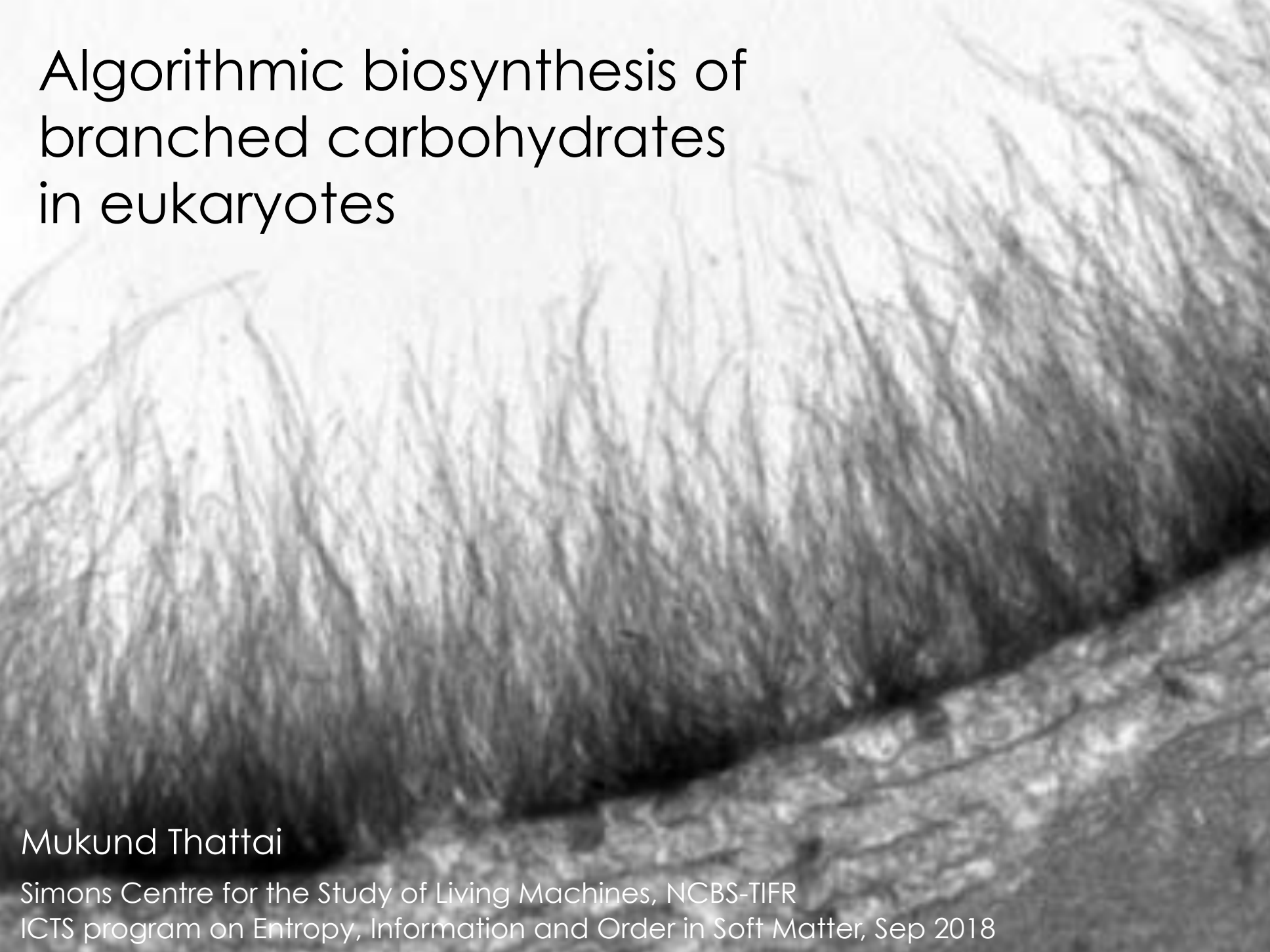
Algorithmic biosynthesis of branched carbohydrates in eukaryotes

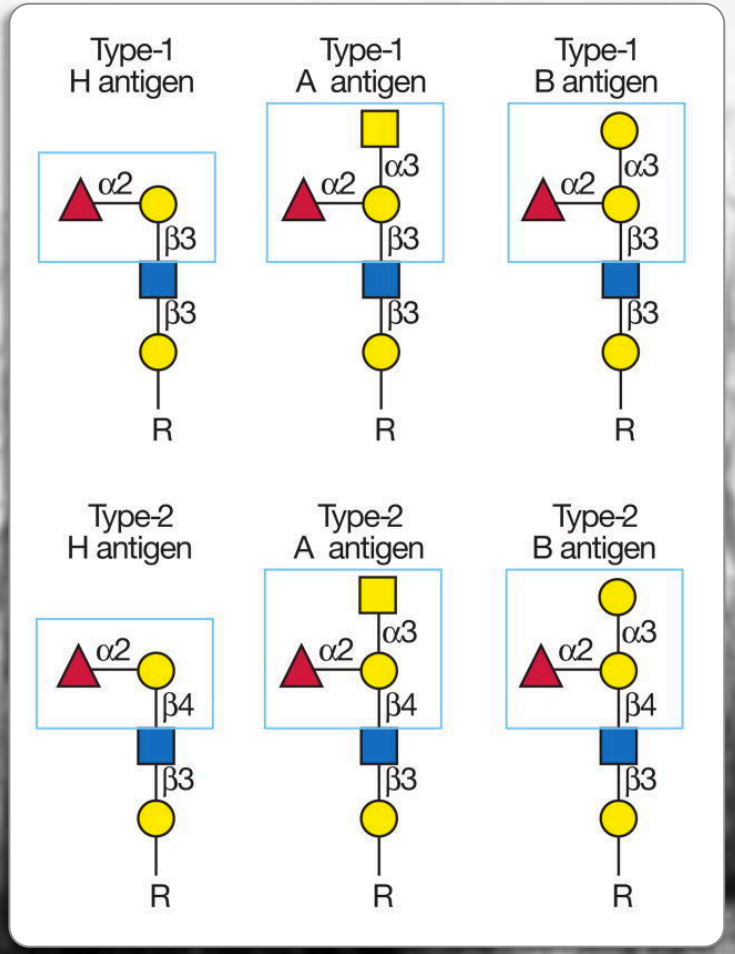


Mukund Thattai

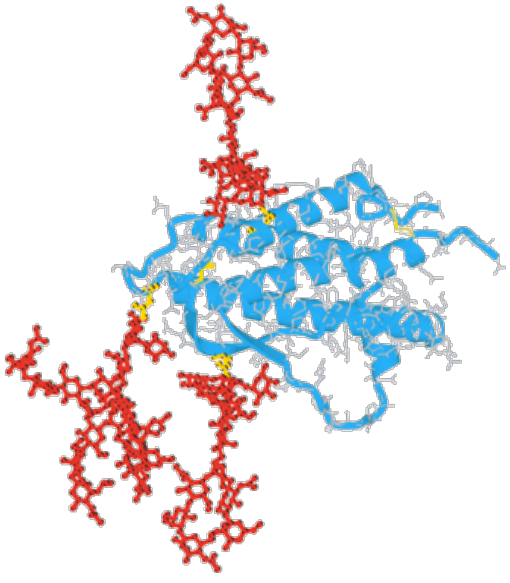
Simons Centre for the Study of Living Machines, NCBS-TIFR

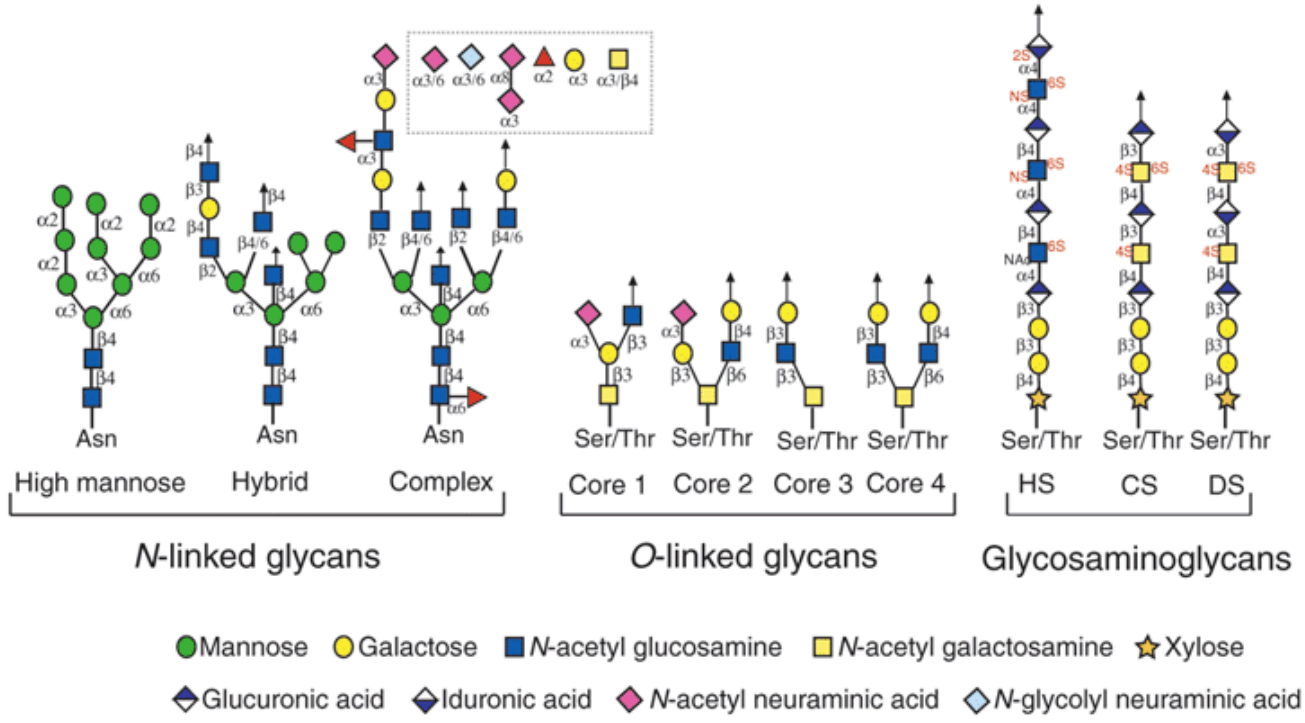
ICTS program on Entropy, Information and Order in Soft Matter, Sep 2018

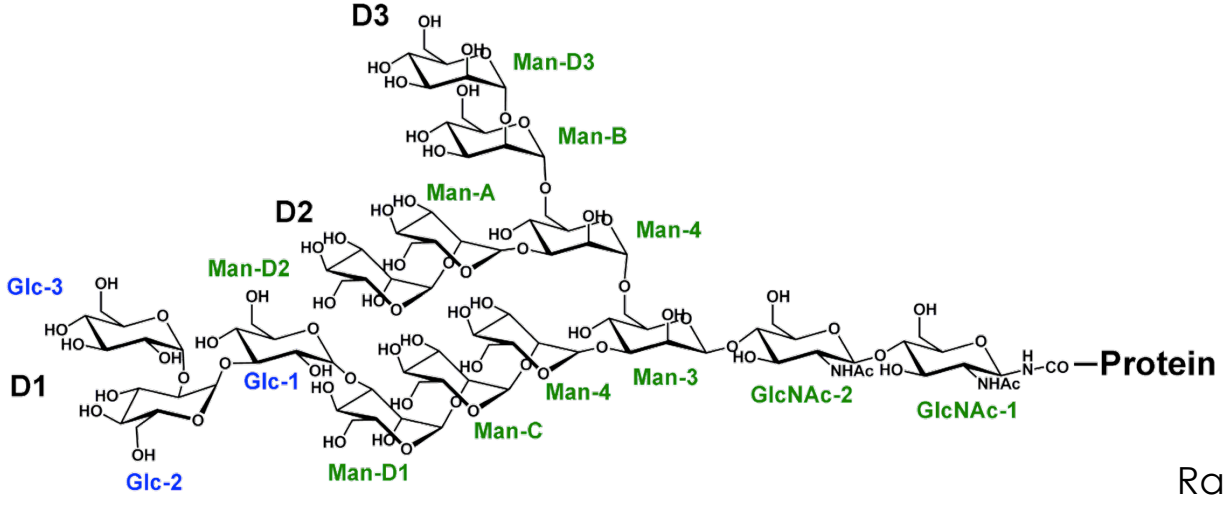
Glycans are branched carbohydrates that decorate the surface of every living cell



Meuwese, 2008; Varki et al., Essentials of Glycobiology

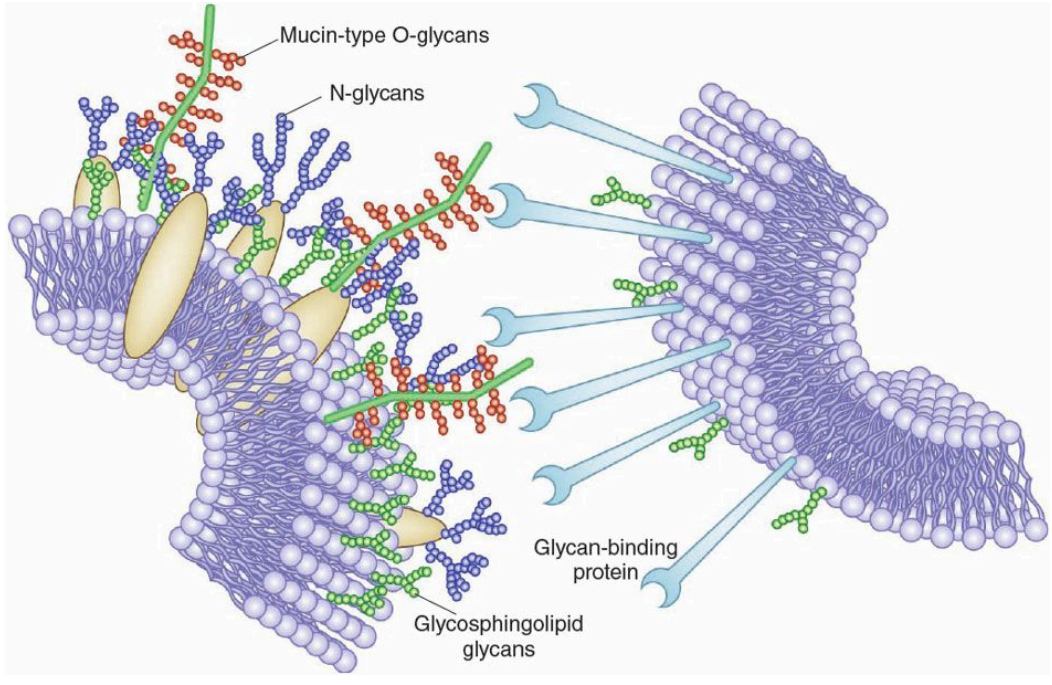




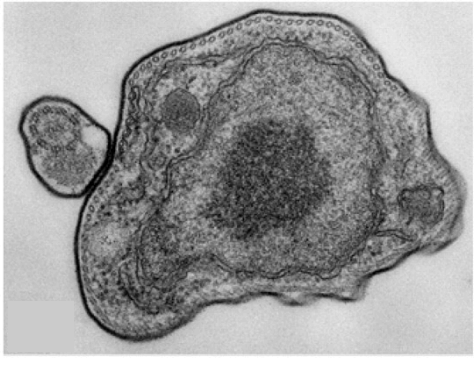


Raman et al., Nat Methods 2005;
Satoh et al., Molecules 2015;
Sheridan, Nature Biotechnol 2007

Glycans convey information about cell identity



Host-pathogen interface



Sheader et al., PNAS 2005

Cellular aggregation

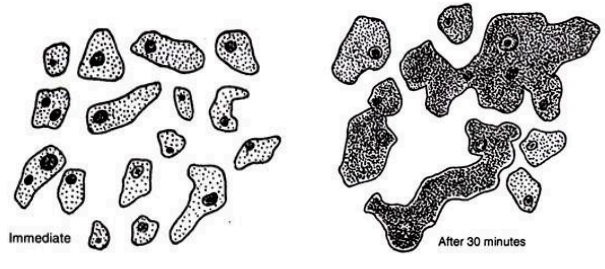
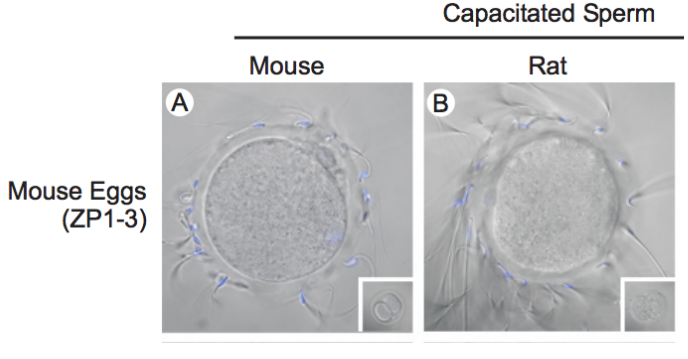


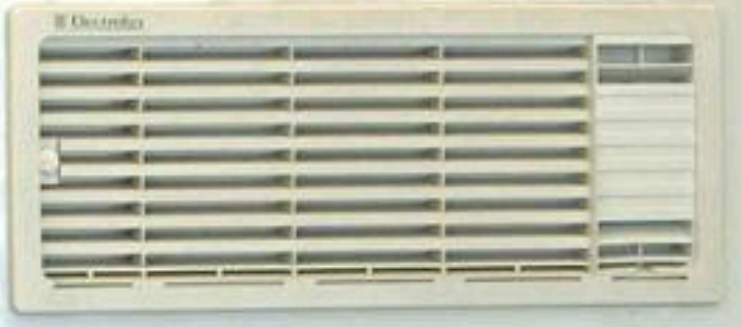
Image credit: Ganguly

Species-specific fertilization



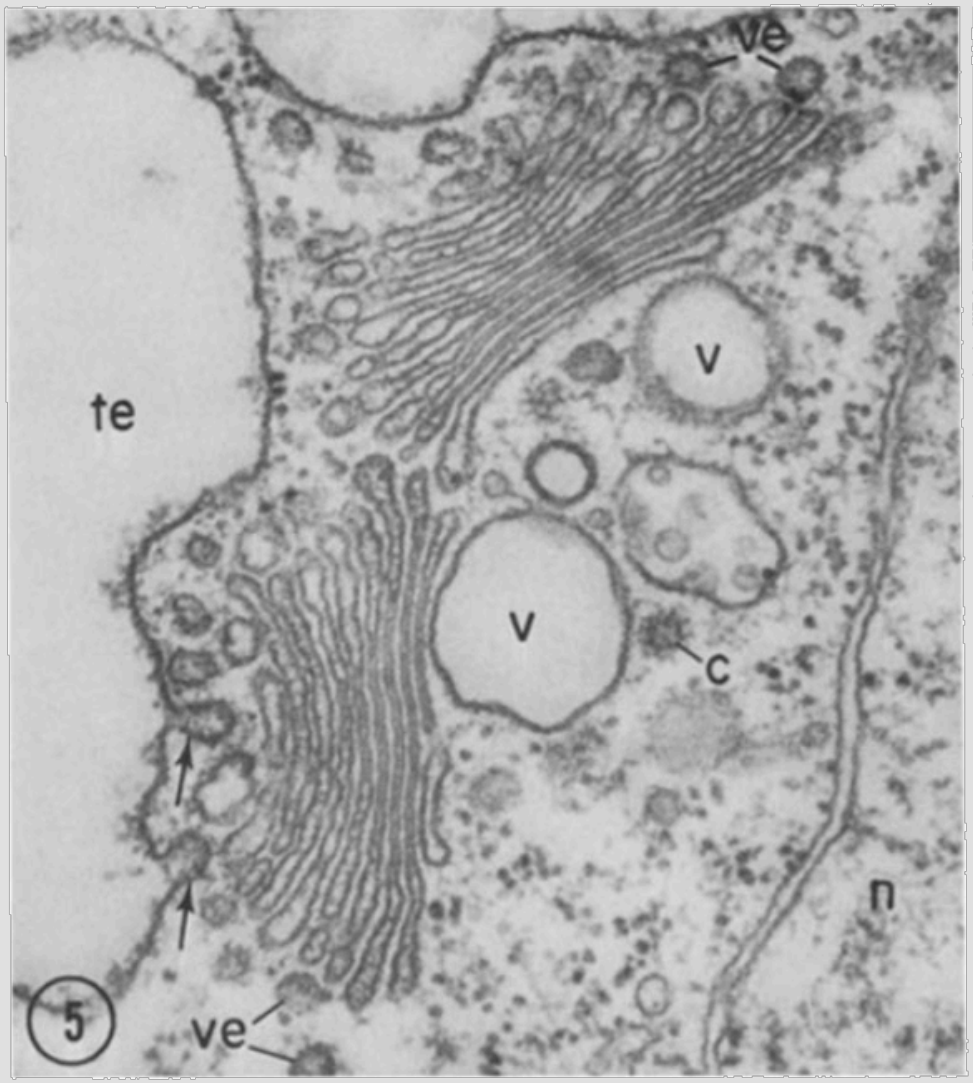
Hoodbhoy et al., JBC 2005

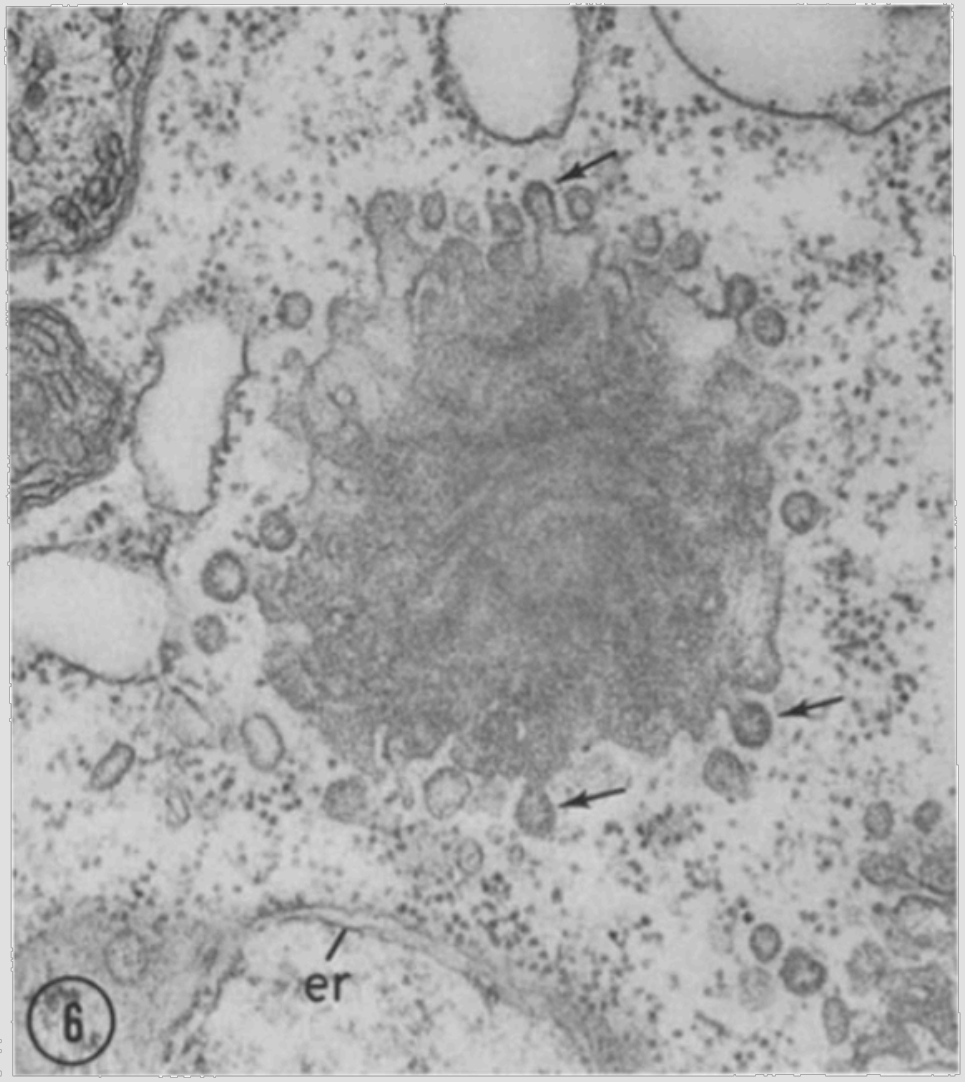
Contrôle Anti-Dopage



02 LE TOUR DE FRANCE

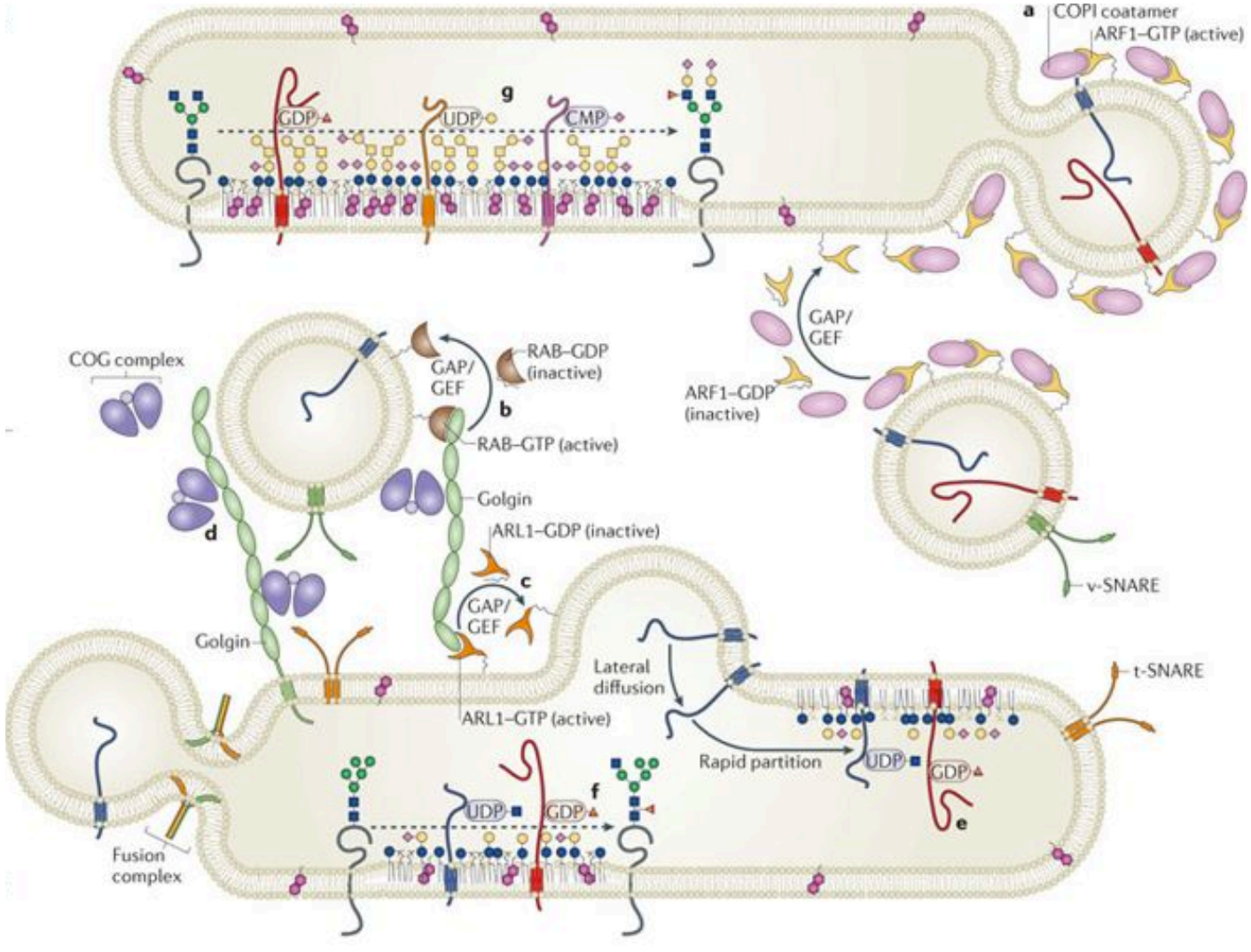
Eukaryotic glycans are built in the Golgi apparatus





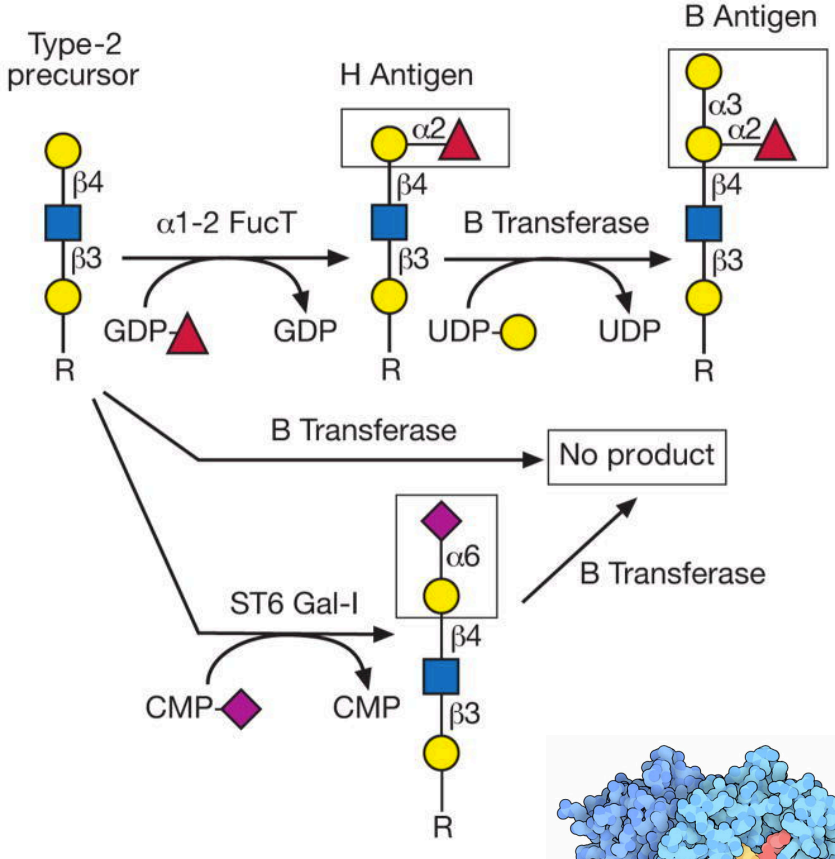
Farquhar & Palade, J Cell Biol 1981

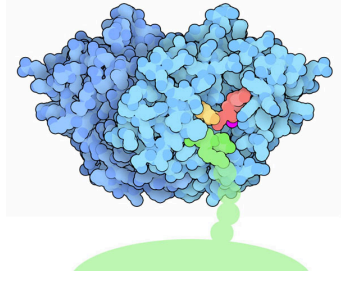
Eukaryotic glycans are built in the Golgi apparatus

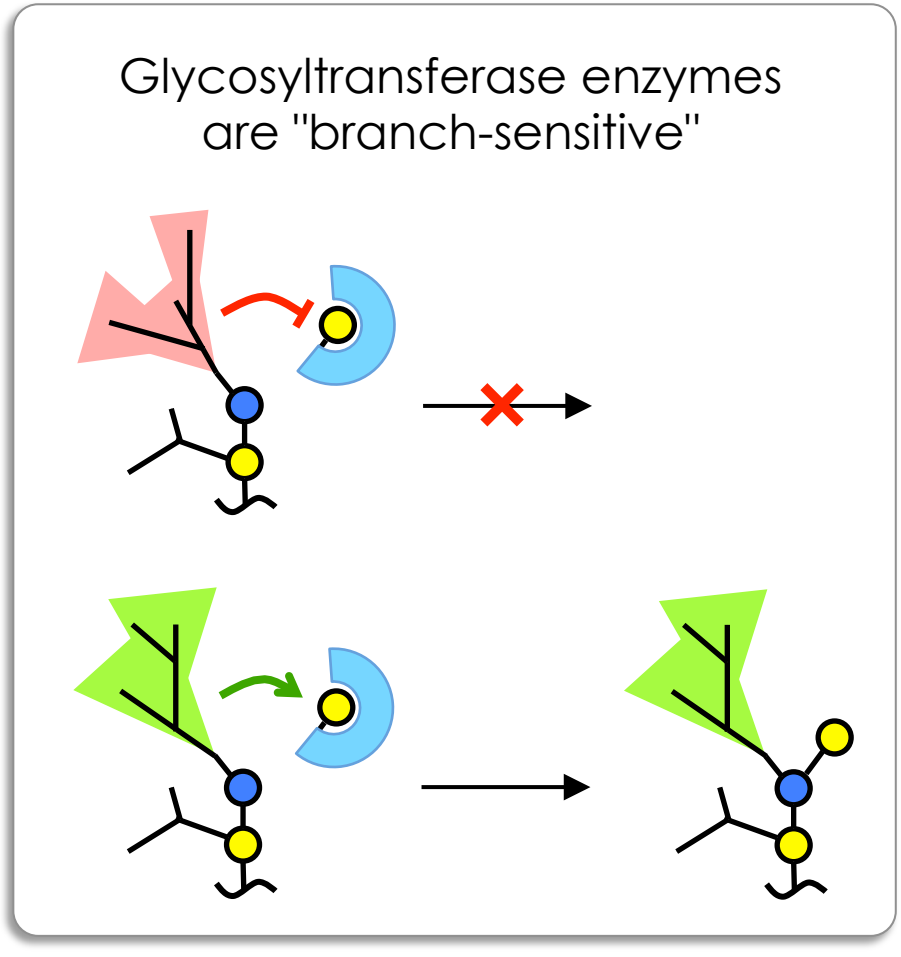


Moremen et al., Nat Rev Mol Cell Biol 2012

Glycans are built by adding sugar monomers to a growing oligomer



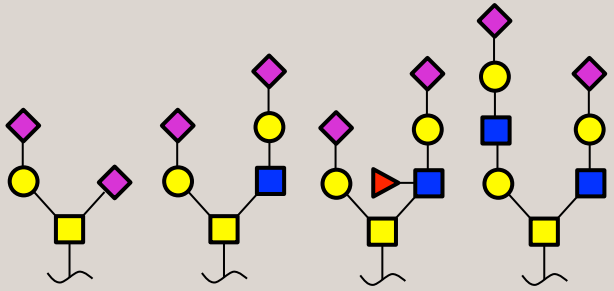




Essentials of Glycobiology; PDB 3i0g

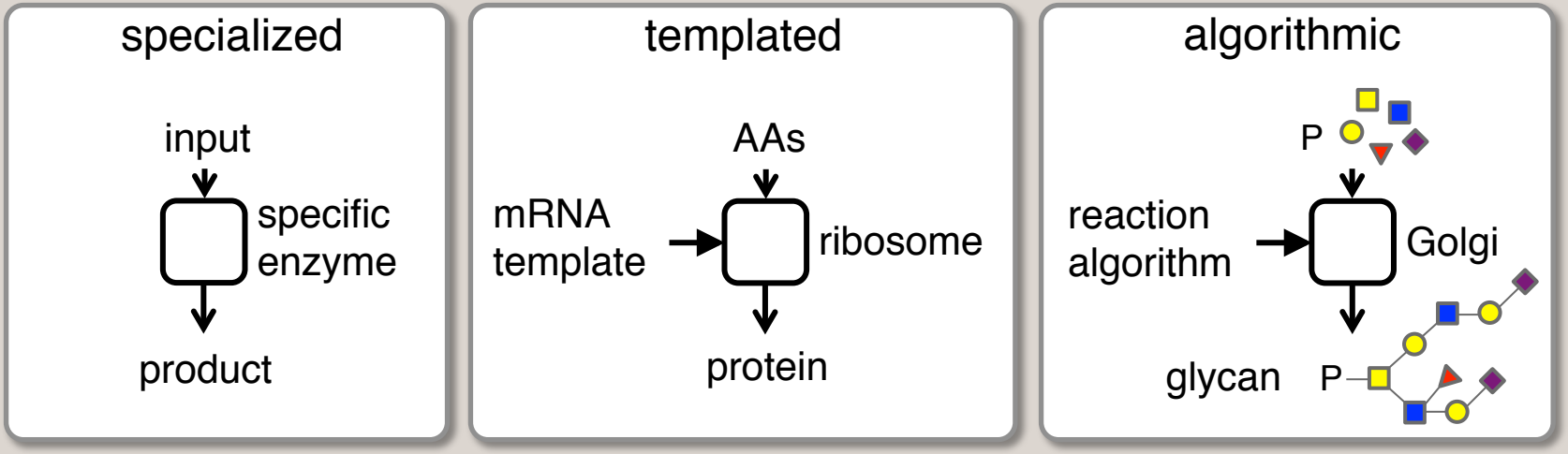
Where is the information encoded?

Why <u>these</u> structures, and not any more, or fewer?

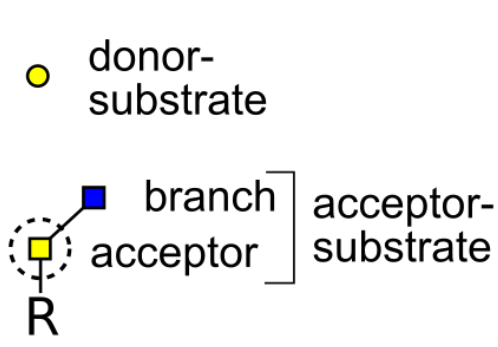


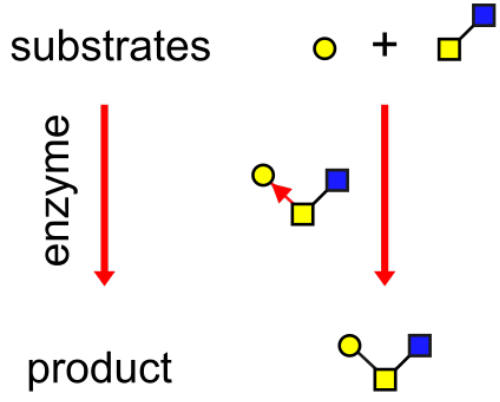
Hård et al. (1992) The carbohydrate chains of the beta subunit of human chorionic gonadotropin.

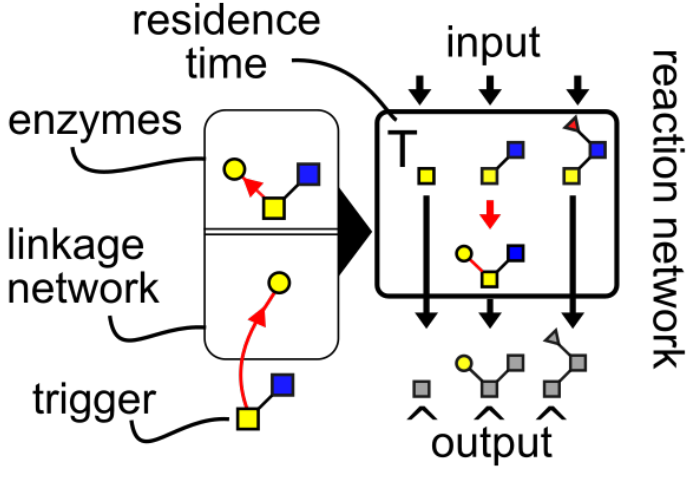
Modes of biosynthesis



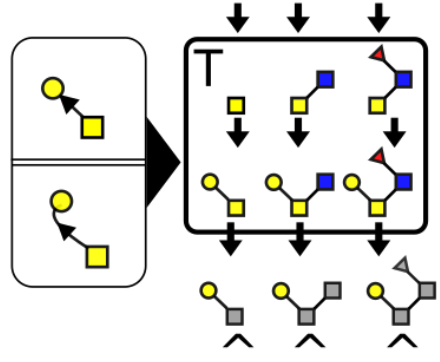
Basics of glycan biosynthesis





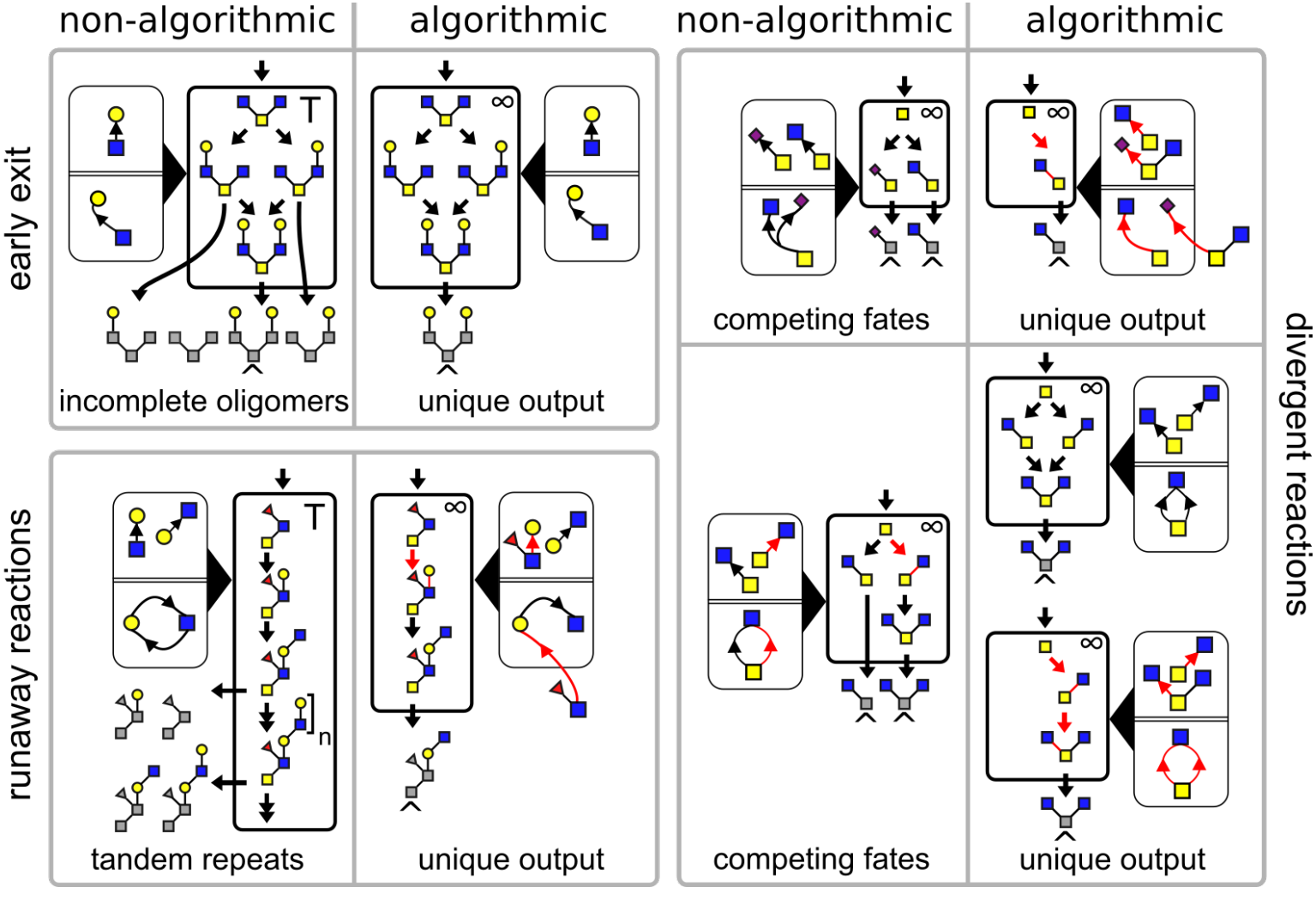


branch sensitive



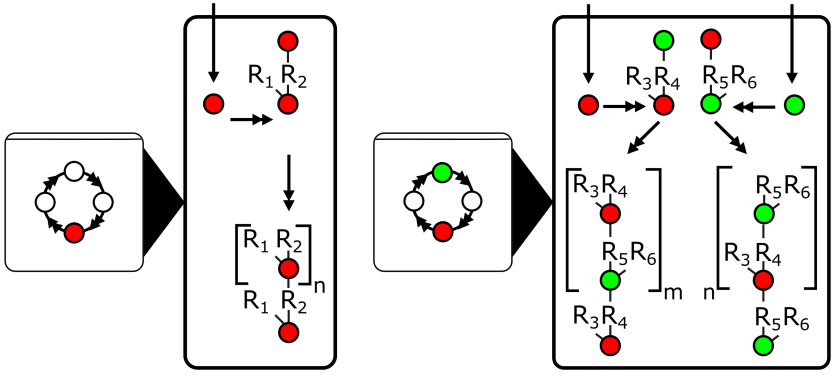
branch insensitive

Sources of glycan diversity

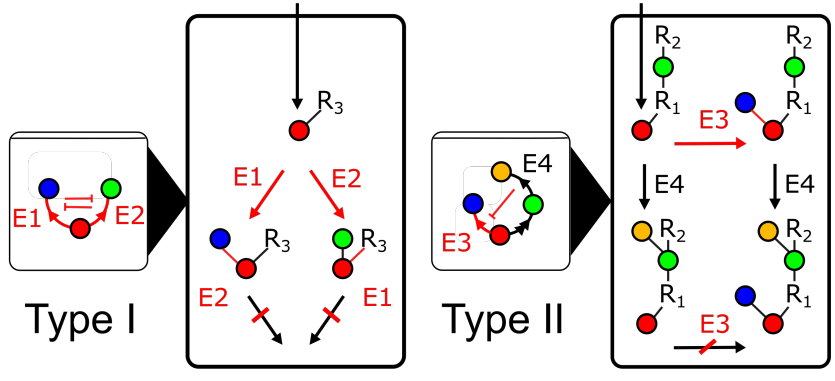


Runaway reactions and divergent reactions

runaway reactions
⇔ linkage loop

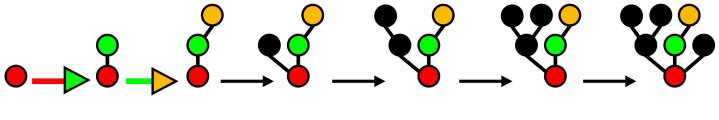


divergent reactions
⇒ acceptor conflict

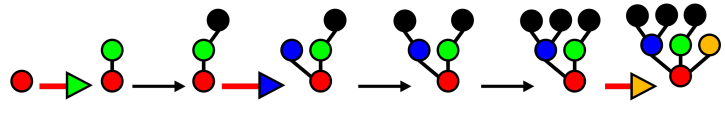


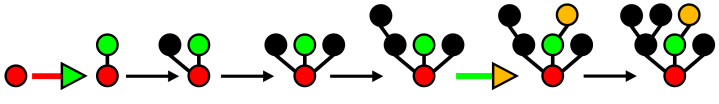
partial order on chains

strict order on branches

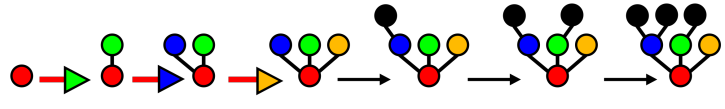


depth-first growth

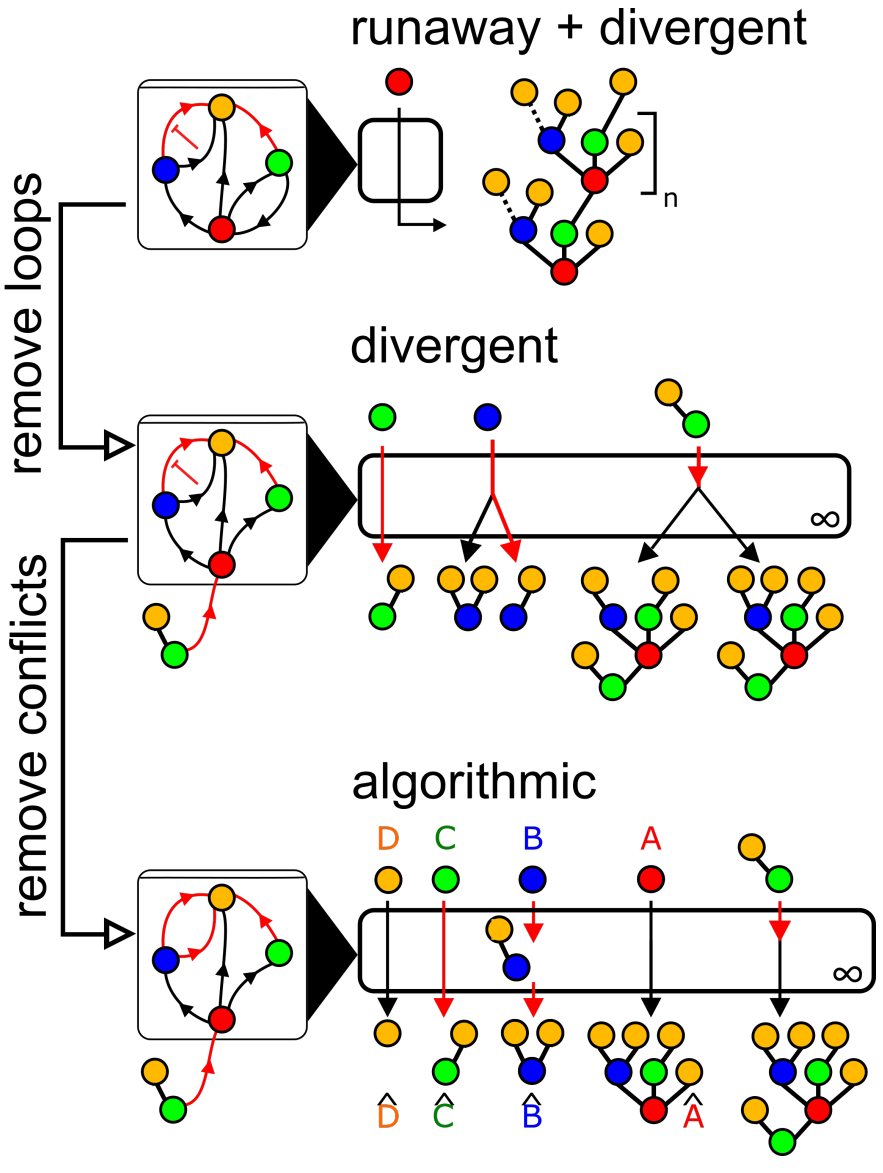




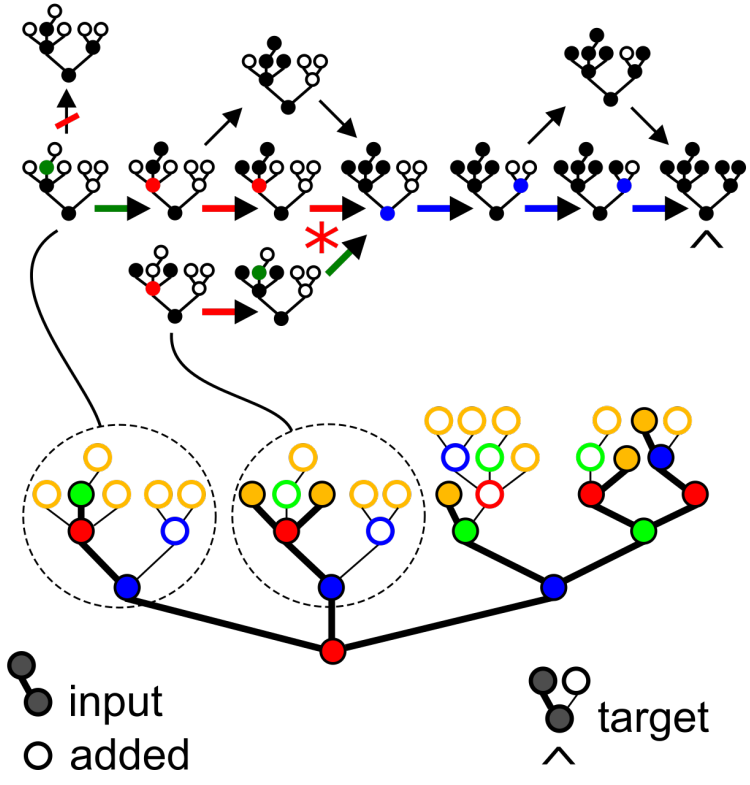
breadth-first growth



Algorithmic compartments

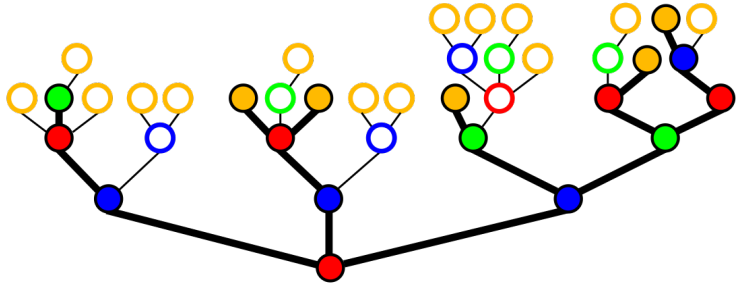


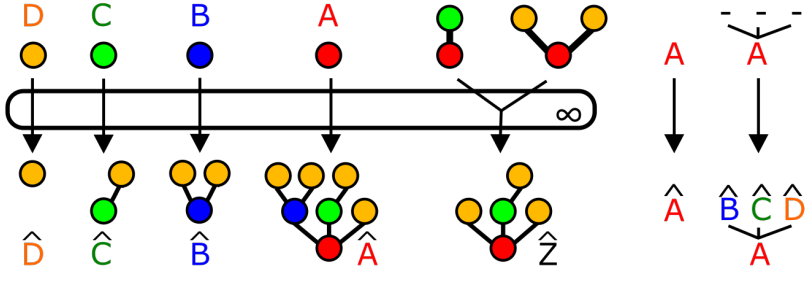
The inverse problem: building a target oligomer



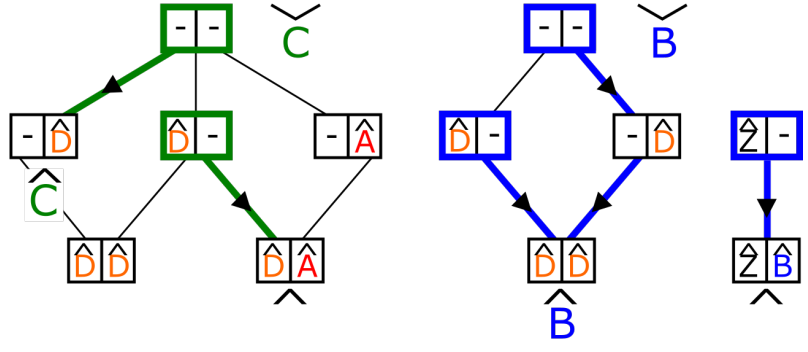
Theorem:
An input/target oligomer pair is algorithmically achievable in a single compartment if and only if there is a uniform depth-first growth order from the input to the target.

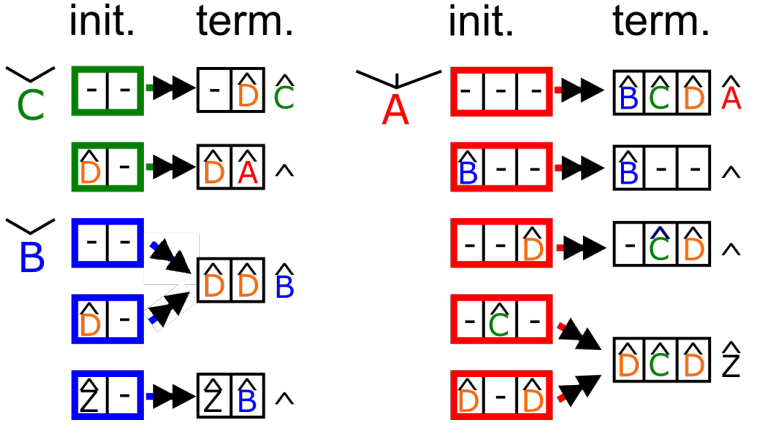
The inverse problem: building a target oligomer

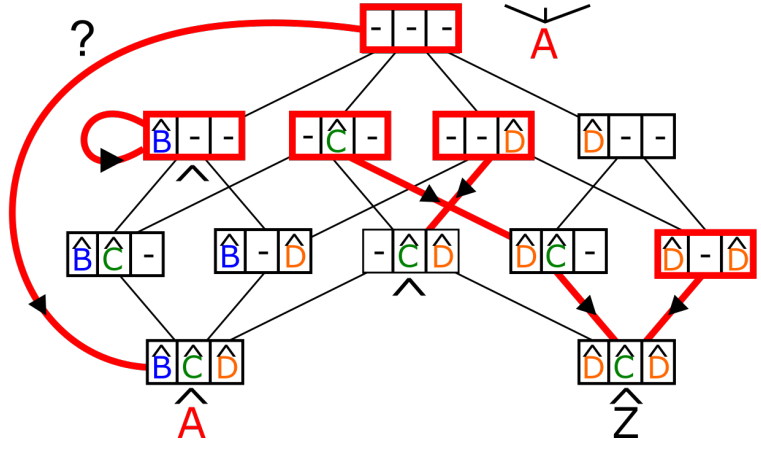




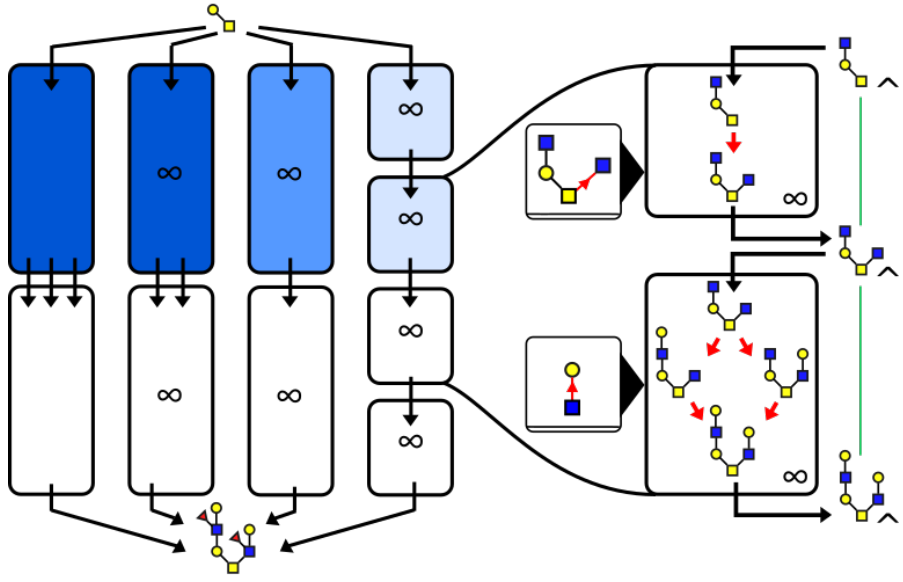
allowed branch orders







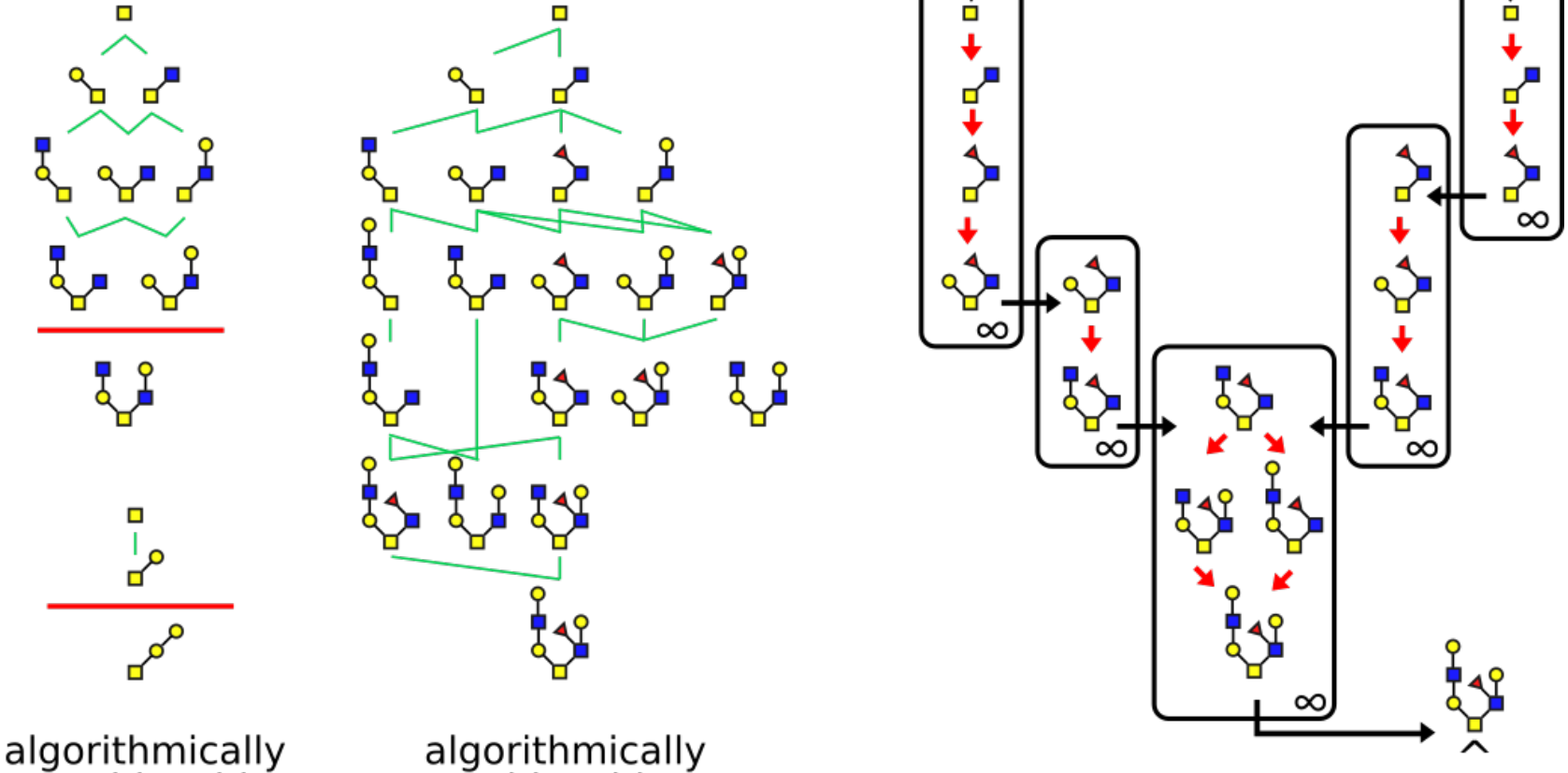
Building oligomers in multilple compartments



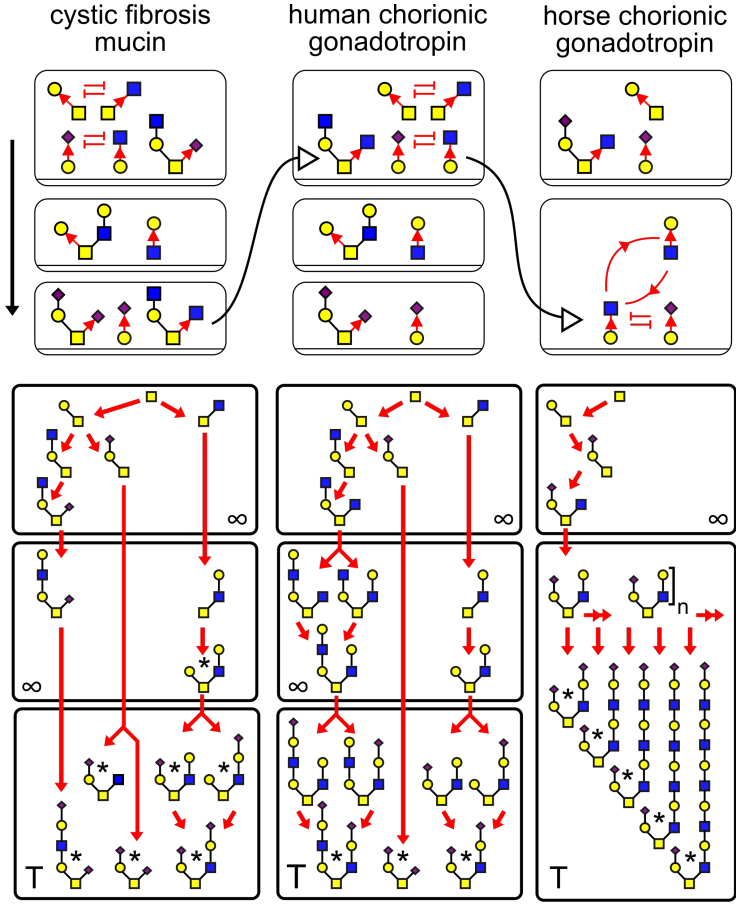
Theorem:
An input/target oligomer pair is algorithmically achievable in a series of N compartments if and only if there is a growth order from the input to the target that can be fully decomposed into N uniform depth-first stretches.

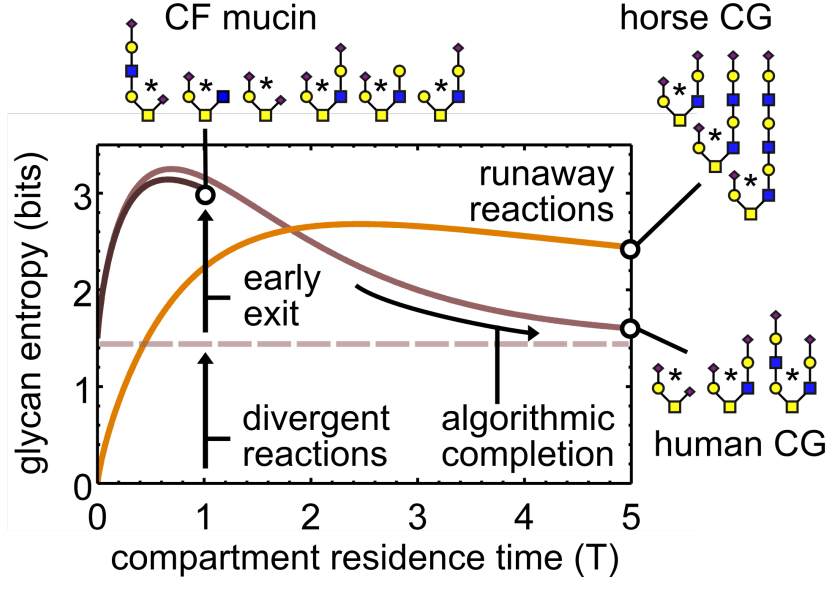
Corollary:
An input/target oligomer pair is algorithmically achievable if and only if there is a series of single-enzyme infinite-residence-time compartments that converts the input to the target as the unique final output.

Building oligomers in multilple compartments



Algorithmic biosynthesis of real glycans





Jaiman & Thattai, in prep., 2018

Glycan guru: Ajit Varki
Algorithms guru: Arnab Bhattacharyya

NCBS: Anjali Jaiman,
Somya Mani, Ramya Purkanti,
Mugdha Sathe, Anjali Jaiman,
Sachit Daniel, Rahul Kumar, ...

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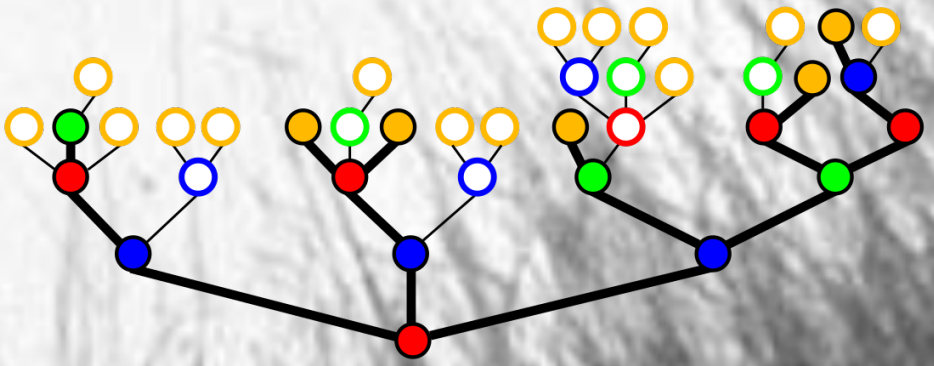

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