signalHsmm: prediction of malarial signal peptides

Michał Burdukiewicz[1]*, Piotr Sobczyk[2], Paweł Błażej[1], Paweł Mackiewicz[1]

[1]University of Wrocław, Department of Genomics,
[2]Wrocław University of Science and Technology, Faculty of Pure and Applied Mathematics,
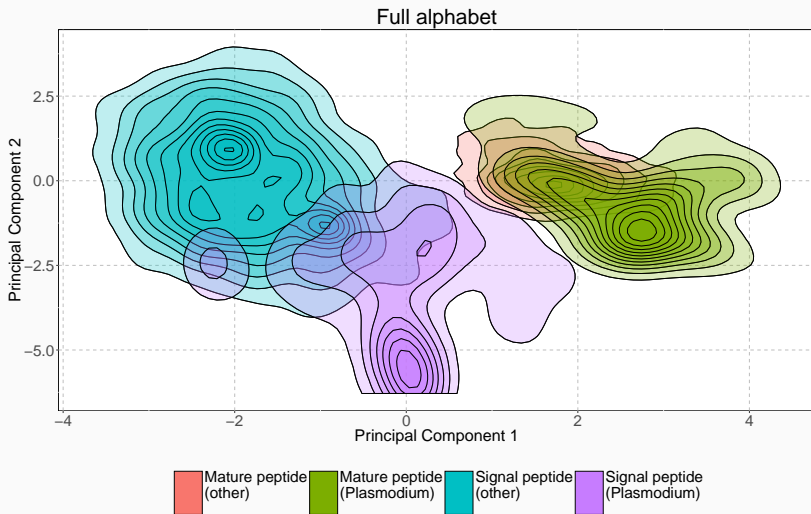
Signal peptides

Secretory signal peptides:

- are short (20-30 residues) N-terminal amino acid sequences,
- direct a protein to the endomembrane system and next to the extracellular localization,
- are universal enough to direct properly proteins in different secretory systems; artifically introduced bacterial signal peptides can guide proteins in mammals (Nagano and Masuda, 2014) and plants (Moeller et al., 2009),
- tag among others hormons, immune system proteins, structural proteins, and metabolic enzymes.
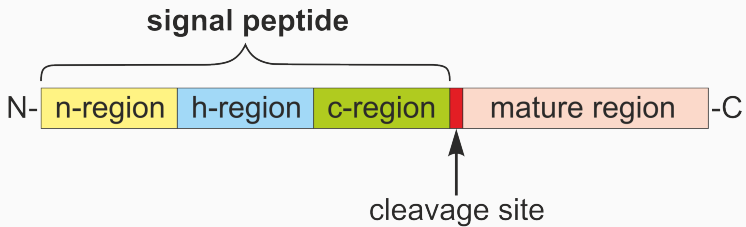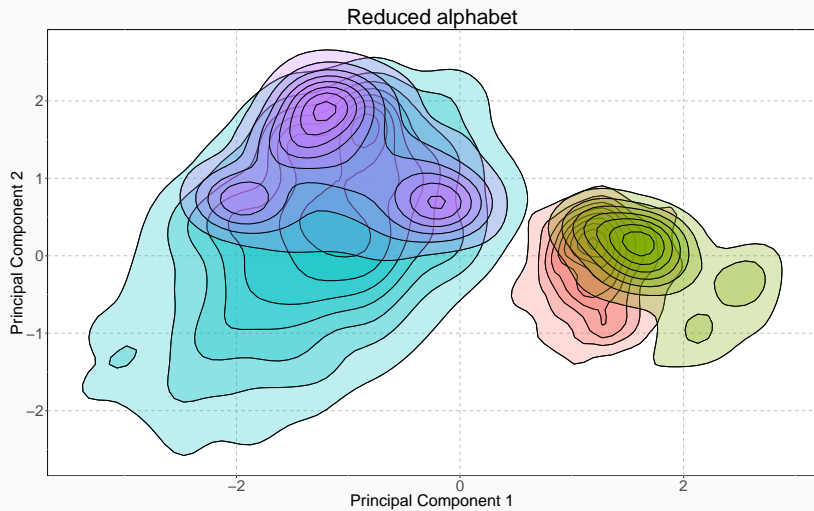
Signal peptides possess three distinct domains with variable length and characteristic amino acid composition (Hegde and Bernstein, 2006):
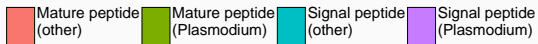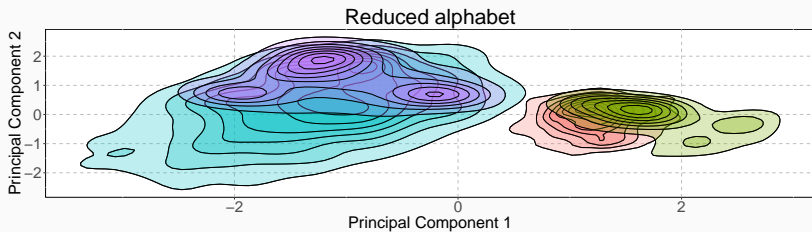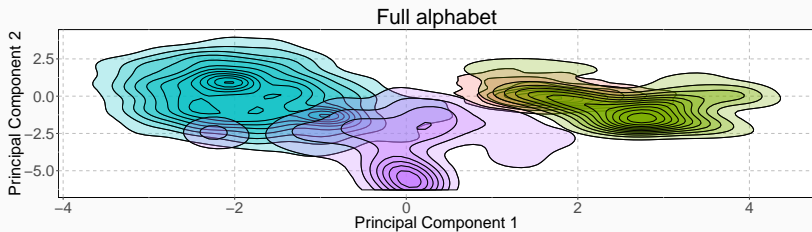
- n-region: mostly basic residues (Nielsen and Krogh, 1998),
- h-region: strongly hydrophobic residues (Nielsen and Krogh, 1998),
- c-region: a few polar, uncharged residues (Jain et al., 1994).

Heavy adenine-thymine bias of parasitic genomes (Tonkin et al., 2008) alters amino acid composition of malarial signal peptides.

Full alphabet

Group	Amino acids
1	D, E, H, K, N, Q, R
2	G, P, S, T, Y
3	F, I, L, M, V, W
4	A, C

Reduced alphabet

Full alphabet

Reduced alphabet

Mature peptide (other) · Mature peptide (Plasmodium) · Signal peptide (other) · Signal peptide (Plasmodium)

Countour plot of first two components in Pricincipal Compoment Analysis of amino acid frequency. The signal peptides from malaria and other taxons differ significantly when the full amino acid alphabet is employed. After the reduction of the alphabet, the signal peptides group together despite their origin.

Acknowledgements and funding

9

References

Hegde, R. S. and Bernstein, H. D. (2006). The surprising complexity of signal sequences. *Trends in Biochemical Sciences*, 31(10):563–571.

Jain, R. G., Rusch, S. L., and Kendall, D. A. (1994). Signal peptide cleavage regions. functional limits on length and topological implications. *The Journal of Biological Chemistry*, 269(23):16305–16310.

Moeller, L., Gan, Q., and Wang, K. (2009). A bacterial signal peptide is functional in plants and directs proteins to the secretory pathway. *Journal of Experimental Botany*, 60(12):3337–3352.

Nagano, R. and Masuda, K. (2014). Establishment of a signal peptide with cross-species compatibility for functional antibody expression in both escherichia coli and chinese hamster ovary cells. *Biochemical and Biophysical Research Communications*, 447(4):655 – 659.

Nielsen, H. and Krogh, A. (1998). Prediction of signal peptides and signal anchors by a hidden markov model. *Proceedings / ... International Conference on Intelligent Systems for Molecular Biology ; ISMB. International Conference on Intelligent Systems for Molecular Biology*, 6:122–130.

Tonkin, C. J., Foth, B. J., Ralph, S. A., Struck, N., Cowman, A. F., and McFadden, G. I. (2008). Evolution of malaria parasite plastid targeting sequences. *Proc Natl Acad Sci U S A*, 105(12):4781–4785.