

Online Monitoring of the Respiration Activity in 96-Deep-Well Microtiter Plate CHO Cultures Streamlines Kill Curve Experiments

Introduction



Kuhner TOM



Kuhner
microTOM^[3]

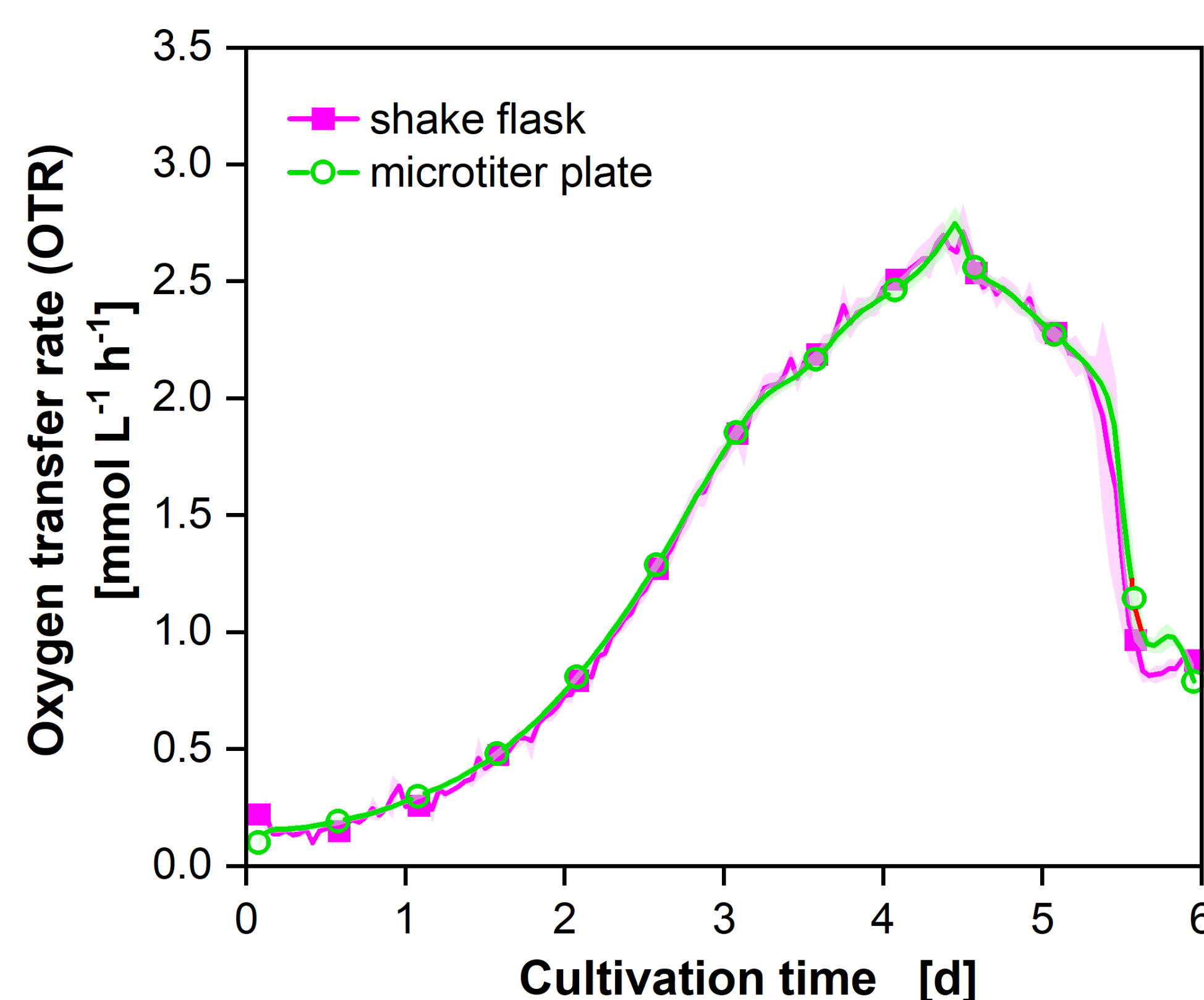
- Online monitoring of the respiration activity simplifies CHO culture characterization in shake flasks^[1]
- High-throughput cultivation is increasingly important for process development with mammalian cells^[2]
- ➔ **Scale-down of oxygen transfer rate monitoring from shake flasks to 96-well microtiter plates**
- Kill curve experiments are labor-intensive and require high-throughput
- ➔ **Streamline kill curve experiments by using 96-well microtiter plate online monitoring**

**Scale-down of CHO
cultivations to 96-well
microtiter plates enables high-
throughput online monitoring
of the oxygen transfer rate**



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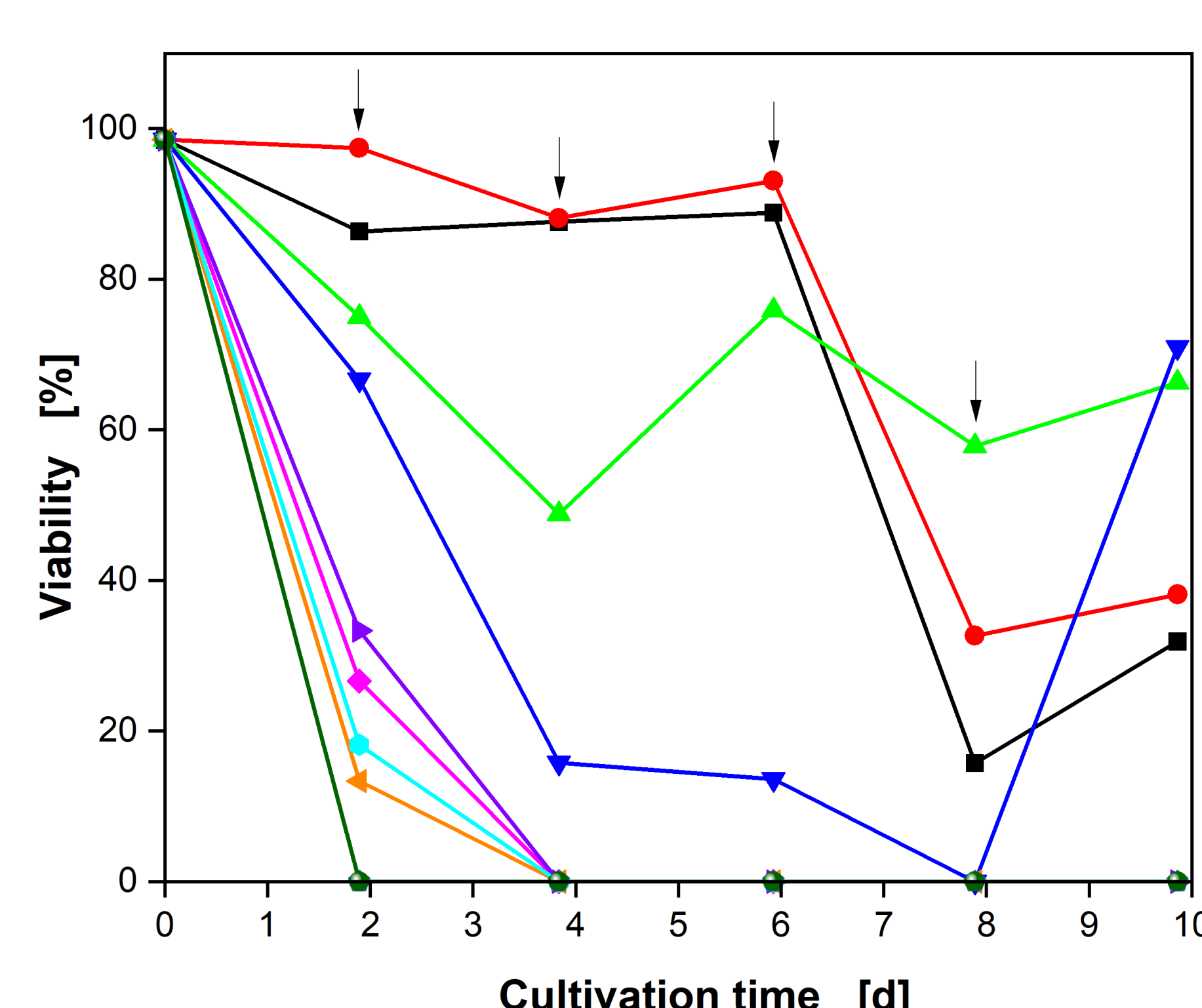
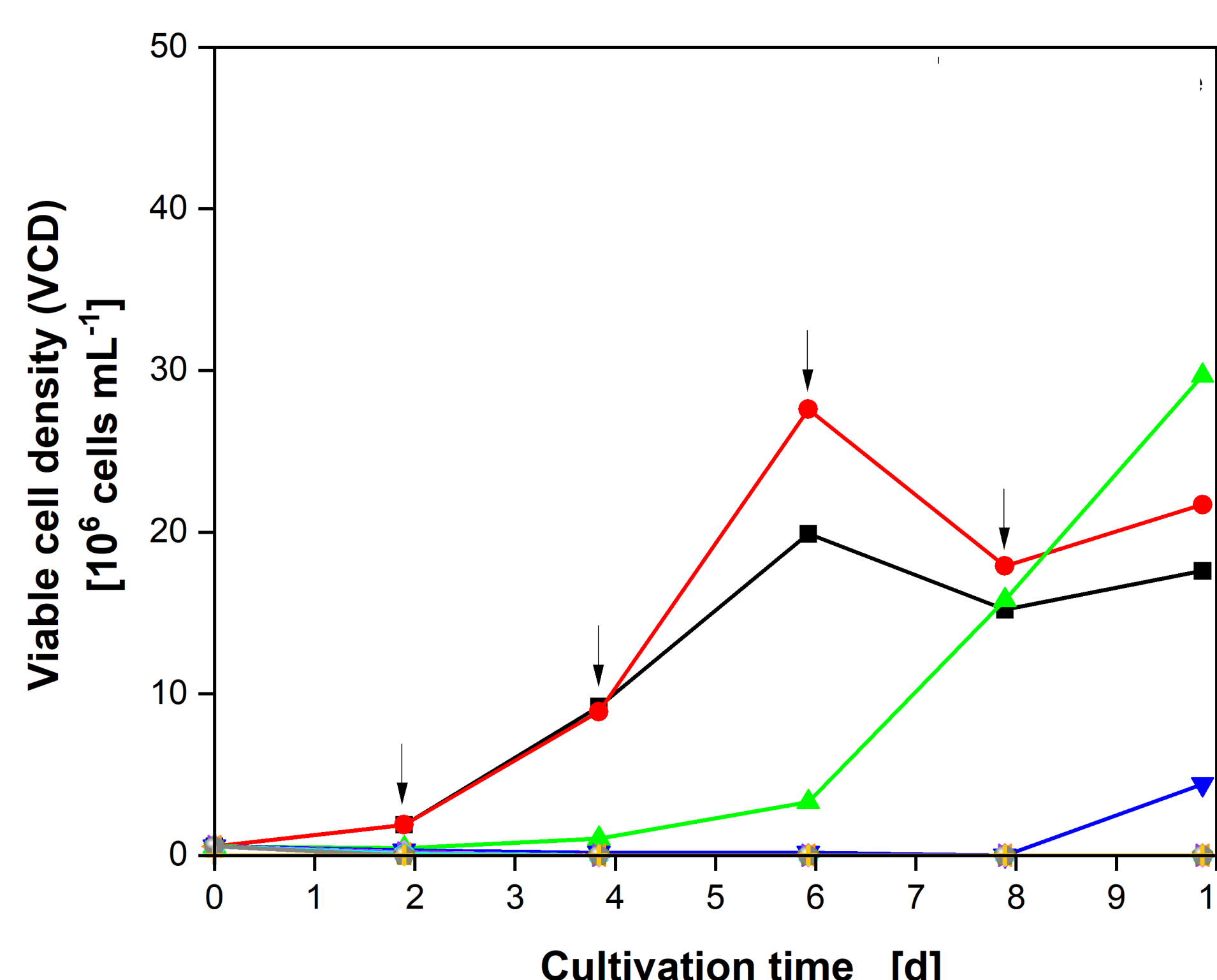
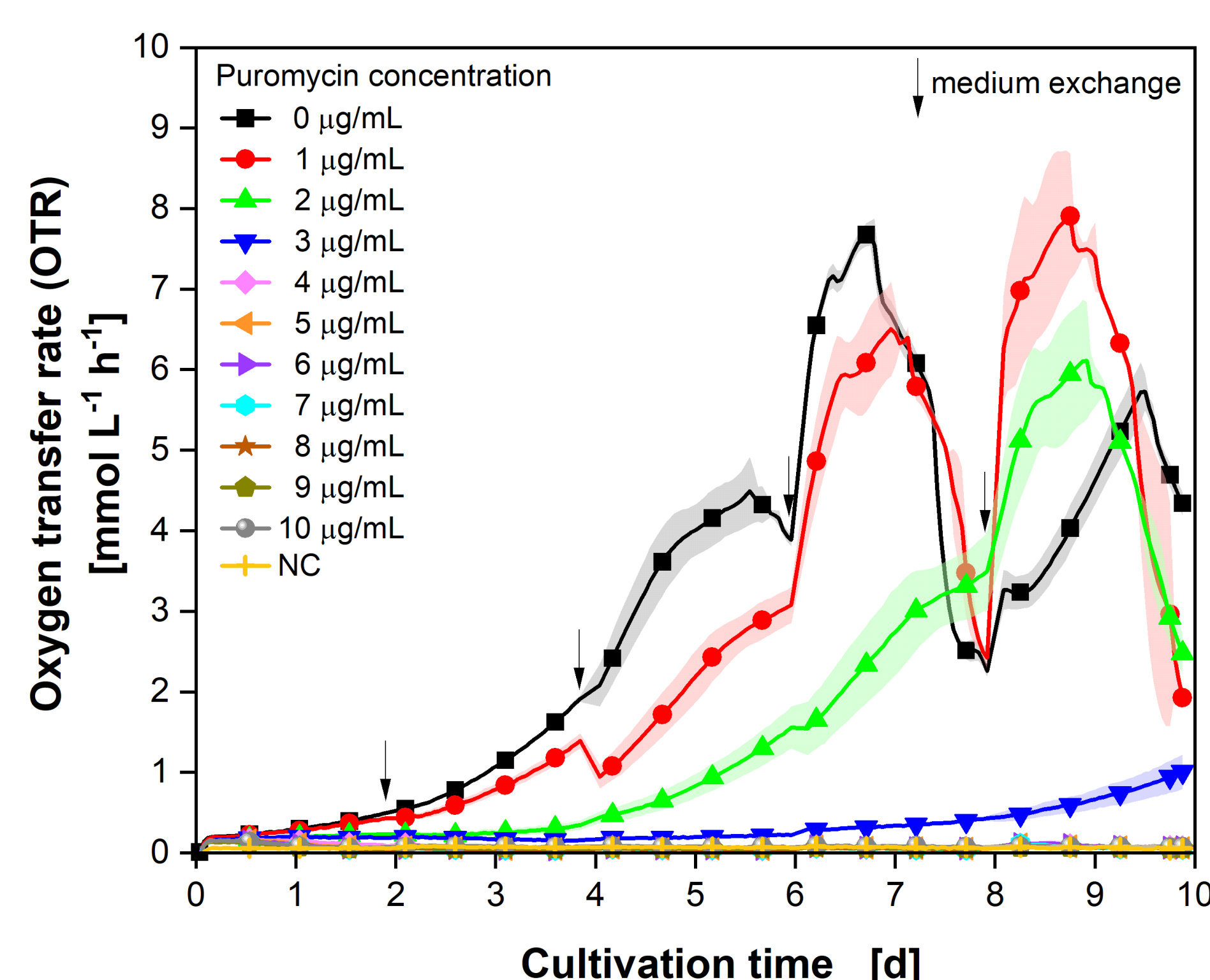
Scale-down of CHO cell cultivations to 96-well microtiter plates



Cultivation of CHO-K1 cells in 100 mL shake flasks (N=3) and 96-deep-well microtiter plates (N=53)
Oxygen transfer rate monitoring in the Kuhner TOM (shake flasks) and the Kuhner microTOM (microtiter plates) devices
TCX6D + 8 mM Gln, 36.5 °C, 5 % CO₂, humidified; TOM: 140 rpm, 50 mm; microTOM: 850 rpm, 3 mm
Standard deviations marked as shaded areas

- Scale-down parameter: maximum oxygen transfer capacity (OTR_{max})^[4]
- High reproducibility indicated by standard deviations
- compared to shake flasks:
20-fold reduced media consumption
6-fold increase of reaction vessels

Streamlined kill curve experiments due to microTOM device



Kill curve experiments of CHO-K1 cells with the antibiotic puromycin
Oxygen transfer rate, viable cell density and viability; medium exchange by centrifugation and replacement of medium every 2nd day
TCX6D + 8 mM Gln, 36.5 °C, 5 % CO₂, humidified; 850 rpm, 3 mm, 96-deep-well microtiter plate

- OTR curves clearly indicate the puromycin concentration at which all cells are killed
- Identical results of OTR monitoring and VCD / viability determination
- 95 % medium reduction compared to conventional methods in shake flasks

**Further applications in media
and clone screening, cytotoxicity
tests and scale-up approaches**