Project Title: Passive regulation of gene expression

Polish partner	**German partner**
Dr. Tomasz W. Turowski	Dr. Daniel Schindler
Institute of Biochemistry and Biophysics, PAS	Max Planck Institute for Terrestrial Microbiology, MPG

DNA, the fundamental carrier of genetic information, forms an antiparallel helical structure, hosting genes on both the forward and reverse strands. RNA polymerases (RNAP) conduct the transcription of genetic information from DNA to RNA, yielding different types of RNA—non-coding RNA (ncRNA) and messenger RNA (mRNA), which are essential for protein synthesis. The transcription process, orchestrated by three eukaryotic RNAP types, produces rRNA, mRNA, and tRNA, respectively.

While gene expression is actively regulated by transcription factors and the unique spatial distribution of DNA within the nucleus, the active transcription of genes induces supercoiling of the DNA helix. Supercoiling, which involves over- and underwinding of DNA, occurs as a by-product of transcription. The resolution of supercoiling by topoisomerases is well documented in all cells and involves several specialized and conserved enzymes.

This project aims to explore the role of passive regulation of gene expression, focusing on biophysical mechanisms, specifically DNA supercoiling. Recent bacterial studies suggest that DNA can transmit long-range forces and influence other genes. Our goal is to measure the effects of neighboring genes on each other within eukaryotic genomes, thereby unraveling the phenomenon termed "passive regulation". This research has implications for disease development and provides insights for biotechnology applications.

Using an interdisciplinary approach, the project integrates molecular and synthetic biology with mathematical modeling and biophysics at local and global scales. While yeast will serve as the initial model system, the results will be translated to human cells in a later phase of the project.

The collaboration involves the Institute of Biochemistry and Biophysics, PAS in Warsaw, and the Max Planck Institute for Terrestrial Microbiology, MPG in Marburg. The overall goal is to elucidate and predict the molecular mechanisms underlying passive regulation induced by transcription and to provide a comprehensive understanding of their impact.