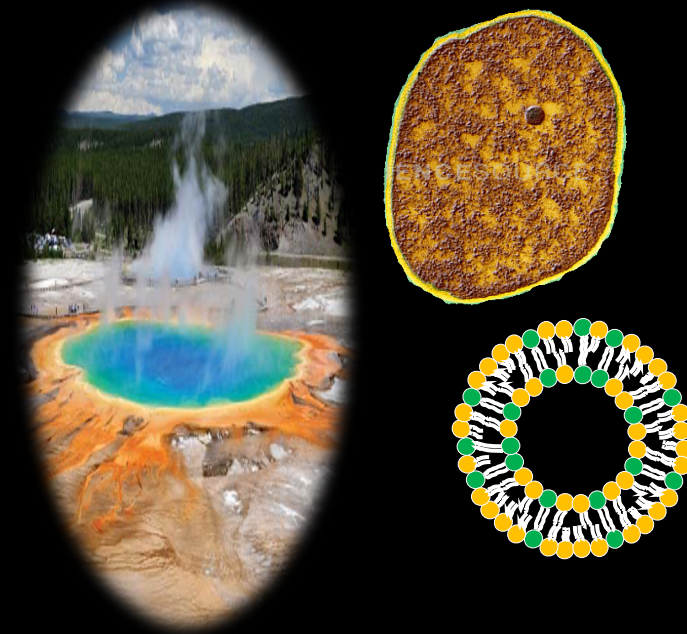


Archaea: weird microorganisms with wonderful lipids

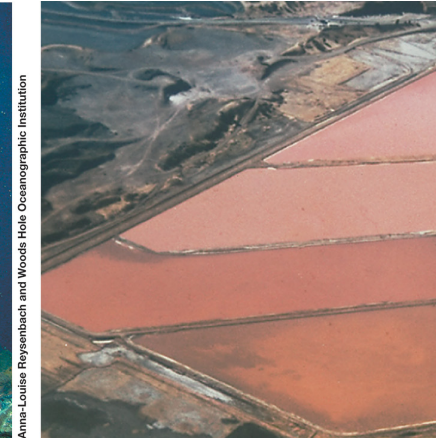
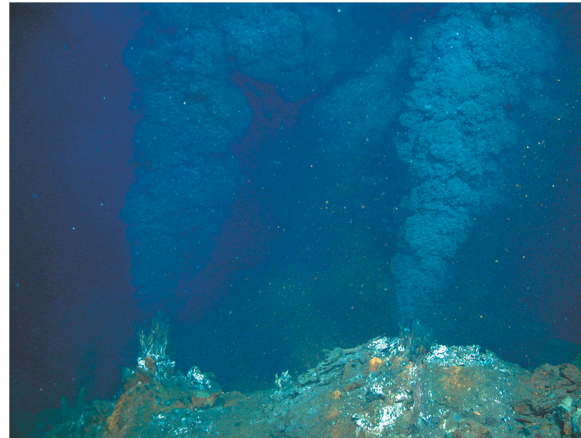
Alexander Treusch

Department of Biology
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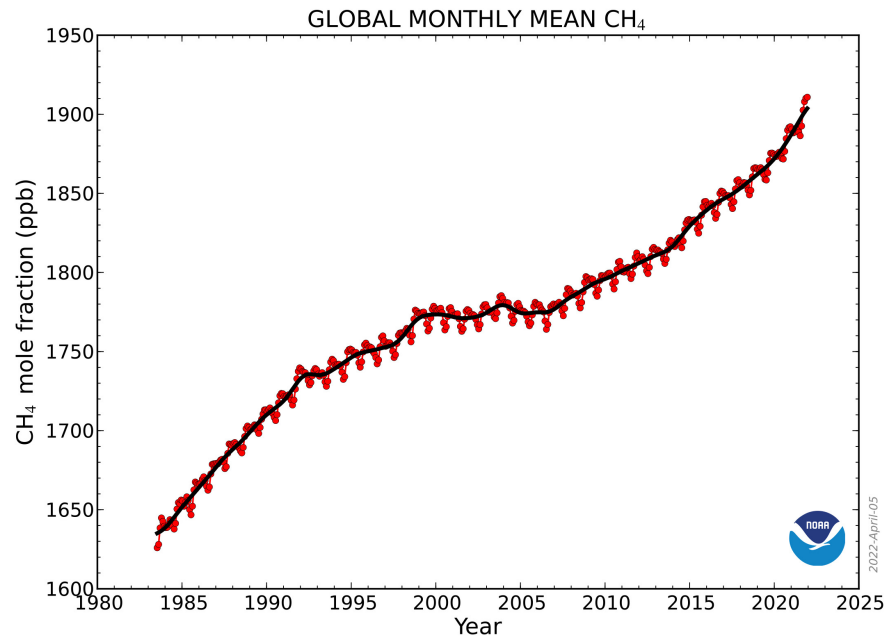
Archaea

- traditionally considered extremophilic microorganisms
- habitats include hot springs, solfatares, hydrothermal vents, salt evaporation ponds, ...

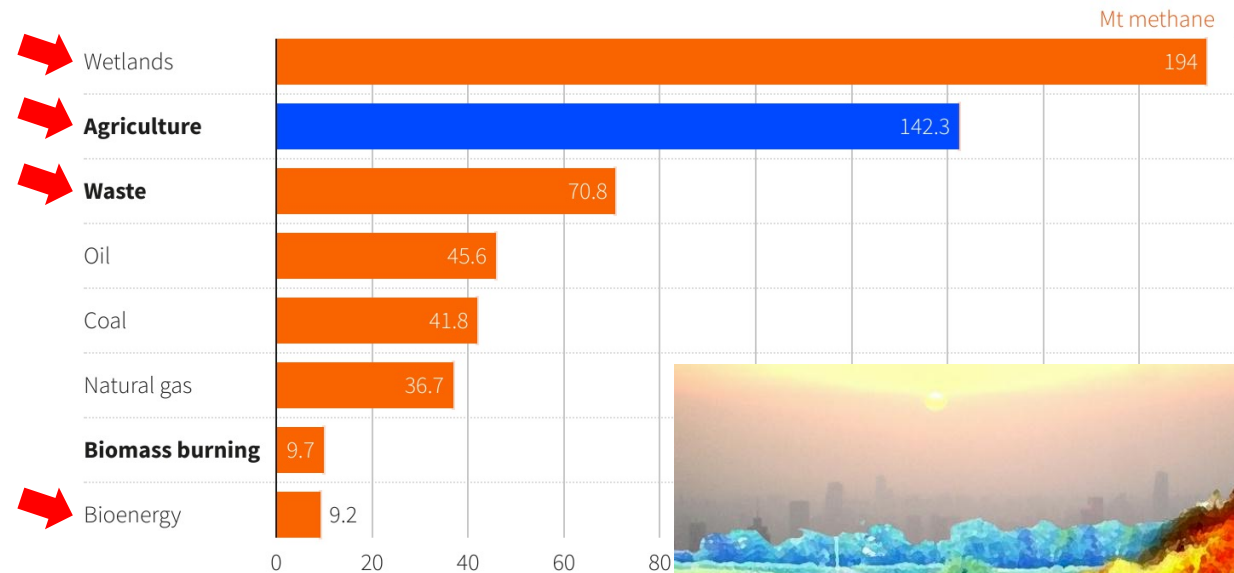


Archaea

- strictly anaerobic methanogens are also Archaea
- only significant biologic producers of methane



Sources of methane emissions



Note: Energy sector emissions are from the 2022 Global Methane Tracker available for 2019, 2020 or 2021.

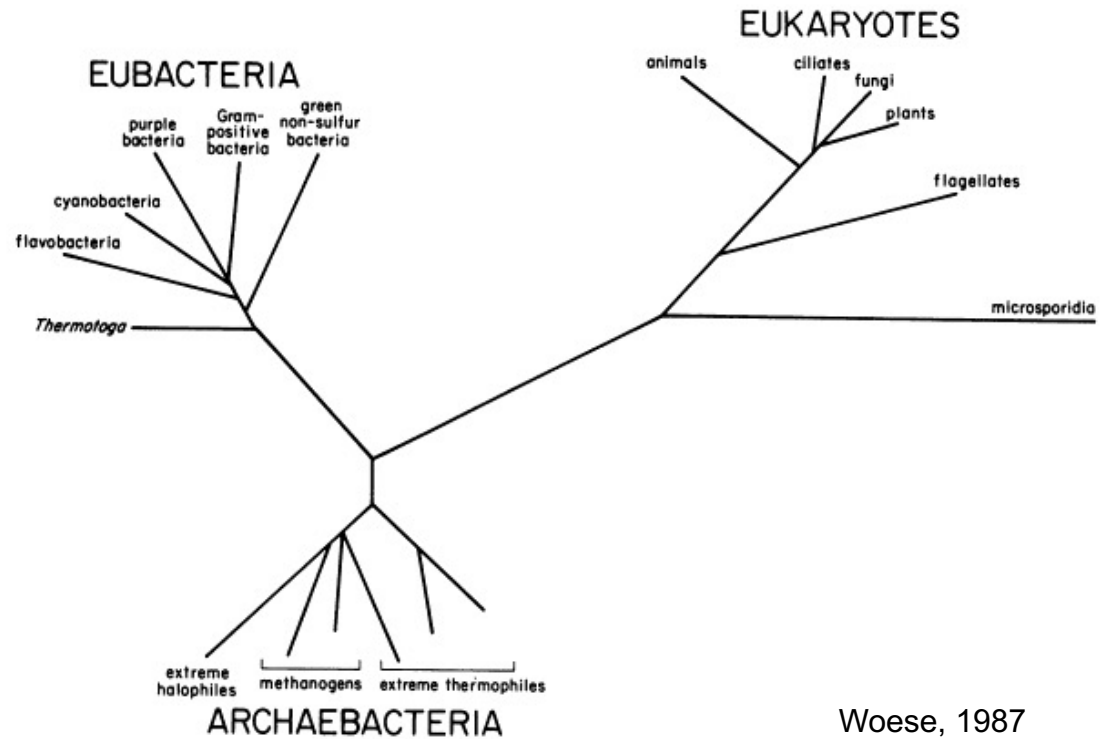
Source: International Energy Agency | Afriq Fitri Alias | Breakingviews |



Archaea form their own domain

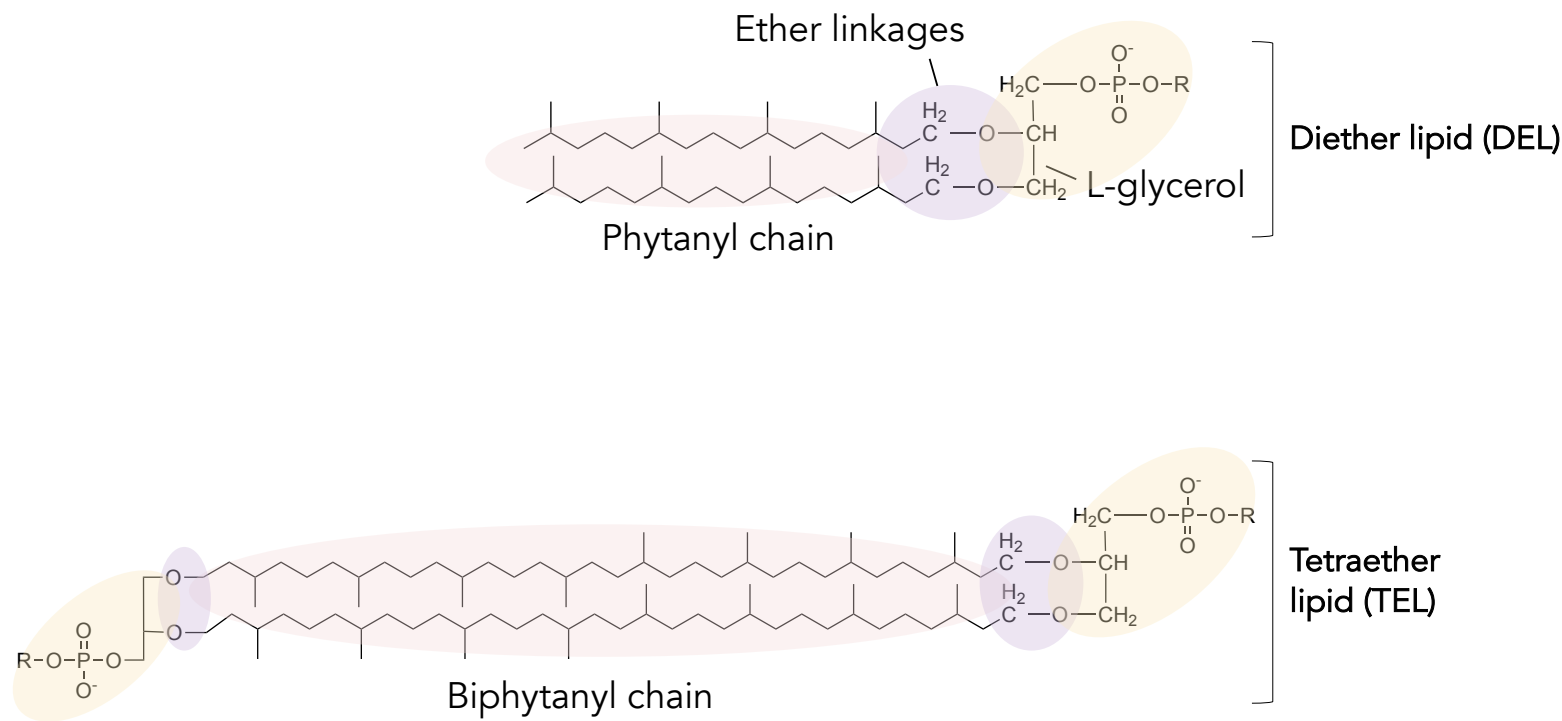


Carl Woese reconstructed their phylogeny based on 16S rRNA sequences in 1987.

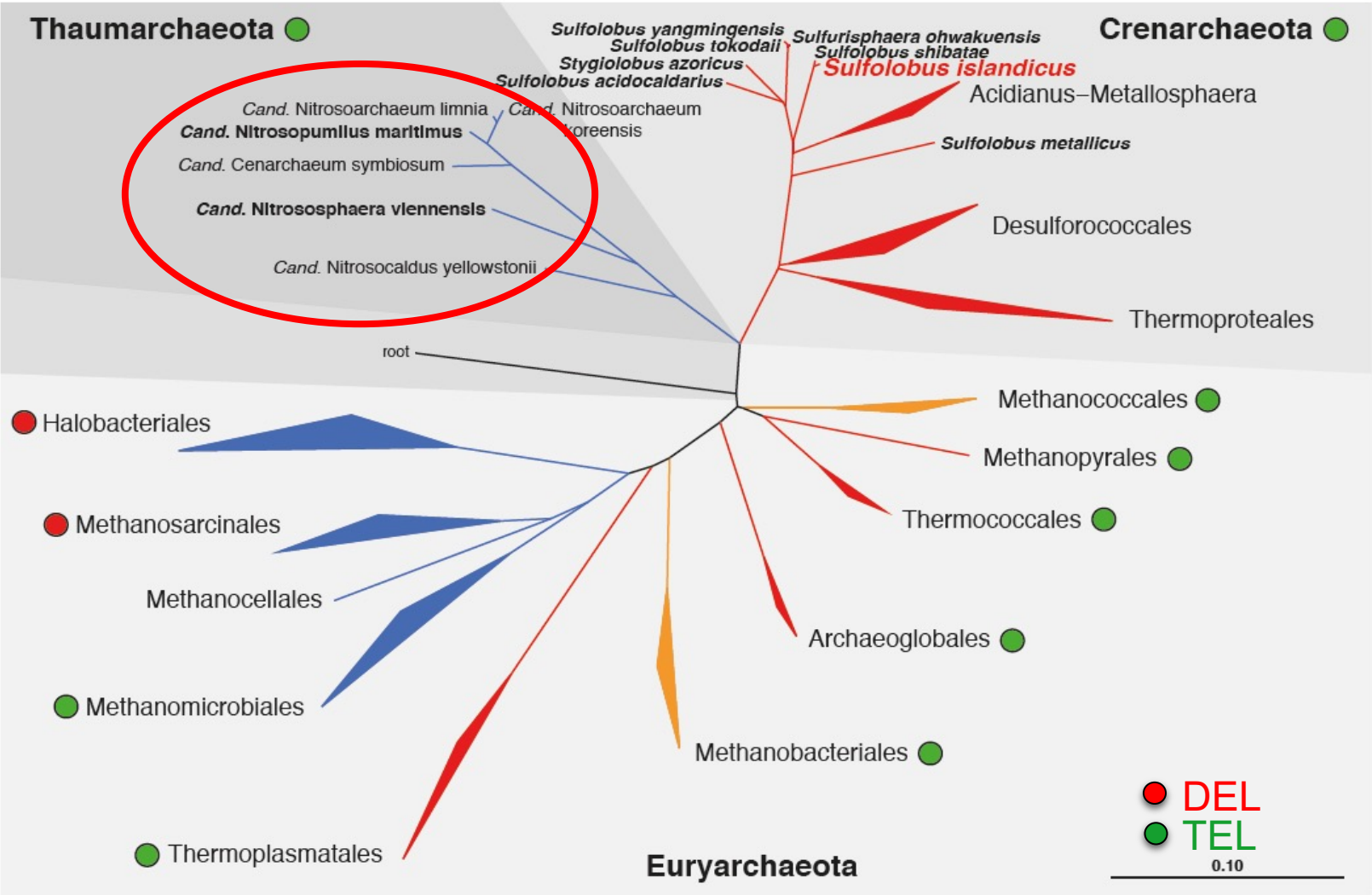


Woese, 1987

Archaeal membrane lipids

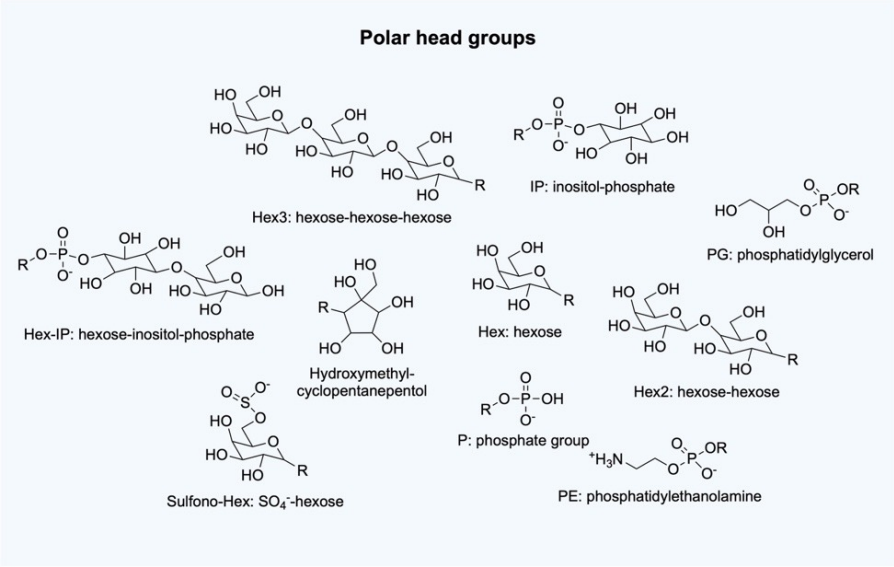
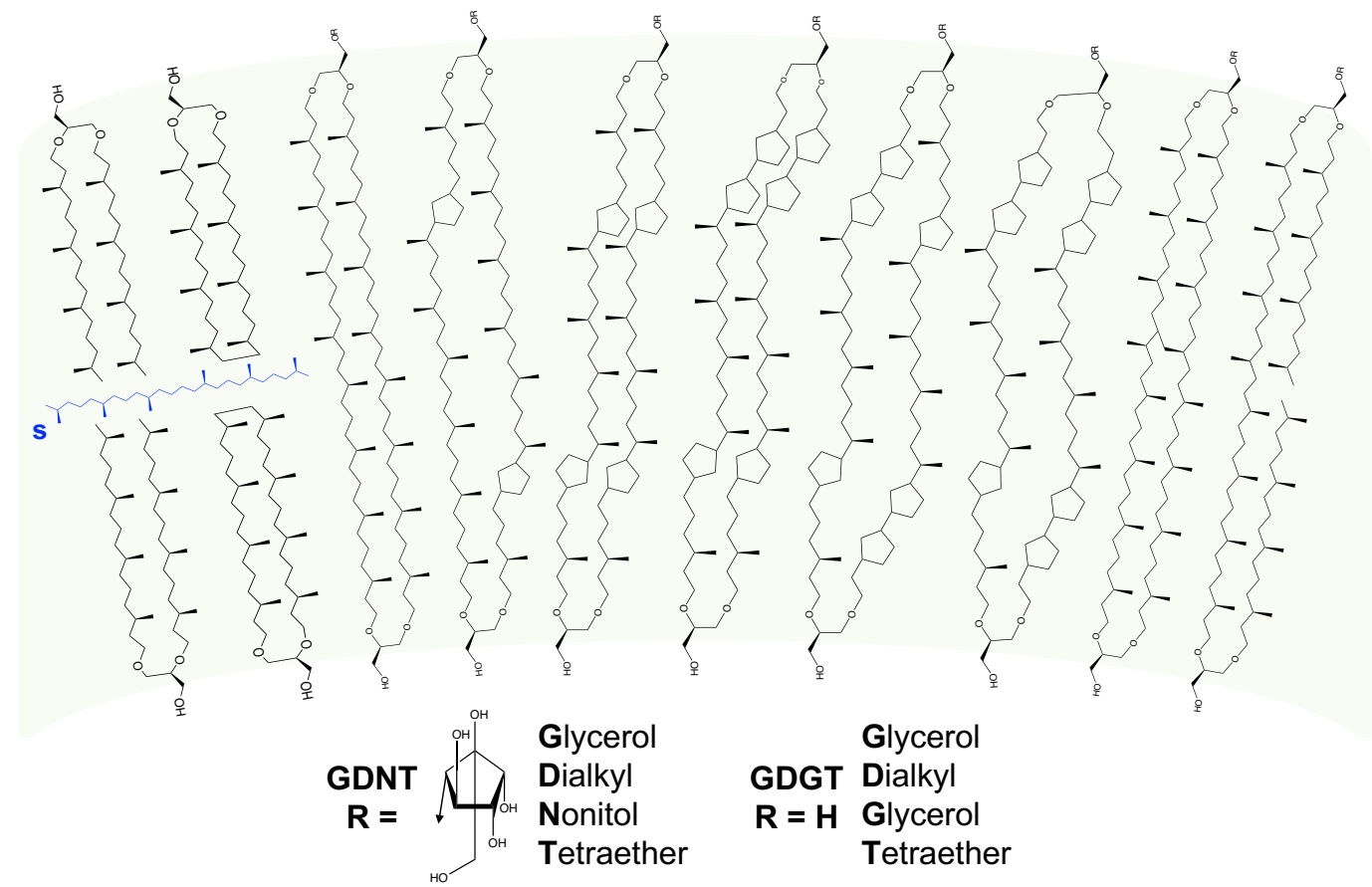


Distribution of TELs



Jacobsen et al., European Journal of Pharmaceutical Sciences (2017)

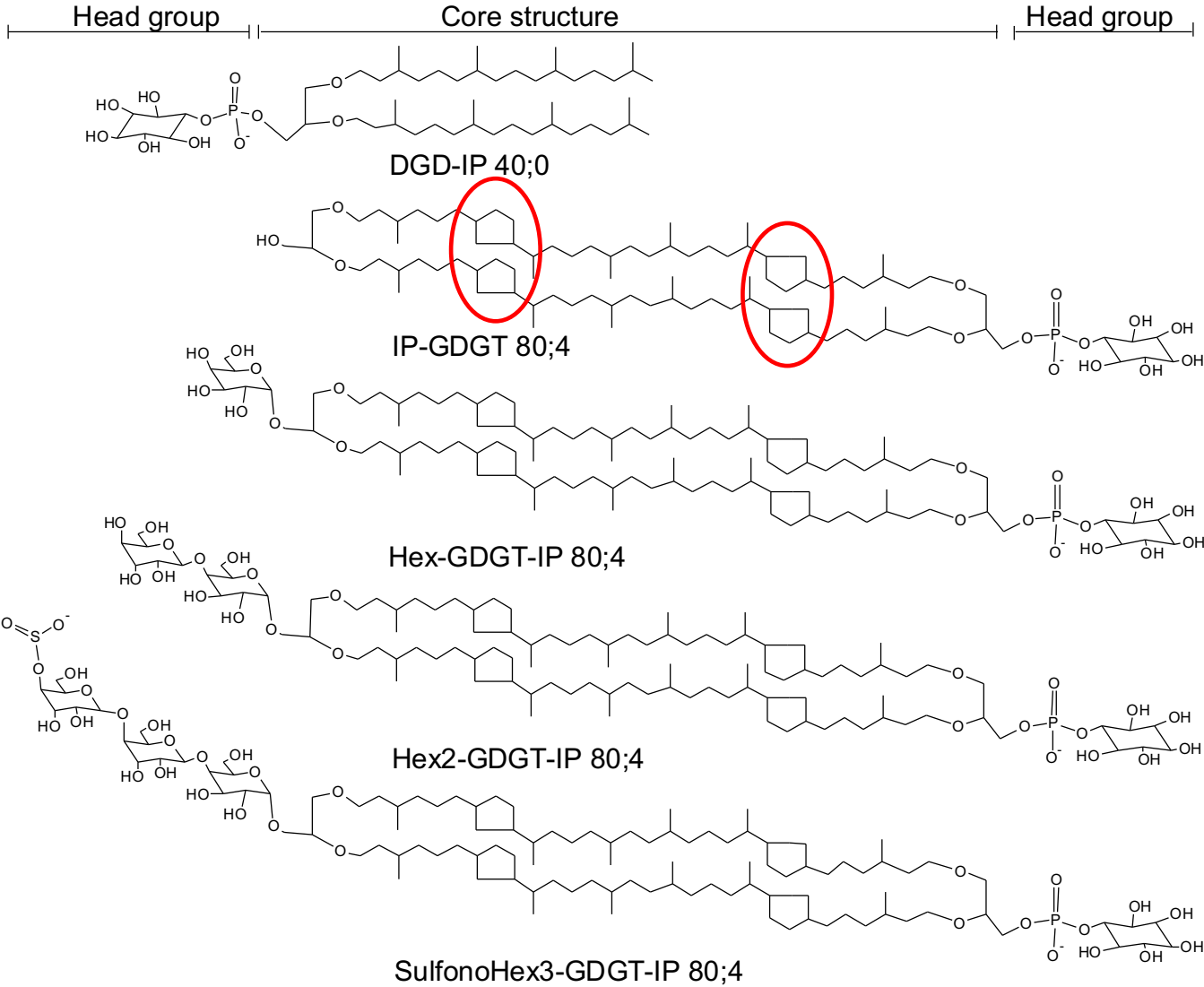
Diversity of archaeal TELs



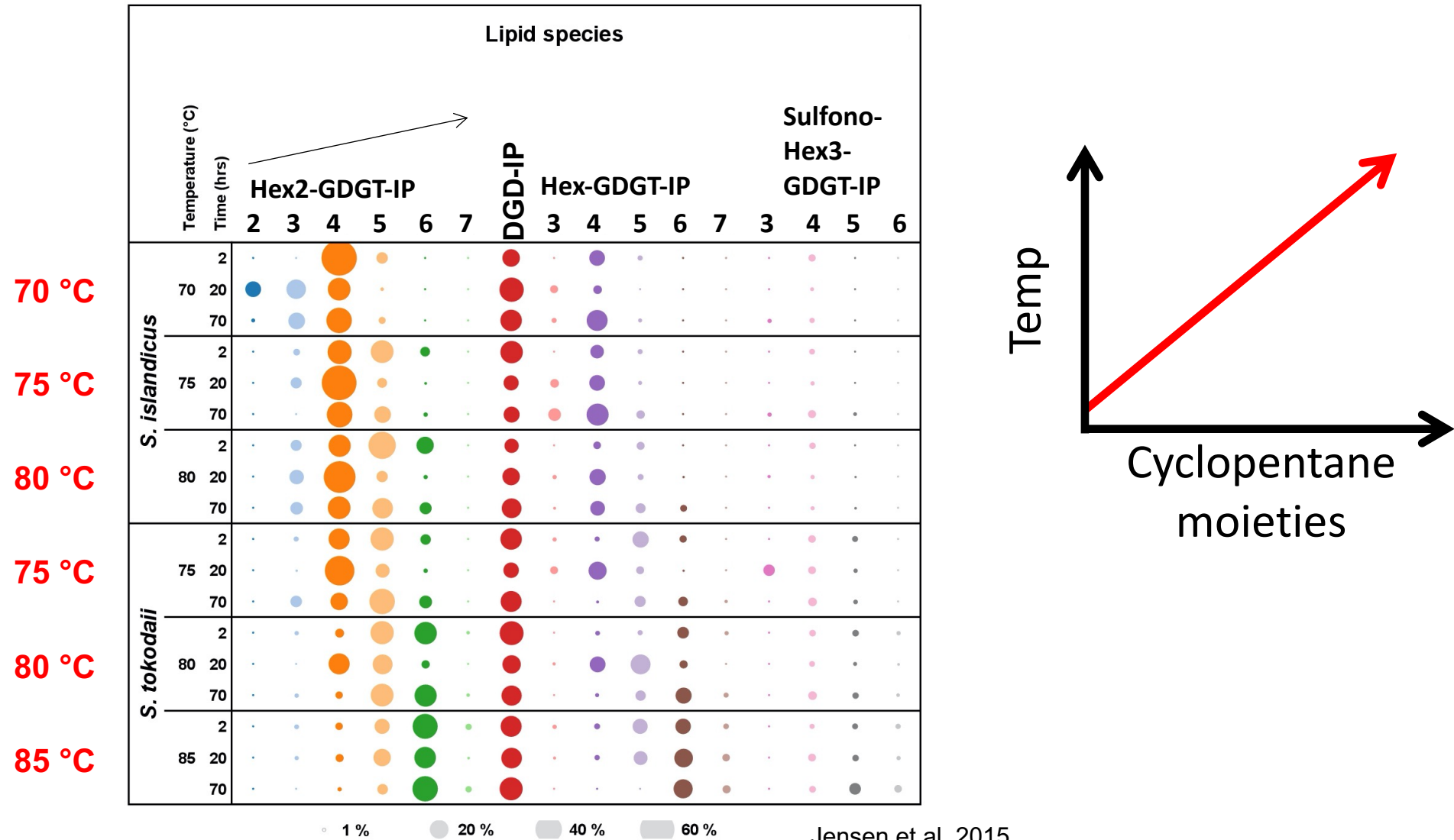
Most common polar head groups found attached to archaeal membrane core lipids

Bohsen *et al.*, in preparation

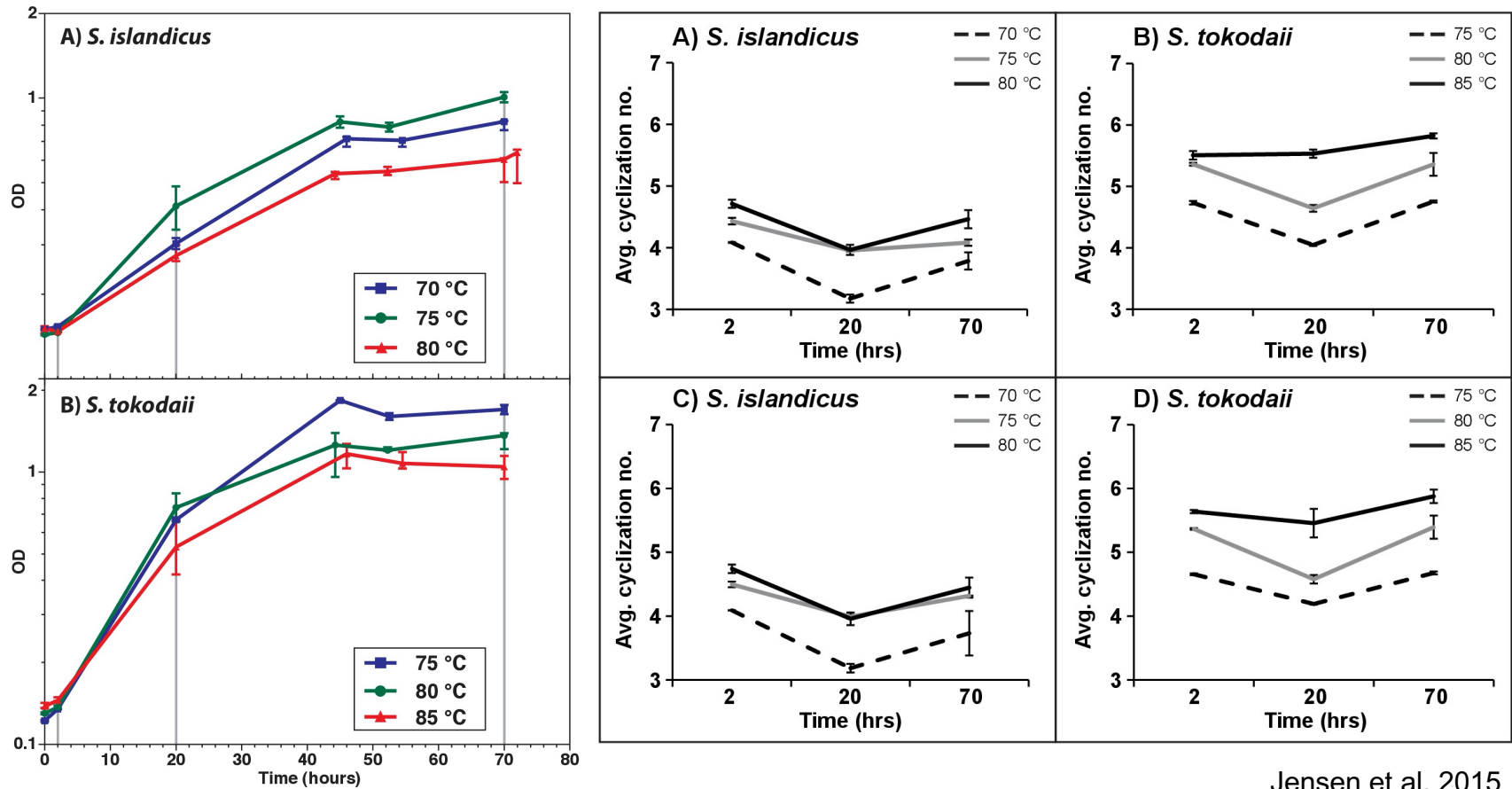
Cyclization of TELs



Effects of Temperature on TEL Composition



Effect of Growth on TEL Composition



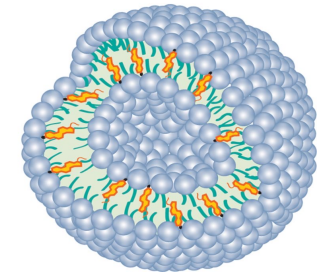
Total lipid pool

Hex2-GDGT-IP

Avg. cyclization no. = average number of cyclopentane moieties in the core lipid

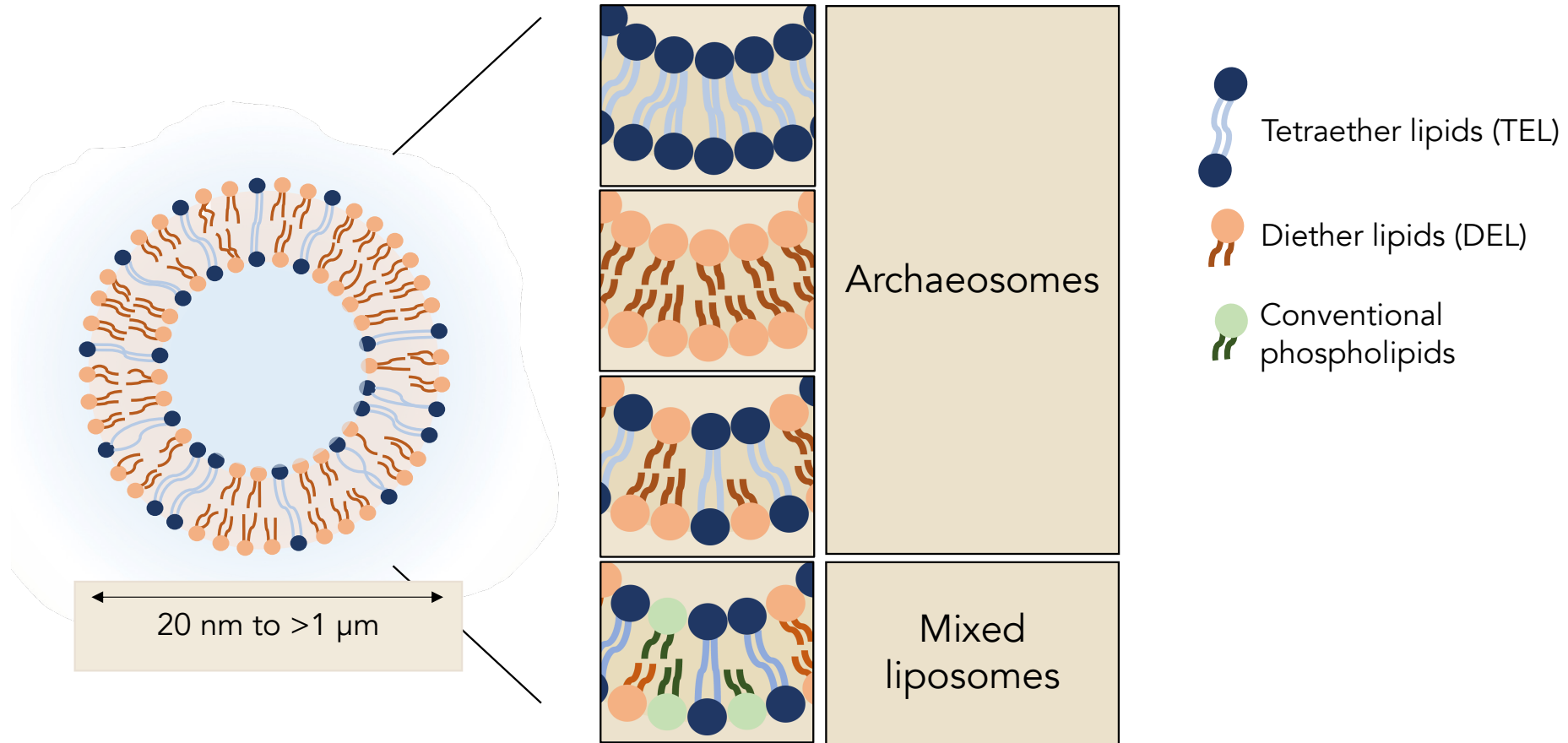
Archaeal lipids in biotechnology

- **Biomarkers for the presence and abundance of Archaea** (Sturt et al., 2004, Pitcher et al., 2009, Huguet et al., 2010)
- **Paleothermometer (TEX₈₆)** (Schouten et al., 2002)
- **Lubricant for engines** (Chang, 1992)
- **Bioelectronics** (De Rosa et al., 1994)
- **Immobilization matrix on implants/catheters** (Liefieith et al., 2018)
- **Vaccine delivery** (e.g. Krishnan and Sprott, 2008)
- **Gene delivery** (e.g. Le Gall et al., 2014)
- **Drug delivery:**
 - **transdermal** (Moghimpour et al., 2013)
 - **intravenous** (Mahmoud et al., 2015, Mahmoud et al., 2017, Plenagl et al., 2019)
 - **pulmonary** (Hemetsberger et al., 2022)
 - **oral** (Li et al., 2010, Parmentier et al., 2011 + 2014, Uhl et al., 2016, 2017, 2021)



Monteiro et al., 2014

Liposomes containing archaeal lipids



Species explored for drug delivery

Methanogens

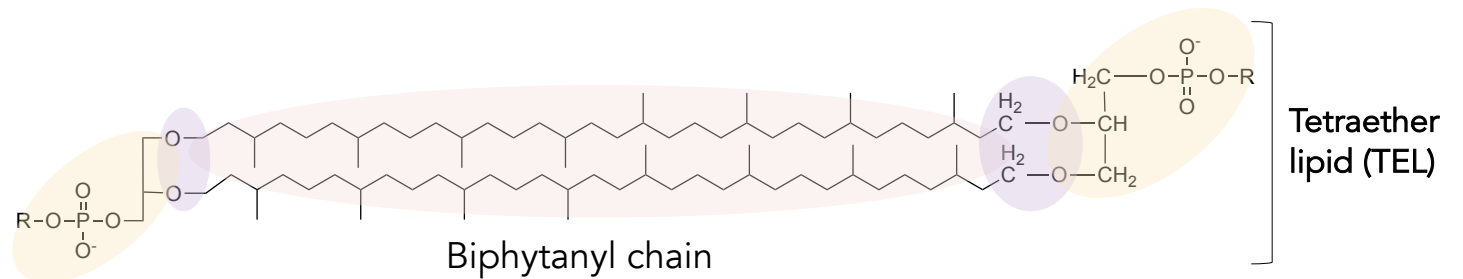
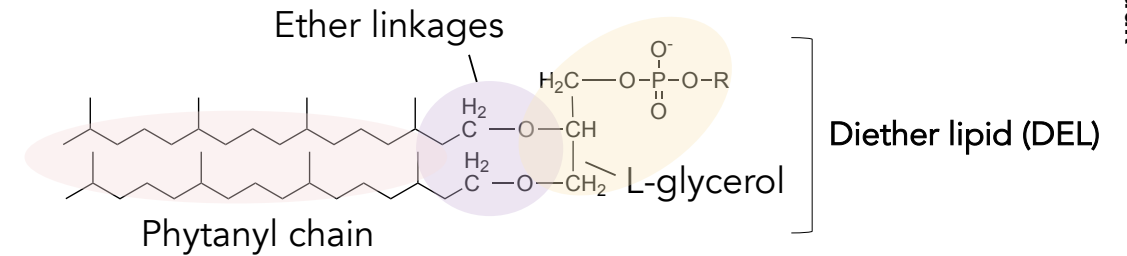
Methanosarcina mazei
Methanobacterium espanolae
Methanospirillum hungatei
Methanococcus jannaschii
Methanococcus voltae
Methanosaeta concilii
Methanosphaera stadtmanae
Methanobrevibacter smithii

Halophiles

Natronobacterium magadii
Halobacterium salinarum

Thermoacidophiles

Sulfolobus acidocaldarius
Thermoplasma acidophilum
Sulfolobus islandicus (Jensen et al. 2015)



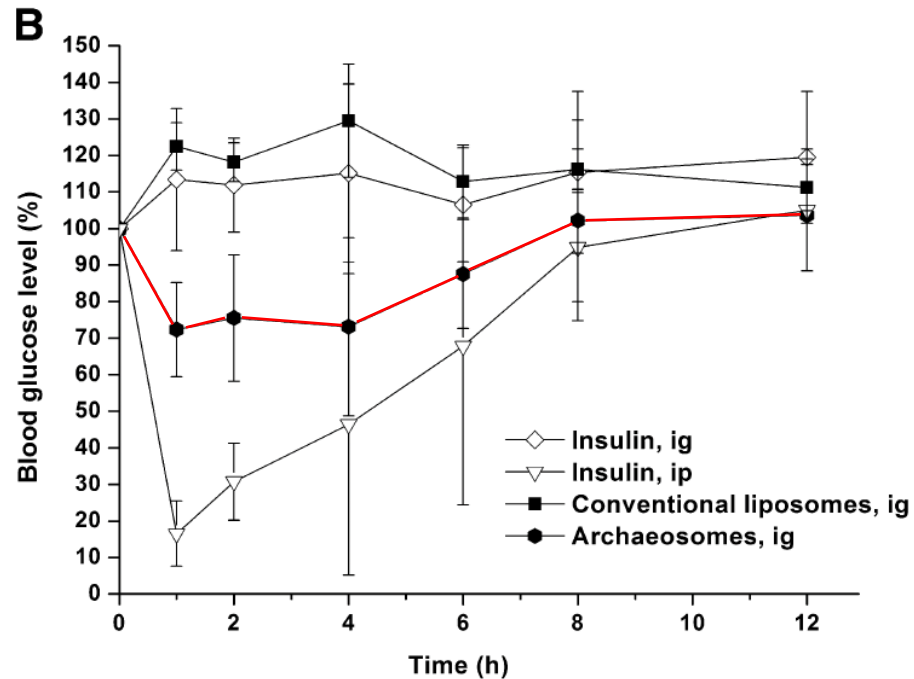
Bohsen et al., in preparation

TEL liposomes work!

Archaeosomes

Sulfolobus acidocaldarius

Li et al. 2010

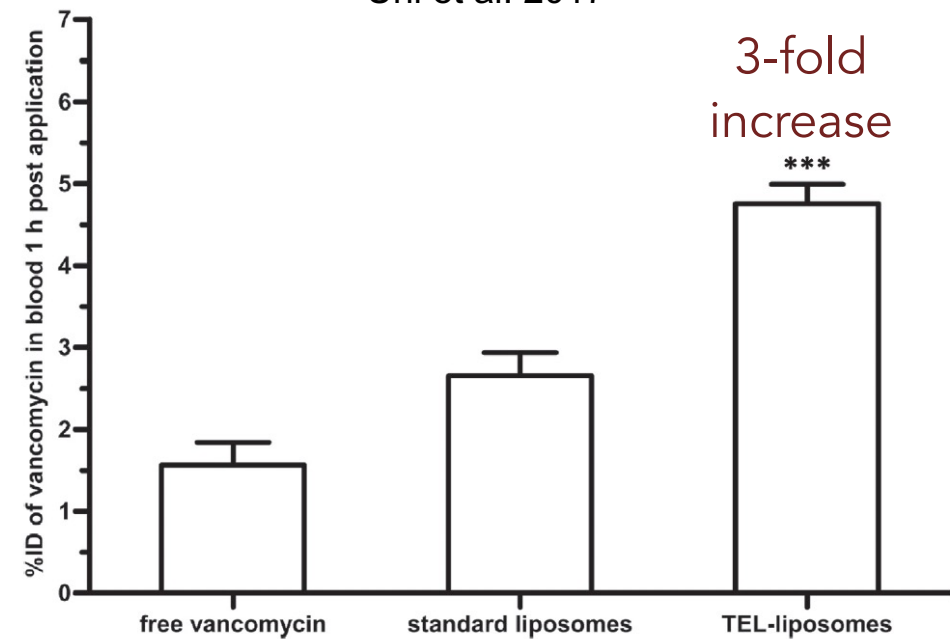


In vivo changes in blood glucose levels following oral administration of insulin to diabetic mice.

Mixed liposomes

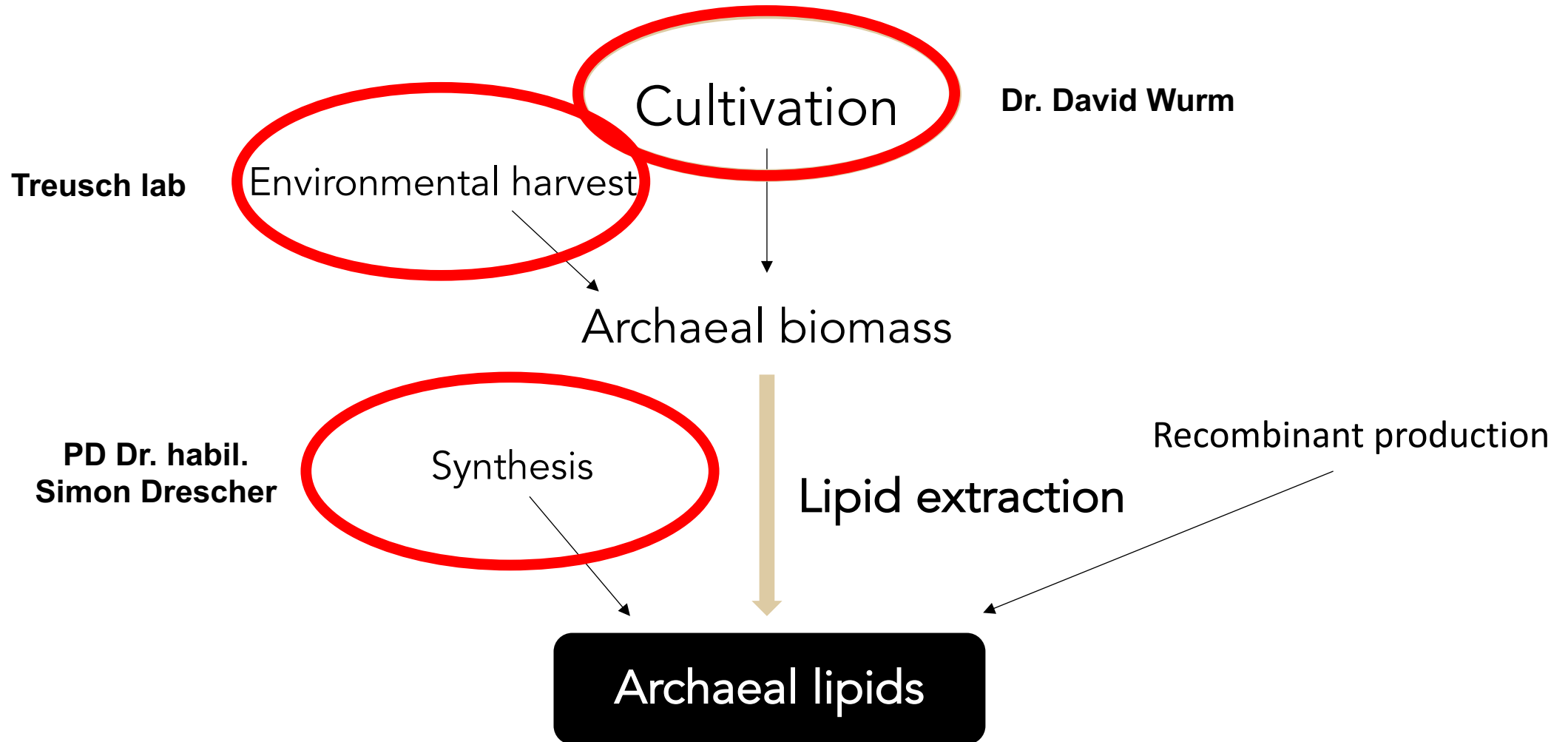
Egg-PC/cholesterol/*Sulfolobus acidocaldarius* lipid fraction E
(85/15/5 mol-%)

Uhl et al. 2017

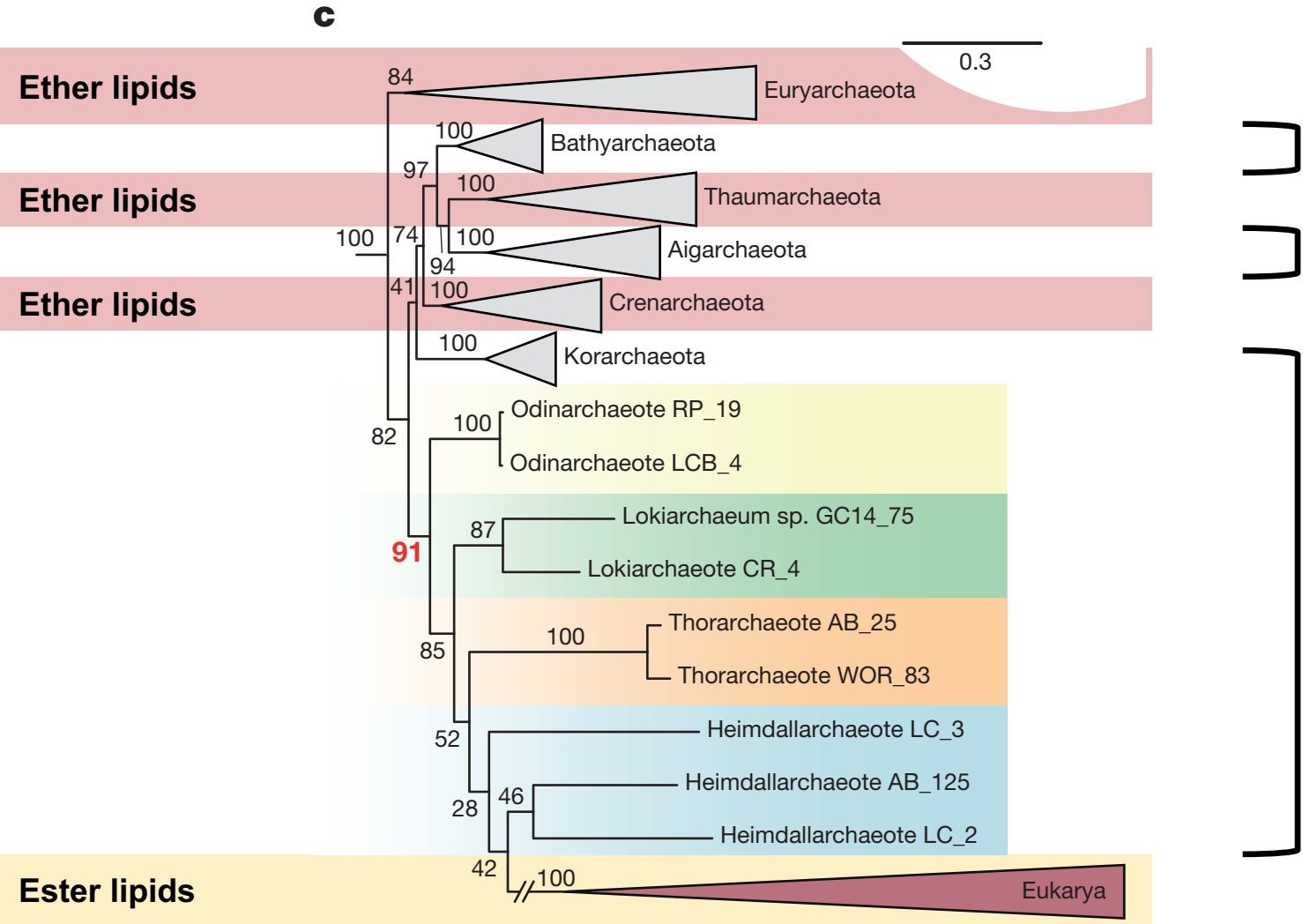


Bioavailability of vancomycin in Wistar rats 1h after oral administration.

Sources for TELs



What about the future?



Summary and conclusions

Archaea...

- ... form their own domain of life (maybe together with Eukaryotes?)
- ... cultivated species are mainly extremophiles
- ... ongoing expansion of known diversity

Archaeal lipids...

- ... have unique properties, making them interesting for biotechnology
- ... are not easy to source
- ... diversity is not fully known
- ... function not completely understood yet

Application of archaeal lipids...

- ... shows great promises in (oral) drug delivery by liposomes and LNPs
- ... will be boosted by better availability of them
- ... will be expanding to new areas

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Phospholipid Research Center