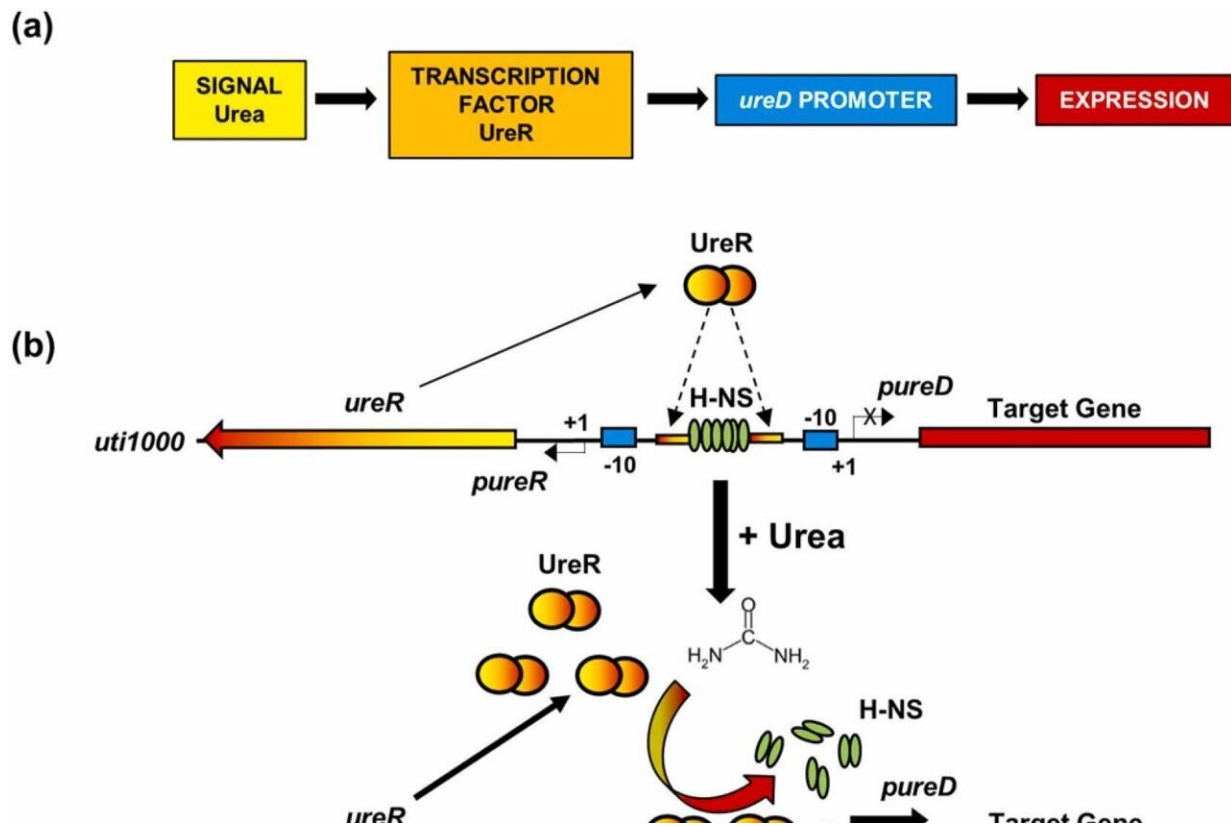


Urine could play key part in future biotech systems

October 27 2022



Experiments with the *uti1000* promoter fragment. (a) Control of gene expression by urea and the UreR transcription activator protein. In the presence of urea, UreR activates transcription from the *ureD* promoter to drive transcription of downstream genes. (b) A schematic representation of the *uti1000* promoter and its regulation by UreR. In the absence of urea, a low basal level of UreR is present allowing the system to be poised and triggered rapidly in response to urea. UreR binds weakly to the two UreR-binding sites within the *ureR-ureD* regulatory region and competes directly with the nucleoid associated protein H-

NS. In the presence of urea, UreR undergoes a conformational change and occupies both of its binding sites within the ureR-ureD intergenic region, outcompeting H-NS to activate transcription from the ureD and ureR promoters. The ureR and ureD -10 promoter elements are shown as rectangles, and transcript start sites (+1) are indicated by bent arrows. (c) The panel shows measured β -galactosidase activities in wild-type JCB387 cells, carrying the *uti1000* promoter fragment cloned into pRW50. Cells were grown in LB medium and supplemented with various concentrations of urea, as indicated. β -Galactosidase activities are expressed as nmol ONPG hydrolysed $\text{min}^{-1} \text{mg}^{-1}$ dry cell mass and represent the average of three independent experiments. Error bars show standard deviation. Values above bars indicate the fold induction at each urea concentration. Credit: *New Biotechnology* (2022). DOI: 10.1016/j.nbt.2022.10.003

A common chemical found in urine can be used to kick-start large-scale production of proteins such as hormones and antibodies used by biotech companies.

Researchers at the University of Birmingham and Aston University, in the U.K., have developed a system that uses [urea](#) to [trigger](#) the production of these proteins in the large quantities needed by the biotech industry.

Typically, in this process, small pieces of DNA are introduced into bacteria such as *E.coli* to persuade them to overproduce certain proteins. It is a well-understood technology that was first developed in the 1970s. Overproduction, however, is typically triggered by "inducer" molecules, which can be costly, and often need careful handling, such as refrigeration.

By using urea instead, the researchers have developed a method that is cheaper, more straightforward, and uses easily accessible materials.

In a new study, published in *New Biotechnology*, the team investigated both purified urea and the urea contained in common garden fertilizers. They showed that similar results could be achieved using either source.

Co-author Professor Steve Busby, in the University of Birmingham's School of Biosciences, said, "Our aim is to make this technology available to biotech companies who want to explore how to optimize their processes and also keep their costs down."

The team also showed it was possible to fine-tune the amounts of [protein](#) triggered by the urea molecule, by varying the concentrations used. This is important to avoid harming or exhausting the host bacteria. They found it was possible to optimize production to quantities similar to those produced using medium-strength promoters currently used as standard by the biotech industry.

The study builds on earlier work in which the team successfully demonstrated that nitrate, a cheap, stable and abundant inorganic ion, could also be used as a trigger. Nitrate is commonly found in many commercial fertilizers and even in some garden fertilizers, meaning that it is always readily available, even in areas where other types of promoter chemicals might be inaccessible.

Co-author Dr. Joanne Hothersall, also in the School of Biosciences, added, "Both urea and [nitrate](#) will be much more readily available, and easy to use, in locations where infrastructure limits access, for example where maintaining a cold supply chain is challenging. We hope these new approaches will open up new avenues of research for biotech industries."

More information: Joanne Hothersall et al, New vectors for urea-inducible recombinant protein production, *New Biotechnology* (2022). [DOI: 10.1016/j.nbt.2022.10.003](https://doi.org/10.1016/j.nbt.2022.10.003)

Provided by University of Birmingham

Citation: Urine could play key part in future biotech systems (2022, October 27) retrieved 1 April 2023 from <https://phys.org/news/2022-10-urine-key-future-biotech.html>

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