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Systems biology of *Clostridium acetobutylicum*

A renewed interest in the development of biofuels has emerged in recent years, principally due to dwindling crude oil reserves and concerns over the environmental impact of fossil fuels. Bacterial fermentation is a possible solution to questions over the source of future biofuels.

Clostridium acetobutylicum is an anaerobic, non-pathogenic, Gram-positive bacterium capable of producing the solvents acetone, butanol and ethanol. Though each of these can be used as a biofuel, the properties of butanol make it the most promising energy source of the three. For butanol production by *C. acetobutylicum* to be exploited on an industrial scale, however, genetically-engineered strains must be designed which can produce butanol at much higher levels than those achieved by wild-type strains.

The SysMO and SysMO2 programmes COSMIC (*Clostridium acetobutylicum* Systems Microbiology) were established to apply a systems approach to understanding the complex mechanisms behind solvent production by *C. acetobutylicum* and to establish this bacterium as the paradigm for clostridial systems biology. An iterative approach is adopted whereby experimental work is designed to complement mathematical models of solventogenesis which in turn generate experimentally-testable hypotheses. Notably, the gene regulation networks governing solvent production and the connected process of sporulation are modelled and parametrised according to experimental data. Systematic *in silico* alteration of gene expression for each component of the networks enables identification of those genes most crucial for butanol production and will elucidate the optimal genetic engineering strategies for maximising butanol yield.