Technological progress, present in almost every science field, is tightly related to gathering the huge amounts of data. The key example here is molecular biology, which thanks to automated diagnostics can provide a description of given patient with gigabytes of data from high throughput technologies. One of such technologies are micro-array methods for gene expression measurements or spectrometric determination of metabolites concentrations in cells that. Nevertheless, whatever the type of technology is, provided datasets carry important and useful information that can and should be retrieved and used in diagnostics, personalized medicine or drug design procedures.

On the other hand, an ongoing, joint work of molecular biologists, bio-physicists and -chemists results in systematic description of processes that occur in human organisms and reveals possibilities for highly specific inference. A good example of a molecular mechanism description are singaling pathways, that with their formal representation can be deeply studied to better understand the complex system of a human cell.

Nonetheless, the formal representation can vary, but the most important thing that comes up with systematic and progressive understanding of molecular mechanisms is the possibility for more sublime inference from biomedical data that were discussed above.

This project aims to derive an integrative model that will analyse series of high throughput experimental data in two interrelated contexts:

- locally, i.e. the independent analysis of individual signalling pathways, that will allow to select the most significantly (in a statistical sense) perturbed signalling cascades in inter-cellular communication;
- globally, i.e. the analysis of full metabolic network, that would describe all possible sources and of phenotypic perturbations (with respect to homoeostatic profile) in a given experimental dataset.

In our studies the core is the Bayesian inference methodology. We plan to derive a model, that will draw from the Metropolis-Hastings algorithm ideas and provide a way to integrate the transcriptomic measurements with the current knowledge about signalling and metabolic pathways. One of the important steps of the modelling process will be the introduction of expression matrix decomposition into cell- and/or functional-specific sub-profiles.

The model itself will be verified with high quality transcriptomic data provided by MD Anderson Centre from patients with diagnosed with various types of bladder cancer (the preliminary, sequential analysis of transcriptomic profiles was published in the mid-march this year).

We expect that our derived methods and tools, thanks to the use of analytical and computational procedures, will provide the next step to a better understanding of the molecular mechanisms responsible for the formation and development of this type of cancer.

In the context of the local analysis, we hope to identify new biomarkers for molecular characterics of the analyzed types and subtypes of bladder cancer. Here, the term biomarker should be understood as the identification and description of the most significantly deregulated signalling pathways. On the other hand, the global analysis is designed to identify a metabolic profile of human cancers. In particular, we expect to discover the relationship between various signalling cascades, which can lead to designation of the potential source, or independent sources, of the process of carcinogenesis.

It seems that the greatest value of the proposed research, assuming that it will be resolved successfully, will be its cognitive (the metabolic etiology of cancer and its progression mechanisms) and diagnostic (dysregulations in signalling pathways indicating an increased risk of the disease). Moreover, there is a potential use of the outcome of this research in the drug design procedures (tracking the possible sources or critical elements of metabolic disorders, may result in determination of the potential areas for targeted therapy).

It is known that nowadays cancer is slowly gaining a status of a chronic disease and both the earlier diagnosis and appropriately selected therapy can facilitate a potential patient treatment and lead to a complete cure. For us it is very strong motivation why conducting the proposed research is important not only in the scientific context, but also in the broadly understood social context.