On the appropriateness of use of a continuous formulation for the modelling of discrete multireactant systems following Michaëlis–Menten kinetics

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Abstract The possibility of solving the mass balances to a multiplicity of substrates within a CSTR in the presence of a chemical reaction following Michaelis-Menten kinetics using the assumption that the discrete distribution of said substrates is well approximated by an equivalent continuous distribution on the molecular weight is explored. The applicability of such reasoning is tested with a convenient numerical example. In addition to providing the limiting behavior of the discrete formulation as the number of homologous substrates increases, the continuous formulation yields in general simpler functional forms for the final distribution of substrates than the discrete counterpart due to the recursive nature of the solution in the latter case.

List of Symbols

Symbol	Units	Description
$C\{N.\Delta M\}$	$\mathrm{mol/m^3}$	concentration of substrate containing N monomer residues each with molecular weight ΔM
$\bar{C}\{N.\Delta M\}$	–	normalized value of $C\{N.\Delta M\}$
$C^*\{M\}$	$\mathrm{mol/m^3\,da}$	concentration of substrate of molecular weight M
$\bar{C}^*_{(i)}$	–	normalized value of $C^*\{M\}$ at the i-th iteration of a finite difference method
$\bar{C}^*\{M\}$	–	normalized value of $C^*\{M\}$
$C_0\{N.\Delta M\}$	$\mathrm{mol/m^3}$	inlet concentration of substrate containing N monomer residues each with molecular weight ΔM
$\bar{C}_0\{N.\Delta M\}$	–	normalized value of $C_0\{N.\Delta M\}$
$\bar{C}^*_{0,(i)}$	–	normalized value of $C^*_0\{M\}$ at the i-th iteration of a finite difference method
$C^*_0\{M\}$	$\mathrm{mol/m^3\,da}$	initial concentration of substrate of molecular weight M
C_{tot}	$\mathrm{mol/m^3}$	(constant) overall concentration of substrates (discrete model)
C^*_{tot}	$\mathrm{mol/m^3}$	(constant) overall concentration of substrates (continuous model)
D	–	deviation of the continuous approach relative to the discrete approach
i	–	dummy integer variable
I	–	arbitrary integration constant
j	–	dummy integer variable
k	–	dummy integer variable
K_m	$\mathrm{mol/m^3}$	Michaëlis–Menten constant for the substrates
l	–	dummy integer variable
M	da	molecular weight of substrate
M^*	–	normalized value of M
M_∞	da	maximum molecular weight of a reacting substrate
N	–	number of monomer residues of a reacting substrate
N_∞	–	maximum number of monomer residues of a reacting substrate
N^*_∞	–	total number of increments for the finite difference method
Q	$\mathrm{m^3/s}$	volumetric flow rate of liquid through the reactor
S	–	inert product molecule
S_i	–	substrate containing i monomer residues
V	$\mathrm{m^3}$	volume of the reactor
$v_{\max}$	$\mathrm{mol/m^3\,s}$	reaction rate under saturating conditions of the enzyme active site with substrate
$v_{\max}\{N.\Delta M\}$	$\mathrm{mol/m^3\,s}$	reaction rate under saturating conditions of the enzyme active site with substrate containing N monomer residues with molecular weight ΔM
$\bar{v}_{\max}\{N.\Delta M\}$	–	dimensionless value of $v_{\max}\{N.\Delta M\}$ (discrete model)
$\bar{v}^*_{\max}\{M\}$	–	dimensionless value of $v^*_{\max}\{M\}$ (continuous model)
$\hat{v}_{\max}$	$\mathrm{mol/m^3\,s}$	molecular weight-averaged value of $v_{\max}$ (discrete model)
$\hat{v}^*_{\max}$	$\mathrm{mol.da/m^3\,s}$	molecular weight-averaged value of $v_{\max}$ (continuous model)
$v^*_{\max}\{M\}$	$\mathrm{mol.da/m^3\,s}$	reaction rate under saturating conditions of the enzyme active site with substrate with molecular weight M
$\bar{v}^*_{\max}\{M\}$	–	dimensionless value of $v_{\max}\{M\}$

| $\bar{v}^{*}_{\max, (i)}$ | – | dimensionless value of $v_{\max}\{M\}$ at the i-th iteration of a finite difference method |
| $v^{\theta}_{\max}$ | $mol/m^3\,s$ | reference constant value of $v_{\max}$ |

Greek symbols

β	–	dimensionless operating parameter (discrete distribution)
β^*	–	dimensionless operating parameter (continuous distribution)
ΔM	da	(average) molecular weight of a monomeric subunit
ΔM^*	–	selected increment for the finite difference method
Ξ	–	auxiliary corrective factor (discrete model)

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Mathematical statement

Although most enzymes possess a very high degree of specificity towards their substrates due to their catalytic role *in vivo*, some enzymes exhibit a large affinity to a wide variety of polymeric substrates provided that these substrates share a common type of labile covalent bond [1]. In such situation, the various reactants compete with one another for the active site of the enzyme irrespective of their sequence of monomer residues or overall molecular weight. Examples documented in the literature include the action of such hydrolases as lysozyme on mucopolysaccharides of bacterial cell walls [2], amylo-glucosidase on amylose [3, 4], and peptidases on various peptides derived from paracaseins [5].

Of particular interest here are the reactions effected by soluble exo-hydrolases (i.e., enzymes that cleave ester, glycosidic or peptide bonds next to the ends of polymeric carbon backbones, thus releasing monomeric subunits) on complex mixtures of substrates consisting of bipolymers of various chain lengths. The general stoichiometry can be represented as follows:

$$S_i \rightarrow S_{i-1} + S \quad (2 \leqslant i \leqslant N_{\infty}), \tag{1}$$

where S_i denotes a substrate consisting of i monomeric subunits and N_{∞} is the number of subunits of the largest molecule existing in non-negligible concentration which is susceptible to enzymatic transformation. In this mechanism, both S_i and S_{i-1} can bind and be transformed by the enzyme, but the monomeric units S and S_1 do not bind significantly to the enzyme (hence the enzyme is not active upon either of them).

The chemical reaction is assumed to be carried out in a continuous stirred tank reactor (CSTR) under isothermal conditions and absence of enzyme deactivation. In this type of reactor the ease of operation, low construction costs, and absence of concentration gradients of the stirred batch counterpart are coupled with the possibility of steady-state operation and lack of disturbance on the reacting fluid upon sampling which are characteristic of continuous flow reactors [6]. A state of perfect micromixing within the reacting fluid is assumed throughout [7], which eliminates the need for taking residence time distributions into account in the mass balances. The enzyme kinetics is assumed to be accurately described by a multisubstrate Michaëlis–Menten rate equation [1] for which the dissociation constant (also known as Michaëlis–Menten constant) associated with the enzyme-substrate complex, K_m, has the same value irrespective of the type of moiety bound thereto. This type of behavior, i.e., variable $v_{\max}$ (where $v_{\max}$ is the maximum rate of reaction under saturation conditions of substrate) and constant K_m, has been observed previously, e.g. in the hydrolytic action of horse liver esterase on fatty acid moieties of different chain lengths [8].

If one uses the discrete, multireactant approach, the mass balance to every type of substrate reads

$$v_{\max}\{N.\Delta M\}\ C\{N.\Delta M\} = 0, \quad N > N_{\infty},$$

$$QC_0\{N.\Delta M\} + \frac{Vv_{\max}\{(N+1).\Delta M\}\ C\{(N+1).\Delta M\}}{K_m + C_{tot}} = QC\{N.\Delta M\} + \frac{Vv_{\max}\{N.\Delta M\}\ C\{N.\Delta M\}}{K_m + C_{tot}}, \quad 2 \leqslant N \leqslant N_{\infty}, \tag{2}$$

$$QC_0\{N.\Delta M\} + \frac{Vv_{\max}\{(N+1).\Delta M\}\ C\{(N+1).\Delta M\}}{K_m + C_{tot}} = QC\{N.\Delta M\}, \quad N = 1.$$

where Q is the volumetric flow rate of reacting fluid, subscript o denotes inlet conditions, V is the volume of the reactor, N is the number of monomeric subunits in each molecule, ΔM is the (average) molecular weight of each monomeric unit, $C\{N.\Delta M\}$ and $C\{(N+1).\Delta M\}$ are the molar concentrations of molecules with molecular weights equal to $N.\Delta M$ and $(N+1)\Delta M$, respectively, and $v_{\max}\{N.\Delta M\}$ and $v_{\max}\{(N+1).\Delta M\}$ are the maximum rates of reaction under saturation conditions of the enzyme with molecules of molecular weights equal to $N.\Delta M$ and $(N+1)\Delta M$, respectively. The constant C_{tot} is given by:

$$C_{tot} \equiv \sum_{N=1}^{N_{\infty}} C_0\{N.\Delta M\} = \sum_{N=1}^{N_{\infty}} C\{N.\Delta M\}, \tag{3}$$

where advantage was taken from the one to one stoichiometry for the active reactants as depicted in Eq. (1). In Eq. (2) and for $1 \leqslant N \leqslant N_{\infty}$, the first term in the LHS represents the inlet molar flow rate of molecules with molecular weight equal to $N.\Delta M$, the second term in the LHS represents the molar rate of production of molecules with molecular weight equal to $N.\Delta M$ [or, equivalently, of consumption of molecules with molecular weight equal to $(N+1).\Delta M$], the first term in the RHS accounts for the outlet molar flow rate of molecules with molecular weight equal to $N.\Delta M$, and the second term in the RHS (in the case where it exists) arises from the molar rate of consumption of molecules with molecular weight equal to $N.\Delta M$. Equation (2) is equivalent to the following recursive relation:

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$$\bar{C}\{N/N_\infty\} = \frac{\bar{C}_0\{N/N_\infty\}}{1+\beta\,\bar{v}_{\max}\{N/N_\infty\}}, \quad N=N_\infty,$$

$$\bar{C}\{N/N_\infty\} = \frac{\bar{C}_0\{N/N_\infty\}+\beta\,\bar{v}_{\max}\{(N+1)/N_\infty\}\,\bar{C}\{(N+1)/N_\infty\}}{1+\beta\,\bar{v}_{\max}\{N/N_\infty\}}, \quad 2\leqslant N\leqslant N_\infty-1, \tag{4}$$

$$\bar{C}\{N/N_\infty\} = \bar{C}_0\{N/N_\infty\}+\beta\,\bar{v}_{\max}\{(N+1)/N_\infty\}\,\bar{C}\{(N+1)/N_\infty\}, \quad N=1.$$

The situation of $N>N_\infty$ was no longer taken into account due to its inherent lack of practical interest here. The dimensionless operating parameter β, which is the ratio of the time scale associated with convection through the reactor, V/Q, to the time scale associated with the enzymatic reaction, $(K_m+C_{tot})/\hat{v}_{\max}$, is defined as:

$$\beta \equiv \frac{V\hat{v}_{\max}}{Q(K_m+C_{tot})}, \tag{5}$$

where $\hat{v}_{\max}$ is the molecular weight-averaged value of $v_{\max}$:

$$\hat{v}_{\max} \equiv \frac{\sum_{N=1}^{N_\infty} v_{\max}\{N.\Delta M\}.\Delta M}{\sum_{N=1}^{N_\infty} \Delta M}. \tag{6}$$

$\bar{C}$ is a normalized concentration given by:

$$\bar{C} \equiv \frac{C}{C_{tot}}, \tag{7}$$

and $\bar{v}_{\max}$ is a dimensionless maximum rate of reaction defined as:

$$\bar{v}_{\max} \equiv \frac{v_{\max}}{\hat{v}_{\max}}. \tag{8}$$

Combination of Eq. (4) from $N=N_\infty$ down to $N=1$, one obtains [9]:

with the generic reaction depicted in Eq. (1):

$$\frac{dM}{dt} = -\frac{v_{\max}^\star\{M\}}{K_m+C_{tot}^\star}, \tag{11}$$

where $v_{\max}^\star\{M\}\,dM$ is the maximum rate of reaction under saturation conditions of molecules with molecular weight comprised between M and $M+dM$, and where the constant $C_{tot}^\star$ is given by:

$$C_{tot}^\star \equiv \int_0^{M_\infty} C_0^\star\{M\}\,dM = \int_0^{M_\infty} C^\star\{M\}\,dM, \tag{12}$$

where M_∞ denotes the limit in molecular weight above which either the substrate concentration is virtually nil or the enzyme is virtually inactive ($M_\infty = N_\infty.\Delta M$ as required for consistency). In Eq. (10), the term in the LHS represents the net molar rate of production of molecules with molecular weight comprised between M and $M+dM$ or, equivalently, the difference between the molar rate of consumption of molecules with molecular weight comprised between $M+dM$ and $M+2dM$ and the molar rate of consumption of molecules with molecular weight comprised between M and $M+dM$. The first term in the RHS accounts for the inlet molar flow rate of molecules with molecular weight comprised between M and $M+dM$, whereas the second term in the

$$\bar{C}\{N/N_\infty\} = \frac{\bar{C}_0\{N/N_\infty\}}{1+\beta\,\bar{v}_{\max}\{N/N_\infty\}}, \quad N=N_\infty,$$

$$\bar{C}\{N/N_\infty\} = \frac{\bar{C}_0\{N/N_\infty\}}{1+\beta\,\bar{v}_{\max}\{N/N_\infty\}} + \sum_{j=1}^{N_\infty-N} \frac{\bar{C}_0\{(N+j)/N_\infty\}\prod_{l=0}^{j-1}(\beta\,\bar{v}_{\max}\{(N+j-l)/N_\infty\})}{\prod_{k=0}^{j}(1+\beta\,\bar{v}_{\max}\{(N+j-k)/N_\infty\})}, \quad 2\leqslant N\leqslant N_\infty-1, \tag{9}$$

$$\bar{C}\{N/N_\infty\} = \bar{C}_0\{N/N_\infty\} + \sum_{j=1}^{N_\infty-N} \frac{\bar{C}_0\{(N+j)/N_\infty\}\prod_{l=0}^{j-1}(\beta\,\bar{v}_{\max}\{(N+j-l)/N_\infty\})}{\prod_{k=0}^{j}(1+\beta\,\bar{v}_{\max}\{(N+j-k)/N_\infty\})}, \quad N=1.$$

If a continuous formulation is employed, then the material balance under steady state conditions to the (infinity of) substrates should be mathematically expressed in terms of the local population density in a way similar to the population balance to a MSMPR crystallizer operating under steady state conditions [10]:

$$V\frac{d}{dM}\left\{C^\star\{M\}\left(\frac{dM}{dt}\right)\right\} = Q(C_0^\star\{M\}-C^\star\{M\}), \tag{10}$$

where $C^\star\{M\}\,dM$ is the molar concentration of molecules with molecular weight comprised between M and $M+dM$. The analogy between the continuous and the discrete distribution of substrate concentrations is apparent by making $M=N.\Delta M$ in Eq. (10). The rate of variation of the molecular weight of a substrate with a given molecular weight is essentially equal to the negative of the pseudo-first order rate constant associated

RHS represents the outlet molar flow rate of molecules with molecular weight comprised between M and $M+dM$.

Rearrangement of Eq. (10) yields:

$$\bar{C}^\star\{M^\star\} - \beta^\star\frac{d}{dM^\star}\{\bar{v}_{\max}^\star\{M^\star\}\,\bar{C}^\star\{M^\star\}\} = \bar{C}_0^\star\{M^\star\}$$

$$\bar{C}^\star\{M^\star\} = \frac{\bar{C}_0^\star\{M^\star\}}{1+\beta^\star\,\bar{v}_{\max}^\star\{M^\star\}}, \quad M^\star=1 \tag{13}$$

$$\bar{v}_{\max}^\star\{M^\star\}\,\bar{C}^\star\{M^\star\} = 0, \quad M^\star>1$$

where

$$M^\star \equiv \frac{M}{M_\infty}, \tag{14}$$

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and, in a similar fashion to Eqs. (7), (5), and (8), one obtains:

$$\bar{C}^* \equiv \frac{C^*}{C_{tot}^*}, \tag{15}$$

$$\beta^* \equiv \frac{V \hat{v}_{max}^*}{M_\infty Q (K_m + C_{tot}^*)}, \tag{16}$$

and

$$\bar{v}_{max}^* \equiv \frac{v_{max}^*}{\hat{v}_{max}^*}, \tag{17}$$

respectively, under the assumption that:

$$\hat{v}_{max}^* \equiv \frac{\int_0^{M_\infty} v_{max}^* \{M\} \, dM}{\int_0^{M_\infty} dM}. \tag{18}$$

Equation (13) may be rewritten as:

$$\frac{d}{dM^*} \{\beta^* \, \bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\}\}$$

$$- \left(\frac{1}{\beta^* \, \bar{v}_{max}^* \{M^*\}}\right) (\beta^* \, \bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\}) = -\bar{C}_0^* \{M^*\}, \tag{19}$$

$$\bar{C}^* \{M^*\} = \frac{\bar{C}_0^* \{M^*\}}{1 + \bar{v}_{max}^* \{M^*\}}, \quad M^* = 1$$

where, as before, the situation of $M > M_\infty$ was discarded.

The above equation has the form of an ordinary first order liner differential equation with $\beta^* \, \bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\}$ as the dependent variable and M as the independent variable. The general solution of Eq. (19) can be written as [11]:

$$\beta^* \, \bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\} =$$

$$\frac{I - \int \bar{C}_0^* \{M^*\} \exp\left\{-\frac{1}{\beta^*} \int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right\} dM^*}{\exp\left\{-\frac{1}{\beta^*} \int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right\}},$$

$$\bar{C}^* \{M^*\} = \frac{\bar{C}_0^* \{M^*\}}{1 + \beta^* \, \bar{v}_{max}^* \{M^*\}}, \quad M^* = 1 \tag{20}$$

where I denotes an arbitrary integration constant.

The general analytical form of Eqs. (9) and (20) depends on the shape of the distribution of inlet concentrations of substrates susceptible to enzymatic action, i.e., $\bar{C}_0 \{M\}$ and $\bar{C}_0^* \{M\}$, respectively. If the following condition is satisfied:

$$\bar{C}_0^* \{M^*\} = \frac{1}{\bar{v}_{max}^* \{M^*\}}, \tag{21}$$

then Eq. (20) can be simplified to:

$$\bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\} =$$

$$\frac{I + \beta^* \exp\left\{-\frac{1}{\beta^*} \int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right\}}{\beta^* \exp\left\{-\frac{1}{\beta^*} \int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right\}},$$

$$\bar{C}^* \{M^*\} = \frac{1}{\bar{v}_{max}^* \{M^*\} (1 + \beta^* \, \bar{v}_{max}^* \{M^*\})}, \quad M^* = 1 \tag{22}$$

Application of the limiting condition listed in Eq. (22) finally yields:

$$\bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M^*\} = 1 - \left(1 - \frac{1}{1 + \beta^* \, \bar{v}_{max}^* \{M^*\}}\right) \exp\left\{-\frac{1}{\beta^*} \left(\left(\int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right)_{M^*=1} - \int \frac{dM^*}{\bar{v}_{max}^* \{M^*\}}\right)\right\}. \tag{23}$$

If β^* tends to zero, then Eq. (23) becomes:

$$\lim_{\beta^* \to 0} \bar{v}_{max}^* \{M^*\} \, \bar{C}^* \{M\} = 1. \tag{24}$$

Eq. (24) can also read:

$$\lim_{\beta^* \to 0} \bar{C}^* \{M^*\} = \frac{1}{\bar{v}_{max}^* \{M^*\}} = \bar{C}_0^* \{M^*\}. \tag{25}$$

This result is expected because the conversion in the reactor should be negligible when the reactor residence time is very small when compared with the time constant associated with the enzyme-catalyzed reaction; remember that, as discussed before, β^* is the ratio of these two time scales.

In the general case, which encompasses Eq. (22) as a special situation, Eq. (13) can be solved by a finite difference method:

$$\bar{C}_{(i-1)}^* = \frac{\frac{\bar{C}_{0,(i)}^* \Delta M^*}{\beta^*} + \left(\bar{v}_{max,(i)}^* - \frac{\Delta M^*}{\beta^*}\right) \bar{C}_{(i)}^*}{\bar{v}_{max,(i-1)}^*}, \quad 1 \leqslant i \leqslant N_\infty^* \tag{26}$$

$$\bar{C}_{0(N_\infty^*)}^* = \frac{\bar{C}_{0(N_\infty^*)}^*}{1 + \beta^* \, \bar{v}_{max,(N_\infty^*)}^*},$$

where ΔM^* is the selected increment for the finite difference method, N_∞^* is the total number of increments, and (i) denotes the i-th iteration.

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Numerical example
Assume that:

$$v_{max} \{N . \Delta M\} = \left(\frac{v_{max}^\theta}{\sqrt{M_\infty}}\right) \sqrt{N . \Delta M}, \tag{27}$$

and, in a similar way:

$$v_{max}^* \{M\} = (V_{max}^\theta \sqrt{M_\infty}) \sqrt{M}, \tag{28}$$

where v_{max}^θ denotes a reference value of the maximum rate of reaction. Under these circumstances, Eqs. (6) and (8) give:

$$\bar{v}_{max} = \Xi \{N_\infty\} \sqrt{N/N_\infty}, \tag{29}$$

where Ξ is a corrective factor given by:

$$\Xi \{N_\infty\} \equiv \frac{N_\infty^{3/2}}{\sum_{i=1}^{N_\infty} \sqrt{i}}, \tag{30}$$

whereas Eqs. (17) and (18) give:

$$\bar{v}_{max}^* = \frac{3}{2} \sqrt{M^*}, \tag{31}$$

Assuming in addition that:

$$\bar{C}_0 = \frac{1}{\bar{v}_{max} \{N, N_\infty\}} = \frac{1}{\Xi \{N_\infty\} \sqrt{N/N_\infty}}, \tag{32}$$

as well as

$$\bar{C}_0^* = \frac{1}{\bar{v}_{max}^* \{M^*\}} = \frac{2}{3\sqrt{M^*}}, \tag{33}$$

and using Eqs. (29), (30), and (32) in Eq. (9), and Eq. (31) in Eq. (23), one finally obtains:

$$\bar{v}_{max}\{N/N_\infty\}\,\bar{C}\{N/N_\infty\} = 0, \quad N > N_\infty$$

$$\bar{C}\{N/N_\infty\} = \frac{1}{\Xi\{N_\infty\}\sqrt{N/N_\infty} + \beta\Xi^2\{N_\infty\}(N/N_\infty)}, \quad N = N_\infty$$

$$\bar{C}\{N/N_\infty\} = \frac{1}{\Xi\{N_\infty\}\sqrt{N/N_\infty} + \beta\Xi^2\{N_\infty\}(N/N_\infty)} + \sum_{j=1}^{N_\infty - N} \frac{\beta^j\Xi\{N_\infty\}^{j-1}\prod_{l=0}^{j-1}\sqrt{(N+j-l)/N_\infty}}{\sqrt{(N+j)/N_\infty}\prod_{k=0}^{j}(1+\beta\Xi\{N_\infty\}\sqrt{(N+j-k)/N_\infty})}, \quad 2 \leqslant N \leqslant N_\infty - 1, \tag{34}$$

$$\bar{C}\{N/N_\infty\} = \frac{1}{\Xi\{N_\infty\}\sqrt{N/N_\infty}} + \sum_{j=1}^{N_\infty - N} \frac{\beta^j\Xi\{N_\infty\}^{j-1}\prod_{l=0}^{j-1}\sqrt{(N+j-l)/N_\infty}}{\sqrt{(N+j)/N_\infty}\prod_{k=0}^{j}(1+\beta\Xi\{N_\infty\}\sqrt{(N+j-k)/N_\infty})}, \quad N = 1$$

and:

$$\bar{v}_{max}^*\{M^*\}\,\bar{C}_{max}^*\{M^*\} = 0, \quad M^* > 1$$

$$\bar{C}^*\{M^*\} = \frac{2\left(1 - \frac{3\beta^*}{2+3\beta^*}\exp\left\{-\frac{4}{3\beta^*}(1-\sqrt{M^*})\right\}\right)}{3\sqrt{M^*}}, \tag{35}$$

$$0 < M^* \leqslant 1$$

respectively. Equations (34) and (35) are graphically plotted in Fig. 1 for five values of N_∞ and three values of β.

3
Discussion

The constraint that the integrals and summations of v_{max} and C_0 in M remain upperly bounded for every value of M and N. ΔM in the range under scrutiny, which does not necessarily imply that v_{max} and C_0 remain upperly bounded themselves in that range, can not be violated; otherwise the average values $\hat{v}_{max}$ (or $\hat{v}_{max}^*$) and C_{tot} (or C_{tot}^*) may not be defined by Eq. (6) or Eq. (18), and Eq. (3) and (12), respectively.

The continuous approximation is, in general, good for every value of β, covering the range from small conversions (i.e. small β, or, equivalently, kinetic control) to large conversions (i.e. large β, or, equivalently, convection control). In the case documented (see Fig. 1), the differences between the two approaches at high values of β are particularly impressive for the concentrations of the monomeric substrate because, since all polymeric substrates will eventually be transformed into monomeric forms via the enzyme-catalyzed reaction, the peaks for the monomer will be very large although their areas can be balanced by the area below the continuous distribution, which is especially steep as it tends to infinity when M tends to zero. Note that the dimensionless concentrations can be higher than unity for certain ranges of molecular weights provided that in other ranges they are below unity. The normalizing factor is the total concentration of substrates rather than the maximum local concentration of any given substrate.

The continuous approximation improves in accuracy as N_∞ increases (as expected, since the number of distinct substrate

molecules increases). The deviation between the continuous and the discrete approximation, defined as:

$$D \equiv \sum_{N=1}^{N_\infty}\left(\int_{(N-1)/N_\infty}^{N/N_\infty} \bar{C}^*\{M^*\}\,dM^* - \bar{C}\{N/N_\infty\}\right), \tag{36}$$

is virtually zero due to the fact that the overall concentration of

substrates, C_{tot} and C_{tot}^*, is in both cases a constant which is supposed to take virtually the same value. In general, it can be stated that if more than 50 substrates of a homologous series are considered as the feedstock, then the approximation of the continuous approach to the discrete approach is very good.

Although it might be argued that at $M^* = 1$, $\bar{v}_{max}^*\{M^*\}\,\bar{C}^*\{M^*\} = 0$, this boundary condition yields very poor results in terms of agreement of the continuous distribution with the discrete counterparts, because the imposition of a nil boundary condition at $M^* = 1$ affects the behavior of $\bar{C}^*\{M^*\}$ in its neighborhood in a strong fashion since smooth, rather than steep changes are allowed in any vicinity; such effect gets attenuated as M^* gets further apart from unity. Therefore, one has to resort to the alternative boundary condition that, at $M^* = 1$ (or, in a more appropriate fashion, at $M^* = 1^-$), $\bar{C}^*\{M^*\} = \bar{C}_0^*\{M^*\}/(1+\beta^*\bar{v}_{max}^*\{M^*\})$; the latter value is obtained as the limiting behavior in terms of substrate concentration of a CSTR characterized by parameter β^* where the substrate with a dimensionless molecular weight equal to unity is being converted to a substrate with a vanishingly smaller molecular weight.

Continuous formulations of discrete problems have found some use in the past, e.g. in the simulation of distillation operations of multicomponent mixtures consisting of a great variety of homologous hydrocarbons. The advantage of using a continuous distribution instead of a discrete distribution for the case of enzymatic reactions is the ease of definition of a continuous solution rather than a recursive solution in several situations of practical interest. Although major differences between the simple form given by Eq. (35) and the involved form given by Eq. (34) are apparent, other concentration and maximum rate distributions might lead to not so dramatically distinct results especially if the recursive relations denoted as Eq. (4) and (26) are to be employed in numerical algorithms. In any case, the method developed in this communication is relevant from the applied point of view because it suggests that the fractional accuracy in predicting the actual discrete distribution of concentrations is good especially for the larger substrates, i.e. the ones which often exist in larger concentrations. It should be noted that one of the most common goals underlying the
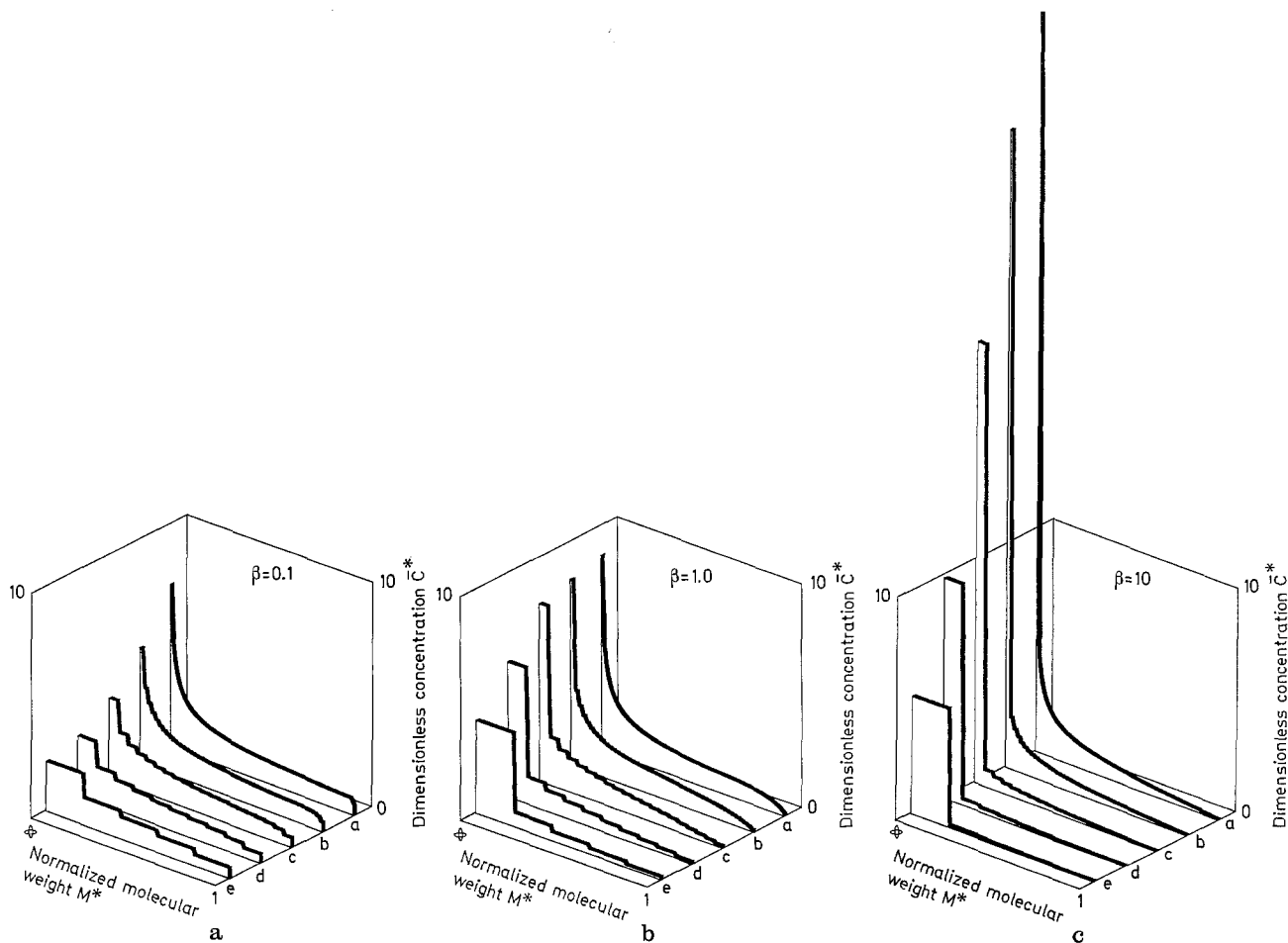
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Fig. 1a–c. Plots of the concentration distributions as continuous functions of the molecular weight for (a) $N_\infty = \infty$ (continuous distribution), (b) $N_\infty = 50$, (c) $N_\infty = 20$, (d) $N_\infty = 10$, and (e) $N_\infty = 5$, for (1a) $\beta = 0.1$, (1b) $\beta = 1$, and (1c) $\beta = 10$ in all cases it was assumed that $M_\infty = 100$, and hence $\beta^* = \beta / 100$

utilization of a reaction system of the type described above is the general decrease in the degree of polymerization of the heavier substrates rather than the accurate description of the rates of production of monomers and dimers at the expense of such molecules.

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