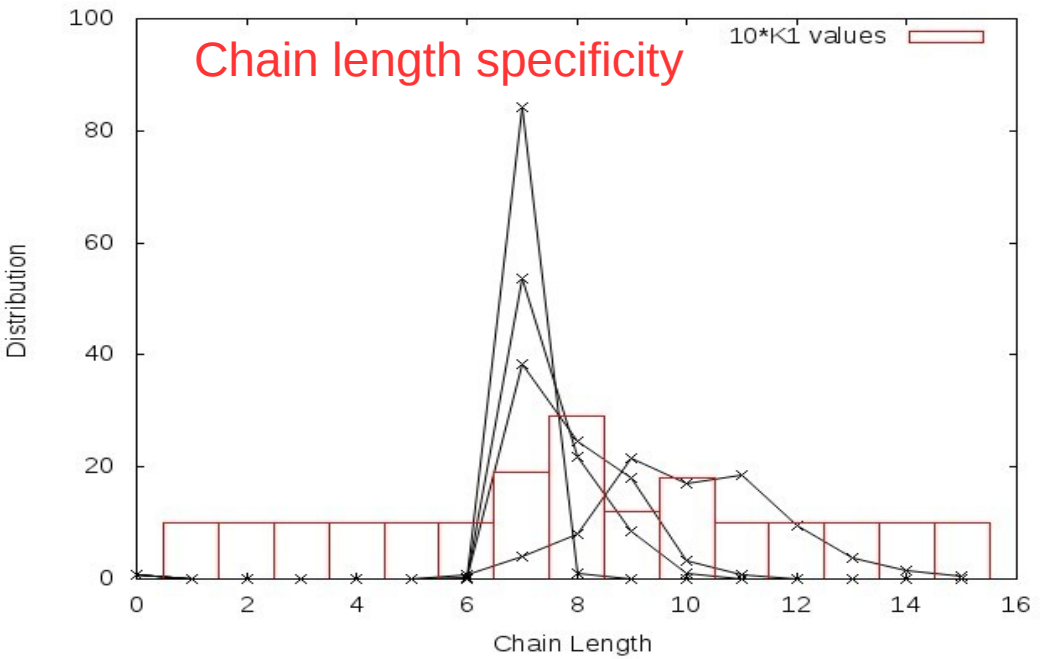


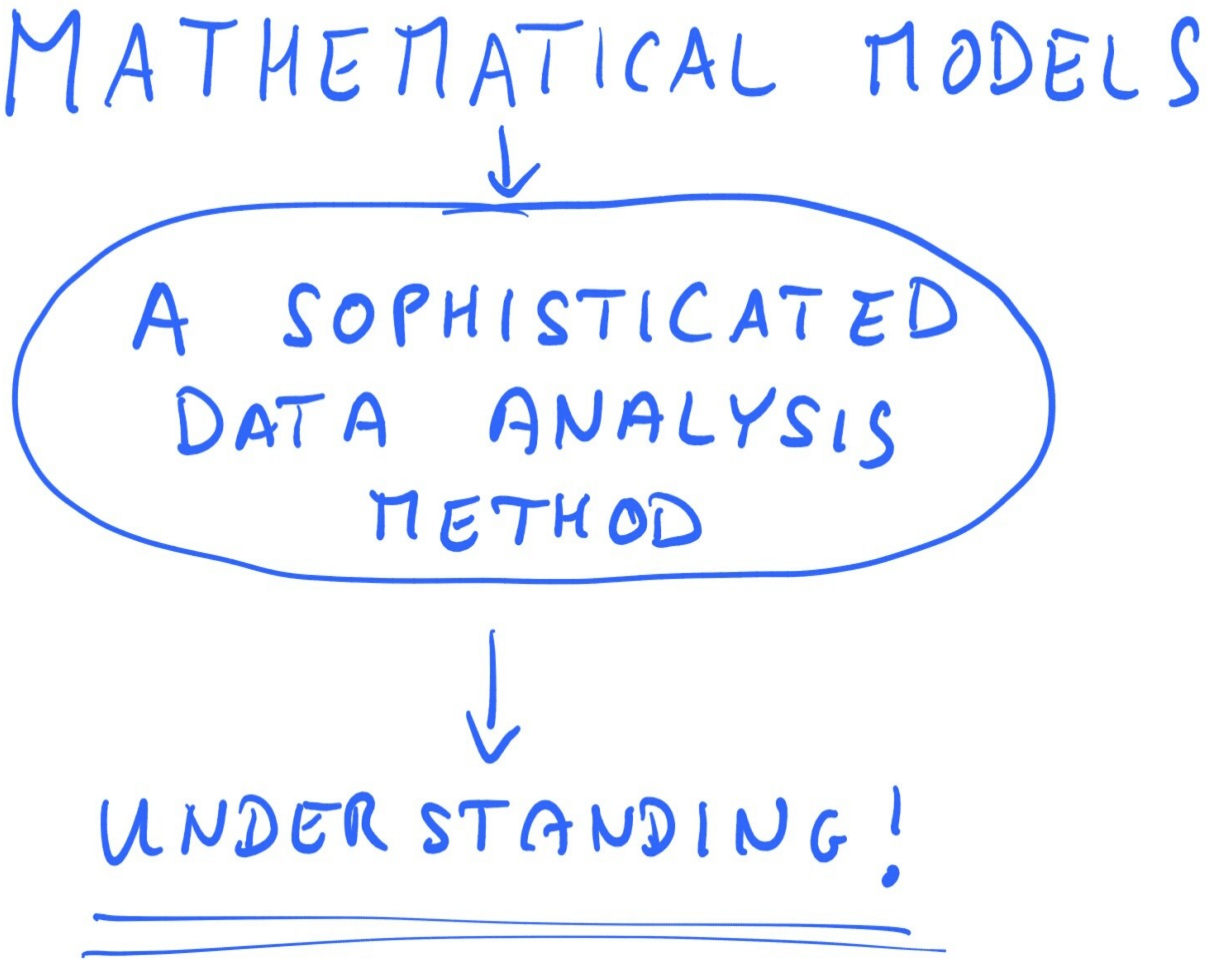
SS1 (Starch Synthase I):

$$\mathrm{ADPG} + G_n \rightleftharpoons \mathrm{ADP} + G_{n+1}$$

data from Henrike Brust, U Potsdam
(see also Brust el al, 2013, J Appl Glycosci 60)






MATHEMATICAL MODELS
A SOPHISTICATED DATA ANALYSIS METHOD
UNDERSTANDING!