

Systems Biology: The Science of Interconnections

Engineering microbial consortia for plastic degradation

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Life in nature depends on interconnections to survive. Ecosystems, organisms, cells, and molecules all function as intricate networks that react dynamically to one another. Systems biology is an interdisciplinary field that combines biology, engineering, and computational modelling. It seeks to understand these connections and responses by looking at systems in a holistic manner, rather than by breaking them down into individual parts to be studied separately. Recent research by Dharmasiddhi et al. from the University of Waterloo demonstrates how systems biological approaches can be used to tackle one of humanity's biggest challenges – plastic pollution.

Plastics like polyethylene terephthalate (PET) and nylon are extremely durable. While this makes them useful for daily use products, it makes them difficult to degrade when disposed as waste in the environment. While there has been progress towards identifying microbes that can degrade these plastics, natural degradation remains slow and inefficient, especially when a combination of different plastics are present. There is also a need to design strategies to utilise the monomers formed after plastic is degraded. Systems and synthetic biology offer an interesting avenue to tackle this problem.

In their study, Dharmasiddhi et al. engineer a synthetic microbial consortium to efficiently degrade a mixture of PET and nylon monomers. Rather than relying on a single bacterial chassis, they design a cross-feeding community of two bacteria in which each species performs a specialised task that contributes to the overall goal. This division of labour is a unique aspect of systems biology, which advocates the use of modular but interconnected parts to form a completely functional whole.

The team chose the strains *Escherichia coli* Nissle 1917 and *Pseudomonas putida*

KT2440 for their engineered consortium. The *E. coli* strain was evolved to consume ethylene glycol (EG), one of the monomers of PET, as its sole carbon source, while the *P. putida* strain was evolved to consume hexamethylenediamine (HD), the nylon monomer, as its sole nitrogen source. The idea was that *E. coli* will perform carbon metabolism using the supplied EG and provide essential carbon compounds to *P. putida*, which in turn will perform nitrogen metabolism using HD and provide *E. coli* with nitrogen compounds.

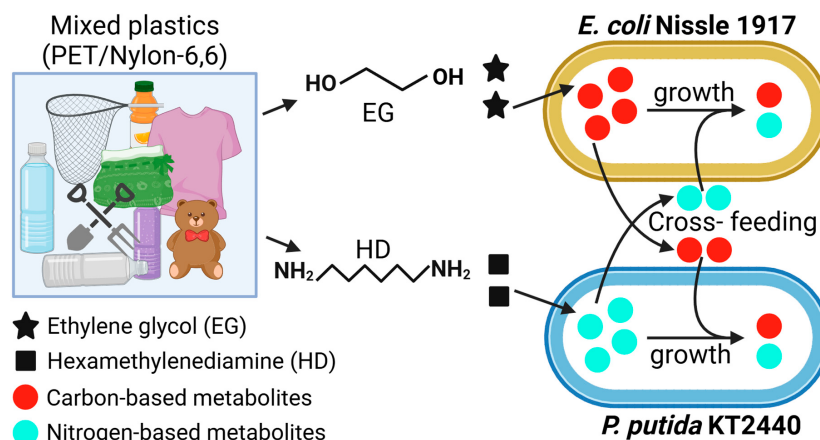


Figure 1: The proposed design for the microbial consortium

Initially, the wildtype strains were subjected to iterative rounds of adaptive evolution. *E. coli* populations were gradually exposed to increasing EG concentrations, while *P. putida* populations grew in media with increasing HD levels. This produced two evolved strains, EcEG1 and PpHD1. Following this, these evolved strains were co-cultured in a chemostat supplied with EG and HD to observe whether they demonstrate the expected mutually beneficial behaviour. After 25 days, this produced two further evolved strains, EcEG2 and PpHD2.

Unexpectedly, the consortium did not display the designed cross-feeding pattern. Instead, a new metabolic interaction emerged. PpHD2, while still efficiently utilising HD for its nitrogen needs, began to oxidise EG into glycolate, a compound that accumulates and becomes toxic if not further metabolised. On the other hand, EcEG2 lost its ability to use EG as a carbon source but evolved to use glycolate instead. As a result, PpHD2 would consume EG, produce toxic glycolate, export

it out of the cell, and then EcEG2 would utilise it to drive carbon metabolism and biomass formation. This emergent cross-feeding led to significantly higher overall biomass yields and greater community stability than either monoculture was able to achieve.

The researchers elucidated the mechanisms of this cross-feeding computationally by performing flux balance analysis (FBA) on the genome-scale metabolic models (GSMs) of the two species. This revealed that under high EG uptake and limited HD assimilation by *P. putida*, the bacterium would always export glycolate out of the cell, which would be taken up by *E. coli*. This was validated experimentally by high-performance liquid chromatography (HPLC) to quantify glycolate in the co-culture media over time. In co-culture, the glycolate levels remained relatively constant. However, in the monoculture of *P. putida*, glycolate accumulated over time. This conclusively proved that the two species evolved a novel cross-feeding mechanism involving glycolate. Thus, the team successfully designed a synthetic microbial consortium that could degrade the monomers of PET and nylon.

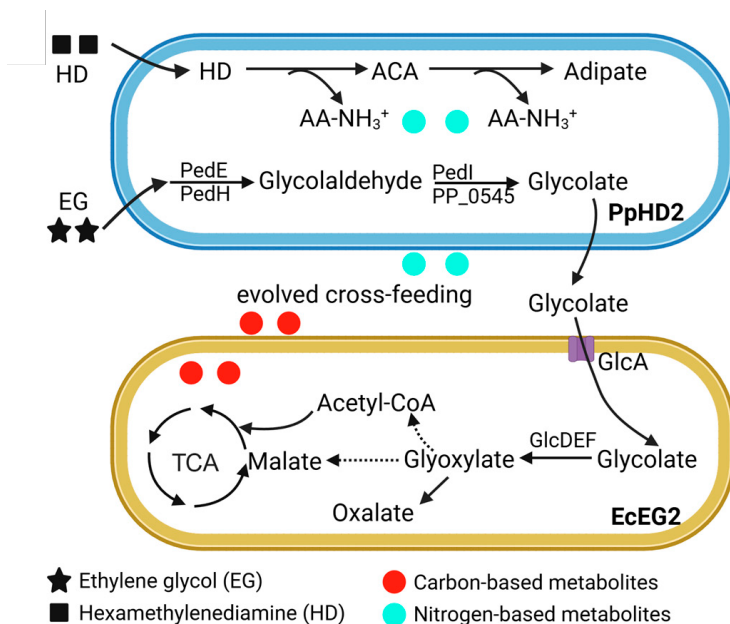


Figure 2: The emergent cross-feeding after adaptive evolution

This work highlights the importance of modular design in systems biology. If one

strain underperforms, its partner can compensate for it, imparting robustness to the system. Modular consortia also would allow for adding a new strain to tackle another type of plastic as this requires only integration with the existing metabolic network, rather than redesigning the entire system from scratch.

In the future, Dharmasiddhi et al. hope to integrate their microbial consortium with physical and chemical pretreatments for plastic depolymerisation. They also aim to further engineer their consortium to valorize the plastic monomers into useful products of human interest, and not just utilise them for microbial growth.

In conclusion, this study is an interesting example of how systems thinking and computational systems biology can be beneficial in designing novel behaviours. In the battle against plastic pollution, synthetic microbial consortia designed by systems biology may be our only complete solution.

Original paper

Dharmasiddhi, I. P. W., et al. (2025). Engineering a Cross-Feeding synthetic bacterial consortium for degrading mixed PET and nylon monomers. *Processes*, 13(2), 375. <https://doi.org/10.3390/pr13020375>
