

## The fairy-tale of Systems Biology

Once upon a time (2006) there was a village (**yeasttown**) with 6200 inhabitants. It was a lively village that grew steadily with a doubling time of 0.5 century. It lived in apparent harmony with its environment, that supplied the village with everything required (**nutrients**). Although the village produced quite some garbage (**CO<sub>2</sub> ethanol, glycerol**) it did not bother about this. The central administration of the country (**systems biology**) was a mess. As a result it was not known what 40% of the inhabitants did for a job (**function unknown**) Moreover, it was not known who was married to whom (**interactomics**) nor what and how much individual inhabitants produced, in terms of goods, services etc. (**transcriptomics**). The administration simply assumed that all work (**physiomics**) could be expressed in terms of money that could be used for the economy of the village (**Y<sub>ATP</sub>**). The central administration only had appropriate knowledge of ingoing goods and outgoing garbage (**fluxomics**). Although it was a peaceful village, sometimes there was a battle between the workhorses (**pathway enzymes**) and those inhabitants that controlled these workhorses (**regulatory genes**) by direct interaction. (**Theveleinomics**) or via bribery with cyclic AMP. Also punishment by decapitation (**catabolite inactivation**) and other procedures for termination of activity (**apoptosis**) were practiced

This cannot go on, the central administration decided. We must, at least before 2021, know:

- What all inhabitants do (**function analysis**)
- Where they do this (**metabolic compartmentation**)
- Which roads they use for going to work (**metabolic network analysis**)
- How we can avoid those horrible traffic jams that obstruct the village (**Metabolic Control Analysis**)
- How much garbage is piled up by all families (**metabolomics**)
- Reduce overall garbage output to reduce greenhouse effects.

On the basis of such knowledge we can introduce a new system: we will excommunicate nasty inhabitants (**gene deletion**) and promote immigration from elsewhere (**heterologous expression**). We must not only produce garbage but also do something useful (**enzymes, primary and secondary metabolites**) but only in the way we want (**metabolic pathway engineering**)

The central government, headed by Merja Penttilä, that kept a keen eye on the activities of all villages in the country, concluded: let us organize a special assembly (**ISSY**) in which we discuss how we keep central control. And so it was decided! However, some villages started fierce competition with others (**killer yeasts**) and a war became unavoidable (**panel discussion**) between local governments of the provinces of the country (**the researchers**). This is not what I wanted queen Merja cried! I do like all villages, although I regard the capital cities (**filamentous fungi**) as my favourite : they are properly organized in long filaments and are more actively looking for their foodsupply (**solid state fermentation of lignocellulosic feedstock**) Anyway, the queen realized that yeasttown had a difficult time ahead: systems biology must bear fruits in all villages (**comparative yeast genomics**) to boost economy, she said.

The founder of the village (**Pasteur**) would have suggested otherwise: an overheated economy (**pasteurisation**) will automatically solve the problem.

Hans van Dijken, June 2006