

Introduction

Shaken bioreactors are outstanding because of their easy handling and their low price. Due to these advantages in comparison to stirred bioreactors, they are irreplaceable in applications that require a high number of experiments, e.g. screening for efficient strains or optimisation of media.

Although shaken bioreactors are frequently used methods that enable online measurement are very limited. This problem is solved by RAMOS (Fig. 1), which determines the oxygen transfer rate (OTR), the carbon dioxide transfer rate (CTR) and the respiratory quotient (RQ) of a biological system online. The respiration rates (OTR, CTR) are the most suitable measurable variables to quantify the physiological state of a culture of aerobic microorganisms.

Principle of Measurement

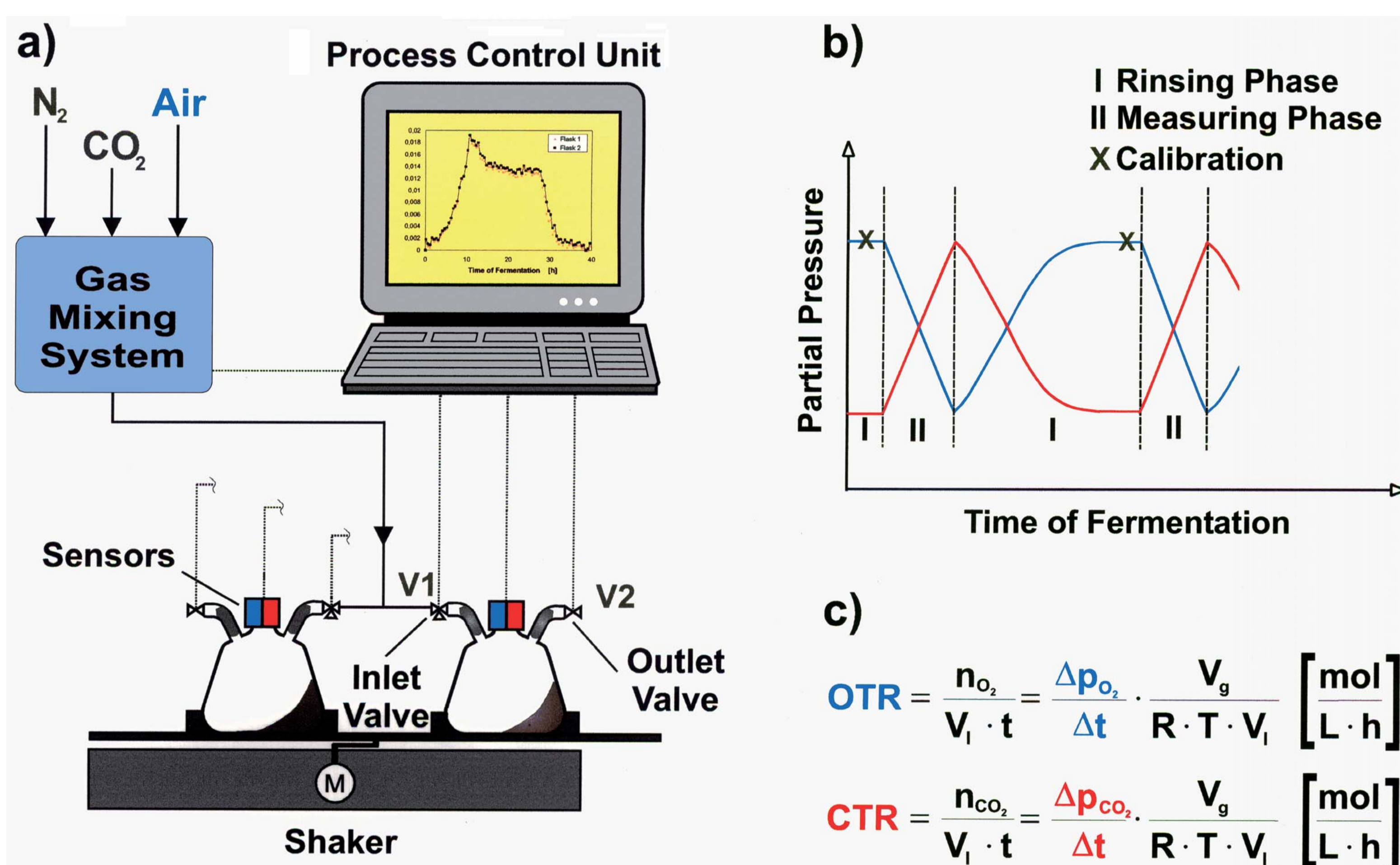


Fig. 1: a) Principle of RAMOS, b) measuring cycle, c) equations of OTR and CTR

During fermentation a measuring cycle is continually repeated. This measuring cycle is separated into a measuring and a rinsing phase (Fig. 1b). During the rinsing phase gas flows through the measuring flasks. At the beginning of the measuring phase the inlet and outlet valves (V1, V2) of the measuring flasks are closed (Fig. 1a). The sustained respiration activities of the microorganisms lead to a change of the partial pressure of oxygen and carbon dioxide in the headspace of the particular measuring flasks. At the end of the measuring phase a computer calculates from the changes of the partial pressures the oxygen (OTR) and the carbon dioxide transfer rate (CTR) in the particular measuring flasks.

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Applications of RAMOS

- Determination of suitable conditions for conventional mass screening (operating conditions, duration of the experiment, ...)
- Recognition and prevention of limitations
- Online tracking of microbial cultures in shake flasks. Many details of the culture behaviour can be clarified at this very early state of bioprocess development (Fig. 2)
- Easy determination of characteristic values for scale up (OTR, CTR, RQ, $k_L a$, μ , ...)
- Calculation of mass balances of a fermentation process based on total oxygen consumption

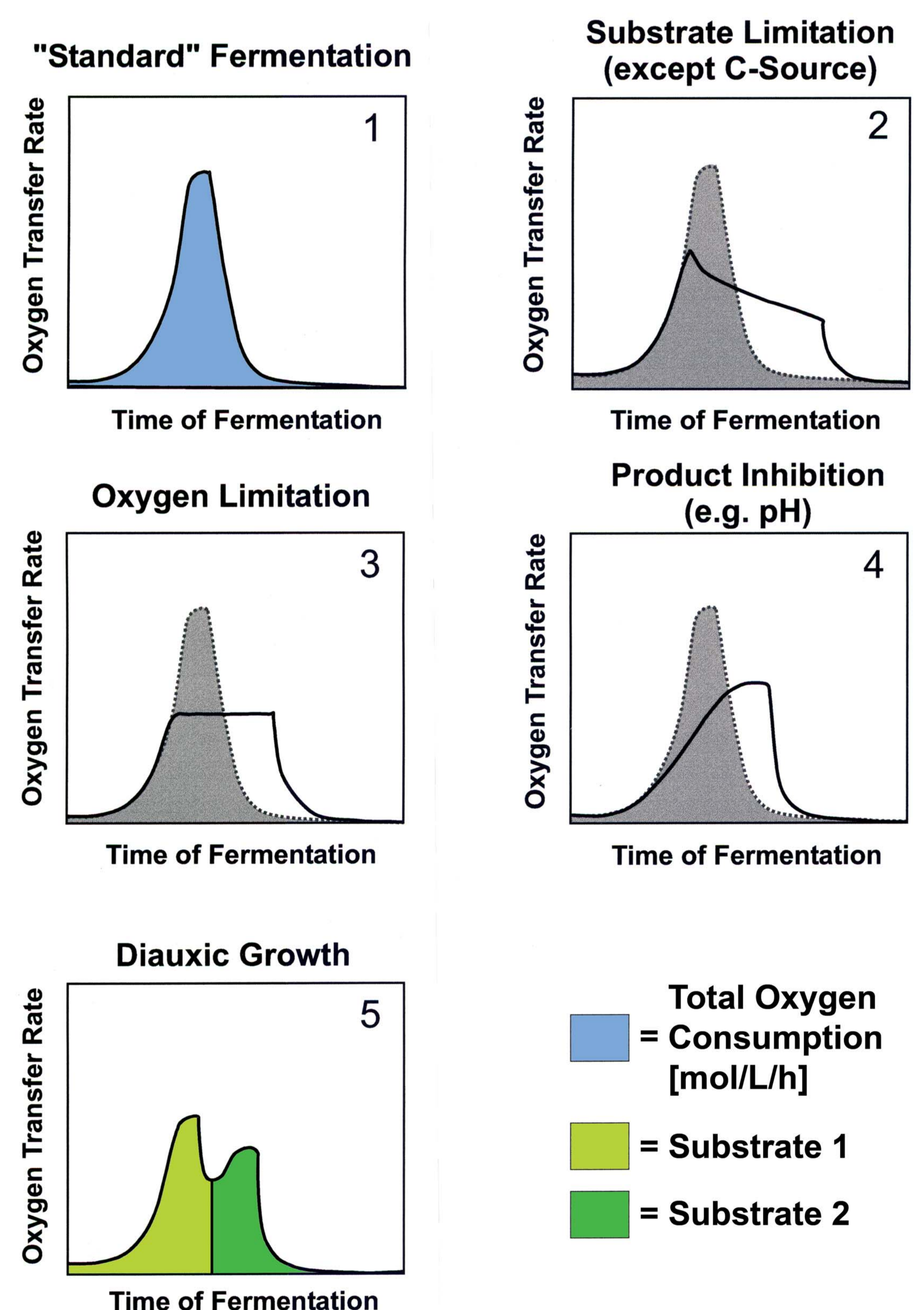


Fig. 2: OTR of typical biological phenomena