

# Development of microbial strains useful in co-culture systems and cell-free systems metabolic engineering.

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## Abstract

**For the study of organic or artificial interactions between cell populations, co-culture techniques have numerous biological applications. As multi-species cell consortia and other natural or synthetic ecology systems are widely acknowledged to hold enormous potential for fundamental research as well as novel industrial, medical, and environmental applications with numerous proof-of-principle studies in recent years, such techniques are of utmost importance in synthetic biology. How can co-cultures reach their full potential? The extracellular environment, which is governed by the experimental set-up, has a significant impact on cell-cell interactions in co-cultures and must be carefully taken into account. Here, the problems and potential of co-culture experiments are reviewed along with an overview of current experimental and theoretical co-culture setups in synthetic biology and related domains.**

**Keywords:** Co-culture techniques, Metabolic engineering, Synthetic biology, Co-culture systems.

## Introduction

Co-culture systems are essential to all investigations of cell-cell interactions and have been used for a long time to examine interactions between cell populations. Synthetic biologists have recently developed a special interest in such systems for researching and creating complex multicellular synthetic systems. A co-culture, at its most basic level, is a cell cultivation setup in which two or more distinct cell populations are cultivated in some degree of interaction with one another. Studying natural interactions between populations, increasing the success of certain populations during cultivation, or creating artificial interactions between populations are some of the reasons for employing such a setup. Researching infections, other natural interactions, and developing experimental models and biomimetic settings of natural systems, such as artificial tissues, are a few examples of studying natural interactions between populations. Because they allow for high-throughput testing and detailed observation of drug effects on cell-cell interactions, co-cultures are much more relevant for drug research than animal models because they give a tissue model that is more comparable to that of the human body *in vivo*. Certain populations require more cultivation success [1].

Some cells are difficult to monoculture *in vitro* or, at the very least; do not exhibit the necessary physiological behaviours *in vivo*. However, the inclusion of a different cell population may increase the effectiveness of culturing or the behaviour of the cells. It is increasingly usual to create synthetic relationships between populations. The development of complex systems

with industrial applications has received significant attention in synthetic biology and other biological sciences, despite the fact that mixed cultures have long been employed for such purposes. Every one of these calls for co-culture systems. Synthetic industrial consortiums, synthetic ecologies, and other complicated relationships are a few examples. Due to their higher productivity and other benefits over monocultures, synthetic ecologies are commonly believed to offer considerable potential for basic research as well as industrial, medicinal, and environmental applications [2,3].

Co-culture systems will be crucial to the development of synthetic biology. Even in hard to culture organisms, studying natural cell-cell interactions will reveal fresh avenues for re-engineering. Delivering societal benefit through industrial, medicinal, and environmental applications is synthetic biology's ultimate goal. Because of this, a lot of synthetic biology systems are created with future industrial, medical, or environmental co-culture applications in mind, like cell-cell communication, toggle switches for population control, and bacterial cells engineered for killing pathogens, targeting tumours, or delivering therapeutics.

These systems must pass stringent safety and function tests before being deployed in industrial, environmental, or medicinal settings, especially with regard to cell-cell interactions and subsequent process optimization. Co-culture systems are extremely complex model systems for tissues or ecologies, with interactions taking place on a variety of temporal and length scales. For these studies, experimental

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systems are needed that enable high-throughput monitoring of complicated cell consortia, massive data collecting, and control and change of experimental parameters.

The connection between genetic engineering and the use of complex systems is represented by co-culture technology. Co-cultures can be found at many different levels of the biological hierarchy, such as organs and ecosystems, hence investing in technological development can benefit research in a variety of fields. Co-culture technology might make it possible to provide answers to a wide range of biological queries. Industrial microbes are expected to exhibit robustness, stability of metabolism in changing environments, tolerance to toxic metabolic waste or compounds in feedstock, and resistance to environmental stresses. These qualities cannot easily be engineered in a single microbe, but they can be achieved using consortia if appropriate enabling technology is available [4-6].

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