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# A generic model-based methodology for quantification of mass transfer limitations in microreactors

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## HIGHLIGHTS

- A generic methodology for assessing potential impact of mass transfer limitations is developed.
- The methodology is independent from the reactor geometry and/or reaction.
- The results correspond well with the traditional approach using dimensionless numbers.
- Dimensionless numbers should always be applied with care.

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## ABSTRACT

Microreactors are becoming more popular in the biocatalytic field to speed up reactions and thus achieve process intensification. However, even these small-scale reactors can suffer from mass transfer limitations. Traditionally, dimensionless numbers such as the second Damköhler number are used to determine whether the reaction is either kinetically or mass transfer limited. However, these dimensionless numbers only give a qualitative measure of the extent of the mass transfer limitation, and are only applicable to simple reactor configurations. In practice, this makes it difficult to rapidly quantify the importance of such mass transfer limitations and compare different reactor configurations. This paper presents a novel generic methodology to quantify mass transfer limitations. It was applied to two microreactor configurations: a microreactor with immobilised enzyme at the wall and a Y-shaped microreactor with one inlet stream containing enzyme and the other containing substrate. The results of the immobilised enzyme microreactor correspond very well with the traditional approach of using the second Damköhler number ($Da_{II}$). However, the results of the Y-shaped microreactor showed that the second Damköhler number is not applicable in this case, indicating that dimensionless numbers should be applied with care. For both configurations, the mass transfer limitations could be quantified and linked with appropriate dimensionless numbers, illustrating the power of the proposed methodology.



## 1. Introduction

Microreactors have received considerable interest in the (bio)chemical field, especially due to their versatility and improved controllability of the process. Indeed, they can be operated in batch or in continuous mode, they consume only limited amounts of chemicals per experiment, which gives them a competitive advantage over conventional lab-scale batch reactors when used for process screening, for biocatalyst screening or for kinetic characterisation of the biocatalyst. These microreactors have small channels with dimensions below 1 mm, which enhances transfer rates for both mass and heat [1,2]. By reducing the distance between reactants, mass transfer limitations are reduced in a microreactor [3]. However, even at such small dimensions, mass transfer limitations can still occur and have an important impact. That is why in the literature the importance of mass transfer limitations in microreactors is discussed frequently [4,1,3]. Mass transfer limitations lead to a reduced volumetric productivity [5], but also obscure the underlying kinetic model parameter values [6]. Kinetic model parameter values which are estimated based on mass transfer limited measurements, yield apparent parameter

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**Nomenclature**

*Abbreviations*

| | |
|---|---|
| CFD | Computational Fluid Dynamics |
| DOF | Degree of Freedom |

*Greek symbols*

| | | |
|---|---|---|
| $\rho$ | [kg/m$^3$] | density of the fluid |
| $\tau_{mod}$ | [min] | modified residence time [1] |
| $\tau$ | [min] | residence time |

*Symbols*

| | | |
|---|---|---|
| [$E$] | [g/L] | enzyme concentration |
| [$P$] | [mM] | concentration of product $P$ |
| [$S$] | [mM] | concentration of substrate $S$ |
| Bo | [–] | Bodenstein number |
| $D$ | [m$^2$/s] | diffusion coefficient solute |
| $D_E$ | [m$^2$/s] | diffusion coefficient enzyme |
| $Da_I$ | [–] | first Damköhler number |
| $Da_{II}$ | [–] | second Damköhler number |
| **D** | [m$^2$/s] | Taylor dispersion coefficient |
| $F_S$ | [mol/L] | flow of substrate $S$ |
| $H$ | [m] | microreactor height |
| $k_{cat}$ | [L/(g·s)] | second-order kinetic constant |
| $l_{char}$ | [m] | characteristic length |
| $L$ | [m] | microreactor length |
| $n_{enzyme}$ | [g] | total amount of enzyme |
| $p$ | [–] | rho-normalised pressure |
| Pe | [–] | Péclet number |
| $Pe_{2D}$ | [–] | two-dimensional Péclet number |
| $RD$ | [–] | relative difference [%] between $[P]_{out,PF}$ and $[P]_{out,CFD}$ |
| Re | [–] | Reynolds number |
| $r_{max}$ | [mM/s] | maximum reaction rate |
| $r_S$ | [mM/s] | substrate consumption rate |
| $TC$ | [–] | total conversion |
| $t$ | [min] | time |
| **u** | [m/s] | velocity vector |
| $u_x$ | [m/s] | fluid velocity in x-direction |
| $W$ | [m] | width of the microreactor |
| $x$ | [m] | average displacement of a Brownian particle |

*Subscripts*

| | |
|---|---|
| 0 | inlet |
| out,CFD | outlet of CFD simulation |
| out,PF | outlet of plug flow |

values which represent the combined effect of both mass transfer limitations and kinetics [7]. In order to retrieve the underlying or so-called intrinsic parameter values, these mass transfer limitations need to be excluded by improving the internal mixing and/or optimising the geometry of the reactor. Given this relevance, it is important to identify whether mass transfer limitations are occurring. Traditionally, dimensionless numbers such as the second Damköhler number ($Da_{II}$) are used to determine the occurrence of mass transfer limitations (Eq. (1)).

$$Da_{II} = \frac{\text{Reaction rate}}{\text{Diffusion rate}} = \frac{\text{Diffusion time}}{\text{Reaction time}} \quad (1)$$

The second Damköhler number ($Da_{II}$) represents the ratio between the reaction rate and the diffusion rate. However, in many cases it is also represented as the ratio of the diffusion time and reaction time [4]. The diffusion time can be calculated by the Einstein equation for the Brownian motion of a particle or molecule suspended in a fluid (Eq. (2)) [8].

$$\overline{x^2} = 2Dt \quad (2)$$

where $\overline{x^2}$ represents the mean quadratic displacement of the molecule under study, $D$ the diffusion coefficient of the molecule and $t$ the time the molecule could diffuse. From Eq. (2), the diffusion time needed by the molecule to reach distance $x$ can be calculated [4]. To extract the reaction time, different definitions of reaction time are available in the literature: Kockmann et al. [4] and Roberge et al. [9] use the half-life time of the reaction to characterise reactions, while Swarts et al. [3] use the time at which 95% conversion is reached. A reaction time yielding 100% conversion cannot be used in most cases, since for many kinetic models the reaction rate approaches zero at very low substrate concentrations, yielding an infinite reaction time [3].

In channel-like microreactors, the second Damköhler number $Da_{II}$ can be easily applied to determine whether a reaction is mass transfer limited or kinetically limited. However, this comes with some limitations. A first drawback of this dimensionless approach is that it only gives a qualitative estimate of the mass transfer limitation. For instance, when $Da_{II}$ is high ($\gg 1$), the reaction is said to be mass transfer limited and when it is low ($\ll 1$), the reaction is kinetically limited. However, for most cases no quantification of the level of mass transfer limitations can be directly extracted. In the literature, the value of the second Damköhler number at which a reaction is changing from mass transfer limited to kinetically limited is around one [10]. Walter et al. [1] state that in the case of circular channels with plug flow, a $Da_{II}$ below 0.1 represents the kinetically limited region, whereas for $Da_{II}$ values above 100 the reaction is mass transfer limited. A $Da_{II}$ value between 0.1 and 100 represents a so-called transient region. Information about the transition of mass transfer limited to kinetically limited conditions is not always available and is only valid for that particular microreactor configuration. Secondly, no quantitative information is given about the reduction in productivity, making it almost impossible to determine whether mass transfer limitations are important in terms of process efficiency.

Next to $Da_{II}$, which is used to identify mass transfer limitations, the first Damköhler number ($Da_I$) represents the ratio between the residence time of the solution in the reactor and the reaction time (Eq. (3)). The same difficulties arise with the definition of the reaction time as with the second Damköhler number. At large values of the first Damköhler number ($Da_I \gg 1$), the reaction has sufficient time to complete. At small $Da_I$ values ($Da_I \ll 1$), the reaction does not have sufficient time to reach full conversion.

$$Da_I = \frac{\text{Residence time}}{\text{Reaction time}} \quad (3)$$

Despite the fact that these dimensionless numbers are widely used in the chemical engineering field, not everyone is familiar with these dimensionless numbers and therefore one sometimes even starts developing "new" but redundant dimensionless numbers. E.g. Kerby et al. [6] propose a criterion $\lambda$ which represents the ratio of reaction rate to mass transfer rate, and they state that it "*was developed to evaluate the importance of flow-dependent,*