



Manual

The CADET Authors **CADET Version 3.0.0**

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1 Models

1.1 Unit operation models

1.1.1 General rate model (GRM)

The general rate model is the most comprehensive model of mass transfer in column liquid chromatography, when only the axial coordinate in the column and the radial coordinate in the beads are considered [Kuř65; Gu95; Gui+06; FG04].

The main assumptions are:

1. The cross sections of the column are homogenous in terms of interstitial volume, fluid flow, and distribution of components. Thus, only one spatial coordinate in axial direction is needed.
2. The bead radii r_p are much smaller than the column radius r_c and the column length L . Therefore, the beads can be seen as continuously distributed inside the column (i.e., at each point there is interstitial and bead volume).

Variable	Domain	Description
i	$\{0, \dots, N_{\text{comp}} - 1\}$	Component index
m_i	$\{0, \dots, N_{\text{bnd},i} - 1\}$	Bound state index of i th component
m	$\{0, \dots, \sum_{i=0}^{N_{\text{comp}}-1} N_{\text{bnd},i} - 1\}$	Total bound state index
t	$[0, T_{\text{end}}]$	Time coordinate
z	$[0, L]$	Axial coordinate
r	$[0, r_p]$	Radial coordinate
$c_i(t, z)$	$[0, T_{\text{end}}] \times [0, L]$	Interstitial concentration of the i th component
$c_{p,i}(t, z, r)$	$[0, T_{\text{end}}] \times [0, L] \times [0, r_p]$	Mobile phase concentration of the i th component
$q_{i,m_i}(t, z, r)$	$[0, T_{\text{end}}] \times [0, L] \times [0, r_p]$	Solid phase concentration of the i th component's m_i th bound state
$j_{f,i}(t, z)$	$[0, T_{\text{end}}] \times [0, L]$	Flux of the i th component through stagnant film into the bead

Table 1.1.1: Variables and unknowns

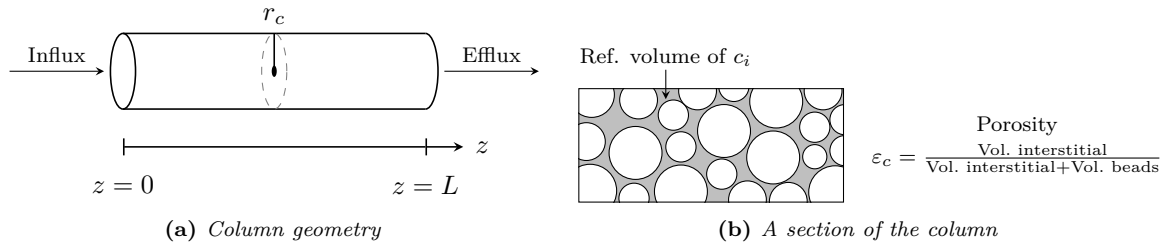


Figure 1.1.1: Column bulk model

The GRM describes transport of solute molecules through the interstitial column volume by convective flow, band broadening caused by axial dispersion, mass transfer resistance through a stagnant film around the beads, pore (and surface) diffusion in the porous beads [MWW96; SS68; Miy07], and adsorption to the inner bead surfaces.

Consider a column of length $L > 0$ filled with spherical beads of radius $r_p \ll L$ (see Fig. 1.1.1). The mass balance in the interstitial column volume is described by

$$\frac{\partial c_i}{\partial t} = -u \frac{\partial c_i}{\partial z} + D_{\text{ax}} \frac{\partial^2 c_i}{\partial z^2} - \frac{1}{\beta_c} \frac{3}{r_p} k_{f,i} [c_i - c_{p,i}(\cdot, \cdot, r_p)]. \quad (1.1)$$

Here, $c_i : [0, T_{\text{end}}] \times [0, L] \rightarrow \mathbb{R}^{\geq 0}$ denotes the concentration in the interstitial column volume, $c_{p,i} : [0, T_{\text{end}}] \times [0, L] \times [0, r_p] \rightarrow \mathbb{R}^{\geq 0}$ the liquid phase concentration in the beads, $k_{f,i}$ the film diffusion coefficient, D_{ax} the dispersion coefficient, u the interstitial velocity, and $\beta_c = \varepsilon_c / (1 - \varepsilon_c)$ the column phase ratio, where ε_c is the column porosity (ratio of interstitial volume to total column volume).

In the liquid phase of the porous beads (see Fig. 1.1.2) the mass balance is given by

$$\frac{\partial c_{p,i}}{\partial t} + \frac{1}{\beta_p} \frac{\partial}{\partial t} \sum_{m_i} q_{i,m_i} = \underbrace{D_{p,i} \left[\frac{\partial^2}{\partial r^2} + \frac{2}{r} \frac{\partial}{\partial r} \right] c_{p,i}}_{\text{Pore diffusion}} + \underbrace{\frac{1}{\beta_p} D_{s,i} \left[\frac{\partial^2}{\partial r^2} + \frac{2}{r} \frac{\partial}{\partial r} \right] \sum_{m_i} q_{i,m_i}}_{\text{Surface diffusion}}, \quad (1.2)$$

where $q_{i,m_i} : [0, T_{\text{end}}] \times [0, L] \times [0, r_p] \rightarrow \mathbb{R}^{\geq 0}$ denotes the solid phase concentration of the i th component's m_i th bound state in the beads, $D_{p,i}$ the effective diffusion coefficient in the beads, $D_{s,i}$ the surface diffusion coefficient, and $\beta_p = \varepsilon_p / (1 - \varepsilon_p)$ the particle phase ratio, where ε_p is the particle porosity (ratio of pore volume to total bead volume). The GRM is used with both quasi-stationary (Eq. (1.3)) and dynamic (Eq. (1.4)) binding models.

$$\text{quasi-stationary: } 0 = f_{\text{ads}}(c_p, q), \quad (1.3)$$

$$\text{dynamic: } \frac{\partial q}{\partial t} = f_{\text{ads}}(c_p, q). \quad (1.4)$$

Note that c_p and q denote the vector of all $c_{p,i}$ and q_{i,m_i} , respectively. The boundary conditions of the bead model the film diffusion and are given for all $t \in (0, \infty)$ and $z \in [0, L]$ by

$$k_{f,i} [c_i - c_{p,i}(\cdot, \cdot, r_p)] = \varepsilon_p D_{p,i} \frac{\partial c_{p,i}}{\partial r}(\cdot, \cdot, r_p) + (1 - \varepsilon_p) D_{s,i} \sum_{m_i} \frac{\partial q_{i,m_i}}{\partial r}(\cdot, \cdot, r_p), \quad (1.5)$$

$$\frac{\partial c_{p,i}}{\partial r}(\cdot, \cdot, 0) = 0. \quad (1.6)$$

By default, the following initial conditions are applied for all $z \in [0, L]$ and $r \in [0, r_p]$:

$$c_i(0, z) = 0, \quad c_{p,i}(0, z, r) = 0, \quad q_{i,m_i}(0, z, r) = 0. \quad (1.7)$$

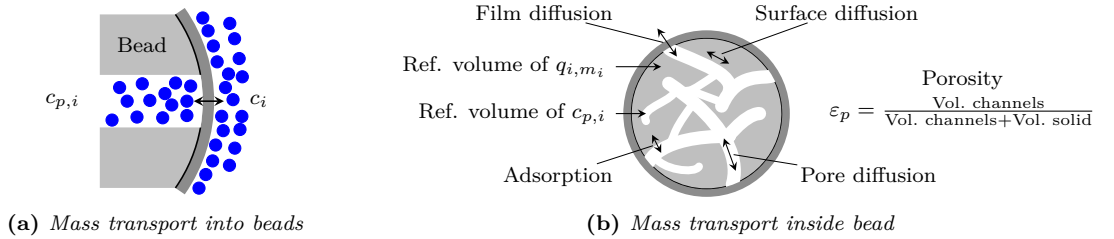


Figure 1.1.2: Column bead model

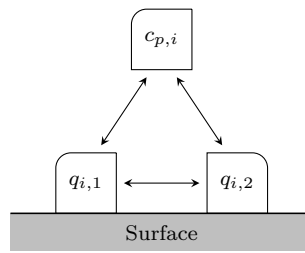


Figure 1.1.3: *Binding with multiple bound states*

1.2 Binding models

The following binding models are presented in dynamic binding mode. By replacing all occurrences of dq/dt with 0, quasi-stationary (rapid-equilibrium) binding mode is achieved. In quasi-stationary binding it is assumed that ad- and desorption take place on a much faster time scale than the other transport processes such that bead liquid phase $c_{p,i}$ (or bulk liquid phase c_i for certain unit operation models) are always in equilibrium with the solid phase q_i .

Equilibrium constants For the quasi-stationary binding mode, adsorption and desorption rate are no longer separate entities. Instead, the quotient $k_{eq} = k_a/k_d$ of adsorption and desorption coefficient is the relevant parameter as shown for the linear binding model (see Section 1.2.1):

$$\frac{dq_i}{dt} = k_{a,i}c_{p,i} - k_{d,i}q_i \quad \Rightarrow 0 = k_{a,i}c_{p,i} - k_{d,i}q_i \quad \Leftrightarrow q_i = \frac{k_{a,i}}{k_{d,i}}c_{p,i} = k_{eq,i}c_{p,i}.$$

The equilibrium constant $k_{eq,i}$ is used in CADET by setting $k_{d,i} = 1$ and $k_{a,i} = k_{eq,i}$.

Correlation of ad- and desorption rates Note that adsorption rate $k_{a,i}$ and desorption rate $k_{d,i}$ are linearly correlated in both binding modes due to the form of the equilibrium constant k_{eq} :

$$k_{a,i} = k_{eq}k_{d,i}.$$

This correlation can potentially degrade performance of some optimization algorithms. While in quasi-stationary binding mode this is prevented by using the technique above, a dynamic binding model has to be reparameterized in order to decouple parameters:

$$\frac{dq_i}{dt} = k_{a,i}c_{p,i} - k_{d,i}q_i = k_{d,i} [k_{eq,i}c_{p,i} - q_i] = k_{a,i} \left[c_{p,i} - \frac{1}{k_{eq,i}}q_i \right].$$

This can be achieved by a (nonlinear) parameter transform

$$F(k_{eq,i}, k_{d,i}) = \begin{pmatrix} k_{eq,i}k_{d,i} \\ k_{d,i} \end{pmatrix} \text{ with Jacobian } J_F(k_{eq,i}, k_{d,i}) = \begin{pmatrix} k_{d,i} & k_{eq,i} \\ 0 & 1 \end{pmatrix}.$$

Dependence on external function A binding model may depend on an external function or profile $T: [0, T_{end}] \times [0, L] \rightarrow \mathbb{R}$, where L denotes the physical length of the unit operation, or $T: [0, T_{end}] \rightarrow \mathbb{R}$ if the unit operation model has no axial length. By using an external profile it is possible to account for effects that are not directly modeled in CADET (e.g., temperature). The dependence of each parameter is modeled by a polynomial of third degree. For example, the adsorption rate k_a is really given by

$$k_a(T) = k_{a,3}T^3 + k_{a,2}T^2 + k_{a,1}T + k_{a,0}.$$

While $k_{a,0}$ is set by the original parameter `XXX_KA` of the file format (XXX being a placeholder for the binding model), the parameters $k_{a,3}$, $k_{a,2}$, and $k_{a,1}$ are given by `XXX_KA_TTT`, `XXX_KA_TT`, and `XXX_KA_T`, respectively. The identifier of the externally dependent binding model is constructed from the original identifier by prepending `EXT_` (e.g., `MULTI_COMPONENT_LANGMUIR` is changed into `EXT_MULTI_COMPONENT_LANGMUIR`). This pattern applies to all parameters and supporting binding models (see Table 1.2.1). Note that the parameter units have to be adapted to the unit of the external profile by dividing with an appropriate power.

Each parameter of the externally dependent binding model can depend on a different external source. The 0-based indices of the external source for each parameter is given in the dataset `EXTFUN`. By assigning only one index to `EXTFUN`, all parameters use the same source. The ordering of the parameters in `EXTFUN` is given by the ordering in the file format specification in Section 2.5.4.

Binding model feature matrix A short comparison of the most prominent binding model features is given in Table 1.2.1. The implemented binding models can be divided into two main classes: Single-state and multi-state binding. While single-state models only have one bound state per component (or less),

multi-state models provide multiple (possibly different) bound states for each component, which may correspond to different binding orientations or binding site types. The models also differ in whether a mobile phase modifier (e.g., salt) is supported to modulate the binding behaviour.

Binding model	Competitive	Mobile phase modifier	External function	Multi-state
Linear	✗	✗	✓	✗
Multi component Langmuir	✓	✗	✓	✗
Multi component Anti-Langmuir	✓	✗	✓	✗
Steric mass action	✓	✓	✓	✗
Self association	✓	✓	✓	✗
Mobile phase modulator Langmuir	✓	✓	✓	✗
Kumar-Langmuir	✓	✓	✓	✗
Saska	✗	✗	✓	✗
Multi component Bi-Langmuir	✓	✗	✓	✓
Bi steric mass action	✓	✓	✓	✓

Table 1.2.1: Supported features of the different binding models

Reference concentrations Some binding models use reference concentrations c_{ref} and q_{ref} of the mobile phase modulator (e.g., salt) in the particle liquid and solid phase, respectively. The reference values are mainly used for normalizing adsorption and desorption rates, but also for other parameters that appear with those concentrations. They amount to a simple parameter transformation that is exemplified at one equation of the steric mass action binding model

$$\frac{dq_i}{dt} = k_{a,i} c_{p,i} \bar{q}_0^{\nu_i} - k_{d,i} q_i c_{p,0}^{\nu_i},$$

where $c_{p,0}$ denotes the mobile phase salt concentration and

$$\bar{q}_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} (\nu_j + \sigma_j) q_j$$

is the number of available binding sites which is related to the number of bound salt ions. Using the parameter transformation

$$\begin{aligned} k_{a,i} &= \tilde{k}_{a,i} q_{\text{ref}}^{-\nu_i}, \\ k_{d,i} &= \tilde{k}_{d,i} c_{\text{ref}}^{-\nu_i}, \end{aligned}$$

we obtain the modified model equation

$$\frac{dq_i}{dt} = \tilde{k}_{a,i} c_{p,i} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{\nu_i} - \tilde{k}_{d,i} q_i \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{\nu_i}.$$

This transformation serves as a (partial) nondimensionalization of the adsorption and desorption rates and, by properly choosing the reference concentrations c_{ref} and q_{ref} , may improve the optimizer performance.

Recommended choices for c_{ref} are the average or maximum inlet concentration of the mobile phase modifier c_0 , and for q_{ref} the ionic capacity Λ . Note that setting the reference concentrations to 1.0 each results in the original binding model.

1.2.1 Linear

A linear binding model, which is often employed for low concentrations or in analytic settings [Gui+06].

$$\frac{dq_i}{dt} = k_{a,i} c_{p,i} - k_{d,i} q_i \quad i = 0, \dots, N_{\text{comp}} - 1.$$

See Table 2.5.12.

1.2.2 Multi Component Langmuir

The Langmuir binding model includes a saturation term and takes into account the capacity of the resin [Lan16; Gui+06]. All components compete for the same binding sites.

$$\frac{dq_i}{dt} = k_{a,i} c_{p,i} q_{\text{max},i} \left(1 - \sum_{j=0}^{N_{\text{comp}}-1} \frac{q_j}{q_{\text{max},j}} \right) - k_{d,i} q_i \quad i = 0, \dots, N_{\text{comp}} - 1.$$

See Table 2.5.13.

1.2.3 Multi Component Anti-Langmuir

The Anti-Langmuir (or generalized Langmuir) binding model extends the Langmuir model (see Section 1.2.2). The factor $p_j \in \{-1, 1\}$ determines the shape of the isotherm. For $p_j = 1$ (standard Langmuir) the chromatograms have sharp fronts and a dispersed tail (isotherm is concave). In case of the Anti-Langmuir ($p_j = -1$) it is the other way around (isotherm is convex).

$$\frac{dq_i}{dt} = k_{a,i} c_{p,i} q_{\text{max},i} \left(1 - \sum_{j=0}^{N_{\text{comp}}-1} p_j \frac{q_j}{q_{\text{max},j}} \right) - k_{d,i} q_i \quad i = 0, \dots, N_{\text{comp}} - 1.$$

See Table 2.5.14.

1.2.4 Steric Mass Action

The steric mass action model takes charges of the molecules into account [BC92] and is, thus, often used in ion-exchange chromatography. Each component has a characteristic charge ν that determines the number of available binding sites Λ (ionic capacity) used up by a molecule. Due to the molecule's shape, some additional binding sites (steric shielding factor σ) may be shielded from other molecules and are not available for binding.

$$\frac{dq_i}{dt} = k_{a,i} c_{p,i} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{\nu_i} - k_{d,i} q_i \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{\nu_i} \quad i = 1, \dots, N_{\text{comp}} - 1,$$

where $c_{p,0}$ and q_0 denote the salt concentrations in the liquid and solid phase of the beads, respectively. The number of free binding sites

$$\bar{q}_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} (\nu_j + \sigma_j) q_j = q_0 - \sum_{j=1}^{N_{\text{comp}}-1} \sigma_j q_j$$

is calculated from the number of bound counter ions q_0 by taking steric shielding into account. In turn, the number of bound counter ions q_0 (electro-neutrality condition) is given by

$$q_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} \nu_j q_j,$$

which also compensates for the missing equation for $\frac{dq_0}{dt}$. See Table 2.5.16.

The concept of reference concentrations (c_{ref} and q_{ref}) is explained in the respective paragraph in Section 1.2.

1.2.5 Self Association

This binding model is similar to the steric mass action model (see Section 1.2.4) but is also capable of describing dimerization [Mol08; Wes+12]. The dimerization, which is the immobilization of protein at some already bound protein, is also termed “self-association”. It is modeled by adding a quadratic (in $c_{p,i}$) term to the adsorption part of the equation.

$$\begin{aligned} \frac{dq_i}{dt} &= c_{p,i} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{\nu_i} [k_{a,i,1} + k_{a,i,2} c_{p,i}] - k_{d,i} q_i \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{\nu_i} & i = 1, \dots, N_{\text{comp}} - 1, \\ q_0 &= \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} \nu_j q_j, \end{aligned}$$

where the number of available binding sites is given by

$$\bar{q}_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} (\nu_j + \sigma_j) q_j = q_0 - \sum_{j=1}^{N_{\text{comp}}-1} \sigma_j q_j.$$

See Table 2.5.17.

The concept of reference concentrations (c_{ref} and q_{ref}) is explained in the respective paragraph in Section 1.2.

1.2.6 Mobile Phase Modulator Langmuir

This model is a modified Langmuir model (see Section 1.2.2) which can be used to describe hydrophobic interaction chromatography [MEH89; Kar+04]. A modulator component (termed “salt”, $c_{p,0}$ and q_0) influences ad- and desorption processes:

$$\frac{dq_i}{dt} = k_{a,i} e^{\gamma c_{p,0}} c_{p,i} q_{\text{max},i} \left(1 - \sum_{j=1}^{N_{\text{comp}}-1} \frac{q_j}{q_{\text{max},j}} \right) - k_{d,i} c_{p,0}^{\beta} q_i \quad i = 1, \dots, N_{\text{comp}} - 1.$$

where $c_{p,0}$ and q_0 denote the salt concentrations in the liquid and solid phase of the beads respectively. Salt is considered to be inert, therefore either

$$\frac{dq_0}{dt} = 0$$

is used if salt has one bound state, or salt can be used without a bound state. Parameter γ describes the hydrophobicity and β the ion-exchange characteristics. See Table 2.5.15.

1.2.7 Kumar-Langmuir

This extension of the Langmuir isotherm (see Section 1.2.2) developed in [Kum+15] was used to model charge variants of monoclonal antibodies in ion-exchange chromatography. A non-binding salt component $c_{p,0}$ is added to modulate the ad- and desorption process.

$$\frac{dq_i}{dt} = k_{a,i} \exp\left(\frac{k_{\text{act},i}}{T}\right) c_{p,i} q_{\text{max},i} \left(1 - \sum_{j=0}^{N_{\text{comp}}-1} \frac{q_j}{q_{\text{max},j}} \right) - k_{d,i} (c_{p,0})^{\nu_i} q_i \quad i = 1, \dots, N_{\text{comp}} - 1$$

In this model, the true adsorption rate $k_{a,i,\text{true}}$ is governed by the Arrhenius law in order to take temperature into account

$$k_{a,i,\text{true}} = k_{a,i} \exp\left(\frac{k_{\text{act},i}}{T}\right).$$

Here, $k_{a,i}$ is the frequency or pre-exponential factor, $k_{\text{act},i} = E/R$ is the activation temperature (E denotes the activation energy and R the Boltzmann gas constant), and T is the temperature. The characteristic charge ν of the protein is taken into account by the power law. See Table 2.5.20.

1.2.8 Saska

In this binding model an additional quadratic term is added to the linear model [Sas+92]. The quadratic term allows to take interactions of liquid phase components into account.

$$\frac{dq_i}{dt} = H_i c_{p,i} + \sum_{j=0}^{N_{\text{comp}}-1} k_{ij} c_{p,i} c_{p,j} - q_i \quad i = 0, \dots, N_{\text{comp}} - 1$$

See Table 2.5.18.

1.2.9 Multi Component Bi-Langmuir

The multi component Bi-Langmuir model [Gui+06] adds $M - 1$ *additional* types of binding sites $q_{i,j}$ ($0 \leq j \leq M - 1$) to the Langmuir model (see Section 1.2.2) without allowing an exchange between the different sites $q_{i,j}$ and $q_{i,k}$ ($k \neq j$). Therefore, there are no competitiveness effects between the different types of binding sites and they have independent capacities.

$$\frac{dq_{i,j}}{dt} = k_{a,i}^{(j)} c_{p,i} q_{\text{max},i}^{(j)} \left(1 - \sum_{k=0}^{N_{\text{comp}}-1} \frac{q_{k,j}}{q_{\text{max},k}^{(j)}}\right) - k_{d,i}^{(j)} q_{i,j} \quad i = 0, \dots, N_{\text{comp}} - 1, j = 0, \dots, M - 1.$$

Note that all binding components must have exactly the same number of binding site types $M \geq 1$. See the Langmuir isotherm in Section 1.2.2 and Table 2.5.19.

Originally, the Bi-Langmuir model is limited to two different binding site types. Here, the model has been extended to arbitrary many binding site types.

1.2.10 Bi Steric Mass Action

Similar to the Bi-Langmuir model (see Section 1.2.9), the Bi-SMA model adds $M - 1$ *additional* types of binding sites $q_{i,j}$ ($0 \leq j \leq M - 1$) to the SMA model (see Section 1.2.4) without allowing an exchange between the different sites $q_{i,j}$ and $q_{i,k}$ ($k \neq j$). Therefore, there are no competitiveness effects between the two types of binding sites and they have independent capacities.

$$\frac{dq_{i,j}}{dt} = k_{a,i,j} c_{p,i} \left(\frac{\bar{q}_{0,j}}{q_{\text{ref},j}}\right)^{\nu_{i,j}} - k_{d,i,j} q_{i,j} \left(\frac{c_{p,0}}{c_{\text{ref},j}}\right)^{\nu_{i,j}} \quad i = 1, \dots, N_{\text{comp}} - 1, j = 0, \dots, M - 1,$$

where $c_{p,0}$ and $q_{0,j}$ ($0 \leq j \leq M - 1$) denote the salt concentrations in the liquid and solid phases of the beads respectively. The number of available salt ions $\bar{q}_{0,j}$ for each binding site type $0 \leq j \leq M - 1$ is given by

$$\bar{q}_{0,j} = \Lambda_j - \sum_{k=1}^{N_{\text{comp}}-1} (\nu_{k,j} + \sigma_{k,j}) q_{k,j}.$$

Electro-neutrality conditions compensating for the missing equations for $\frac{dq_{0,j}}{dt}$ are required:

$$q_{0,j} = \Lambda_j - \sum_{k=1}^{N_{\text{comp}}-1} \nu_{k,j} q_{k,j} \quad j = 0, \dots, M-1.$$

Note that all binding components must have exactly the same number of binding site types $M \geq 1$. See Table 2.5.21.

The reference concentrations $c_{\text{ref},j}$ and $q_{\text{ref},j}$ can be specified for each binding site type $0 \leq j \leq M-1$. The concept of reference concentrations is explained in the respective paragraph in Section 1.2.

Originally, the Bi-SMA model is limited to two different binding site types. Here, the model has been extended to arbitrary many binding site types.

2 CADET File Format Specifications

The CADET framework is designed to work on a file format structured into groups and datasets. This concept may be implemented by different file formats. At the moment, CADET natively supports HDF5 and XML as file formats. The choice is not limited to those two formats but can be extended as needed. In this section the general layout and structure of the file format is described.

2.1 Global structure

The global structure (see Fig. 2.1.1) is divided into three parts: **input**, **output**, and **meta**. Every valid CADET file needs an **input** group (see Fig. 2.1.2) which contains all relevant information for simulating a model. It does not need an **output** (see Fig. 2.1.4) or **meta** (see Fig. 2.1.1) group, since those are created when results are written. Whereas the **output** group is solely used as output and holds the results of the simulation, the **meta** group is used for input and output. Details such as file format version and simulator version are read from and written to the **meta** group.

If not explicitly stated otherwise, all datasets are mandatory. By convention all group names are lowercase, whereas all dataset names are uppercase. Note that this is just a description of the file format and not a detailed explanation of the meaning of the parameters. For the latter, please refer to the corresponding sections in the previous chapter.

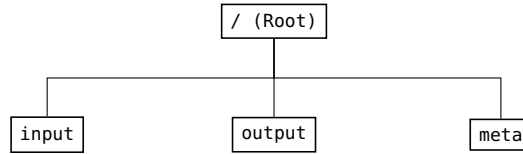


Figure 2.1.1: Structure of the groups in the root group of the file format

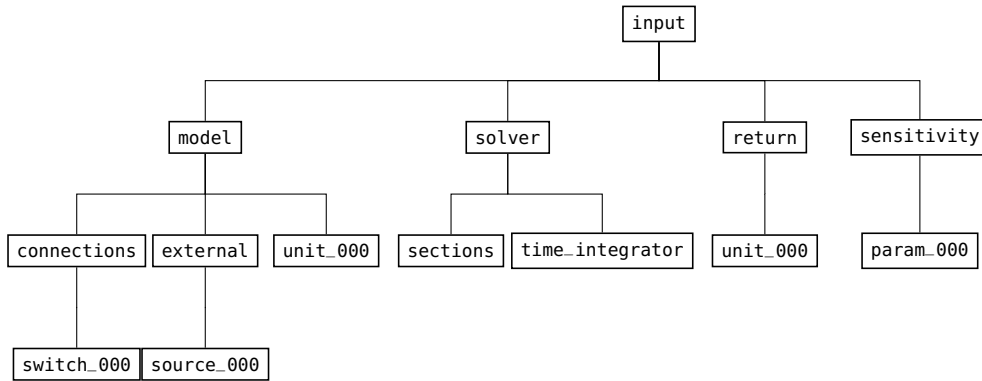


Figure 2.1.2: High-level structure of the groups in the input part of the file format

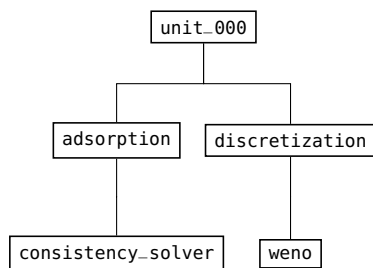


Figure 2.1.3: Structure of the groups in a column unit operation (/input/model group)

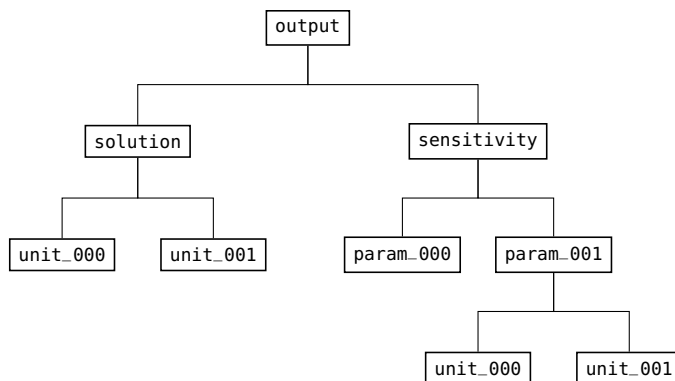


Figure 2.1.4: Structure of the groups in the output part of the file format

2.2 Notation and identifiers

Reference volumes are denoted by subscripts:

m_{IV}^3 Interstitial volume

m_{MP}^3 Bead mobile phase volume

m_{SP}^3 Bead solid phase volume

Common notation and identifiers that are used in the subsequent description are listed in Table 2.2.1.

Identifier	Meaning
NCOMP	Number of components of a unit operation
NTOTALCOMP	Total number of components in the system (sum of all unit operation components)
NBND _i	Number of bound states of component <i>i</i> of a unit operation
NTOTALBND	Total number of bound states of a unit operation (sum of all bound states of all components)
NSTATES	Maximum of the number of bound states for each component of a unit operation
NDOF	Total number of degrees of freedom of the current unit operation model or system of unit operations
NSEC	Number of time integration sections
PARAM_VALUE	Value of a generic unspecified parameter

Table 2.2.1: Common notation and identifiers used in the file format description

2.3 Ordering of multi dimensional data

Some model parameters, especially in certain binding models, require multi dimensional data. Since CADET only reads one dimensional arrays, the layout of the data has to be specified (i.e., the way how

the data is linearized in memory). The term “*xyz-major*” means that the index corresponding to *xyz* changes the slowest.

For instance, suppose a model with 2 components and 3 bound states has a “component-major” dataset. Then, the requested matrix is stored in memory such that all bound states are listed for each component (i.e., the component index changes the slowest and the bound state index the fastest):

`comp0bnd0, comp0bnd1, comp0bnd2, comp1bnd0, comp1bnd1, comp1bnd2.`

This linear array can be represented as a 2×3 matrix in “row-major” storage format, or a 3×2 matrix in “column-major” ordering.

2.4 Section dependent model parameters

Some model parameters (see Table 2.4.1) can be assigned different values for each section. For example, the velocity a column is operated with could differ in the load, wash, and elution phases. Section dependency is recognized by specifying the appropriate number of values for the parameters (see *Length* column in the following tables). If a parameter depends on both the component and the section, the ordering is section-major.

For instance, the *Length* field of the parameter **VELOCITY** reads “1 / NSEC” which means that it is not recognized as section dependent if only 1 value (scalar) is passed. However, if NSEC many values (vector) are present, it will be treated as section dependent.

Note that all components of component dependent datasets have to be section dependent (e.g., you cannot have a section dependency on component 2 only while the other components are not section dependent).

Dataset	Component dependent	Section dependent
COL_DISPERSION		✓
FILM_DIFFUSION	✓	✓
PAR_DIFFUSION	✓	✓
PAR_SURFDIFFUSION	✓	✓
VELOCITY		✓

Table 2.4.1: Section dependent datasets in the unit operation models (*/input/model/unit_XXX* group)

2.5 Input group

2.5.1 System of unit operations

Dataset	Group <i>/input/model</i> Description	Unit	Type	Range	Length
NUNITS	Number of unit operations in the system	–	int	≥ 1	1
INIT_STATE_Y	Initial full state vector (optional, unit operation specific initial data is ignored)	–	double	≥ 0	NDOF
INIT_STATE_YDOT	Initial full time derivative state vector (optional, unit operation specific initial data is ignored)	–	double	≥ 0	NDOF
INIT_STATE_SENSY_XXX	Initial full state vector of the XXXth sensitivity system (optional, unit operation specific initial data is ignored)	–	double	≥ 0	NDOF
INIT_STATE_SENSYDOT_XXX	Initial full time derivative state vector of the XXXth sensitivity system (optional, unit operation specific initial data is ignored)	–	double	≥ 0	NDOF

Table 2.5.1: Datasets in the */input/model/* group

Dataset	Group /input/model/connections Description	Unit	Type	Range	Length
NSWITCHES	Number of valve switches	–	int	≥ 1	1

Table 2.5.2: *Datasets in the /input/model/connections group*

Dataset	Group /input/model/connections/switch_XXX Description	Unit	Type	Range	Length
SECTION	Index of the section which activates this connection set	–	int	≥ 0	1
CONNECTIONS	Matrix with list of connections in row-major storage. Columns are <i>UnitOpID from</i> , <i>UnitOpID to</i> , <i>Component from</i> , <i>Component to</i> . If the last two entries are -1 , all components are connected.	–	int	≥ -1	$\text{NCONNECTIONS} \times 4$

Table 2.5.3: *Datasets in the /input/model/connections/switch_XXX group*

Dataset	EXTFUN_TYPE = LINEAR_INTERP_DATA – Group /input/model/external/source_XXX Description	Unit	Type	Range	Length
VELOCITY	Velocity of the external profile in positive column axial direction	s^{-1}	double	≥ 0	1
DATA	Function values T at the data points	[T]	double	\mathbb{R}	Arbitrary
TIME	Time of the data points	s	double	≥ 0.0	Same as DATA

Table 2.5.4: *Datasets in the /input/model/external/source_XXX group*

Dataset	EXTFUN_TYPE = PIECEWISE_CUBIC_POLY – Group /input/model/external/source_XXX Description	Unit	Type	Range	Length
VELOCITY	Velocity of the external profile in positive column axial direction	s^{-1}	double	≥ 0	1
CONST_COEFF	Constant coefficients of piecewise cubic polynomial	[T]	double	\mathbb{R}	Arbitrary
LIN_COEFF	Linear coefficients of piecewise cubic polynomial	[T] s^{-1}	double	\mathbb{R}	Same as CONST_COEFF
QUAD_COEFF	Quadratic coefficients of piecewise cubic polynomial	[T] s^{-2}	double	\mathbb{R}	Same as CONST_COEFF
CUBE_COEFF	Cubic coefficients of piecewise cubic polynomial	[T] s^{-3}	double	\mathbb{R}	Same as CONST_COEFF
SECTION_TIMES	Simulation times at which a new piece begins (breaks of the piecewise polynomial)	s	double	≥ 0.0	CONST_COEFF+1

Table 2.5.5: *Datasets in the /input/model/external/source_XXX group*

2.5.2 Unit operation models

Inlet

Dataset	UNIT_TYPE = INLET – Group /input/model/unit_XXX Description	Unit	Type	Range	Length
UNIT_TYPE	Specifies the type of unit operation model	–	string	INLET	1
NCOMP	Number of chemical components in the chromatographic media	–	int	≥ 1	1
INLET_TYPE	Specifies the type of inlet profile	–	string	PIECEWISE_CUBIC_POLY	1

Table 2.5.6: *Datasets for the inlet unit operation (/input/model/unit_XXX group)*

Dataset	Group /input/model/unit_XXX/sec_XXX Description	Unit	Type	Range	Length
CONST_COEFF	Constant coefficients for inlet concentrations	$\text{mol m}_{\text{IV}}^{-3}$	double	\mathbb{R}	NCOMP
LIN_COEFF	Linear coefficients for inlet concentrations	$\text{mol m}_{\text{IV}}^{-3} \text{s}^{-1}$	double	\mathbb{R}	NCOMP
QUAD_COEFF	Quadratic coefficients for inlet concentrations	$\text{mol m}_{\text{IV}}^{-3} \text{s}^{-2}$	double	\mathbb{R}	NCOMP
CUBE_COEFF	Cubic coefficients for inlet concentrations	$\text{mol m}_{\text{IV}}^{-3} \text{s}^{-3}$	double	\mathbb{R}	NCOMP

Table 2.5.7: *Datasets in the /input/model/unit_XXX/sec_XXX groups*

General rate model

Dataset	UNIT_TYPE = GENERAL_RATE_MODEL – Group /input/model/unit_XXX Description	Unit	Type	Range	Length
UNIT_TYPE	Specifies the type of unit operation model	–	string	GENERAL_RATE_MODEL	1
NCOMP	Number of chemical components in the chromatographic media	–	int	≥ 1	1
ADSORPTION_MODEL	Specifies the type of adsorption model	–	string	See Section 2.5.4	1
INIT_C	Initial concentrations for each comp. in the bulk mobile phase	$\text{mol m}_{\text{IV}}^{-3}$	double	≥ 0.0	NCOMP
INIT_CP	Initial concentrations for each comp. in the bead liquid phase (optional, INIT_C is used if left out)	$\text{mol m}_{\text{MP}}^{-3}$	double	≥ 0.0	NCOMP
INIT_Q	Same as INIT_C but for the bound phase	$\text{mol m}_{\text{SP}}^{-3}$	double	≥ 0.0	NTOTALBND
INIT_STATE	Full state vector for initialization (optional, INIT_C, INIT_CP, and INIT_Q will be ignored; if length is $2 * \text{NDOF}$, then the second half is used for time derivatives)	various	double	–	NDOF
COL_DISPERSION	Axial dispersion coefficient	$\text{m}_{\text{IV}}^2 \text{s}^{-1}$	double	≥ 0.0	1 / NSEC
COL_LENGTH	Column length	m	double	> 0.0	1
COL_POROSITY	Column porosity	–	double	≥ 0.0	1
FILM_DIFFUSION	Film diffusion coefficients	m s^{-1}	double	≥ 0.0	NCOMP / NCOMP \times NSEC
PAR_DIFFUSION	Effective particle diffusion coefficients	$\text{m}_{\text{MP}}^2 \text{s}^{-1}$	double	≥ 0.0	NCOMP / NCOMP \times NSEC
PAR_POROSITY	Particle porosity	–	double	> 0.0	1
PAR_RADIUS	Particle radius	m	double	> 0.0	1
PAR_SURFDIFFUSION	Particle surface diffusion coefficients	$\text{m}_{\text{SP}}^2 \text{s}^{-1}$	double	≥ 0.0	NTOTALBND / NTOTALBND \times NSEC
VELOCITY	Interstitial velocity of the mobile phase	m s^{-1}	double	> 0.0	1 / NSEC

Table 2.5.8: Datasets for the general rate model unit operation (/input/model/unit_XXX group)

UNIT_TYPE = GENERAL_RATE_MODEL – Group /input/model/unit_XXX/discretization					
Dataset	Description	Unit	Type	Range	Length
NCOL	Number of column (axial) discretization cells	–	int	≥ 1	1
NPAR	Number of particle (radial) discretization cells	–	int	≥ 1	1
NBOUND	Number of bound states for each component	–	int	≥ 0	NCOMP
PAR_DISC_TYPE	Specifies the discretization scheme inside the particles	–	string	EQUIDISTANT_PAR EQUIVOLUME_PAR USER_DEFINED_PAR	1
PAR_DISC_VECTOR	Node coordinates for the cell boundaries (ignored if PAR_DISC_TYPE \neq USER_DEFINED_PAR)	m	double	[0, 1]	NPAR+1
USE_ANALYTIC_JACOBIAN	Use analytically computed jacobian matrix (faster) instead of jacobian generated by algorithmic differentiation (slower)	–	int	0/1	1
RECONSTRUCTION	Type of reconstruction method for fluxes	–	string	WENO	1
GS_TYPE	Type of Gram-Schmidt orthogonalization, see IDAS guide 4.5.7.3, 41f.	–	int	0 (CLASSICAL_GS) 1 (MODIFIED_GS)	1
MAX_KRYLOV	Defines the size of the Krylov subspace in the iterative linear SPGMR solver (0: MAX_KRYLOV = NCOL)	–	int	0 – NCOL	1
MAX_RESTARTS	Maximum number of restarts in the GMRES algorithm. If lack of memory isn't an issue, better use a larger Krylov space than restarts	–	int	≥ 0	1
SCHUR_SAFETY	Schur safety factor; Influences the tradeof between linear iterations and nonlinear error control; see IDAS guide 2.1, 5	–	double	≥ 0.0	1

Table 2.5.9: *Datasets for the discretization of the general rate model unit operation (/input/model/unit_XXX/discretization group)*

2.5.3 Flux reconstruction methods

Dataset	WENO parameters – Group /input/model/unit_XXX/discretization/weno	Description	Type	Range
BOUNDARY_MODEL	Boundary model type: 0 = Lower WENO order (stable), 1 = Zero weights (unstable for small D_{ax}), 2 = Zero weights for $p \neq 0$ (stable?), 3 = Large ghost points		int	0 – 3
WENO_EPS	WENO ε		double	≥ 0.0
WENO_ORDER	WENO Order: 1 = standard upwind scheme, 2, 3; also called WENO K		int	1 – 3

Table 2.5.10: *Datasets for the WENO reconstruction (/input/model/unit_XXX/discretization/weno group)*

2.5.4 Adsorption models

Externally dependent binding models Some binding models have a variant that can use external sources as specified in Section 2.5.1 (also see Section 1.2 and Table 1.2.1 on which binding models support this feature). For the sake of brevity, only the standard variant of those binding models is specified below. In order to obtain the format for the externally dependent variant, first replace the binding model name XXX by EXT_XXX. Each parameter p (except for reference concentrations XXX_REFC0 and XXX_REFQ) depends on a (possibly distinct) external source in a polynomial way:

$$p(T) = p_{\text{TTT}}T^3 + p_{\text{TT}}T^2 + p_{\text{T}}T + p.$$

Thus, a parameter XXX_YYY of the standard binding model variant is replaced by the four parameters EXT_XXX_YYY, EXT_XXX_YYY_T, EXT_XXX_YYY_TT, and EXT_XXX_YYY_TTT. Since each parameter can depend on a different external source, the dataset EXTFUN (not listed in the standard variants below) should contain a vector of 0-based integer indices of the external source of each parameter. The ordering of the parameters in EXTFUN is given by the ordering in the standard variant. However, if only one index is passed in EXTFUN, this external source is used for all parameters.

Dataset	Nonlinear consistency solver parameters – Group /input/model/unit_XXX/adsorption/consistency_solver	Description	Type	Range	Length
SOLVER_NAME	Name of the solver		string	LEVMAR ATRN_RES ATRN_ERR COMPOSITE	1
INIT_DAMPING	Initial damping factor (default is 0.01)		double	≥ 0.0	1
MIN_DAMPING	Minimal damping factor (default is 0.0001; ignored by LEVMAR)		double	≥ 0.0	1
MAX_ITERATIONS	Maximum number of iterations (default is 50)		int	> 0	1
SUBSOLVERS	Vector with names of solvers for the composite solver (only required for composite solver)		string	see SOLVER_NAME	> 1

Table 2.5.11: *Datasets for the nonlinear consistency solver (/input/model/unit_XXX/adsorption/consistency_solver group)*

Dataset	ADSORPTION_MODEL = LINEAR – Group /input/model/unit_XXX/adsorption	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary		–	int	0/1	1
LIN_KA	Adsorption rate constants		$\text{m}_{\text{MP}}^3 \text{m}_{\text{SP}}^{-3} \text{s}^{-1}$	double	≥ 0.0	NCOMP
LIN_KD	Desorption rate constants		s^{-1}	double	≥ 0.0	NCOMP

Table 2.5.12: *Datasets for the linear adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = MULTI_COMPONENT_LANGMUIR – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
MCL_KA	Adsorption rate constants	$m_{MP}^3 \text{ mol}^{-1} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
MCL_KD	Desorption rate constants	s^{-1}	double	≥ 0.0	NCOMP
MCL_QMAX	Maximum adsorption capacities	$\text{mol } m_{SP}^{-3}$	double	> 0.0	NCOMP

Table 2.5.13: *Datasets for the multi component Langmuir adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = MULTI_COMPONENT_ANTILANGMUIR – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
MCAL_KA	Adsorption rate constants	$m_{MP}^3 \text{ mol}^{-1} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
MCAL_KD	Desorption rate constants	s^{-1}	double	≥ 0.0	NCOMP
MCAL_QMAX	Maximum adsorption capacities	$\text{mol } m_{SP}^{-3}$	double	> 0.0	NCOMP
MCAL_ANTILANGMUIR	Anti-Langmuir coefficients (optional)	–	double	$\{-1, 1\}$	NCOMP

Table 2.5.14: *Datasets for the multi component Anti-Langmuir adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = MOBILE_PHASE_MODULATOR – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
MPM_KA	Adsorption rate constants	$m_{MP}^3 \text{ mol}^{-1} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
MPM_KD	Desorption rate constants	$m_{MP}^{3\beta} \text{ mol}^{-\beta} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
MPM_QMAX	Maximum adsorption capacities	$\text{mol } m_{SP}^{-3}$	double	≥ 0.0	NCOMP
MPM_BETA	Parameters describing the ion-exchange characteristics (IEX)	–	double	≥ 0.0	NCOMP
MPM_GAMMA	Parameters describing the hydrophobicity (HIC)	$m_{MP}^3 \text{ mol}^{-1}$	double	≥ 0.0	NCOMP

Table 2.5.15: *Datasets for the mobile phase modulator adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = STERIC_MASS_ACTION – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
SMA_KA	Adsorption rate constants	$m_{MP}^3 m_{SP}^{-3} s^{-1}$	double	≥ 0.0	NCOMP
SMA_KD	Desorption rate constants	s^{-1}	double	≥ 0.0	NCOMP
SMA_NU	Characteristic charges of the protein; The number of sites ν that the protein interacts with on the resin surface	–	double	≥ 0.0	NCOMP
SMA_SIGMA	Steric factors of the protein; The number of sites σ on the surface that are shielded by the protein and prevented from exchange with the salt counterions in solution	–	double	≥ 0.0	NCOMP
SMA_LAMBDA	Stationary phase capacity (monovalent salt counterions); The total number of binding sites available on the resin surface	$mol m_{SP}^{-3}$	double	≥ 0.0	1
SMA_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$mol m_{MP}^{-3}$	double	> 0.0	1
SMA_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$mol m_{SP}^{-3}$	double	> 0.0	1

Table 2.5.16: Datasets for the steric mass action adsorption model (/input/model/unit_XXX/adsorption group)

ADSORPTION_MODEL = SELF_ASSOCIATION – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
SAI_KA1	Adsorption rate constants	$m_{MP}^3 m_{SP}^{-3} s^{-1}$	double	≥ 0.0	NCOMP
SAI_KA2	Adsorption rate constants of dimerization	$m_{MP}^6 m_{SP}^{-6} s^{-1}$	double	≥ 0.0	NCOMP
SAI_KD	desorption rate constants	s^{-1}	double	≥ 0.0	NCOMP
SAI_NU	Characteristic charges ν of the protein	–	double	≥ 0.0	NCOMP
SAI_SIGMA	Steric factors σ of the protein	–	double	≥ 0.0	NCOMP
SAI_LAMBDA	Stationary phase capacity (monovalent salt counterions); The total number of binding sites available on the resin surface	$mol m_{SP}^{-3}$	double	≥ 0.0	1
SAI_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$mol m_{MP}^{-3}$	double	> 0.0	1
SAI_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$mol m_{SP}^{-3}$	double	> 0.0	1

Table 2.5.17: Datasets for the self association adsorption model (/input/model/unit_XXX/adsorption group)

ADSORPTION_MODEL = SASKA – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
SASKA_H	Henry coefficient	$m_{MP}^3 m_{SP}^{-3} s^{-1}$	double	\mathbb{R}	NCOMP
SASKA_K	Quadratic factors	$m_{MP}^6 m_{SP}^{-3} mol^{-1} s^{-1}$	double	\mathbb{R}	NCOMP ²

Table 2.5.18: Datasets for the Saska adsorption model (/input/model/unit_XXX/adsorption group)

ADSORPTION_MODEL = MULTI_COMPONENT_BILANGMUIR – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
MCBL_KA	Adsorption rate constants in state-major ordering	$m_{MP}^3 \text{ mol}^{-1} \text{ s}^{-1}$	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
MCBL_KD	Desorption rate constants in state-major ordering	s^{-1}	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
MCBL_QMAX	Maximum adsorption capacities in state-major ordering	mol m_{SP}^{-3}	double	> 0.0	$\text{NSTATES} \cdot \text{NCOMP}$

Table 2.5.19: Datasets for the Bi-Langmuir adsorption model (/input/model/unit_XXX/adsorption group)

ADSORPTION_MODEL = KUMAR_MULTI_COMPONENT_LANGMUIR – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
KMCL_KA	Adsorption pre-exponential factors	$m_{MP}^3 \text{ mol}^{-1} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
KMCL_KD	Desorption rate	$m_{MP}^{3\nu_i} \text{ mol}^{-\nu_i} \text{ s}^{-1}$	double	≥ 0.0	NCOMP
KMCL_KACT	Activation temperatures	K	double	≥ 0.0	NCOMP
KMCL_QMAX	Maximum adsorption capacities	mol m_{SP}^{-3}	double	> 0.0	NCOMP
KMCL_NU	Salt exponents / characteristic charges	–	double	> 0.0	NCOMP
KMCL_TEMP	Temperature	K	double	≥ 0	1

Table 2.5.20: Datasets for the Kumar-Langmuir adsorption model (/input/model/unit_XXX/adsorption group)

ADSORPTION_MODEL = BI_STERIC_MASS_ACTION – Group /input/model/unit_XXX/adsorption					
Dataset	Description	Unit	Type	Range	Length
IS_KINETIC	Selects kinetic or quasi-stationary adsorption mode: 1 = kinetic, 0 = quasi-stationary	–	int	0/1	1
BISMA_KA	Adsorption rate constants in state-major ordering	$m_{MP}^3 m_{SP}^{-3} \text{ s}^{-1}$	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
BISMA_KD	Desorption rate constants in state-major ordering	s^{-1}	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
BISMA_NU	Characteristic charges $\nu_{i,j}$ of the i th protein with respect to the j th binding site type in state-major ordering	–	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
BISMA_SIGMA	Steric factors $\sigma_{i,j}$ of the i th protein with respect to the j th binding site type in state-major ordering	–	double	≥ 0.0	$\text{NSTATES} \cdot \text{NCOMP}$
BISMA_LAMBDA	Stationary phase capacity (monovalent salt counterions) of the different binding site types λ_j	mol m_{SP}^{-3}	double	≥ 0.0	NSTATES
BISMA_REFC0	Reference liquid phase concentration for each binding site type or one value for all types (optional, defaults to 1.0)	mol m_{MP}^{-3}	double	> 0.0	$1/\text{NSTATES}$
BISMA_REFQ	Reference solid phase concentration for each binding site type or one value for all types (optional, defaults to 1.0)	mol m_{SP}^{-3}	double	> 0.0	$1/\text{NSTATES}$

Table 2.5.21: Datasets for the bi steric mass action adsorption model (/input/model/unit_XXX/adsorption group)

2.5.5 Return data

Dataset	Group /input/return Description	Type	Range
WRITE_SOLUTION_TIMES	Write times at which a solution was produced (optional, defaults to 1)	int	0/1
WRITE_SOLUTION_LAST	Write full solution state vector at last time point (optional, defaults to 0)	int	0/1
WRITE_SENS_LAST	Write full sensitivity state vectors at last time point (optional, defaults to 0)	int	0/1
SPLIT_COMPONENTS_DATA	Determines whether a joint dataset (matrix) for all components is created or if each component is put in a separate dataset (XXX_COMP_000, XXX_COMP_001, etc.) (optional, defaults to 1)	int	0/1

Table 2.5.22: *Datasets in the /input/model/return group*

Dataset	Group /input/return/unit_XXX Description	Type	Range
WRITE_SOLUTION_COLUMN_INLET	Write solutions at column inlet $c_i(t, 0)$	int	0/1
WRITE_SOLUTION_COLUMN_OUTLET	Write solutions at column outlet (chromatograms) $c_i(t, L)$	int	0/1
WRITE_SOLUTION_COLUMN	Write solutions of the column bulk volume c_i	int	0/1
WRITE_SOLUTION_PARTICLE	Write solutions of the particle phases $c_{p,i}$, $q_{i,j}$	int	0/1
WRITE_SOLUTION_FLUX	Write solutions of the bead fluxes $j_{f,i}$	int	0/1
WRITE_SOLDOT_COLUMN_INLET	Write solution time derivatives at column inlet $\partial c_i(t, 0)/\partial t$	int	0/1
WRITE_SOLDOT_COLUMN_OUTLET	Write solution time derivatives at column outlet (chromatograms) $\partial c_i(t, L)/\partial t$	int	0/1
WRITE_SOLDOT_COLUMN	Write solution time derivatives of the column bulk volume $\partial c_i/\partial t$	int	0/1
WRITE_SOLDOT_PARTICLE	Write solution time derivatives of the particle phases $\partial c_{p,i}/\partial t$, $\partial q_{i,j}/\partial t$	int	0/1
WRITE_SOLDOT_FLUX	Write solution time derivatives of the bead fluxes $\partial j_{f,i}/\partial t$	int	0/1
WRITE_SENS_COLUMN_INLET	Write sensitivities at column inlet $\partial c_i(t, 0)/\partial p$	int	0/1
WRITE_SENS_COLUMN_OUTLET	Write sensitivities at column outlet (chromatograms) $\partial c_i(t, L)/\partial p$	int	0/1
WRITE_SENS_COLUMN	Write sensitivities of the column bulk volume $\partial c_i/\partial p$	int	0/1
WRITE_SENS_PARTICLE	Write sensitivities of the particle phases $\partial c_{p,i}/\partial p$, $\partial q_{i,j}/\partial p$	int	0/1
WRITE_SENS_FLUX	Write sensitivities of the bead fluxes $\partial j_{f,i}/\partial p$	int	0/1
WRITE_SENSDOT_COLUMN_INLET	Write sensitivity time derivatives at column inlet $\partial^2 c_i(t, 0)/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_COLUMN_OUTLET	Write sensitivity time derivatives at column outlet (chromatograms) $\partial^2 c_i(t, L)/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_COLUMN	Write sensitivity time derivatives of the column bulk volume $\partial^2 c_i/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_PARTICLE	Write sensitivity time derivatives of the particle phases $\partial^2 c_{p,i}/(\partial p, \partial t)$, $\partial^2 q_{i,j}/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_FLUX	Write sensitivity time derivatives of the bead fluxes $\partial^2 j_{f,i}/(\partial p, \partial t)$	int	0/1

Table 2.5.23: *Datasets in the /input/model/return/unit_XXX group*

2.5.6 Parameter sensitivities

Dataset	Group /input/sensitivity Description	Type	Range
NSENS	Number of sensitivities to be computed	int	≥ 0
SENS_METHOD	Method used for computation of sensitivities (algorithmic differentiation)	string	ad1

Table 2.5.24: *Datasets in the /input/sensitivity group*

Dataset	Group /input/sensitivity/param_XXX Description	Type	Range	Length
SENS_UNIT	Unit operation index	int	≥ 0	≥ 1
SENS_NAME	Name of the parameter	string	*1	≥ 1
SENS_COMP	Component index (−1 if parameter is independent of components)	int	≥ -1	≥ 1
SENS_REACTION	Reaction index (−1 if parameter is independent of reactions)	int	≥ -1	≥ 1
SENS_BOUNDPHASE	Bound phase index (−1 if parameter is independent of bound phases)	int	≥ -1	≥ 1
SENS_SECTION	Section index (−1 if parameter is independent of sections)	int	≥ -1	≥ 1
SENS_ABSTOL	Absolute tolerance used in the computation of the sensitivities (optional). Rule of thumb: $ABSTOL / PARAM_VALUE$	double	≥ 0.0	≥ 1
SENS_FACTOR	Linear factor of the combined sensitivity (optional, taken as 1.0 if left out)	double	\mathbb{R}	≥ 1

Table 2.5.25: *Datasets in the /input/sensitivity/param_XXX groups*

2.5.7 Solver configuration

Dataset	Group /input/solver Description	Unit	Type	Range	Length
NTHREADS	Number of used OpenMP threads	–	int	≥ 1	1
USER_SOLUTION_TIMES	Vector with timepoints at which a solution is desired	s	double	≥ 0.0	Arbitrary
CONSISTENT_INIT_MODE	Consistent initialization mode (optional, defaults to 1)	–	int	0 (none) 1 (full) 2 (once, full) 3 (lean) 4 (once, lean)	1
CONSISTENT_INIT_MODE_SENS	Consistent initialization mode (optional, defaults to 1)	–	int	0 (none) 1 (full) 2 (once, full) 3 (lean) 4 (once, lean)	1

Table 2.5.26: *Datasets in the /input/solver group*

Dataset	Group /input/solver/time_integrator Description	Type	Range	Length
ABSTOL	Absolute tolerance in the solution of the original system	double	> 0.0	1
ALGTOL	Tolerance in the solution of the nonlinear consistency equations	double	> 0.0	1
RELTOL	Relative tolerance in the solution of the original system	double	≥ 0.0	1
RELTOL_SENS	Relative tolerance in the solution of the sensitivity systems	double	≥ 0.0	1 / NSENS
INIT_STEP_SIZE	Initial time integrator step size for each section or one value for all sections (0.0: IDAS default value), see IDAS guide 4.5, 36f.	double	≥ 0.0	1 / NSEC
MAX_STEPS	Maximum number of timesteps taken by IDAS (0: IDAS default = 500), see IDAS guide 4.5, 36	int	≥ 0	1

Table 2.5.27: *Datasets in the /input/solver/time_integrator group*

Dataset	Group /input/solver/sections Description	Unit	Type	Range	Length
NSEC	Number of sections	–	int	≥ 1	1
SECTION_TIMES	Simulation times at which the model changes or behaves discontinuously; including start and end times	s	double	≥ 0.0	NSEC+1
SECTION_CONTINUITY	Continuity indicator for each section transition	–	int	0 (discontinuous) 1 (continuous)	NSEC-1

Table 2.5.28: *Datasets in the /input/solver/sections group*

2.6 Output group

Dataset	Group /output/solution Description	Unit	Type
LAST_STATE_Y	Full state vector at the last time point of the time integrator	–	double
LAST_STATE_YDOT	Full time derivative state vector at the last time point of the time integrator	–	double
LAST_STATE_SENSY_XXX	Full state vector of the XXXth sensitivity system at the last time point of the time integrator	–	double
LAST_STATE_SENSYDOT_XXX	Full time derivative state vector of the XXXth sensitivity system at the last time point of the time integrator	–	double

Table 2.6.1: *Datasets in the /output group*

Dataset	Group /output/solution Description	Unit	Type
SOLUTION_TIMES	Time points at which the solution is written	s	double

Table 2.6.2: *Datasets in the /output/solution group*

Dataset	Group /output/solution/unit_XXX Description	Unit	Type
SOLUTION_COLUMN	Interstitial solution as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLUTION_PARTICLE	Solution inside the beads as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{MP\&SP}}^{-3}$	double
SOLUTION_FLUX	Flux solution as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}^{-2} \text{s}^{-1}$	double
SOLUTION_COLUMN_OUTLET	Matrix of solutions at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLUTION_COLUMN_INLET	Matrix of solutions at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLUTION_COLUMN_OUTLET_COMP_XXX	Component XXX of the solution at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLUTION_COLUMN_INLET_COMP_XXX	Component XXX of the solution at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLDOT_COLUMN	Interstitial solution time derivative as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLDOT_PARTICLE	Solution time derivative inside the beads as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{MP\&SP}}^{-3}$	double
SOLDOT_FLUX	Flux solution time derivative as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}^{-2} \text{s}^{-1}$	double
SOLDOT_COLUMN_OUTLET	Matrix of solution time derivatives at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLDOT_COLUMN_INLET	Matrix of solution time derivatives at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLDOT_COLUMN_OUTLET_COMP_XXX	Component XXX of the solution time derivative at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SOLDOT_COLUMN_INLET_COMP_XXX	Component XXX of the solution time derivative at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double

Table 2.6.3: *Datasets in the /output/solution/unit_XXX group*

Dataset	Group /output/sensitivity/param_XXX/unit_YYY Description	Unit	Type
SENS_COLUMN	Interstitial sensitivity as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{IV}}^{-3}$	double
SENS_PARTICLE	Sensitivity inside the beads as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{MP\&SP}}^{-3}$	double
SENS_FLUX	Flux sensitivity as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}^{-2} \text{s}^{-1}$	double
SENS_COLUMN_OUTLET	Matrix of sensitivities at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENS_COLUMN_INLET	Matrix of sensitivities at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENS_COLUMN_OUTLET_COMP_XXX	Component XXX of the sensitivity at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENS_COLUMN_INLET_COMP_XXX	Component XXX of the sensitivity at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENSDOT_COLUMN	Interstitial sensitivity time derivative as $n_{\text{Time}} \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{IV}}^{-3}$	double
SENSDOT_PARTICLE	Sensitivity time derivative inside the beads as $n_{\text{Time}} \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}_{\text{MP\&SP}}^{-3}$	double
SENSDOT_FLUX	Flux sensitivity time derivative as $n_{\text{Time}} \times \text{UNITOPORDERING}$ tensor in row-major storage	$\text{mol m}^{-2} \text{s}^{-1}$	double
SENSDOT_COLUMN_OUTLET	Matrix of sensitivity time derivatives at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENSDOT_COLUMN_INLET	Matrix of sensitivity time derivatives at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENSDOT_COLUMN_OUTLET_COMP_XXX	Component XXX of the sensitivity time derivative at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double
SENSDOT_COLUMN_INLET_COMP_XXX	Component XXX of the sensitivity time derivative at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol m}_{\text{IV}}^{-3}$	double

Table 2.6.4: *Datasets in the /output/sensitivity/param_XXX/unit_YYY groups*

2.7 Meta group

Dataset	Group /meta Description	In / out	Type
FILE_FORMAT	Version of the file format (defaults to 3.0 if omitted)	In	string
CADET_VERSION	Version of the executed CADET simulator	Out	string
CADET_COMMIT	Git commit SHA1 from which the CADET simulator was built	Out	string
CADET_BRANCH	Git branch from which the CADET simulator was built	Out	string
TIME_SIM	Time that the time integration took in seconds (excluding any preparations and postprocessing)	Out	double

Table 2.7.1: *Datasets in the /meta group*

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