WAVE BIOREACTOR CHARACTERIZATION – RESIDENCE TIME DISTRIBUTION

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Introduction

Mammalian cell culture systems are the current focus of biopharmaceutical production. This has led to the development of several technologies and bioreactors to achieve large-scale production.

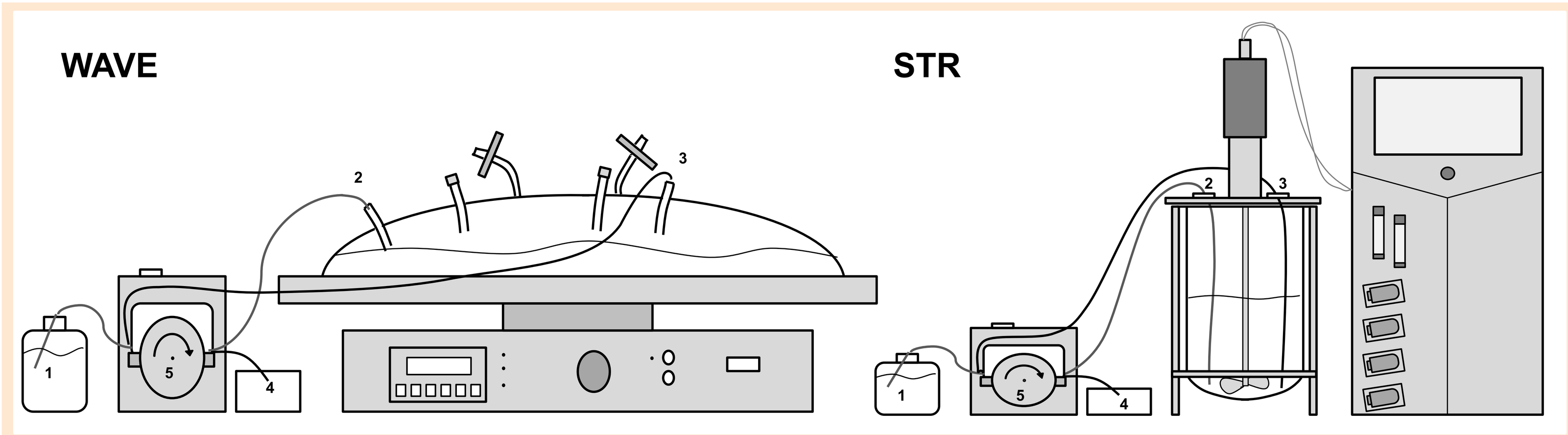
Among the bioreactors available, the **Stirred Tank Reactor** (STR) is the most commonly used. However, disposable reactors have been attracting increased attention lately, with particular relevance to the **Wave bioreactor**. This recently developed bioreactor offers several advantages such as ease of operation, protection against cross-contamination (due to the absence of cleaning or sterilization requirements), as well as good mixing and oxygen transfer without causing shear damage to the cells. This last advantage relates to the undulation movement induced to the culture, a characteristic that is unique to the Wave bioreactor. However, due to its recentness, this reactor still needs a better characterization of its operation.

Thus, in this work, an evaluation of the **residence time distribution** (RTD) in a Wave reactor was performed in order to characterize its mixing and flow, and to compare its behavior with ideal models and with a commercial STR available for mammalian cell culture.

Methods

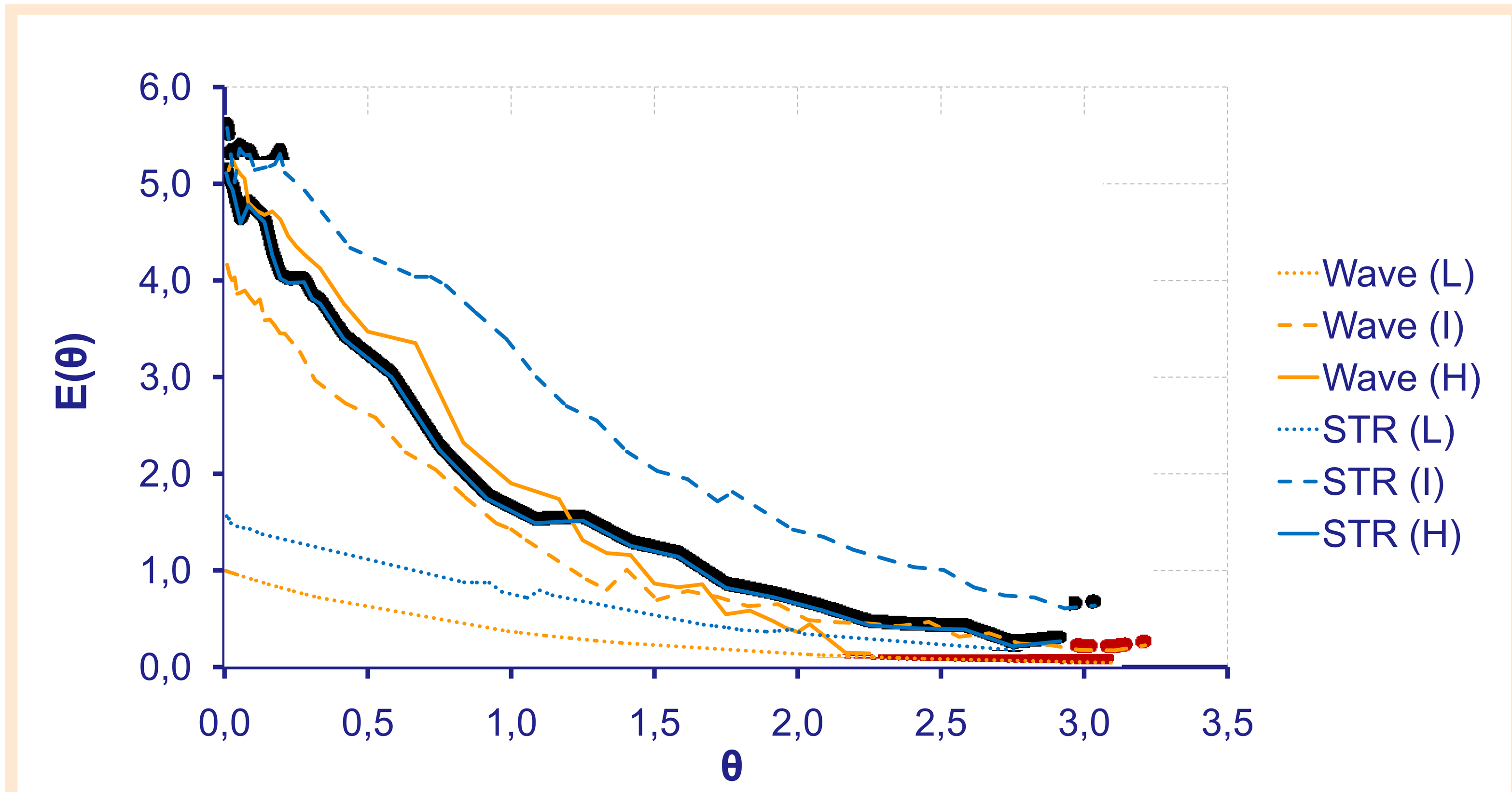
The RTD of the Wave and STR bioreactors was determined as follows:

1. A known concentration (2.67 mg/L) of the tracer methylene blue was added at the reactor inlet, using a pulse input methodology.
2. Three distinct flow rates within the range commonly used in mammalian cell culture were tested: a low flow **(L)** of 3.3x10^{-5} m^3/h, an intermediate flow **(I)** of 7.9x10^{-5} m^3/h, and a high flow **(H)** of 1.25x10^{-4} m^3/h.



3. Throughout the experiment, samples were taken at the outlet of both reactors, and the samples' absorbance was read at 660 nm.

Results



Behavior of Wave reactor at low flow (L) approximates that of the ideal and experimental continuous STR. For the higher flow rates (I and H), behavior of Wave departs from any ideal model.

Assay		Q (m3/h)	τ (h)	tr (h)	R^2	Ideal Model
Wave	L: 3.30x10^{-5}		22.73	25.94	0.28	Continuous stirred tank reactor
	I: 7.90x10^{-5}		9.49	11.84	0.16	Plug-flow reactor
	H: 1.25x10^{-4}		6.00	5.08	-0.13	Plug-flow reactor
STR	L: 3.30x10^{-5}		22.73	21.73	0.25	Continuous stirred tank reactor
	I: 7.90x10^{-5}		9.49	8,72	-1.90	Continuous stirred tank reactor
	H: 1.25x10^{-4}		6.00	4.04	-0.33	Plug-flow reactor

Indeed, the high least squares for flows I and H indicates a considerable deviation from the ideal models.

Comparison of average residence time (tr) with time of passage (τ) provides a possible explanation for the non-ideality of the reactors behavior.

tr < τ – non-ideality might be due to the presence of dead zones.

tr > τ – non-ideality might be due to the presence of short-circuits.

Conclusions

Studies that characterize the behavior of bioreactors are extremely helpful to achieve their best performance. In this study, an RTD characterization of the Wave bioreactor was performed, for flow rates used in mammalian cell culture. In these conditions, it was concluded that:

- The choice of the flow rate will strongly influence the behavior of the Wave bioreactor.
- The use of a low flow rate in Wave seems to be a choice that provides a behavior closer to an ideal model (continuous STR).