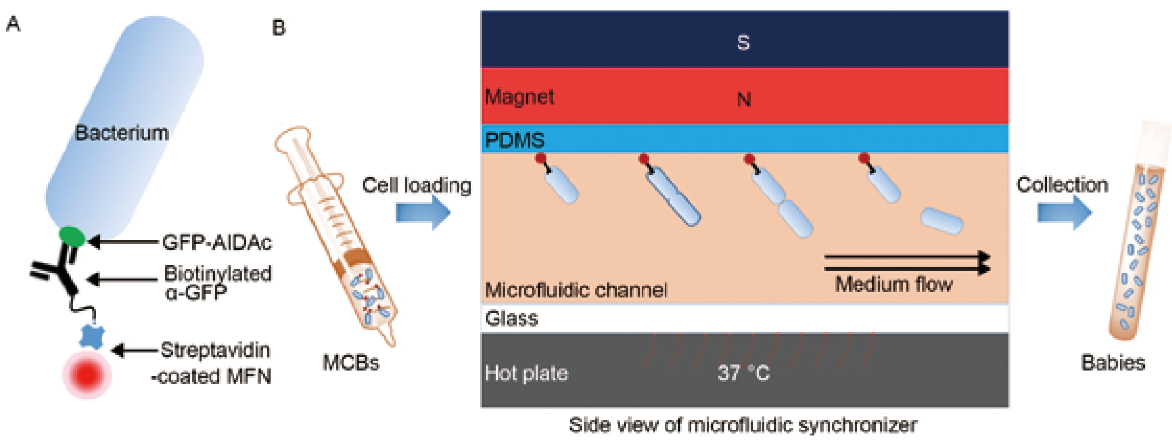
Harvest Synchronous Baby Cells from Microfluidic Channels

The growth and division of bacteria are precisely regulated by a vital process known as the cell cycle. Just like the lifetime of a human being, a bacterial cell's lifetime is composed of different events that occur at different stages of the cell cycle, with the size and physiology of the cell changing as the cycle proceeds. In normal bacterial culture, cells at different stages of the cell cycle are mixed together, so it is difficult to study separate events within the cycle. To gain insight into how the cell cycle regulates events in an orderly way, different methods have been developed to obtain synchronous cells.

Recently, a team led by Professor LIU Chenli at the CAS Shenzhen Institutes of Advanced Technology (SIAT) created a novel microfluidic synchronizer using a synthetic magnetic bacterium to obtain populations of minimally-disturbed, normal, synchronized cells.

In their work, synthetic biology was applied to establish an artificial magnetic "stalk" at one pole of *Escherichia coli* (*E. coli* for short). The inducible stalk was constructed from a chimeric fusion protein, eGFP-AIDAc that was heterologously expressed in the E. coli strain. This protein was subsequently translocated to the cell poles, where it specifically binds to streptavidin-coated magnetic nanoparticles via biotinylated anti-eGFP antibodies. After one cell division, at most one cell pole retained a magnetic "stalk".

One end of these synthetic magnetic bacteria can be attached to a microfluidic channel wall by using a permanent magnet. As these "mother" cells grow and



Engineered *E. coli* cells are cross-linked to magnetic fluorescent nanoparticles (MFN) to form the magnetic capped bacteria (MCBs). After being flowed into the microfluidic channel, these magnetically capped cells are immobilized to the upper chamber wall by a magnet placed above the channels. Under proper culture conditions, these fixed "mother" cells start to grow and give birth to "baby" cells, which are free of magnetic caps and hence are flushed out, yielding a synchronous population of baby cells. (Credit: Dr. LIU Chenli, SIAT) divide in the flowing culture medium, "daughter" cells are born without the inducible, assembled "stalk". They are hence not affected by the magnet and are eluted and collected as shown in the figure.

The construction of such a magnetic bacterium is not limited to *E. coli* strains. The inducible and modularized magnetic "stalk" can be easily assembled in a wide range of bacterial strains.

The microfluidic chip used in this study provides fine control of the micro-environment of cultured cells. Important features such as temperature, growth medium, and added chemical reagents can be adjusted easily. This novel microfluidic synchronizer significantly reduces the consumption of culture medium and increases the concentration of synchronous cells.

Synthetic biology is an interdisciplinary subject applying different disciplines, such as biotechnology, genetic engineering, biophysics, and computer science, to build artificial, modularized biological systems for useful purposes. In the research described here, a novel "baby machine" demonstrated that synthetic biology has great potential for applications in studies of bacterial physiology.

The study entitled "Microfluidic Synchronizer Using a Synthetic Nanoparticle-Capped Bacterium" was published in *ACS Synthetic Biology*.

(SIAT)

Reference:

Z. Chang *et al*., Microfluidic Synchronizer Using a Synthetic Nanoparticle-Capped Bacterium. *ACS synthetic biology* 8, 962 (Published: April 9, 2019). doi: 10.1021/acssynbio.9b00058.