

# Genome-scale Metabolic Network Reconstruction of the Pathogen *Treponema pallidum* ssp. *pallidum*

## Background

The spirochaete bacterium *Treponema pallidum* causes the sexually transmitted infectious disease syphilis [1] as well as yaws, a tropical skin, and bones infection. Without antibiotics treatment, both diseases can lead to persistent physical damages and even lethality. In recent years, however, antibiotic resistances are spreading worldwide while at the same time the discovery pipeline for new pharmaceuticals is lean [2]. For this reason, new concepts for fighting infectious diseases need to be made accessible. Computational models of metabolism have already been demonstrated to increase our understanding of cellular functions of a variety of organisms [3] and have the potential to identify new potential therapeutic targets. Until now, no such model exists for *Treponema pallidum* (see image on the right, source: Wikipedia).



## Specific aims

This thesis focuses on the molecular causes of syphilis. To this end, the full metabolic activity of *T. pallidum* ssp. *pallidum* will be reconstructed on a genome scale. To this end, the necessary steps of the protocol for constructing high-quality metabolic reconstructions will be applied to this organism [4]. This bottom-up assembly procedure will include a combination of computational methods and careful manual checking of the model content. Test cases will be created, knowledge gaps will be filled, and confidence of model components will be documented.

## Requirements

Understanding of biochemistry, basic knowledge of Python programming, interest in computational systems biology, patience, and passion for detail.

## References

- [1] Pinto, Miguel, Vítor Borges, Minia Antelo, Miguel Pinheiro, Alexandra Nunes, Jacinta Azevedo, Maria José Borrego, et al. 2016. "Genome-Scale Analysis of the Non-Cultivable *Treponema Pallidum* Reveals Extensive within-Patient Genetic Variation." *Nature Microbiology* 2 (1). Nature Publishing Group: 1–11. doi:10.1038/nmicrobiol.2016.190.
- [2] Laxminarayan, Ramanan, Adriano Duse, Chand Wattal, Anita K M Zaidi, Heiman F L Wertheim, Nithima Sumpradit, Erika Vlieghe, et al. 2013. "Antibiotic Resistance-the Need for Global Solutions." *The Lancet Infectious Diseases* 13 (12): 1057–98. doi:10.1016/S1473-3099(13)70318-9.
- [3] Bordbar, Aarash, Jonathan M Monk, Zachary a King, and Bernhard O Palsson. 2014. "Constraint-Based Models Predict Metabolic and Associated Cellular Functions." *Nature Reviews. Genetics* 15 (January): 107–20. doi:10.1038/nrg3643.
- [4] Thiele, Ines, and Bernhard Ø Palsson. 2010. "A Protocol for Generating a High-Quality Genome-Scale Metabolic Reconstruction." *Nature Protocols* 5 (1). Nature Publishing Group: 93–121. doi:10.1038/nprot.2009.203.