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Natural carbon assimilation and synthetic pathways: Exploring the chemical space of carbon fixation

Anne-Susann Abel

MARIE CURIE ACTIONS

Founded by the European Union

This project has received funding from the European Unions Horizon 2021 research and innovation programme under the Marie-Skłodowska-Curie grant agreement No 101072930

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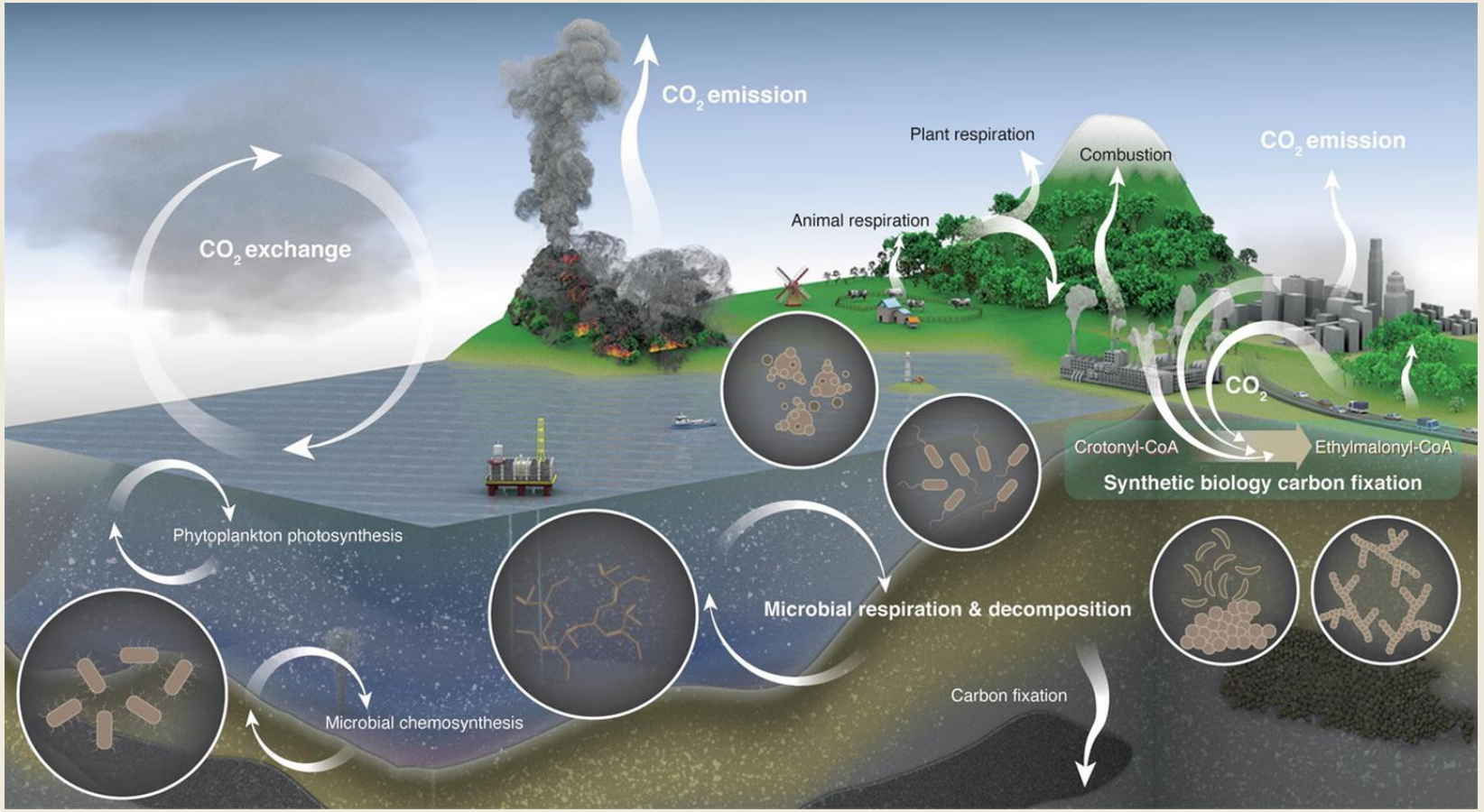
Carbon fixation

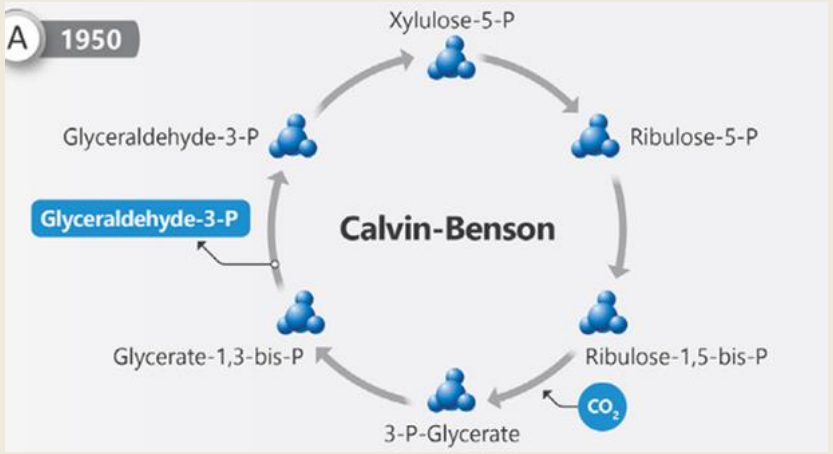


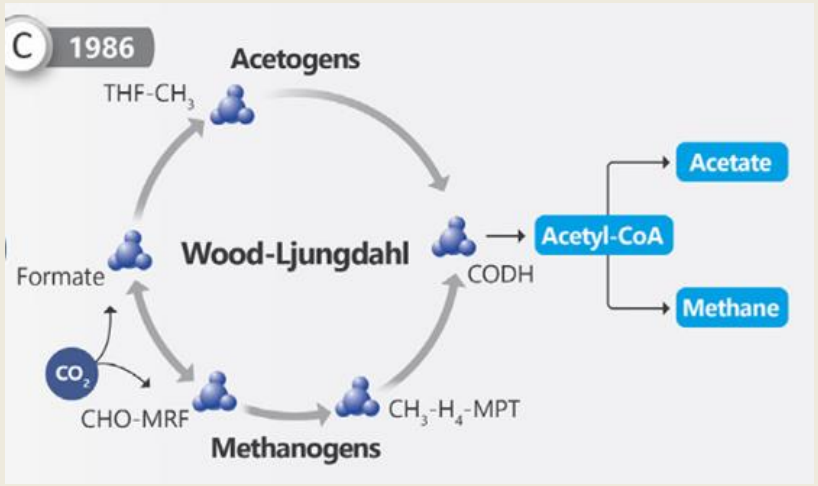
- carbon cycle

- removing CO_2
- value-added chemicals
- agricultural improvements

Santos Correa S, Schultz J, Lauersen KJ, Soares Rosado A (2023) Natural carbon fixation and advances in synthetic engineering for redesigning and creating new fixation pathways. J Adv Res 47:75–92. https://doi.org/10.1016/j.jare.2022.07.011

Natural pathways





- Calvin-Benson-Basham = reductive pentose phosphate pathway
  - Aerobic
  - Eukaryotes
  - Rubisco

- Wood-Ljungdahl = reductive acetyl-CoA pathways (linear)
  - Anaerobic
  - Acetogens
  - Methanogens
- reductive glycine pathway
  - Glycine cleavage system (GCS)

modified after:
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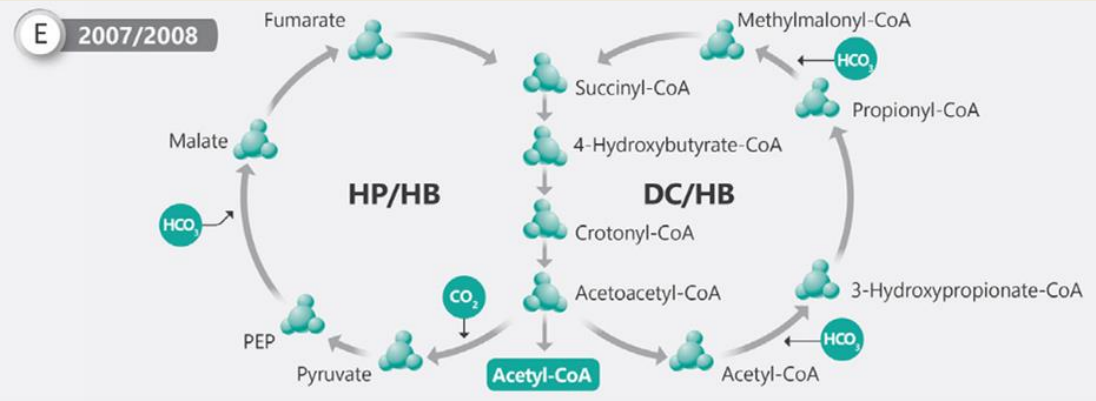

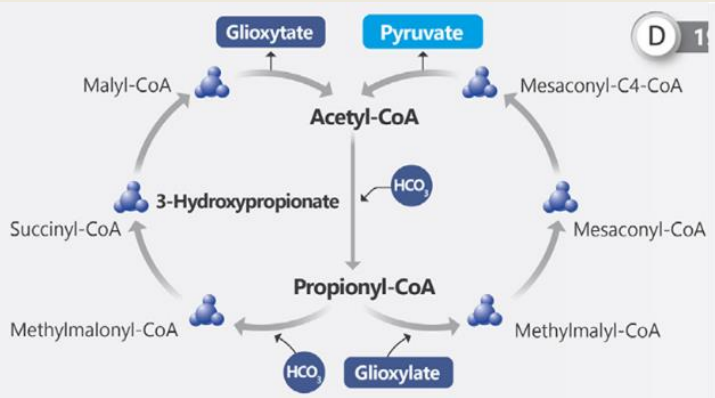

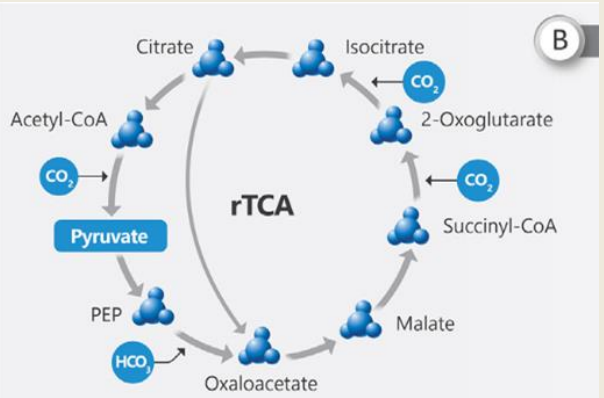

- 3-Hydroxypropionate/4-hydroxybutyrate (3HP/4HB) cycle
  - Aerobic
  - Bacteria
- Dicarboxylate/4HB cycle
  - Anaerobic
  - Archaea

- 3-HP bicycle
  - Anaerobic
  - Bacteria
- reductive TCA cycle
  - Anaerobic
  - Bacteria

modified after:
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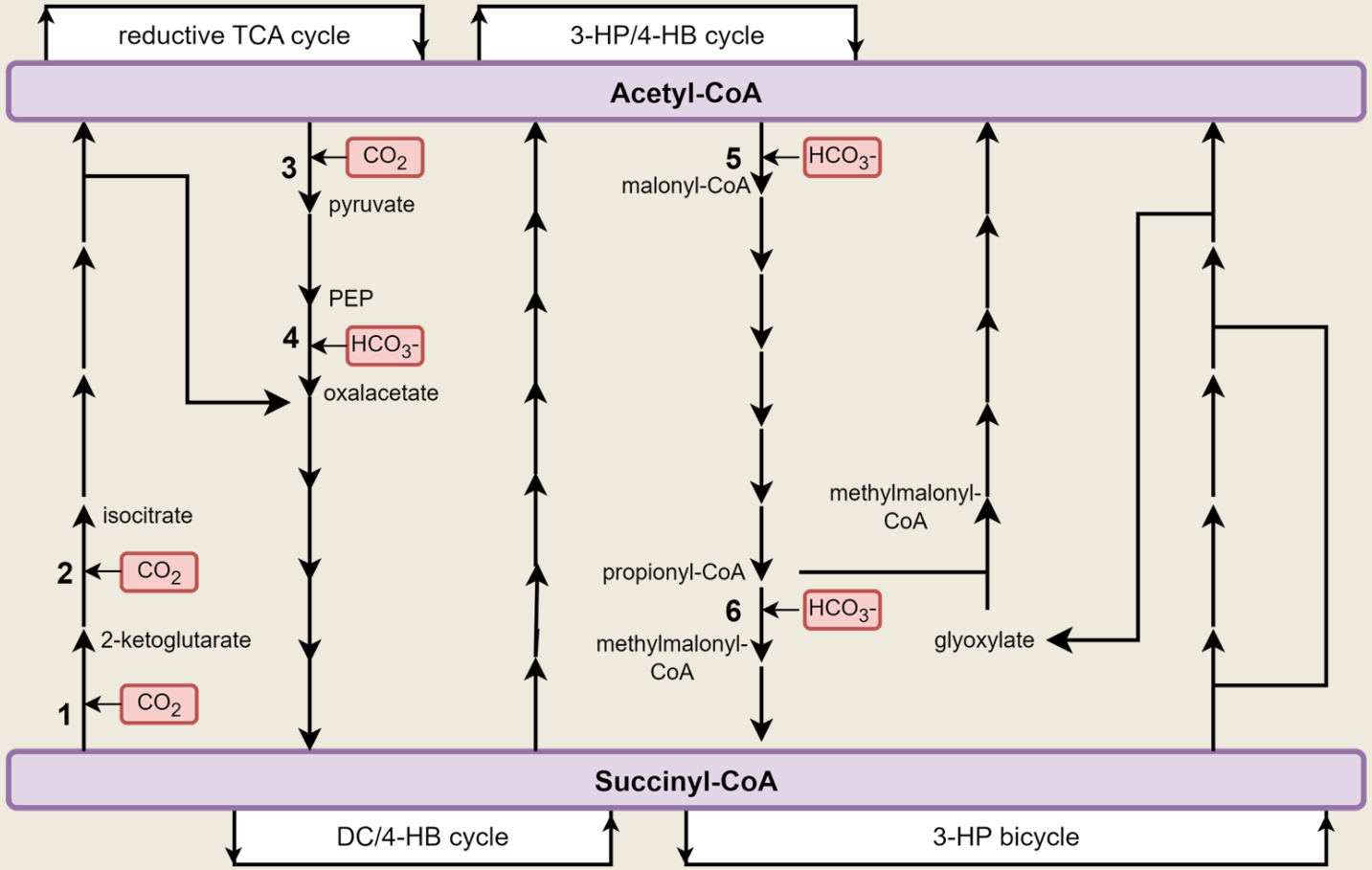
4 Acetyl-CoA-succinyl-CoA carbon fixation



1. 2-Ketoglutarate synthase
2. Isocitrate dehydrogenase
3. Pyruvate synthase
4. **PEP carboxylase**
5. Acetyl-CoA carboxylase
6. Propionyl-CoA carboxylase

modified after:
Bar-Even A, Flamholz A, Noor E, Milo R (2012) Thermodynamic constraints shape the structure of carbon fixation pathways. Biochim Biophys Acta BBA - Bioenerg 1817:1646–1659. https://doi.org/10.1016/j.bbabio.2012.05.002

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Synthetic pathways

"Better" pathways?

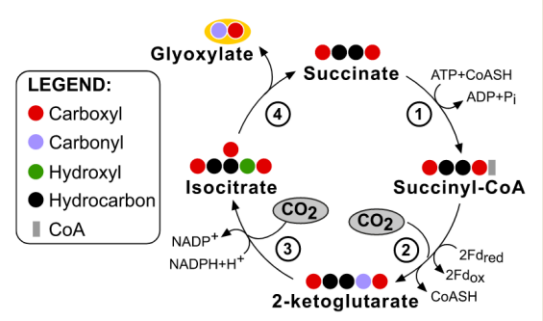
Measures of feasibility

- thermodynamics
- kinetics
- topology
- efficiency
- oxygen-sensitivity

Bar-Even A, Noor E, Lewis NE, Milo R (2010) Design and analysis of synthetic carbon fixation pathways. Proc Natl Acad Sci 107:8889–8894. https://doi.org/10.1073/pnas.0907176107
Bierbaumer S, Nattermann M, Schulz L, Zschoche R, Erb TJ, Winkler CK, Tinzl M, Glueck SM (2023) Enzymatic Conversion of CO 2 : From Natural to Artificial Utilization. Chem Rev 123:5702–5754. https://doi.org/10.1021/acs.chemrev.2c00581

Synthetic pathways

shortest pathway



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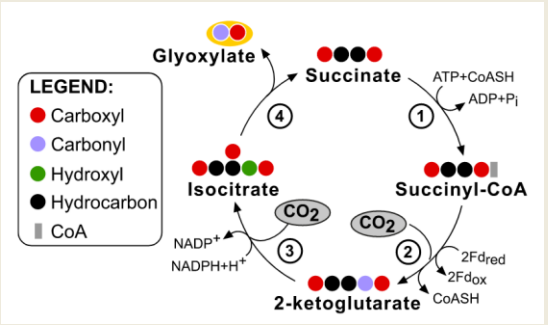
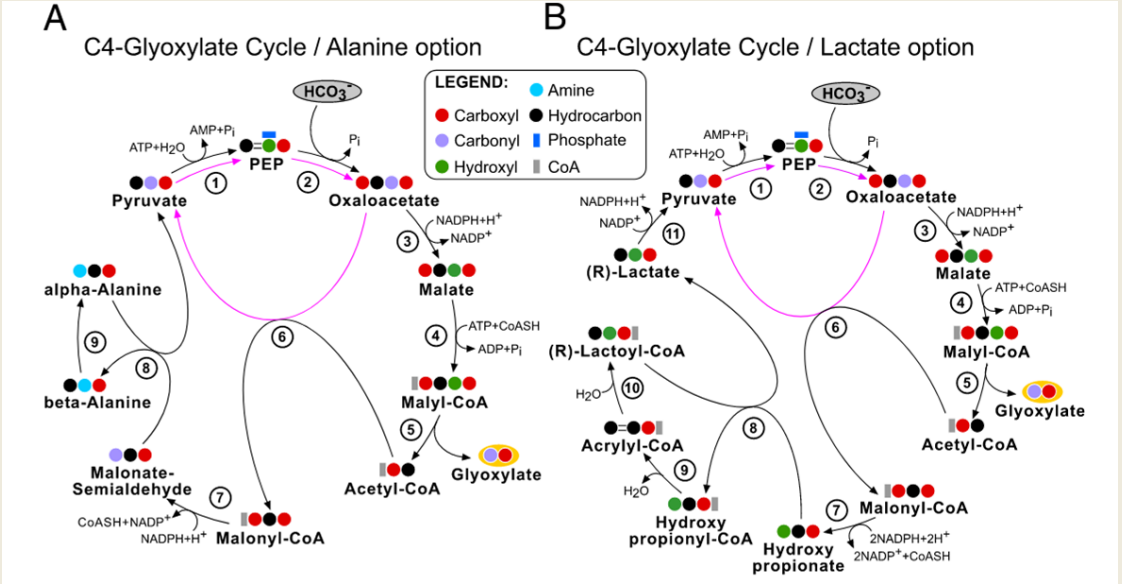


highest activities



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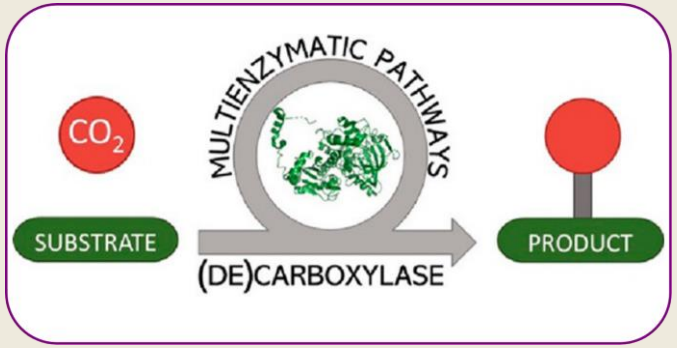
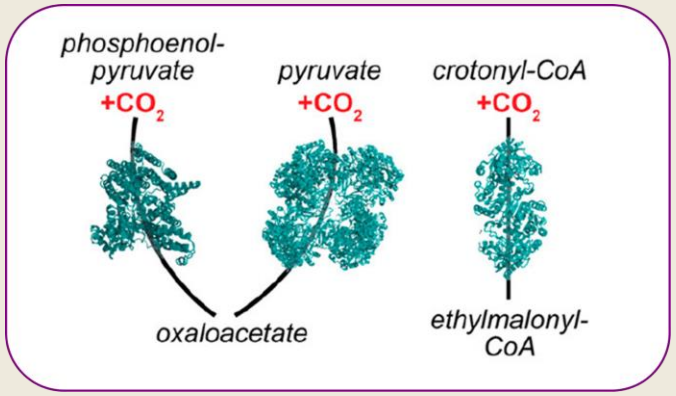
Exploring carbon fixation chemical space

MØD



Co-factors
Carbon source



re-write rules for carbon fixation

focus on acetyl-CoA-succinyl-CoA pathways

NAD(P)H, CoA, Ferredoxin, ATP, Mg2+, biotin, TPP, PLP

HCO3-, CO2

focus on effective carboxylating enzymes

- PEPC
- Pyruvate synthase
- Crotonyl-CoA carboxylase/reductase

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Thank you for your attention!