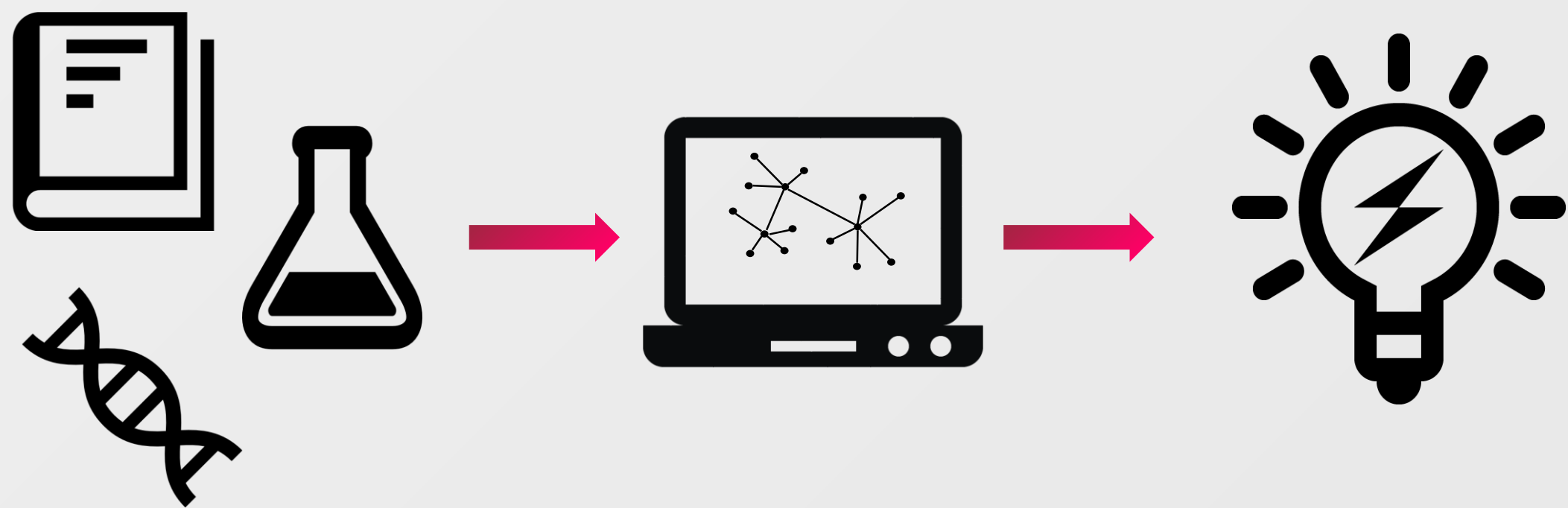# Virtual Cell

Metabolic Switch *in vitro* and *in silico*

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Aim

A genome scale **metabolic network** model is a complex collection of known chemical reactions encoded in the genome of a particular organism. It includes information about **stoichiometric coherences**, **energy requirements** and the **biomass composition**. In combination with metabolomics or transcriptomics, metabolic modeling allows for the detection and in-depth understanding of **molecular mechanisms** and **superordinated regulation networks**.[1]

Model Prediction
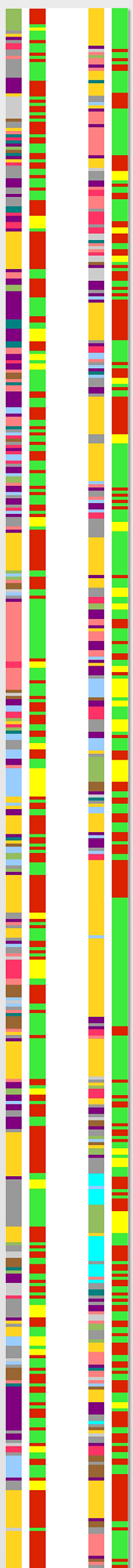
The **metabolic model** of *Streptomyces* sp. Tü6071 consists of 1363 reactions and 1343 metabolites, including pathways for the production of specific natural drugs. With a comparative **Flux Balance Analysis** the different behavior of all reactions between growing and production state can be predicted.

Comparison of the predicted fluxes to genexpression.
Left: Genes included in the model color-encoded by functional subsystem.
Right: Correlation of the predicted to the experimentally measured data. Green: good correlation; yellow: no correlation; red: anti-correlation

Codon Distribution

The transcriptomics data show a very diverse expression of the genes involved in the formation of **tRNA**. Its distribution is a well known **regulation mechanism**. Rare codons, such as the **TTA-codon** for Actinobacteria, often control the formation of specific metabolites.[3]
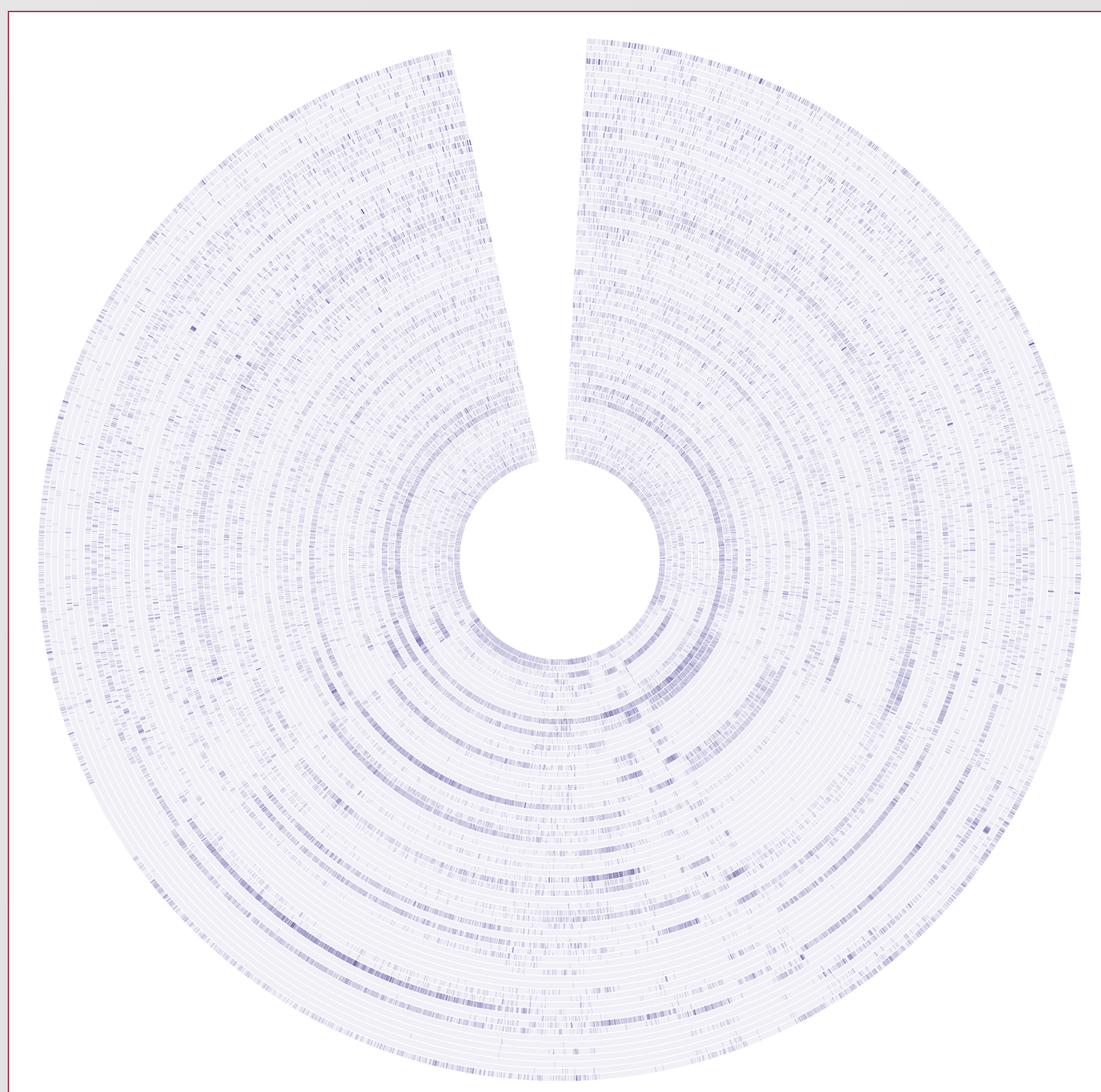
Distribution of possible codons (64) from inside to the outside for all genes (6478) in the genome clustered by codon utilization.

Metabolic Switch

In general, the bacterial metabolism is optimized for the production of **biomass**. With changing environmental conditions, **extensive changes** of the metabolic network take place in order to be able to compete against rival organisms, e.g. by producing of harmful **secondary metabolites,** such as phenalinolactones.[2]
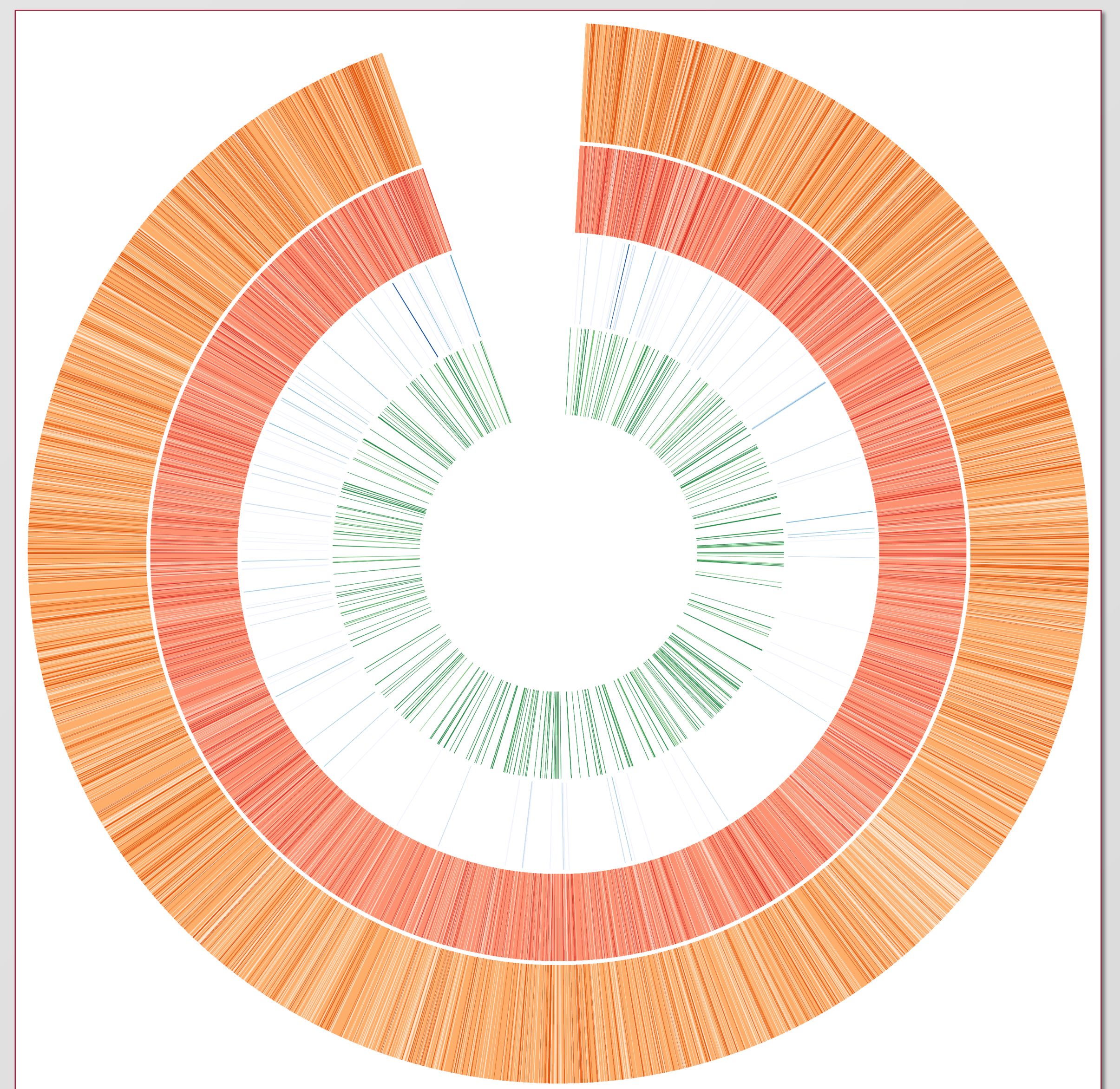
Expression values in growing- and phenalinolactone production state including resulting fold-change from outside to inside for all genes in the genome clustered by codon utilization. Groups of coherent expressed genes are linked in the middle.

Future Prospects

The collected insights and data are now being analyzed and integrated into a **consistent regulatory and metabolic model** (virtual cell). This model can be applied for **rational metabolic engineering** approach of an **overproducer** of important secondary metabolites such as antibiotics.

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References

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[2]   Alam MT, et al., Metabolicmodeling and analysis of the metabolic switch in Streptomyces coelicolor, BMC Genomics. 2010 Mar 26;11:202

[3]   Sen A., et al., Identification of TTA codon containing genes in Frankia and exploration of the role of tRNA in regulating these genes. Arch Microbiol 2012 Jan;194(1):35-45