

Journal club



A VITAL ASSAY

Eduard Buchner's description in 1897 of the first cell-free assay was as important for biochemists as Watson and Cricks' description of the DNA double helix. It was perhaps, in some ways, more important as it laid to rest vitalism, the idea that living cells (and organisms) required some vital force that cannot be explained in chemical or physical terms. This paper laid the foundation for metabolic biochemistry and for the ever-more-complex *in vitro* assays that have defined the minimal components needed for diverse cell functions ranging from protein synthesis to membrane trafficking and that are still used today.

This paper is also a classic example of serendipity. Eduard's brother, Hans, was an immunologist who ground up bacteria to prepare toxins and antitoxins. Yeast was chosen as a model system, given its abundant availability and low cost.



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Hans Buchner's assistant, Martin Hahn, ground up the yeast with fine sand, subjected the paste to a pressure of 500 atmospheres and collected the extract. High pressure led to an undiluted extract that better mimicked the cytoplasm. Also important was the decision to use sand, not glass, which did not change the pH (in the days before buffers). Even the chosen yeast was fortuitous. Louis Pasteur had been trying to prepare similar extracts but he used Paris yeast, which had thicker cell walls than Munich yeast and so resisted breakage.

Buchner's power of observation was also vital. Extracts were preserved using concentrated sugar (a common preservative for fruit), and he noticed a stream of bubbles that he correctly interpreted as CO₂ produced during fermentation. He did the right controls: only sugars that could be fermented by yeast worked; and antiseptics that killed yeast cells did not affect fermentation by the extract. Hence, the observed fermentation was cell-free.

This paper was not without initial controversy, including a prior claim to discovery by Marie von Manassein. It was dismissed by Buchner in a tongue-in-cheek manner: "According to the author air-dried yeast, heated up to 308 °C for 3 hours and 20 minutes, whereby the cells were charred beyond recognition, and likewise yeast boiled for 45 minutes, still had the ability to ferment. Therefore, methodological errors must have occurred." Buchner's achievement soon received wide acclaim with his receipt of the 1907 Nobel Prize in Chemistry, but his talents were prematurely lost when he died at the front in the first World War.

Graham Warren
Max F. Perutz Laboratories (MFPL),
Vienna, Austria.
e-mail: graham.warren@mfpl.ac.at

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ORIGINAL RESEARCH PAPER Buchner, E. Alkoholische Gährung ohne Hefezellen (Alcoholic fermentation without yeast cells). *Ber. Dt. Chem. Ges.* **30**, 117–124 (1897)

FURTHER READING Cornish-Bowden, A. (ed.) *New beer in an old bottle: Eduard Buchner and the growth of biochemical knowledge*. (Universitat de Valencia, 1997) | Kohler, R. The background to Eduard Buchner's discovery of cell-free fermentation. *J. Hist. Biol.* **4**, 35–61 (1971)