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K-mer approaches provide valuable insight into mobilome evolution in the domain Archaea

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K-mer approaches provide valuable insight into mobilome evolution in the domain Archaea

Ariane Bize, Violette Da Cunha, Cédric Midoux,
Sophie Schbath, Patrick Forterre

12th July 2018



K-mer signatures

k-mers = all possible subsequences of length k from a DNA sequence
 4 possible bases: A, T, G, C $\rightarrow 4^k$ different k-mers

e.g. k = 4 \rightarrow 4-mers or tetramers (e.g: ATAA, CGAG, GTTC, ...)
 $\rightarrow 4^4 = 64$ different tetramers

k-mer profile

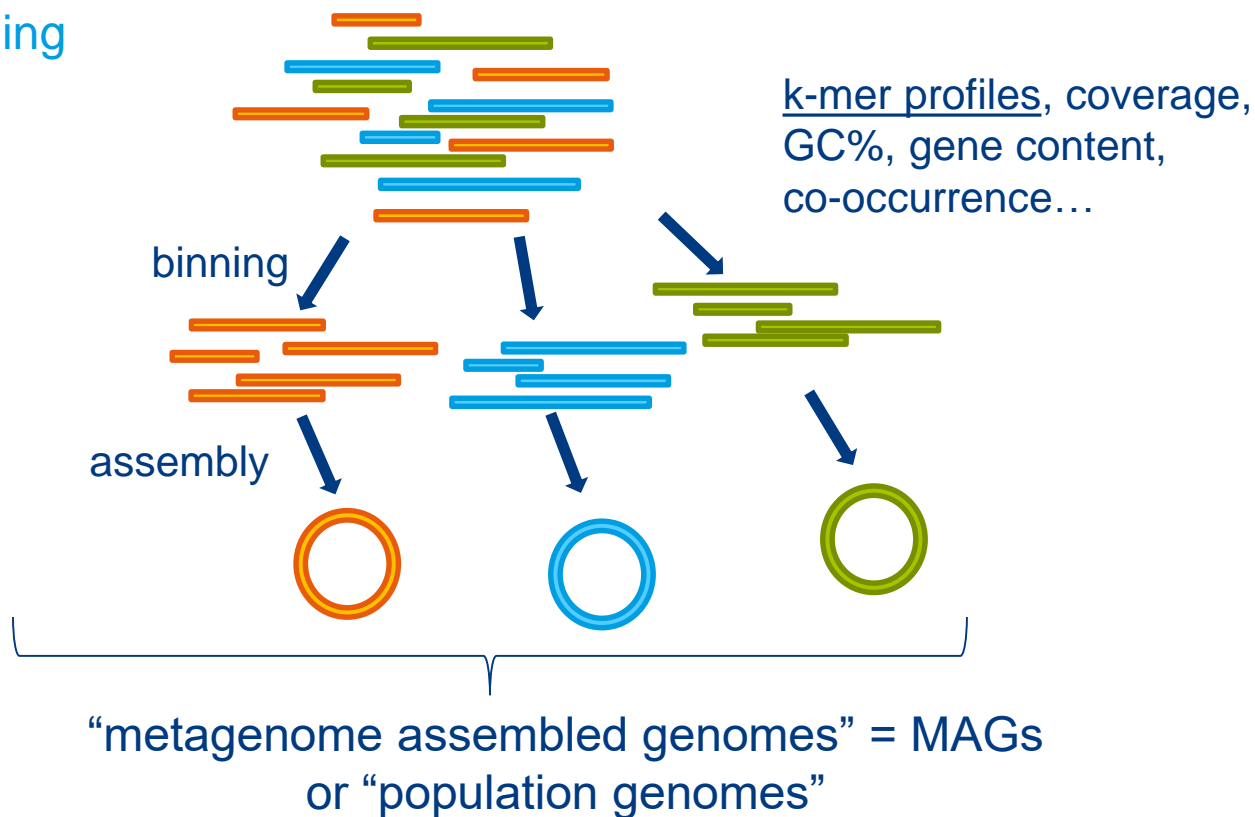
ATTAGGCCGCAAGGGCCTTCATAGTTTTAGCGATTTGGGA

64 words ↑	AGGC	1	Normalization →	AGGC	0.270
	ATTA	1		ATTA	0.270
	GGCC	2		GGCC	0.054
	TAGG	1		TAGG	0.270
	TTAG	2		TTAG	0.054
	
	Counts	Tetramer profile		Frequencies	

- Annotation independent
- Faster computation

K-mer approaches: metagenomics

Contig binning



K-mer approaches: mobilome

Detection of viral or plasmid sequences

VirFinder (Ren et al, Microbiome, 2017)



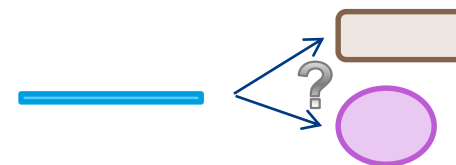
PlasFlow (Krawczyk et al, NAR, 2018)



Host prediction of viruses or plasmids

WiSH (Galiez et al, Bioinformatics, 2017)

PlasFlow (Krawczyk et al, NAR, 2018) [phylum level]



Evolutionary biology? → Also being explored

-Detection and characterization of horizontal transfers in prokaryotes using genomic signature, Dufraigne et al, 2005, NAR

-K-mer natural vector and its application to the phylogenetic analysis of genetic sequences, Wen J, et al, 2014, Gene

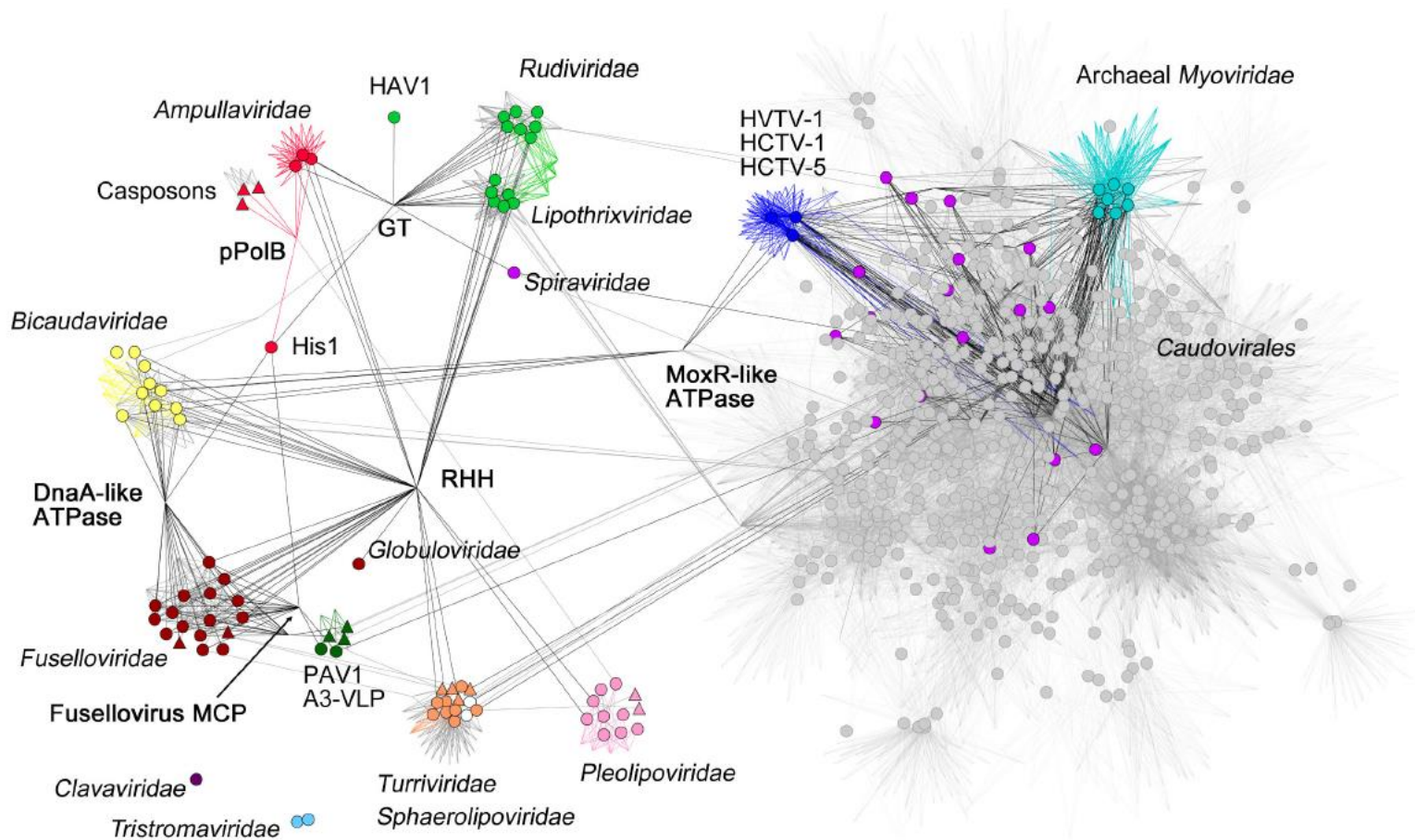
-Phenetic comparison of prokaryotic genomes using k-mer, Désrape et al, 2017, MBE



Present study: plasmids, viruses and hosts from the domain Archaea

- For the hosts, topology based on k-mer signatures consistent with the phylogeny of archaea?
- Regarding archaeal viruses and plasmids, topology similar to that of the hosts?
- Specific signature of archaeal extrachromosomal elements?
- Factors underlying these distributions?

Archaeal viruses



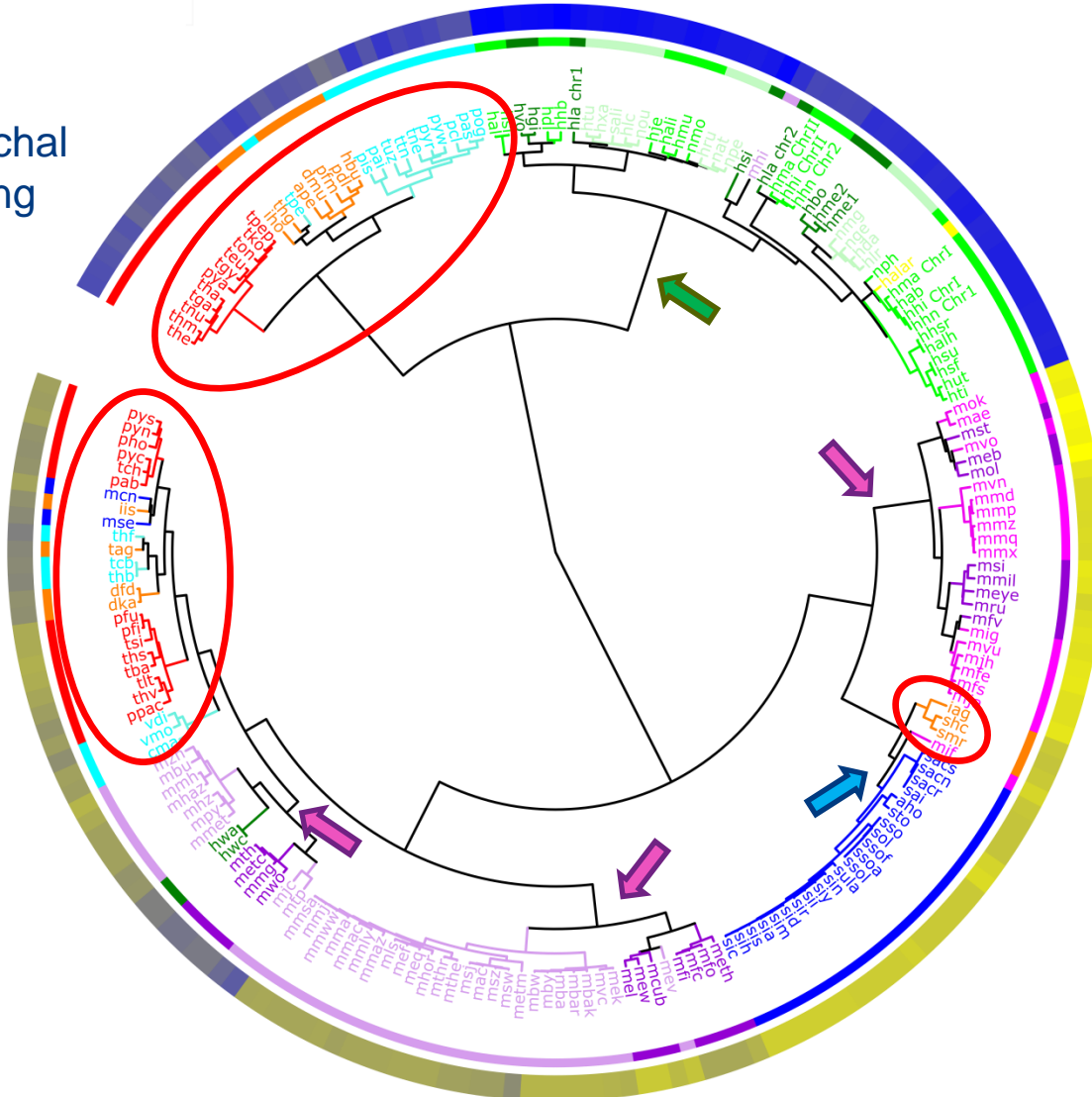
J. Iranzo, M. Krupovic, E.V. Koonin. "The double-stranded DNA virosphere as a modular hierarchical network of gene sharing." MBio 7.4 (2016): e00978-16.

Dataset

	Cells	Conjugative plasmids	Other plasmids	Viruses	Total
Crenarchaeota	55	13	13	51	132
Desulfurococcales	14			4	18
Sulfolobales	24	13	11	41	89
Thermoproteales	17		2	4	23
undet. hyperthermophilic archaea				2	2
Euryarchaeota	141	12	149	39	341
Halobacteriales	22	10	37	15	84
Haloferacales	10	1	29	15	55
Natrialbales	12		29	2	43
undet. haloarchaea	1	1	1	1	4
Gp I { Methanosarcinales	36		12		48
Gp II { Methanococcales	16		9	2	27
Methanobacteriales	19		7	2	28
Thermococcales	25		25	2	52
Total	196	25	162	90	473

Archaeal cells

k=4
Hierarchical
clustering



GC_percent

Minimum

Maximum

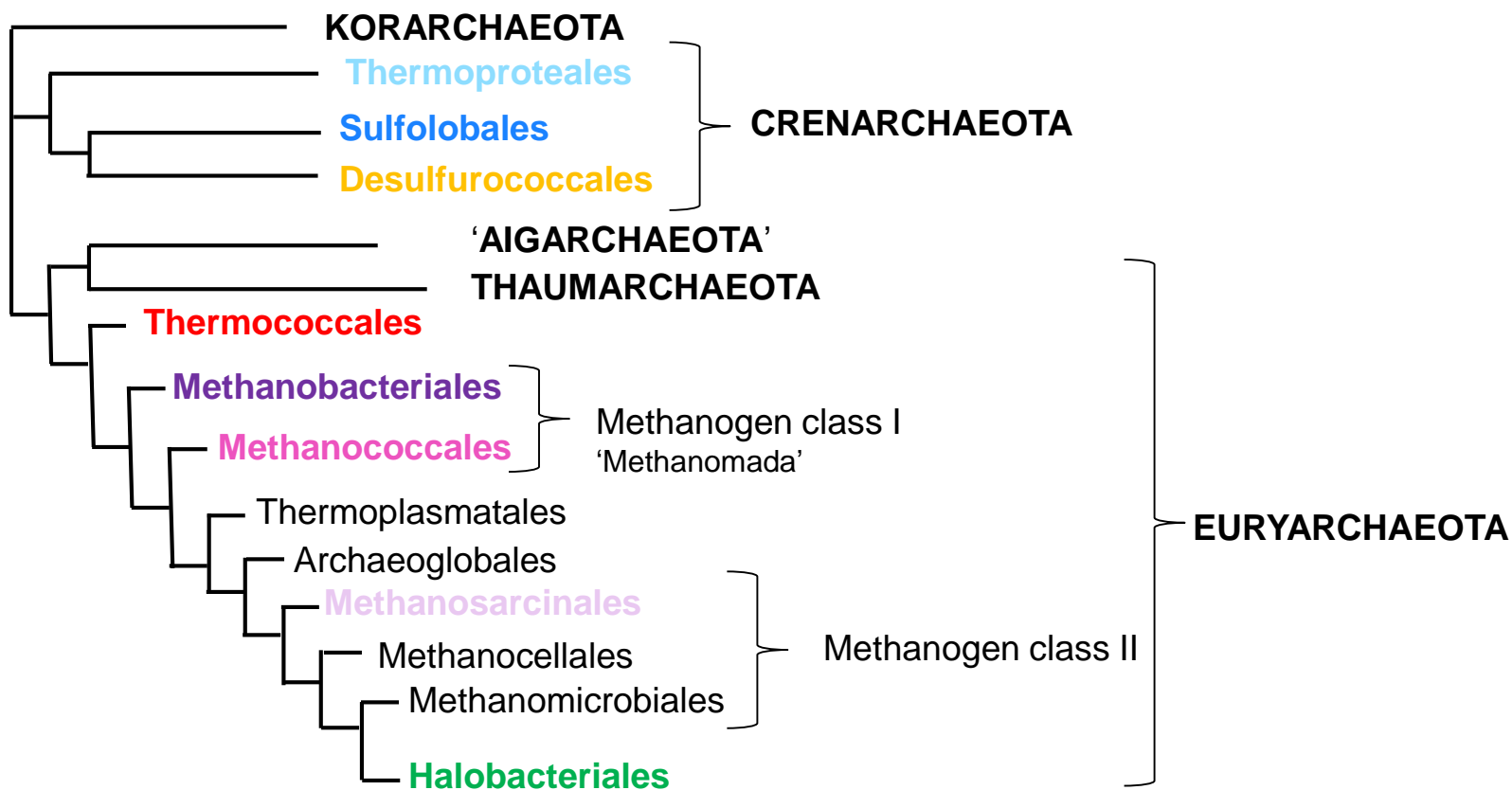
Taxonomic Order

- Halofercales
- Halobacteriales
- Natrialbales
- haloarchaea
- Methanobacteriales
- Methanococcales
- Methanosarcinales
- Thermococcales
- Desulfurococcales
- Thermoproteales
- Sulfolobales



Archaeal cells & phylogeny

- The topology of the dendrogram based on tetramer profiles is **not** consistent with the phylogeny of archaea



Archaeal cells & underlying factors

- Influential inter-related factors (MANOVA):

Factor	% of variance	Statistical significance
Taxonomy (order)	78%	+++
GC% content	74%	+++
“Niche”	67%	+++
Taxonomy (phylum)	6%	+++
Genome length	2%	+

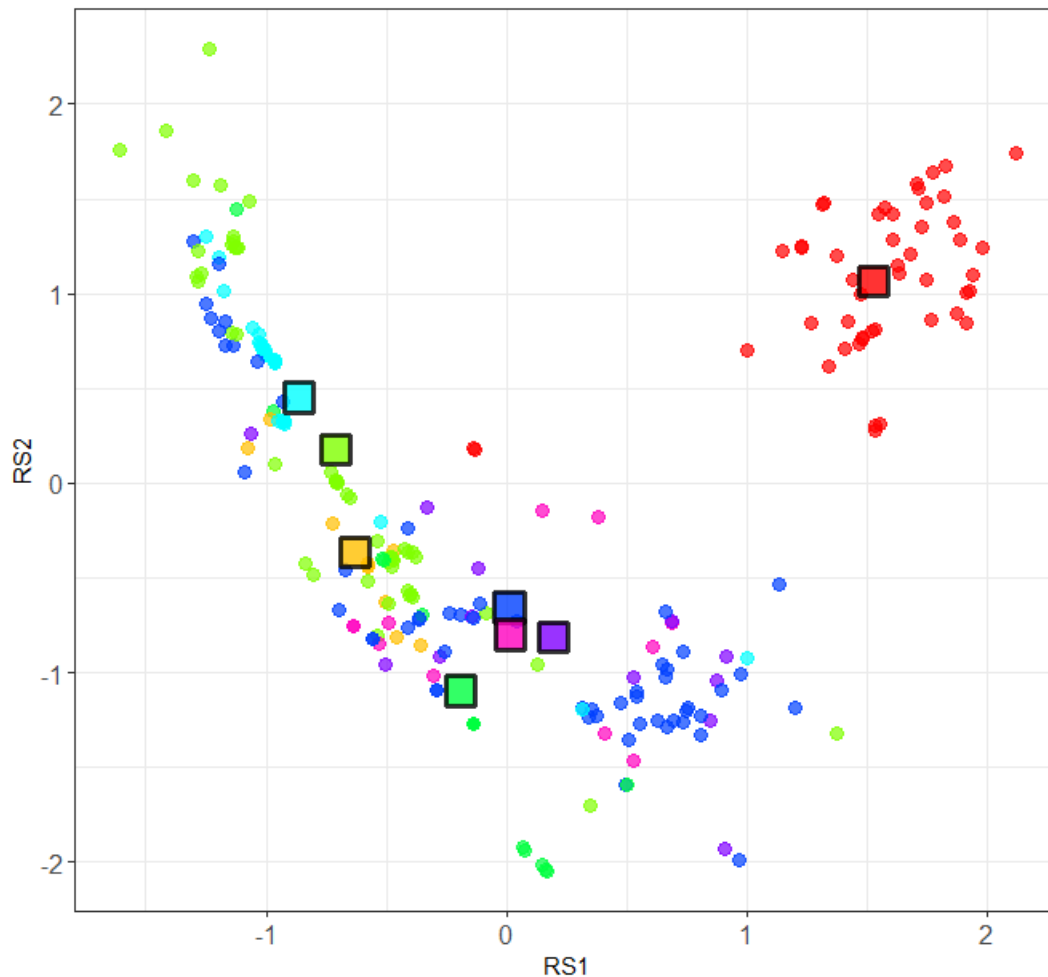
(Link between life style and codon usage: Botzman and Margalit Genome Biology 2011, 12:R109, <http://genomebiology.com/2011/12/10/R109>)

→ Ancient evolutionary links are not detected

- k-mer composition could evolve rapidly (e.g. Thermococcales)

Proteome adaptation to extremophilic conditions?

Principal component analysis, k=3



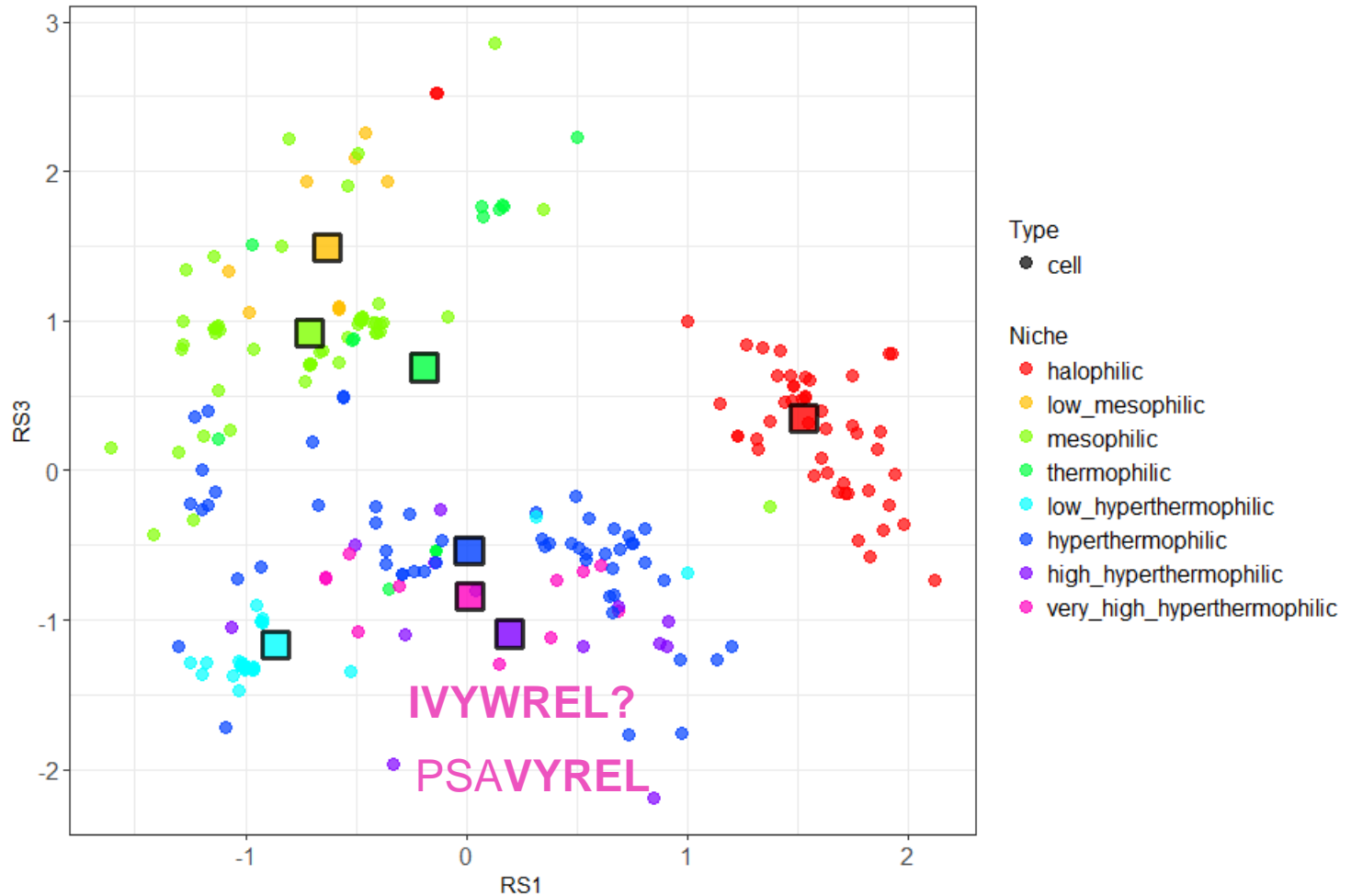
DEVT?

CGA
TCG
GCG
CGC
GAC
GTC
CGT
ACG
CCG
CGG

RSADVTP

Link with proteome adaptation to extremophilic conditions

Principal component analysis. $k=3$



ACIDQLTS*C
TS*CQLIDAC

ACIDQT SCL

GC_percent

Minimum

13

Maximum

Archaeal plasmids and viruses

Type of element

▷ Virus

◀ Plasmid

★ Conjugative plasmid

Taxonomic Order

■ Haloferacales

■ Halobacteriales

■ Natrialbales

■ haloarchaea

■ Methanobacteriales

■ Methanococcales

■ Methanosarcinales

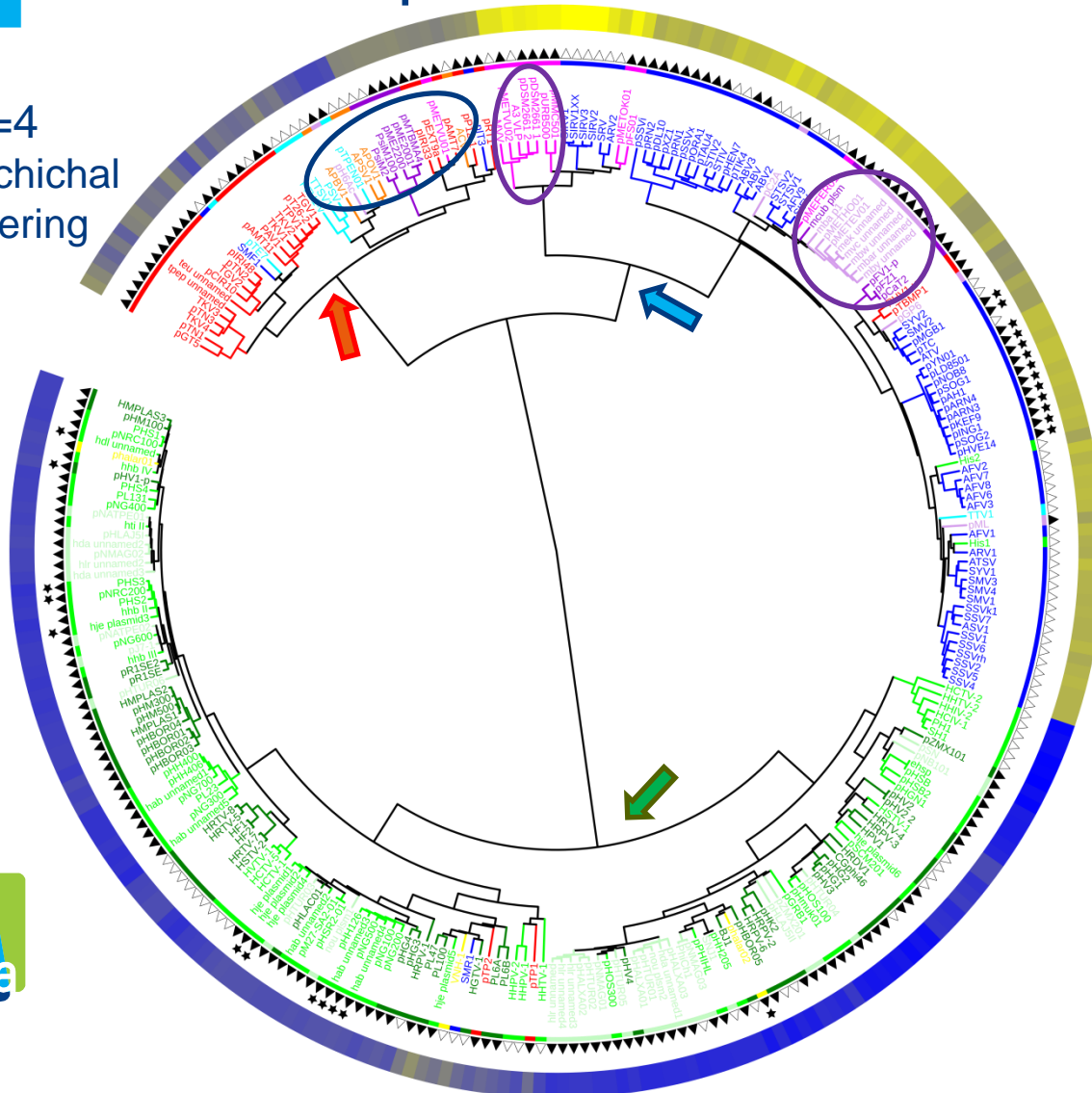
■ Thermococcales

■ Desulfurococcales

■ Thermoproteales

■ Sulfolobales

k=4
Hierarchical
clustering

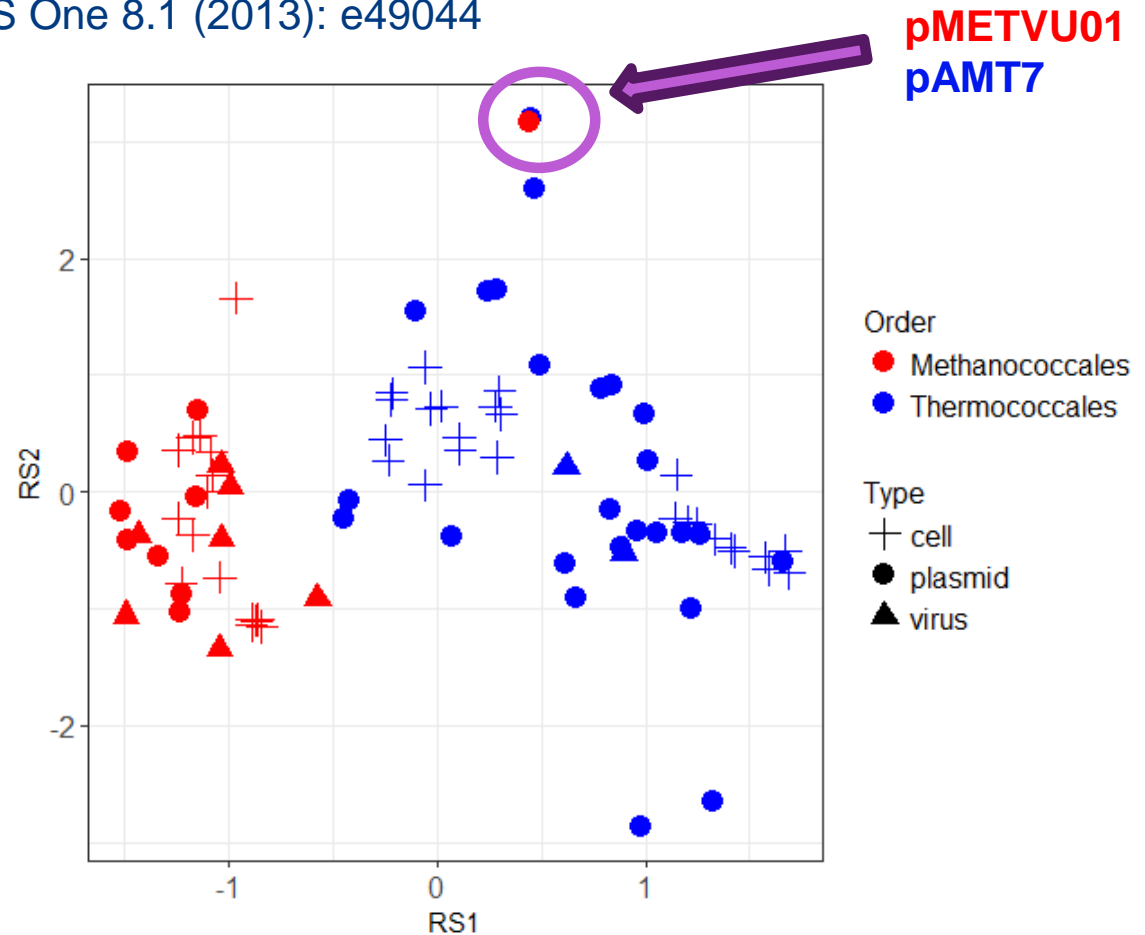


Archaeal plasmids and viruses: conclusions

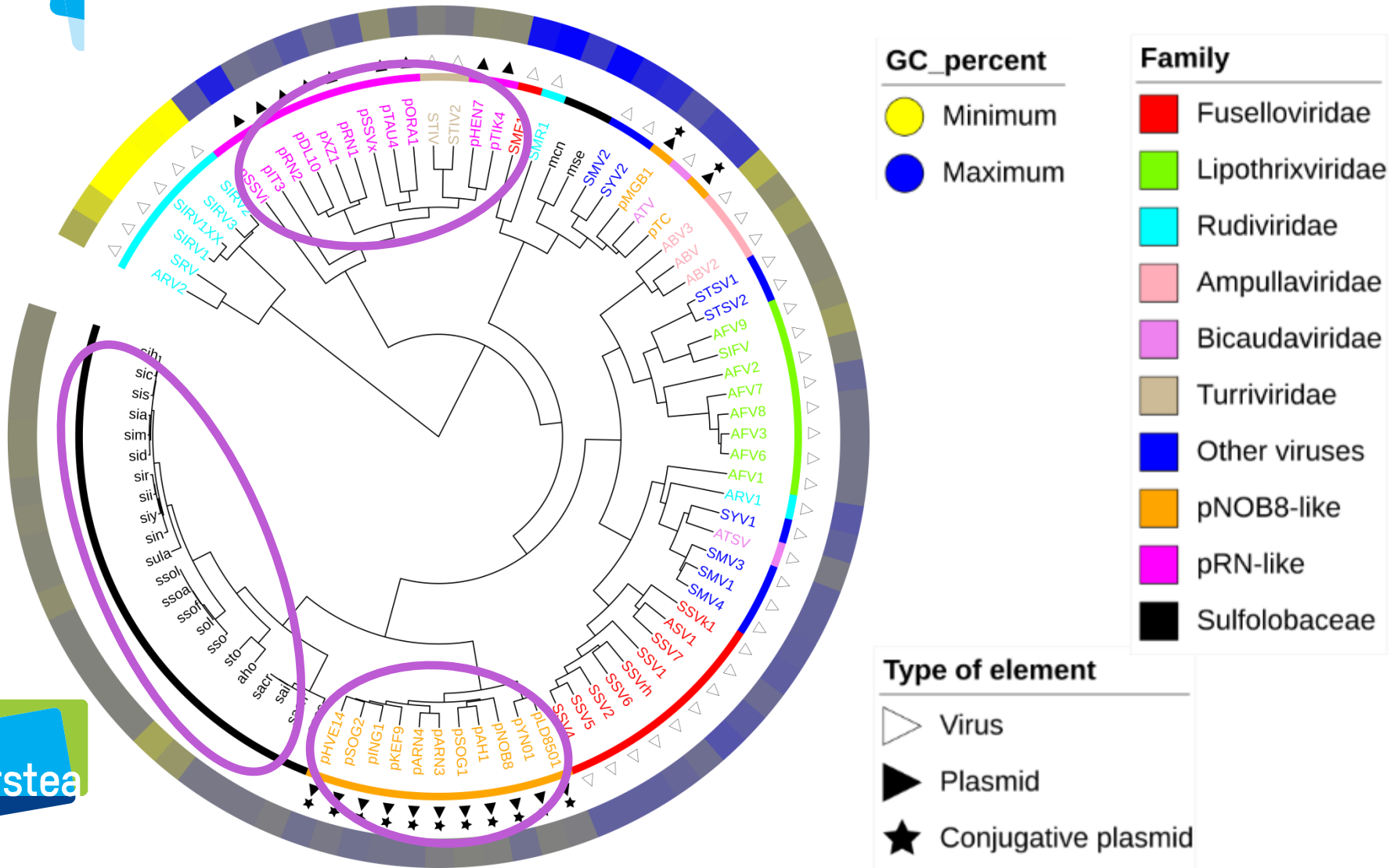
- Compared to cells, a slightly redistributed pattern
→ link with recent evolutionary events?

Krupovic, M, et al. PLoS One 8.1 (2013): e49044

Principal component analysis



Virus, plasmids, hosts: Sulfolobales (Crenarchaeota)





Conclusions, implications

Conclusions

- Phylogenetic position of the host (order), GC%, environment
- **Mobile genetic elements have their own signature**
- Rapidly evolving ? → recent evolutionary events

Implications

- Host prediction: better results on archaea with WiSH than on the whole prokaryote dataset. WiSH also worked for plasmids.
- **Metagenomic binning based on k-mer**
→ possible loss of integrated mobile genetic elements?



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Thank you for your attention!



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