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How to save energy in a cell factory

(Stuttgart) – Insilico Biotechnology is taking active part in a joint research project out to quantify the energy budget of bacteria comprehensively for the first time with a view to optimising them for industrial bioproduction. The researchers' aim is to use the cells' own energy reserves to produce ground substances with minimum energy loss. To achieve this, the scientists are working with methods from systems biotechnology and bioinformatics. In the long run, this will help industrial biotechnology become much more competitive so that it can be applied for a considerably wider range of uses.

Corynebacterium glutamicum is one of today's most exploited organisms and has been used for decades to produce amino acids and other ground substances. In a natural environment, it can be found in soil and it is completely harmless for human beings, which is one of the reasons why this bacterium is so popular for industrial bioproduction. In the last few years, scientists have succeeded in analysing the central metabolism of *C. glutamicum* in detail – both quantitatively and mechanistically, thus paving the way for the first detailed complete model of bacterial metabolism.

In the joint project entitled SysEnCor supported by the Federal Ministry of Education and Research (BMBF), Insilico Biotechnology is now working with academics and other industrial partners from all over Germany to gain a full picture of the energy balance of *C. glutamicum*. This is necessary before the energy balance of the bacterium can be manipulated for more efficient production. Evolution has already provided the bacterium with optimum metabolism but this is dependent on the bacterium's natural way of life whereas cells for bioproduction are found in an artificial environment. Under such circumstances, bacteria do not need survival strategies for adverse conditions as these just do not occur in a laboratory. On the contrary, environmental conditions and nutrient solutions in fermenters are ideal for the bacterium and make it easy to function as a cellular factory for ground substances. Researchers expect that certain metabolic processes involving energy demands can soon be avoided. All this is theory at the moment and practice needs to be carried out to obtain the data and model basis necessary for a targeted manipulation of the energy balance of *C. glutamicum*.

The project will profit from Insilico Biotechnology's know-how on modelling and simulating bacterial metabolic systems. Model experts and lab technicians will collaborate closely to find ways of optimising cellular energy metabolism. »This can only be accomplished with detailed network models and simulations«, explains Klaus Mauch from Insilico's Board of Directors.

In a continuous back and forth between computing rooms and laboratories, data on substance flows and corresponding energy rates will be predicted with high-performance computers and compared with measurements carried out in the lab. Vice versa, results from lab tests will be relayed to the computing experts without delay to improve the project's complex computer models. This type of work cycle and shared labour approach has been chosen to reduce the complexity of the task on hand and to improve the quality of model predictions.

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Energy leaks can then be located exactly and closed immediately. The experts are sure that their results will also help fill up the information gaps still existing for the genome-wide network model of *C. glutamicum*. And, of course, the main goal is to construct energy-optimised strains for amino acid production. Because their biosynthesis is especially energy-intensive for cells, it would be advantageous to be able to save energy during the process. »We are optimistic that our energy-optimised production strains will prove to be so profitable that bio-based production processes will be given an additional boost on their way to more widespread application«, explains Klaus Mauch.

Insilico Biotechnology designs and optimises biotechnological processes for the chemical and pharmaceutical industries. Successful in business since 2001, Insilico has internationally renowned expertise and a unique technology platform for connecting cell model libraries with simulation processes. Insilico analyses the latest biotech data and integrates it in genome-wide network models. With its high-performance computing techniques, Insilico develops new improved solutions for manufacturing biochemicals and biopharmaceuticals and achieves considerable cuts in the time needed for the development of bioprocesses. Insilico is a privately-owned company, located in Stuttgart, Germany.

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