

# Methylation-independent chemotaxis systems are the norm for gastric-colonizing bacteria

UNIVERSITY OF CALIFORNIA  
SANTA CRUZ



Xiaolin Liu, Karen Ottemann

Department of Microbiology and Environmental Toxicology, University of California, Santa Cruz, Santa Cruz, CA

## Introduction

- Chemotaxis signal transduction systems are present in half of archaeal and bacterial species including *Helicobacter* spp.
- Chemotaxis signal transduction systems are comprised of both common and variable proteins. We do not yet understand why these variations exist, or whether there are specific niches that favor particular chemotaxis signaling organization.

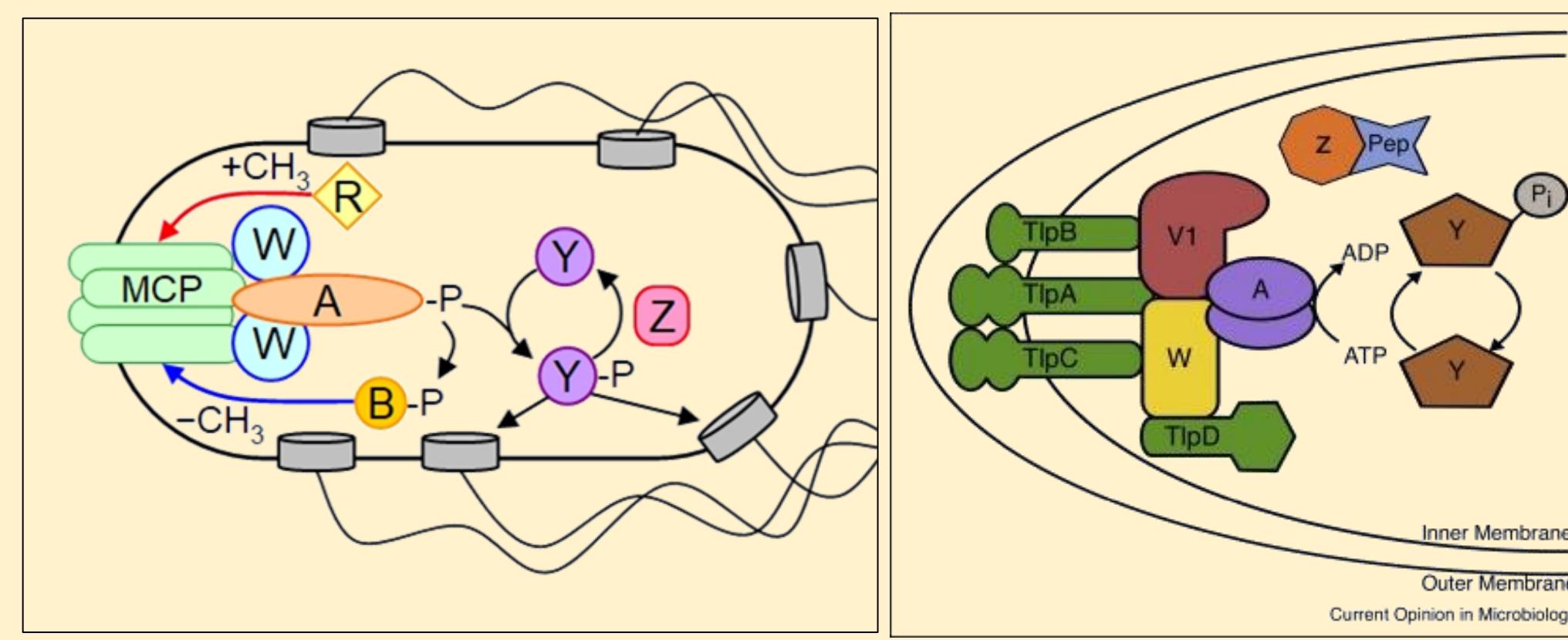


Figure 1. *E. coli* and *H. pylori* chemotaxis system components.

- Most *Helicobacter* species are pathogens, infecting the gastrointestinal tracts of different animals, and they can be divided into gastric or enterohepatic species. Gastric *Helicobacter* species colonize the stomachs of mammals including humans, dogs, cats and other felines, pigs, dolphins, sea otters, and whales, while enterohepatic *Helicobacter* species colonize parts of the gastrointestinal tract outside of stomach including liver and intestine of mammals, birds, and reptiles.

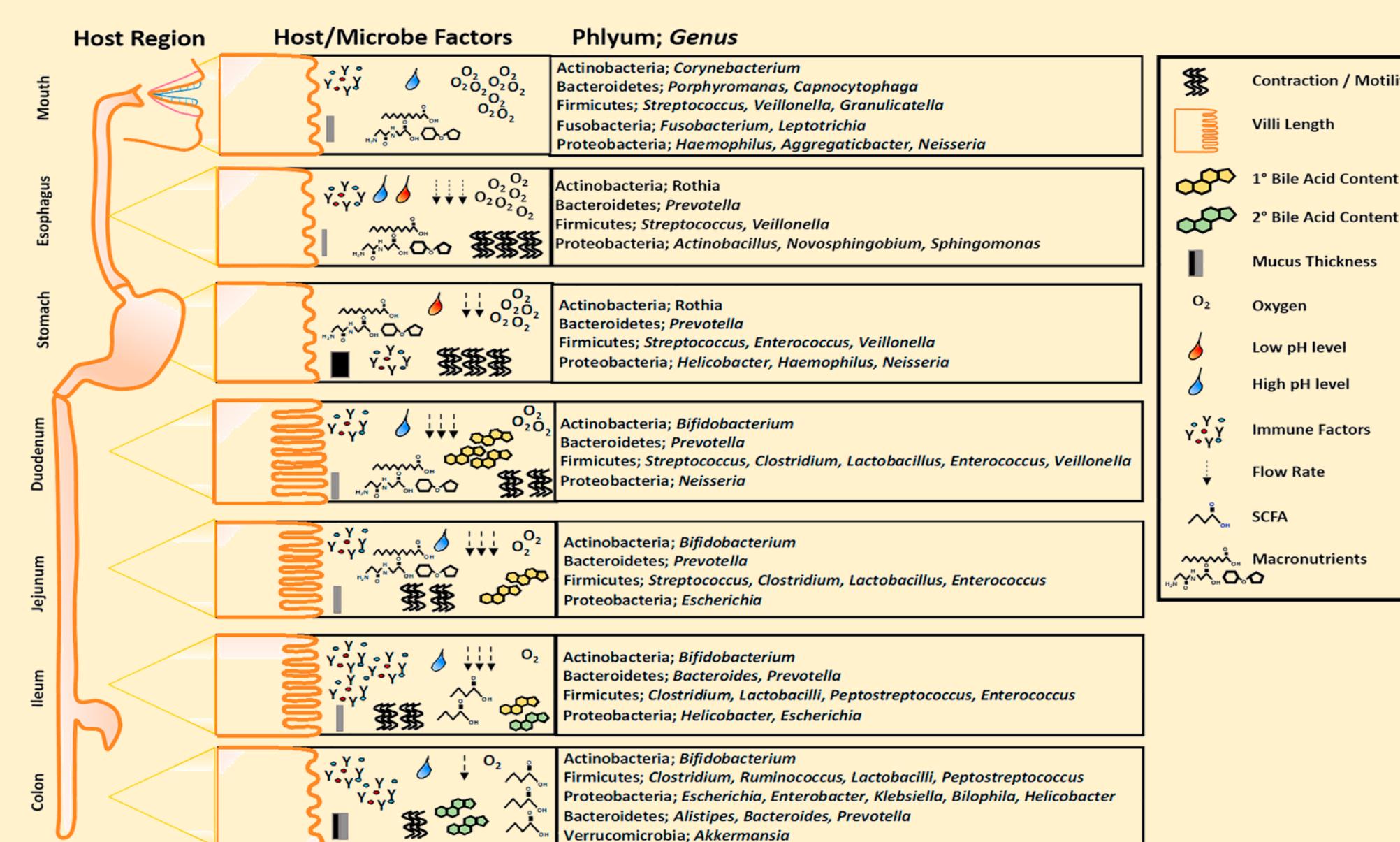


Figure 2. representative host and microbial factors and community membership along the rostral to caudal axis of the GI tract.

- Another on-going challenge is to predict whether a newly-isolated *Helicobacter* sp. is native to the gastric or enterohepatic niche, e.g. when one obtains the sample from feces, rectum or cloaca. Various approaches have historically failed to distinguish gastric from enterohepatic *Helicobacter* species, including analysis of the 16S rRNA sequences, analysis of other single genes, omics analyses, or urease activity. Phylogeny also is not conclusive: Although most gastric or enterohepatic *Helicobacter* species cluster into distinct clades, there are some exceptions. Thus, there is a need for better markers to separate the two groups.

## Results

### CheB and CheR are the two major variations in *Helicobacteraceae* chemotaxis machinery and correlate with *Helicobacter* ecological niche

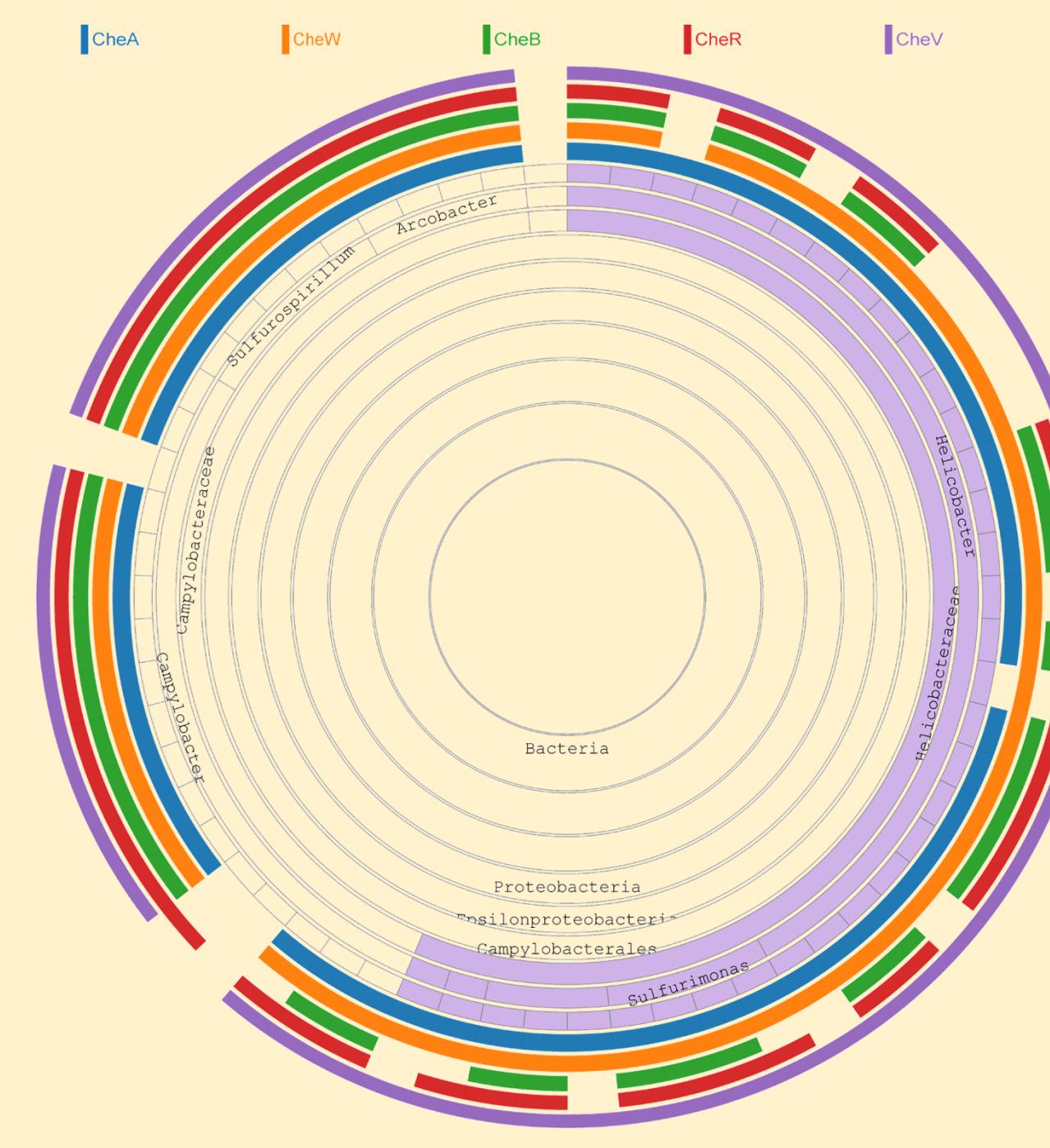
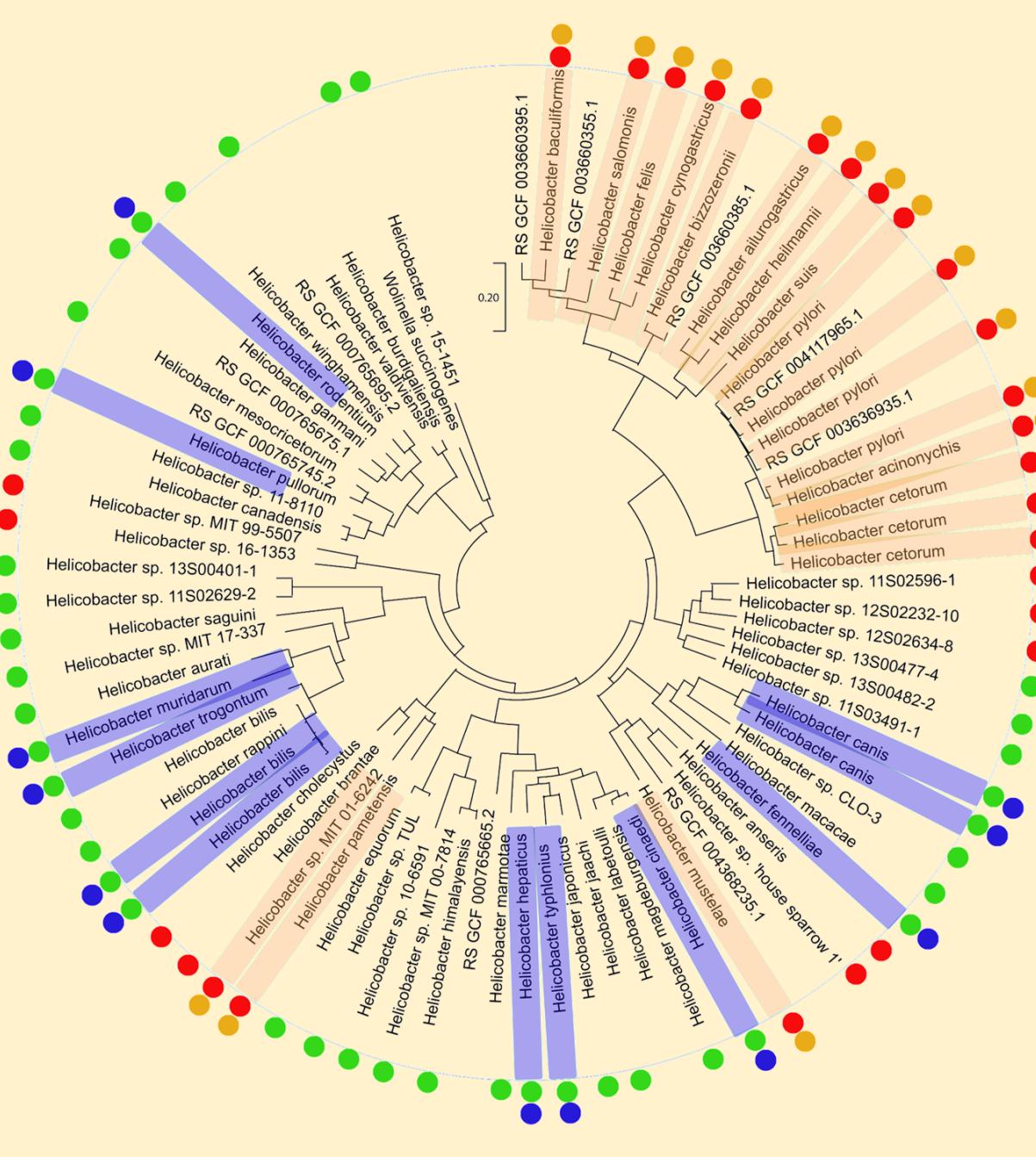


Figure 3. Left panel: Phylogenetic distribution of five kinds of chemotaxis protein genes in the *Campylobacterales* order (left panel).

*Helicobacteraceae* are indicated by light purple shading. In ring just inside the CheA ring, the individual species are denoted by separating lines, with 35 species in the *Helicobacteraceae* family (purple area) and 26 in the *Campylobacteraceae* one.

Right panel: The phylogenetic tree of *Helicobacteraceae* species combined with mapping the niche and presence of *cheB/cheR* on the tree. First layer outside of tree: the presence of *cheB/cheR*. Red dots are genomes without *cheB/cheR*, and green dots are genomes with *cheB/cheR*. The second layer outside of the tree indicates *Helicobacter* species with known gastric (orange) or enterohepatic (blue) niches.



### Methylation sites of chemoreceptors in gastric *Helicobacter* species are degraded

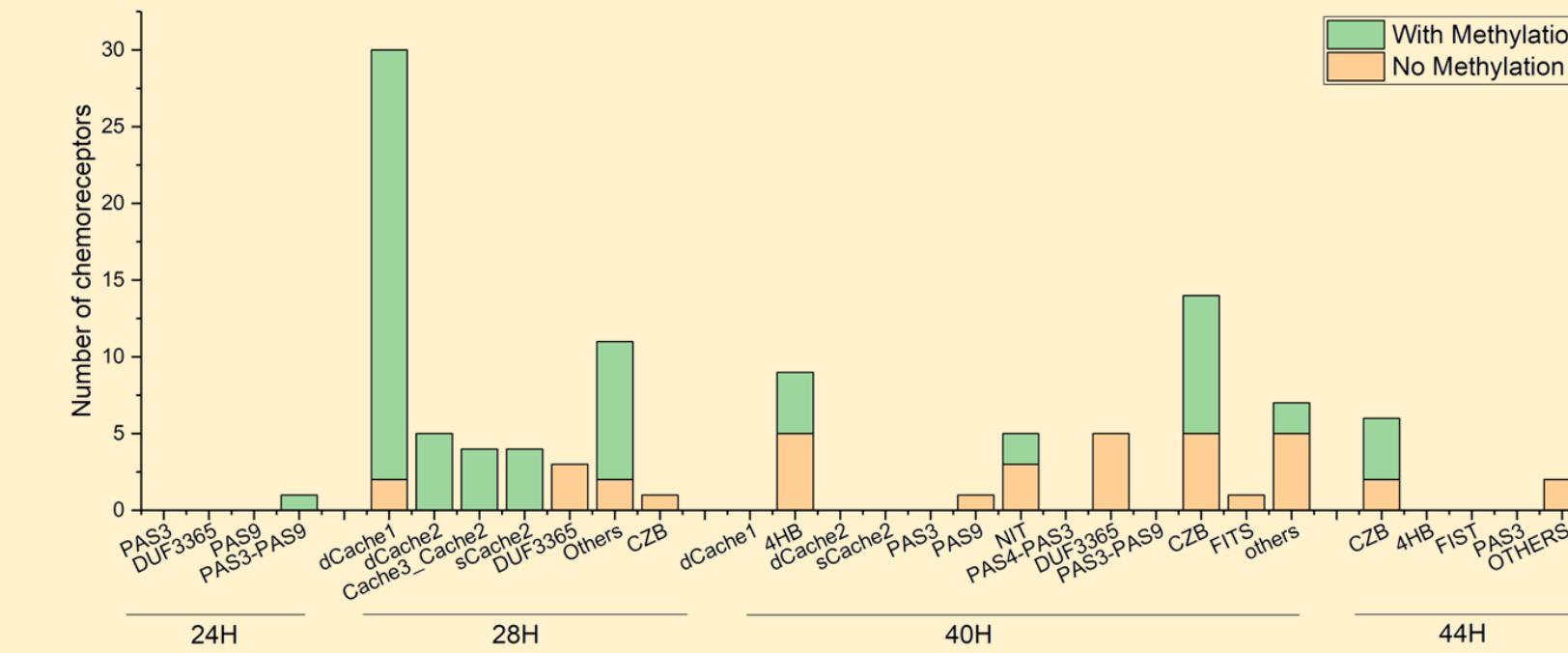
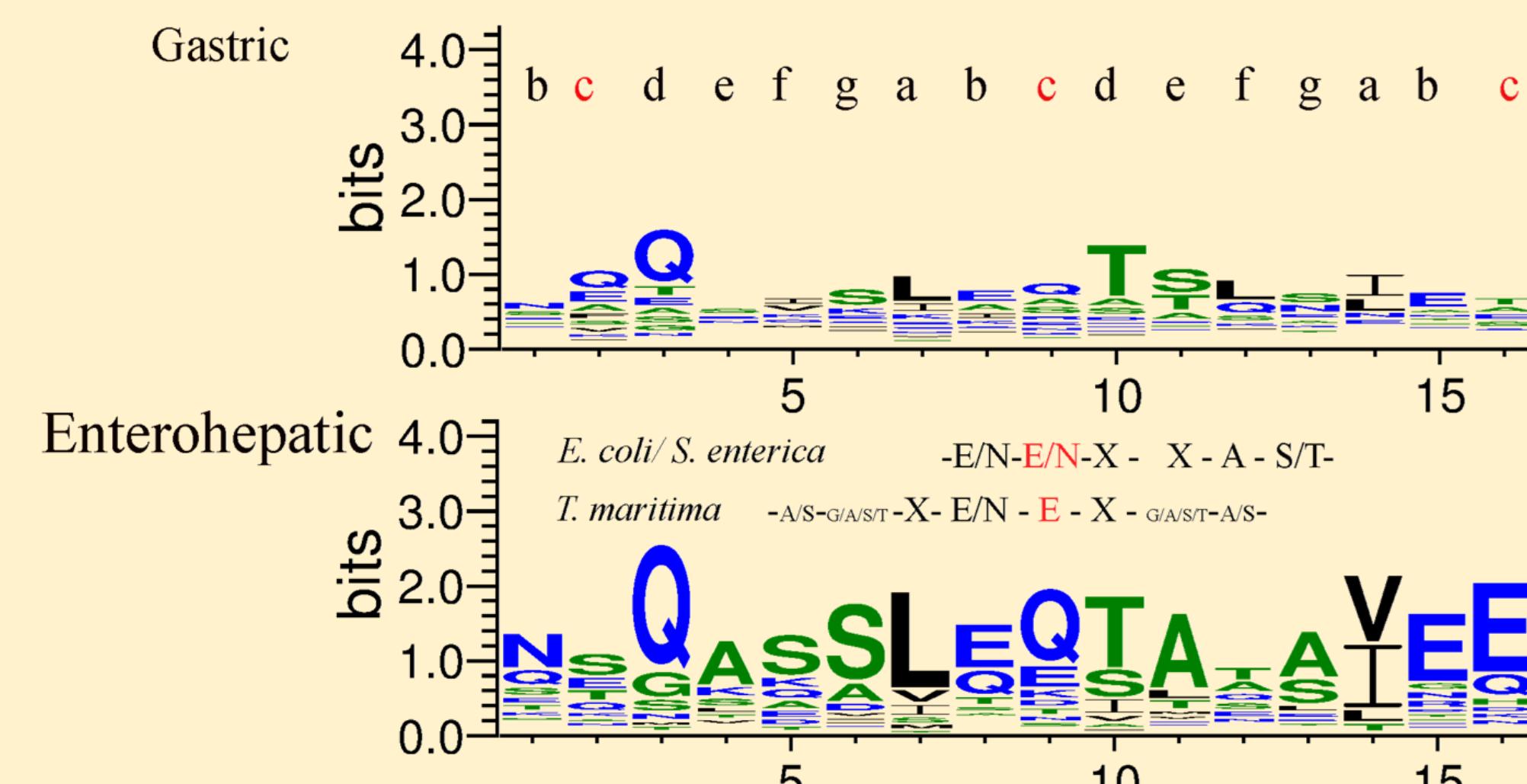


Figure 4. Left panel: Analysis of patterns in the conserved methylation region of chemoreceptors sites 1-2-3, between gastric (Top) and enterohepatic (Bottom) *Helicobacter* species. There is a seven-residue repeat (a-b-c-d-e-f-g) around the methylation sites. The methylation sites are located at position c or d with red color.

Right panel: Analysis of different types of chemoreceptors with methylation sites in enterohepatic *Helicobacter* species.

### *cheB* and *cheR* presence/absence and genome size may have utility to differentiate gastric from enterohepatic *Helicobacter* species

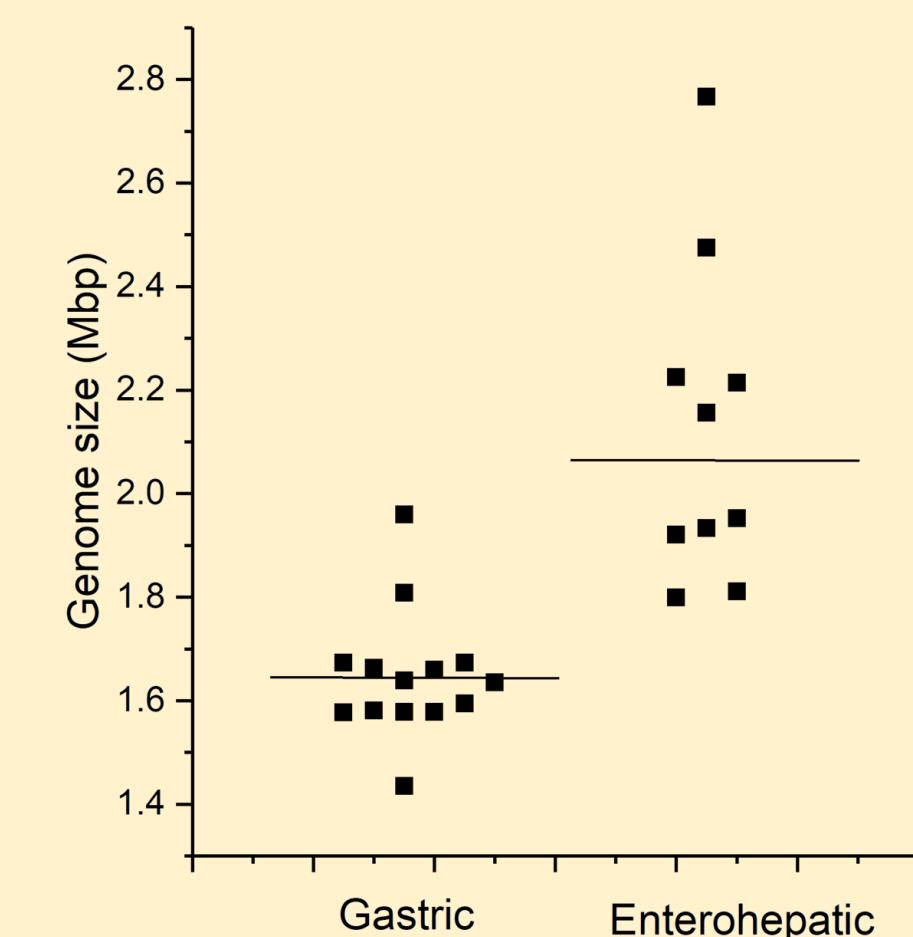
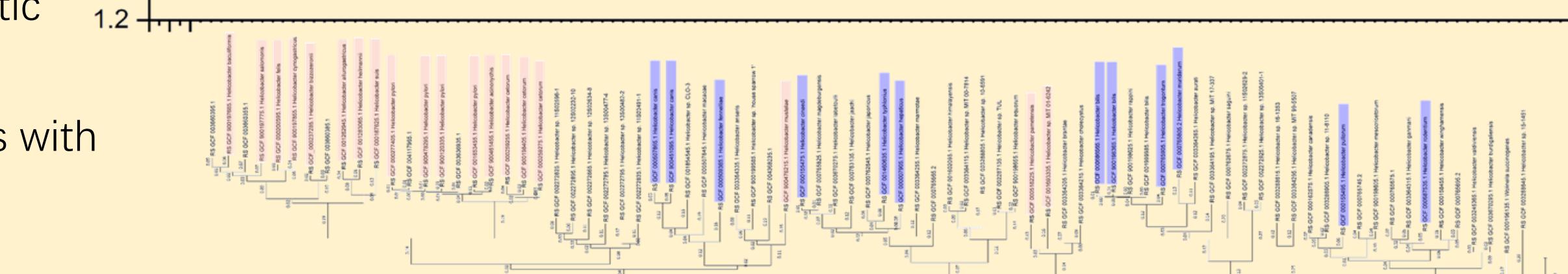


Figure 5. Left panel: The genome size in gastric or enterohepatic *Helicobacter* species. Each dot represents a species.

Right panel: Mapping the genome size of *Helicobacter* species with or without CheB/CheR to the phylogenetic tree of *Helicobacteraceae*. Red squares indicate the genome without CheB/CheR, while the blue squares indicate the genome with CheB/CheR. The strain name with red highlight means confirmed gastric *Helicobacter* species, while strain name with blue color indicates confirmed enterohepatic *Helicobacter* species.



## Conclusion

- Niche mapping supported that CheB/R were present in enterohepatic *Helicobacter* species and absent in gastric ones.
- Methylation-based adaptation is not required in specific environments, particularly the stomach.
- CheB and CheR could serve as markers to indicate whether a *Helicobacter* species was of enterohepatic or gastric origin.