CADET

Chromatography Analysis and Design Toolkit

Manual

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CADET Version 3.1.2

Contents

List of Figures

List of Tables

1 Simulation

This chapter gives an overview of the simulation process and the different steps involved.

CADET uses a backward-differentiation-formula (BDF) time discretization as implemented by the IDAS solver from SUNDIALS [Hin+05]. Each time step requires the solution of a nonlinear algebraic system of equations is performed by a Newton method. Since chromatographic systems can exhibit strong nonlinearity and stiff systems, the Jacobian of the equation system is always updated (i.e., an "exact" Newton method is used).
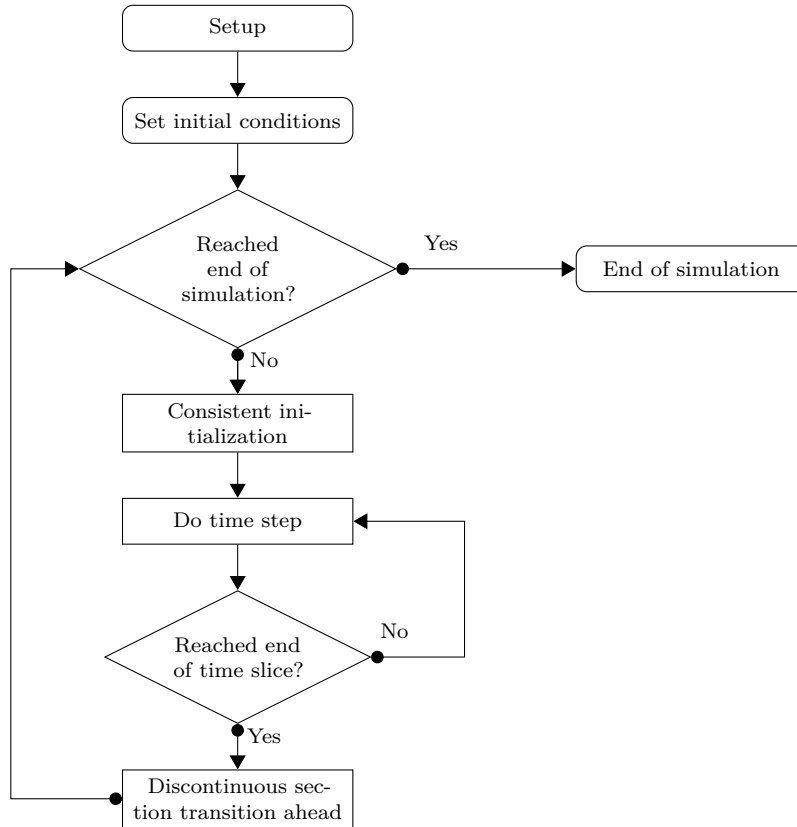
Figure 1.0.1: *General time integration procedure*

The general control flow of a simulation is shown in Fig. 1.0.1. Some aspects of the tasks involved are discussed below.

1.1 Time sections and transitions

The timespan $[t_0, t_{end}]$ of the simulation can be divided into multiple time sections $[t_i, t_{i+1}]$ with

$$t_0 < t_1 < \ldots < t_i < t_{i+1} < \ldots < t_{end}.$$

Time sections are used for various purposes, for example, for defining piecewise polynomials used as inlet profiles or external function, for changing operating conditions such as flow rates, or for changing the connectivity in a network of unit operations. A sequence of (one or more) time sections with smooth transitions is called a time slice (see Fig. 1.1.1).

A transition from one section to the next can either be smooth or discontinuous. On smooth transitions, the time integrator can just step over the section transition. Contrary to smooth transitions, a discontinuous transition requires some extra work in resetting the time integrator and finding consistent initial conditions for the next time slice.
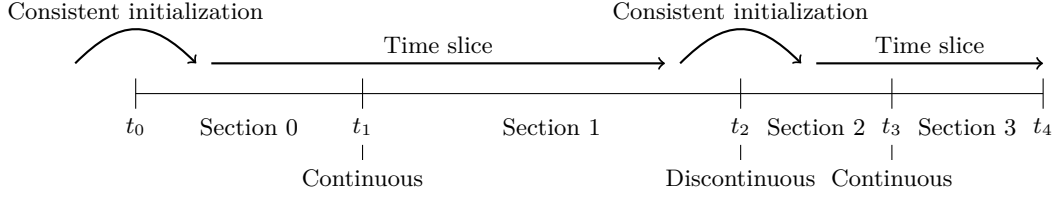
Figure 1.1.1: *Time sections, time slices, and transitions between them*

Time section specification Time sections are specified by an array (`SECTION_TIMES`, see Tab. 3.5.38) which contains the t_i that denote the start- and endpoint of a time section $[t_i, t_{i+1}]$. This means, that the array contains $n+1$ values if there are n sections. The smoothness of a section transition is indicated by the array `SECTION_CONTINUITY`, which contains $n-1$ elements if there are n sections.

1.2 Setup

In the setup phase, the model specification is checked and data structures are prepared for the simulation. The simulation can be run multiple times with different initial conditions, which also allows to continue a simulation. However, the model structure must not change after this point. This means, the different model and submodel types (e.g., unit operation model, binding model) as well as their discretization (i.e., number of cells) and structure (i.e., number of components, number of reactions) are fixed. On the contrary, their parameters (e.g., flow rates, porosities, dispersion coefficients) may change on different runs of a prepared simulation.

This assumption allows an accelerated simulation as there is no memory allocation performed during time integration.

1.3 Consistent initialization

At the beginning of the simulation and on discontinuous section transitions, consistent initial conditions have to be computed. In CADET, the general differential-algebraic equation (DAE)

$$F(t, y, \dot{y}, p) = 0$$

consists of purely algebraic equations that do not contain $\dot{y}$ and dynamic equations. Let $\mathcal{I}_d$ be the index set of dynamic equations and $\mathcal{I}_a$ the index set of algebraic equations. The general DAE can be decomposed into

$$M\dot{y}_{\mathcal{I}_d} + G_{\mathcal{I}_d}(t, y, p) = 0, \tag{1.1}$$
$$G_{\mathcal{I}_a}(t, y, p) = 0, \tag{1.2}$$

where M is the so called "mass matrix", which essentially consist of the state time derivative Jacobian $\partial F/\partial \dot{y}$. Furthermore, it is assumed that the Jacobian of the algebraic equations with respect to the algebraic variables $\partial G_{\mathcal{I}_a}/\partial y_{\mathcal{I}_a}$ is invertible. Hence, the original DAE is of differential index 1.

Given $y_{\mathcal{I}_d}$, consistently initialization means finding $y_{\mathcal{I}_a}$, $y_{\mathcal{I}_d}$, and $\dot{y}$ such that the DAE holds at the initial time point t_0 and can be solved for some non-empty time span. Thus, consistent initial conditions

y_0 and $\dot{y}_0$ satisfy

$$0 = M\dot{y}_{\mathcal{I}_d} + G_{\mathcal{I}_d}(t_0, y, p),$$
$$0 = G_{\mathcal{I}_a}(t_0, y, p),$$
$$0 = \frac{\partial G_{\mathcal{I}_a}}{\partial t}(t_0, y, p) + \frac{\partial G_{\mathcal{I}_a}}{\partial y}(t_0, \dot{y}, p).$$

The last equation, which determines $\dot{y}_{\mathcal{I}_a}$, arises from taking the total derivative with respect to time t of the second equation.

Concluding, a nonlinear algebraic equation system has to be solved in order to compute consistent initial conditions. The error in the solution of these systems is controlled by the `ALGTOL` setting (see Tab. 3.5.37).

1.4 Time stepping

Given the general differential-algebraic equation

$$F(t, y, \dot{y}, p) = 0, \qquad y(t_0) = y_0, \qquad \dot{y}(t_0) = \dot{y}_0$$

with consistent initial values y_0 and $\dot{y}_0$, the BDF discretization uses past time steps $y(t_{\tau-i})$ to compute the current $\dot{y}(t_\tau)$ as

$$\dot{y}(t_\tau) = \frac{1}{\Delta t_\tau} \sum_{i=0}^{q_\tau} \alpha_{\tau,i} y(t_{\tau-i}),$$

where t_τ denotes some time step. The IDAS time integrator adaptively changes the step size $\Delta t_\tau = t_\tau - t_{\tau-1}$ and order $1 \le q_\tau \le 5$ in each time step and automatically determines the corresponding coefficients $\alpha_{\tau,i}$. This *ansatz* is inserted into the DAE and the resulting nonlinear algebraic equation system is solved for $y_\tau = y(t_\tau)$ using a Newton method.

$$H(y_\tau) = F\left(t_\tau, y_\tau, \frac{1}{\Delta t_\tau} \sum_{i=0}^{q_\tau} \alpha_{\tau,i}\, y_{\tau-i}, p\right) = 0 \tag{1.3}$$

This requires (possibly many) solutions of linear equation systems involving the Jacobian of H given by

$$\frac{\mathrm{d}H}{\mathrm{d}y_\tau} = \frac{\partial F}{\partial y} + \frac{\alpha_{\tau,0}}{\Delta t_\tau} \frac{\partial F}{\partial \dot{y}}.$$

The Jacobian of H, which is the linear combination of the partial derivatives $\partial F/\partial y$ and $\partial F/\partial \dot{y}$, can be calculated in two ways. The fastest way is the analytic computation, which is to be preferred if available. However, the implementation of the analytic Jacobian can be time consuming and complicated, especially when quickly testing new models. As a remedy, CADET offers to compute the complicated Jacobian $\partial F/\partial y$ automatically by automatic differentiation (AD). The much simpler Jacobian $\partial F/\partial \dot{y}$ has to be implemented manually.

Adaptivity The BDF order q_τ and size of the time step t_τ are chosen such that the error bounds are satisfied with minimal work. Equation (1.3) is solved with a Newton iteration using very few iterations (`MAX_NEWTON_ITER` from Table 3.5.37) since the starting point is assumed to be close to the solution as the time steps are small. If the solution of the Newton iteration does not pass the *convergence test*, the step size t_τ is reduced and the Newton iteration is tried again. This may happen at most `MAX_CONVTEST_FAIL` times, otherwise time integration is aborted with failure. Having a solution of the Newton iteration at hand, a *local truncation error test* is performed which controls the error of the BDF method. If this test fails, step size t_τ and order q_τ are adapted and the process restarts with solving the nonlinear system Eq. (1.3). The error test may be failed at most `MAX_ERRTEST_FAIL` times before time integration is aborted with failure.

Error bounds for the local truncation error test are specified by an absolute tolerance (`ABSTOL`) and a relative tolerance (`RELTOL`). Note that the relative tolerance only works for non-zero values, whereas zero values are accounted for by the absolute tolerance. For example, a relative tolerance of 10^{-4} and absolute tolerance of 10^{-8} requests 3 significant digits (correct digits after the comma in scientific notation) and considers all numbers with magnitude smaller than 10^{-8} as 0.

The size of the first time step in a time slice is given by `INIT_STEP_SIZE` from Table 3.5.37. If a simulation fails on the first time step, it might help to reduce the initial step size. It can also help to increase the error tolerances, at the cost of imprecise results over the whole course of the simulation.

It can happen that due to severe stiffness or ill-posed models a simulation may exceed its computational budget given by the maximum number of time steps (per time slice) `MAX_STEPS`. In this case, the formulation of the model should be checked and, if necessary, the error tolerances increased. Note that the number of time steps is independent of possible `USER_SOLUTION_TIMES` and refers to internal steps of the time integrator.

On the other extreme, the time integrator might jump over an important change in the solution or not capture some feature of the solution because of too large time steps. This can be avoided by specifying the maximum time step size `MAX_STEP_SIZE`. However, such a situation is unlikely to occur and can also be alleviated by placing a discontinuous section transition at the time of the event.

Note that while the error in time integration is controlled and can (in theory) be made arbitrarily small, the spatial discretization error is not. Hence, it is important and necessary to test different spatial resolutions (number of cells) in order to find a sufficiently accurate (but minimal) number of grid cells. This is particularly relevant for problems with steep fronts as a low spatial resolution adds a substantial amount of numerical dispersion to the solution.

1.5 Parameter sensitivities

Parameter sensitivities $s = \partial y / \partial p$ of a solution y to the DAE with respect to some parameter p are required for various tasks, for example, parameter estimation, process design, and process analysis. The CADET simulator implements the forward sensitivity approach which creates a linear companion DAE for each sensitive parameter

$$0 = \frac{\mathrm{d}}{\mathrm{d}p} F(t, y, \dot{y}, p) = \frac{\partial F}{\partial y}(t, y, \dot{y}, p) \frac{\partial y}{\partial p} + \frac{\partial F}{\partial \dot{y}}(t, y, \dot{y}, p) \frac{\partial \dot{y}}{\partial p} + \frac{\partial F}{\partial p}(t, y, \dot{y}, p)$$
$$= \frac{\partial F}{\partial y}(t, y, \dot{y}, p)s + \frac{\partial F}{\partial \dot{y}}(t, y, \dot{y}, p)\dot{s} + \frac{\partial F}{\partial p}(t, y, \dot{y}, p).$$

These linear DAEs depend on the solution y, $\dot{y}$ of the original DAE system. Consequently, the sensitivity systems are solved together with the original DAE system in a staggered approach [FTB97].

After the nonlinear Eq. (1.3) has been successfully solved using Newton iteration (i.e., it has passed the convergence test), each sensitivity is solved using the same Newton iteration. If direct linear solvers were used, this iteration would convergence with a single iteration as there is no nonlinearity. The Newton method for the sensitivities performs at most `MAX_NEWTON_ITER_SENS` (see Table 3.5.37) iterations. Assuming the convergence test has passed for each sensitivity, the local truncation error test is performed for the full set of variables (i.e., original system and sensitivities). The sensitivities can be excluded from the local truncation error test by setting `ERRORTEST_SENS` appropriately. Note that time integration step size is always affected by sensitivities due to possible convergence test failures.

While the Jacobians $\partial F / \partial y$ and $\partial F / \partial \dot{y}$ can be computed either analytically or via AD, the last term $\partial F / \partial p$ is always computed by AD. In fact, the terms $\partial F / \partial y$ and $\partial F / \partial p$ can be computed by one AD-enabled evaluation of F using the vector mode with appropriate seed vectors [Püt+16].

A parameter sensitivity is specified by identifying the involved parameters, which can be more than one (see below). Parameters are identified by name and multiple indices, which may not all be used (see Tab. 3.5.35). Indices that are not used for identification (e.g., flow rate is independent of bound phase or component) are set to -1. All other indices are zero-based.

Note that the sensitivity systems need to be consistently initialized, too. However, since only linear systems are involved, no nonlinear equation system has to be solved and the procedure is much simpler computationally.

Joint parameters   The use of AD also enables support of meta parameters or joint parameters. Consider the situation in which several parameters $p_1, p_2, \ldots, p_n$ depend (linearly) on a single meta parameter p

$$p_i = p_i(p) = \alpha_i p \qquad \text{for } i = 1, \ldots, n$$

and some coefficients $\alpha_i \in \mathbb{R}$. Hence, the DAE residual function F becomes

$$F(t, y, \dot{y}, p_1(p), \ldots, p_n(p)) = 0$$

and the partial derivative $\partial F / \partial p$ can be computed automatically by AD:

$$\frac{\partial F}{\partial p} = \frac{\partial F}{\partial p_1} \alpha_1 + \ldots + \frac{\partial F}{\partial p_n} \alpha_n.$$

In order to use this functionality, all parameters involved have to be specified in a single sensitivity instance (`param_XXX` group, see Tables 3.5.34 and 3.5.35) by using arrays for the name and indices instead of scalar values. The coefficients α_i are provided in the `SENS_FACTOR` vector.

A simple example for a situation, which benefits from having a single meta parameter, would be a chain of unit operations in a network in which the sensitivity with respect to the flow rate is to be computed. Instead of computing the sensitivity with respect to each single flow rate and fusing them together in a postprocessing step, a meta parameter that maps to all flow rates can be introduced.

Note that nonlinear relationships between original parameter and meta parameters are supported by updating the coefficients α_i before each simulation:

$$\alpha_i = \frac{\partial p_i}{\partial p}.$$

2 Models

2.1 Network of unit operation models

Unit operation models can be composed into a network or graph, in which a node represents a unit operation and an edge denotes a connection between two unit operations. When utilized to full extent, this allows the simulation of complicated setups and processes (e.g., SMB, MCSGP). A more simple use case is the addition of plug flows and stirred tanks up- and downstream of a column in order to account for dead volume and additional dispersion from the tubing.

In a network, outlets of unit operations can be connected to any number of inlets of unit operations. Even direct cycles, where an outlet of a unit operation is connected to its own inlet, are possible. A unit operation does not have to possess both inlet and outlet, but it has to have at least one of them. Pseudo unit operations such as inlet and outlet serve as sources and sinks for the network. However, the latter is not strictly required as any terminal node (i.e., a unit operation that possesses an outlet but does not have an outgoing connection) serves as a sink.

Each connection between two unit operations (i.e., an edge in the graph) is equipped with a volumetric flow rate that determines the mass flow from source to target unit operation. Those flow rates are used to determine the weight of the different incoming feeds at a unit operation's inlet port. Some unit operations can infer their internal flow rate (e.g., interstitial velocity) from their total incoming volumetric flow rate. In general, the mass balance at a unit operation has to be closed, except for unit operations that act as source or sink in the network and variable volume units (e.g., stirred tanks).

The network of unit operations uses "connection"-variables c_{con} to connect the different unit operations with each other. The inlet port variables $c_{\text{in},n}$ of unit operation n are attached to $c_{\text{con},n}$ via

$$c_{\text{in},n,i} = c_{\text{con},n,i}, \qquad i = 1, \ldots, N_{\text{comp},n}. \tag{2.1}$$

The connection variables $c_{\text{con},n,i}$ collect all inflows of component i into unit operation n:

$$c_{\text{con},n,i} = \frac{\sum_{m=1}^{N_{\text{units}}} \sum_{j=1}^{N_{\text{comp},m}} S_{(n,i),(m,j)} F_m c_{\text{out},m,j}}{\sum_{m=1}^{N_{\text{units}}} \hat{S}_{n,m} F_m}, \tag{2.2}$$

where F_m denotes the volumetric flow rate of unit operation m, $S_{(n,i),(m,j)} \in \{0,1\}$ is a connection matrix indicating whether component i of unit operation n is connected to component j of unit operation m, and $\hat{S}_{n,m} \in \{0,1\}$ is another connection matrix indicating whether unit operation n is connected to unit operation m, that is

$$\hat{S}_{n,m} = \begin{cases} 1 & \text{if } \sum_{i=1}^{N_{\text{comp},n}} \sum_{j=1}^{N_{\text{comp},m}} S_{(n,i),(m,j)} \geq 1, \\ 0 & \text{otherwise.} \end{cases}$$

Specification of network connections The connections between the different unit operations in the network are specified by a table. The first two columns specify source and destination unit operation id. The next two columns give source and destination component indices. Finally, the fith column specifies the volumetric flow rate of this connection.

With this setup it is possible to connect single components of unit operations with each other yielding a maximum in flexibility. However, the predominant case is to connect all components of the source unit operations with their respective counterparts in the destination unit. This can easily be done by setting both component indices to -1 instead of writing a separate row for each component of the connection.

Note that in case of multiple rows for one connection between two unit operations (e.g., in case of separate component connections) the flow rate of the first row of that connection is used and all following

flow rates are ignored. Consequently, there can only be one flow rate for a connection between two unit operations regardless of which components are connected.

The connection table is expected in row-major storage format (i.e., the rows are appended to one long array). See Table 3.5.3.

Valve switches The connectivity of the network can only change on a discontinuous section transition. Such a transition with changing connectivity is referred to as valve switch and the connectivity itself as valve configuration.

A list of valve configurations with at least one entry is required. Each valve configuration consists of a network connectivity table as described in Section 2.1 and a section index. The latter denotes the section in which the connectivity table becomes active. Hence, the one required (i.e., the first) entry must have a section index of 0 denoting the initial connectivity.

Note that the section index has to be monotonically increasing throughout the list of valve configurations. See Tables 3.5.2 and 3.5.3.

2.2 Unit operation models

2.2.1 Inlet

A system inlet unit operation is a pseudo unit operation since there is no physical correspondence. The inlet serves as a mass source in the network of unit operations. Consequently, it only possesses an outlet port and no inlet port. Note that an inlet unit operation can provide arbitrary many components and there can be arbitrary many inlet unit operations in a network.

An inlet unit operation provides a feed in which the concentration of each component is given by a profile. The most common profile is a piecewise cubic polynomial, which can both represent discontinuous signals (e.g., pulse or step) and smooth C^2 signals (cubic spline):

$$c_i(t) = \sum_{k=1}^{N_{\text{sect}}} \mathbb{1}_{[t_k, t_{k+1})}(t) \left[a_{k,i} \left(t - t_k \right)^3 + b_{k,i} \left(t - t_k \right)^2 + d_{k,i} \left(t - t_k \right) + f_{k,i} \right],$$

where $0 \leq t_1 < t_2 < \ldots < t_{N_{\text{sect}}+1} \leq T_{\text{sim}}$ is a decomposition of the simulation time interval $[0, T_{\text{sim}}]$ into pieces $[t_k, t_{k+1})$. On each piece, the profile is given by a cubic (fourth order) polynomial shifted to the beginning t_k of the piece.

See Tables 3.5.7 and 3.5.8.

2.2.2 Outlet

A system outlet unit operation is a pseudo unit operation since there is no physical correspondence. The outlet serves as a sink (terminal node) in the network of unit operations. Since any terminal node in the network is a sink (see Section 2.1), outlet unit operations are not strictly necessary. However, in some applications (e.g., SMB) only a certain fraction of a unit operation's output is taken out of the system and the rest is recycled. In this case, outlet unit operations are required in order to avoid unbalanced mass flow in the other unit operations.

Outlets can also be of help if the output of multiple unit operations merges together leaving the network. Instead of manually adding the streams together in a post-processing step, the unit operations can be connected to the same outlet unit.

See Table 3.5.9.

2.2.3 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 [Kuč65; 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 and radial transport is neglected in the column bulk volume.

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	$\{0, \ldots, N_{\text{comp}} - 1\}$	Component index
m_i	$\{0, \ldots, N_{\text{bnd},i} - 1\}$	Bound state index of ith component
m	$\left\{0, \ldots, \sum_{i=0}^{N_{\text{comp}}-1} N_{\text{bnd},i} - 1\right\}$	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 ith component
$c_{p,i}(t, z, r)$	$[0, T_{\text{end}}] \times [0, L] \times [0, r_p]$	Mobile phase concentration of the ith component
$q_{i,m_i}(t, z, r)$	$[0, T_{\text{end}}] \times [0, L] \times [0, r_p]$	Solid phase concentration of the ith component's m_ith bound state
$j_{f,i}(t, z)$	$[0, T_{\text{end}}] \times [0, L]$	Flux of the ith component through stagnant film into the bead

Table 2.2.1: *Variables and unkowns*

(a) *Column geometry*

(b) *A section of the column*
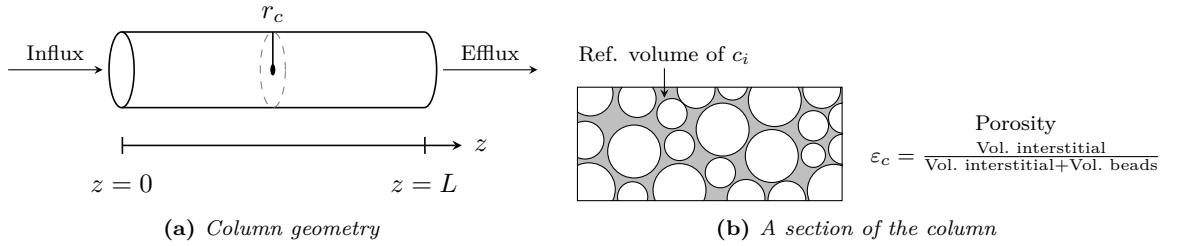
Figure 2.2.1: *Column bulk model*

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. 2.2.1). The mass balance in the interstitial column volume is described by

$$\frac{\partial c_i}{\partial t} = -u\frac{\partial c_i}{\partial z} + D_{\text{ax}}\frac{\partial^2 c_i}{\partial z^2} - \frac{1}{\beta_c}\frac{3}{r_p}k_{f,i}\left[c_i - c_{p,i}(\cdot, \cdot, r_p)\right]. \tag{2.3}$$

Here, $c_i \colon [0, T_{\text{end}}] \times [0, L] \to \mathbb{R}^{\geq 0}$ denotes the concentration in the interstitial column volume, $c_{p,i} \colon [0, T_{\text{end}}] \times [0, L] \times [0, r_p] \to \mathbb{R}^{\geq 0}$ 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).

Danckwerts boundary conditions [Dan53] are applied to inlet and outlet of the column:

$$uc_{\text{in},i}(t) = uc_i(t, 0) - D_{\text{ax}}\frac{\partial c_i}{\partial z}(t, 0) \qquad \forall t > 0, \tag{2.4}$$

$$\frac{\partial c_i}{\partial z}(t, L) = 0 \qquad \forall t > 0. \tag{2.5}$$

Note that the outlet boundary condition Eq. (2.5) is also known as "do nothing" or natural outflow condition.

In the liquid phase of the porous beads (see Fig. 2.2.2) the mass balance is given by

$$\frac{\partial c_{p,i}}{\partial t} + \frac{1 - \varepsilon_p}{F_{\mathrm{acc},i}\varepsilon_p} \frac{\partial}{\partial t} \sum_{m_i} q_{i,m_i} = \underbrace{D_{p,i} \left[\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\right] c_{p,i}}_{\text{Pore diffusion}} + \underbrace{\frac{1 - \varepsilon_p}{F_{\mathrm{acc},i}\varepsilon_p} D_{s,i} \left[\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\right] \sum_{m_i} q_{i,m_i}}_{\text{Surface diffusion}}, \qquad (2.6)$$

where $q_{i,m_i} \colon [0, T_{\mathrm{end}}] \times [0, L] \times [0, r_p] \to \mathbb{R}^{\geq 0}$ denotes the solid phase concentration of the ith component's m_ith bound state in the beads, $D_{p,i}$ the effective diffusion coefficient in the beads, $D_{s,i}$ the surface diffusion coefficient, $F_{\mathrm{acc},i} \in [0, 1]$ the pore accessibility factor, and ε_p the particle porosity (ratio of pore volume to total bead volume). The GRM is used with both quasi-stationary (Eq. (2.7)) and dynamic (Eq. (2.8)) binding models.

$$\text{quasi-stationary:} \quad 0 = f_{\mathrm{ads}}(c_p, q), \qquad (2.7)$$

$$\text{dynamic:} \quad \frac{\partial q}{\partial t} = f_{\mathrm{ads}}(c_p, q). \qquad (2.8)$$

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

$$k_{f,i} [c_i - c_{p,i}(\cdot, \cdot, r_p)] = F_{\mathrm{acc},i}\varepsilon_p D_{p,i} \frac{\partial c_{p,i}}{\partial r}(\cdot, \cdot, r_p) + (1 - \varepsilon_p) D_{s,i} \sum_{m_i} \frac{\partial q_{i,m_i}}{\partial r}(\cdot, \cdot, r_p), \qquad (2.9)$$

$$\frac{\partial c_{p,i}}{\partial r}(\cdot, \cdot, 0) = 0. \qquad (2.10)$$

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

$$c_i(0, z) = 0, \qquad c_{p,i}(0, z, r) = 0, \qquad q_{i,m_i}(0, z, r) = 0. \qquad (2.11)$$

(a) *Mass transport into beads*

(b) *Mass transport inside bead*

Figure 2.2.2: *Column bead model*
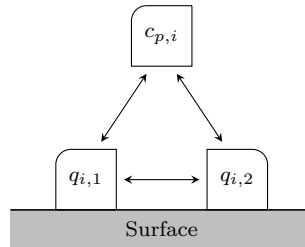
Figure 2.2.3: *Binding with multiple bound states*

See Table 3.5.10.

Size exclusion chromatography The general rate model can be used to simulate size exclusion chromatography (SEC) [Gu95]. The particle porosity ε_p on the mobile phase side of the transport equations

is replaced by the accessible porosity

$$\varepsilon_{p,i} = F_{\mathrm{acc},i}\varepsilon_p \tag{2.12}$$

where the pore accessibility factor $F_{\mathrm{acc},i}$ ranges in $(0,1]$.

Small molecules which can enter any pore have $F_{\mathrm{acc},i} = 1$ whereas larger molecules that can enter some but not small pores have values $0 < F_{\mathrm{acc},i} < 1$. The other extreme is given by molecules so large that they cannot enter any pore and, consequently, $F_{\mathrm{acc},i} = 0$. Note that $F_{\mathrm{acc},i} = 0$ is not allowed in a simulation and a more suitable model should be used instead (e.g., the lumped rate model without pores described in Section 2.2.5).

By default, $F_{\mathrm{acc},i} = 1$ for all components i, which disables size exclusion chromatography. In order to simulate pure SEC, binding is disabled by setting $N_{\mathrm{bnd},i} = 0$ for all components i and applying no binding model. If adsorption is present, it is important to note that any saturation capacity (e.g., $q_{\max}$) is subject to the full pore volume fraction ε_p.

Specification of flow rate / velocity and direction Since volumetric flow rates are specified for each network connection, the unit operation can infer its interstitial velocity via

$$u = u_{\mathrm{int}} = \frac{F_{\mathrm{in}}}{A\varepsilon_c},$$

where F_{in} denotes the volumetric flow rate and A the cross section area. Note that without the bulk porosity ε_c, the superficial velocity would be obtained.

The direction of flow inside the unit operation is governed by the sign of the interstitial velocity u. A positive sign results in (standard) forward flow, whereas a negative sign reverses the flow direction. Note that in case of reversed flow the chromatogram is returned at the unit operation's *inlet*, which may not be returned from simulation by default.

The final behavior is controlled by the interplay of cross section area and interstitial velocity:

1. If cross section area A is given and u is not, u is inferred from the volumetric flow rate.

2. If u is given and A is not, the volumetric flow rate is ignored and the provided interstitial velocity is used.

3. If both cross section area A and interstitial velocity u are given, the magnitude of the actual interstitial velocity u is inferred from the volumetric flow rate and the flow direction is given by the sign of the provided u.

2.2.4 Lumped rate model with pores (LRMP)

The lumped rate model with pores [Gui+06; FG04] deviates from the general rate model (see Section 2.2.3) by neglecting pore diffusion. The particle phase c_p is still there, but no mass transfer happens except for binding and film diffusion. Hence, the model equations are given by

$$\frac{\partial c_i}{\partial t} = -u\frac{\partial c_i}{\partial z} + D_{\mathrm{ax}}\frac{\partial^2 c_i}{\partial z^2} - \frac{1}{\beta_c}\frac{3}{r_p}k_{f,i}\left[c_i - c_{p,i}\right], \tag{2.13}$$

$$\frac{\partial c_{p,i}}{\partial t} + \frac{1-\varepsilon_p}{F_{\mathrm{acc},i}\varepsilon_p}\frac{\partial}{\partial t}\sum_{m_i} q_{i,m_i} = \frac{3}{F_{\mathrm{acc},i}\varepsilon_p r_p}k_{f,i}\left[c_i - c_{p,i}\right] \tag{2.14}$$

with the same meanings of variables and parameters as in the general rate model. The equations are complemented by Danckwerts boundary conditions [Dan53]

$$uc_{\mathrm{in},i}(t) = uc_i(t,0) - D_{\mathrm{ax}}\frac{\partial c_i}{\partial z}(t,0) \qquad\qquad \forall t > 0,$$

$$\frac{\partial c_i}{\partial z}(t,L) = 0 \qquad\qquad \forall t > 0.$$

As for the general rate model, both quasi-stationary and dynamic binding models are supported:

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

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

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

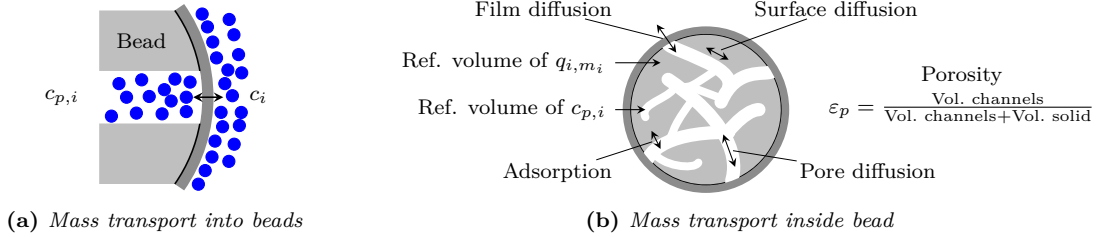$$c_i(0, z) = 0, \qquad c_{p,i}(0, z) = 0, \qquad q_{i,m_i}(0, z) = 0. \qquad (2.15)$$

This model can also be used to simulate size exclusion chromatography (see Section 2.2.3). For the specification of flow rate and direction, the same holds as for the general rate model (see Section 2.2.3). See Table 3.5.12.

2.2.5 Lumped rate model without pores (LRM)

The lumped rate model without pores [Gui+06; FG04] deviates from the lumped rate model with pores (see Section 2.2.4) by neglecting pores completely. The particle phase c_p is removed and the porosity ε_t is taken as total porosity

$$\varepsilon_t = \varepsilon_c + (1 - \varepsilon_c)\,\varepsilon_p. \qquad (2.16)$$

The phase ratio is denoted by $\beta_t = \varepsilon_t/(1 - \varepsilon_t)$ accordingly. The model equations are given by

$$\frac{\partial c_i}{\partial t} + \frac{1}{\beta_t}\frac{\partial}{\partial t}\sum_{m_i} q_{i,m_i} = -u\frac{\partial c_i}{\partial z} + D_{\text{ax}}\frac{\partial^2 c_i}{\partial z^2}, \qquad (2.17)$$

where $\beta_t = \varepsilon_t/(1 - \varepsilon_t)$ denotes the (total) phase ratio. The equations are complemented by Danckwerts boundary conditions [Dan53]

$$uc_{\text{in},i}(t) = uc_i(t, 0) - D_{\text{ax}}\frac{\partial c_i}{\partial z}(t, 0) \qquad\qquad \forall t > 0,$$

$$\frac{\partial c_i}{\partial z}(t, L) = 0 \qquad\qquad \forall t > 0.$$

Both quasi-stationary and dynamic binding models are supported:

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

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

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

$$c_i(0, z) = 0, \qquad\qquad q_{i,m_i}(0, z) = 0. \qquad (2.18)$$

Note that by setting $\varepsilon_t = 1$, removing all bound states by setting $N_{\text{bnd},i} = 0$ for all components i, and applying no binding model, a dispersive plug flow reactor (DPFR) is obtained.

For the specification of flow rate and direction, the same holds as for the general rate model (see Section 2.2.3). See Table 3.5.14.

2.2.6 Continuously stirred tank reactor model (CSTR)

The continuously stirred tank reactor model is a basic building block in unit operation networks and often used to model holdup volume. When combined with a binding model, it can be used to model batch uptake experiments.

Assuming that the fluid inside the tank is well-mixed and that the volume can vary, the governing

equations are given by

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\left[c_i + \frac{1-\varepsilon}{\varepsilon}\sum_{j=0}^{N_{\mathrm{bnd},i}-1} q_{i,j}\right] V\right) = F_{\mathrm{in}}c_{\mathrm{in},i} - F_{\mathrm{out}}c_i,$$

which balances the mass, the binding equation

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

$$\text{dynamic:} \quad \frac{\partial q}{\partial t} = f_{\mathrm{ads}}(c, q),$$

depending on whether quasi-stationary or dynamic binding is used, and the evolution of volume

$$\frac{\mathrm{d}V}{\mathrm{d}t} = F_{\mathrm{in}} - F_{\mathrm{out}} - F_{\mathrm{filter}}.$$

The porosity ε denotes the ratio of liquid phase volume to total tank volume. Thus, setting $\varepsilon = 1$, removing all bound states by setting $N_{\mathrm{bnd},i} = 0$ for all components i, and applying no binding model results in a simple tank. The additional parameter F_{filter}, which denotes the flow rate of pure liquid (without any components) out of the tank, can be used to model a filtering unit.

Note that it is the user's duty to make sure that the volume of the CSTR does not fall below $0\,\mathrm{m}^3$. If it does, the simulation may fail to run or produces unreasonable (e.g., unphysical) results.

See Table 3.5.16.

2.3 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 2.3.1):

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

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:

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

This can be achieved by a (nonlinear) parameter transform

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

Dependence on external function A binding model may depend on an external function or profile $T\colon [0, T_{end}] \times [0, L] \to \mathbb{R}$, where L denotes the physical length of the unit operation, or $T\colon [0, T_{end}] \to \mathbb{R}$ 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 2.3.1). 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 3.5.4.

Binding model feature matrix A short comparison of the most prominent binding model features is given in Table 2.3.1. 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	✓	✗	✓	✓
Multi component spreading	✓	✗	✓	✓
Multi-state steric mass action	✓	✓	✓	✓
Simplified multi-state steric mass action	✓	✓	✗	✓
Bi steric mass action	✓	✓	✓	✓

Table 2.3.1: *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

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

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

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

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

$$k_{a,i} = \tilde{k}_{a,i} q_{\mathrm{ref}}^{-\nu_i},$$
$$k_{d,i} = \tilde{k}_{d,i} c_{\mathrm{ref}}^{-\nu_i},$$

we obtain the modified model equation

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

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.

2.3.1 Linear

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

$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = k_{a,i}c_{p,i} - k_{d,i}q_i \qquad\qquad i = 0,\dots,N_{\mathrm{comp}} - 1.$$

See Table 3.5.19.

2.3.2 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.

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

See Table 3.5.20.

2.3.3 Multi Component Anti-Langmuir

The Anti-Langmuir (or generalized Langmuir) binding model extends the Langmuir model (see Section 2.3.2). 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).

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

See Table 3.5.21.

2.3.4 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.

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

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

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

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

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

which also compensates for the missing equation for $\frac{\mathrm{d}q_0}{\mathrm{d}t}$. See Table 3.5.23.

The concept of reference concentrations (c_{ref} and q_{ref}) is explained in the respective paragraph in Section 2.3.

2.3.5 Self Association

This binding model is similar to the steric mass action model (see Section 2.3.4) 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.

$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = c_{p,i} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{\nu_i} \left[k_{a,i,1} + k_{a,i,2} c_{p,i} \right] - k_{d,i}\, q_i \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{\nu_i} \qquad i = 1, \dots, N_{\text{comp}} - 1,$$

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

where the number of available binding sites is given by

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

See Table 3.5.24.

The concept of reference concentrations (c_{ref} and q_{ref}) is explained in the respective paragraph in Section 2.3.

2.3.6 Mobile Phase Modulator Langmuir

This model is a modified Langmuir model (see Section 2.3.2) 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:

$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = k_{a,i} e^{\gamma_i c_{p,0}} c_{p,i}\, q_{\text{max},i} \left(1 - \sum_{j=1}^{N_{\text{comp}}-1} \frac{q_j}{q_{\text{max},j}} \right) - k_{d,i}\, c_{p,0}^{\beta_i}\, q_i \qquad i = 1, \dots, N_{\text{comp}} - 1.$$

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

$$\frac{\mathrm{d}q_0}{\mathrm{d}t} = 0$$

is used if salt has one bound state, or salt can be used without a bound state. The parameter γ describes the hydrophobicity and β the ion-exchange characteristics. See Table 3.5.22.

2.3.7 Kumar-Langmuir

This extension of the Langmuir isotherm (see Section 2.3.2) 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.

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

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

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

Here, $k_{a,i}$ is the frequency or pre-exponential factor, $k_{\mathrm{act},i} = E/R$ 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 3.5.27.

2.3.8 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.

$$\frac{\mathrm{d}q_i}{\mathrm{d}t} = H_i c_{p,i} + \sum_{j=0}^{N_{\mathrm{comp}}-1} k_{ij} c_{p,i} c_{p,j} - q_i \qquad\qquad i = 0, \ldots, N_{\mathrm{comp}} - 1$$

See Table 3.5.25.

2.3.9 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 2.3.2) without allowing an exchange between the different sites $q_{i,j}$ and $q_{i,k}$ ($k \neq j$). Therefore, there are no competitivity effects between the different types of binding sites and they have independent capacities.

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

Note that all binding components must have exactly the same number of binding site types $M \geq 1$. See the Langmuir isotherm in Section 2.3.2 and Table 3.5.26.

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.

2.3.10 Multi Component Spreading

The multi component spreading model adds a second bound state $q_{i,2}$ to the Langmuir model (see Section 2.3.2) and allows the exchange between the two bound states $q_{i,1}$ and $q_{i,2}$. In the spreading model a second state of the bound molecule (e.g., a different orientation on the surface or a different folding state) is added. The exchange of molecules between the two states is allowed and, since the molecules can potentially bind in both states at the same binding site, competitivity effects are present. This is different to the Bi-Langmuir model in which another type of binding sites is added and no exchange between the different bound states is considered (see Section 2.3.9). For all components $i = 0, \ldots, N_{\mathrm{comp}} - 1$ the equations are given by

$$\frac{\mathrm{d}q_{i,1}}{\mathrm{d}t} = \left(k_a^A c_{p,i} - k_{12} q_{i,1}\right) q_{\mathrm{max},i}^A \left(1 - \sum_{j=0}^{N_{\mathrm{comp}}-1} \frac{q_j^A}{q_{\mathrm{max},j}^A} - \sum_{j=0}^{N_{\mathrm{comp}}-1} \frac{q_j^B}{q_{\mathrm{max},j}^B}\right) - k_d^A q_{i,1} + k_{21} q_{i,2},$$

$$\frac{\mathrm{d}q_{i,2}}{\mathrm{d}t} = \left(k_a^B c_{p,i} + k_{12} q_{i,1}\right) q_{\mathrm{max},i}^A \left(1 - \sum_{j=0}^{N_{\mathrm{comp}}-1} \frac{q_j^A}{q_{\mathrm{max},j}^A} - \sum_{j=0}^{N_{\mathrm{comp}}-1} \frac{q_j^B}{q_{\mathrm{max},j}^B}\right) - \left(k_d^B + k_{21}\right) q_{i,2}.$$

See Table 3.5.28.

2.3.11 Multi-State Steric Mass Action

The multi-state steric mass action model adds $M_i - 1$ *additional* bound states $q_{i,j}$ $(j = 0, \ldots, M_i - 1)$ for each component i to the steric mass action model (see Section 2.3.4) and allows the exchange between the different bound states $q_{i,0}, \ldots, q_{i,M-1}$ of each component. In the multi-state SMA model a variable number of states of the bound molecule (e.g., different orientations on the surface, binding strength of tentacle adsorbers) is added which are more and more strongly bound, i.e.,

$$\nu_{i,j} \leq \nu_{i,j+1} \qquad i = 1, \ldots, N_{\text{comp}} - 1, \quad j = 0, \ldots, M_i - 1.$$

The exchange between the different states of each component is allowed and, since the molecules can potentially bind in all states at the same binding site, competitive effects are present.

$$
\begin{aligned}
\frac{\mathrm{d}q_{i,j}}{\mathrm{d}t} =\ & k_{a,i}^{(j)} c_{p,i} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{\nu_{i,j}} - k_{d,i}^{(j)}\, q_{i,j} \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{\nu_{i,j}} \\
& - \underbrace{\sum_{\ell=0}^{j-1} k_{j\ell}^{(i)}\, q_{i,j} \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{(\nu_{i,j}-\nu_{i,\ell})}}_{\text{to weak state}} - \underbrace{\sum_{\ell=j+1}^{M_i-1} k_{j\ell}^{(i)}\, q_{i,j} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{(\nu_{i,\ell}-\nu_{i,j})}}_{\text{to strong state}} \\
& + \underbrace{\sum_{\ell=0}^{j-1} k_{\ell j}^{(i)}\, q_{i,\ell} \left(\frac{\bar{q}_0}{q_{\text{ref}}} \right)^{(\nu_{i,j}-\nu_{i,\ell})}}_{\text{from weak state}} + \underbrace{\sum_{\ell=j+1}^{M_i-1} k_{\ell j}^{(i)}\, q_{i,\ell} \left(\frac{c_{p,0}}{c_{\text{ref}}} \right)^{(\nu_{i,\ell}-\nu_{i,j})}}_{\text{from strong state}} \qquad \begin{aligned} & i = 1, \ldots, N_{\text{comp}} - 1, \\ & j = 0, \ldots, M_i - 1, \end{aligned}
\end{aligned}
$$

where $c_{p,0}$ and q_0 denote the salt concentrations in the liquid and solid phase of the beads respectively. The number of available salt ions $\bar{q}_0$ is given by

$$\bar{q}_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} \sum_{\ell=0}^{M_j-1} (\nu_{j,\ell} + \sigma_{j,\ell})\, q_{j,\ell}.$$

A neutrality condition compensating for the missing equation for $\frac{\mathrm{d}q_0}{\mathrm{d}t}$ is required:

$$q_0 = \Lambda - \sum_{j=1}^{N_{\text{comp}}-1} \sum_{\ell=0}^{M_j-1} \nu_{j,\ell} q_{j,\ell}.$$

See Table 3.5.29.

The concept of reference concentrations (c_{ref} and q_{ref}) is explained in the respective paragraph in Section 2.3.

2.3.12 Simplified Multi-State Steric Mass Action

The simplified multi-state steric mass action is the same as the multi-state SMA model described above (see Section 2.3.11), but with additional assumptions:

- Molecules are only exchanged between two adjacent states, that is, no transfer from state $q_{i,1}$ to state $q_{i,3}$ is allowed.

- Characteristic charge $\nu_{i,j}$ and shielding factor $\sigma_{i,j}$ only depend on the index of the state j.

Thus, the exchange parameters $k_{j\ell}^{(i)}$, the characteristic charge $\nu_{i,j}$, and the shielding $\sigma_{i,j}$ can be parameterized with few degrees of freedom. For all $i = 1, \ldots, N_{\text{comp}} - 1$ and $j, \ell = 0, \ldots, M_i - 1$ let

$$
k_{j\ell}^{(i)} = \begin{cases} 0, & \text{for } |j - \ell| \neq 1 \\ K_{ws}^{(i)} + jK_{ws,\text{lin}}^{(i)} - K_{ws,\text{quad}}^{(i)}j(j - M_i + 2), & \text{for } \ell = j + 1 \\ K_{sw}^{(i)} + \ell K_{sw,\text{lin}}^{(i)} - K_{sw,\text{quad}}^{(i)}\ell(\ell - M_i + 2), & \text{for } \ell = j - 1, \end{cases}
$$

$$
\nu_{i,j} = \nu_{\min,i} + \frac{j}{M_i - 1}\left(\nu_{\max,i} - \nu_{\min,i}\right) - \nu_{\text{quad},i}j(j - M_i + 1),
$$

$$
\sigma_{i,j} = \sigma_{\min,i} + \frac{j}{M_i - 1}\left(\sigma_{\max,i} - \sigma_{\min,i}\right) - \sigma_{\text{quad},i}j(j - M_i + 1).
$$

Note that the characteristic charge $\nu_{i,j}$ has to be monotonically non-decreasing in the second index j and all other rates and the steric factor $\sigma_{i,j}$ have to be non-negative. See Table 3.5.30.

2.3.13 Bi Steric Mass Action

Similar to the Bi-Langmuir model (see Section 2.3.9), 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 2.3.4) without allowing an exchange between the different sites $q_{i,j}$ and $q_{i,k}$ $(k \neq j)$. Therefore, there are no competitivity effects between the two types of binding sites and they have independent capacities.

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

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

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

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

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

Note that all binding components must have exactly the same number of binding site types $M \geq 1$. See Table 3.5.31.

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 2.3.

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.

3 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.

File format versions The file format may change and evolve over time as new features are added to the simulator. This manual describes the most recent file format version that is also set as default value in `/meta/FILE_FORMAT` (see Tab. 3.7.1). The simulator assumes that the input file uses the most recent format version and does not update old files to the current standard.

3.1 Global structure

The global structure (see Fig. 3.1.1) is divided into three parts: `input`, `output`, and `meta`. Every valid CADET file needs an `input` group (see Fig. 3.1.2) which contains all relevant information for simulating a model. It does not need an `output` (see Fig. 3.1.4) or `meta` (see Fig. 3.1.1) 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.
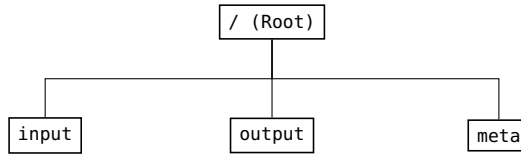
Figure 3.1.1: *Structure of the groups in the root group of the file format*
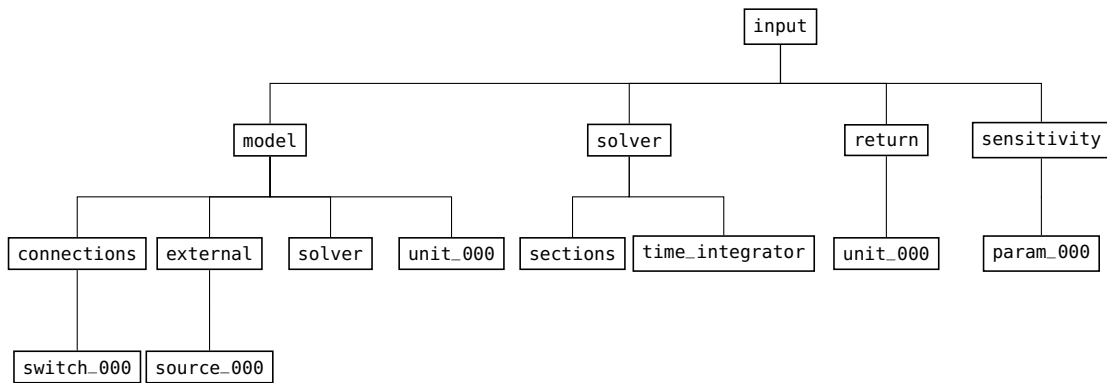
Figure 3.1.2: *High-level structure of the groups in the input part of the file format*
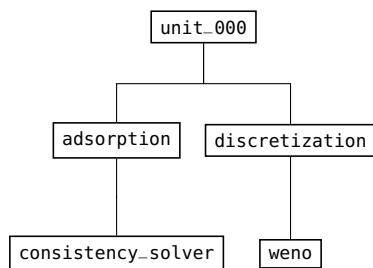
Figure 3.1.3: *Structure of the groups in a column unit operation (`/input/model` group)*
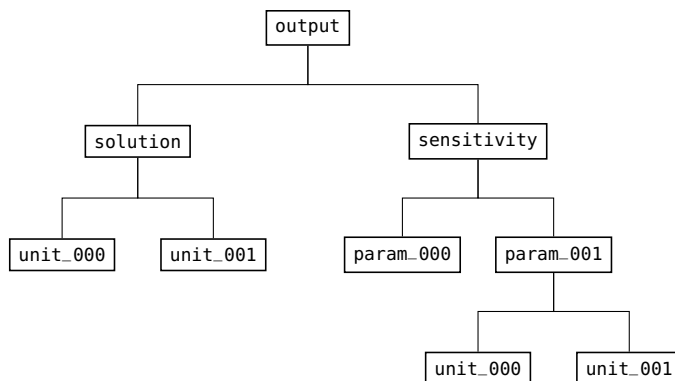
Figure 3.1.4: *Structure of the groups in the output part of the file format*

3.2 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 3.2.1.

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 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 3.2.1: *Common notation and identifiers used in the file format description*

3.3 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.

3.4 Section dependent model parameters

Some model parameters (see Table 3.4.1) 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 3.4.1: *Section dependent datasets in the unit operation models (`/input/model/unit_XXX` group)*

3.5 Input group

3.5.1 System of unit operations

	Group `/input/model`				
Dataset	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 3.5.1: *Datasets in the `/input/model/` group*

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

Table 3.5.2: *Datasets in the /input/model/connections group*

Group /input/model/connections/switch_XXX					
Dataset	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 *UnitOpID from, UnitOpID to, Component from, Component to, volumetric flow rate.* If both component indices are −1, all components are connected.	–	double	≥ -1	NCONNECTIONS $\times$ 5

Table 3.5.3: *Datasets in the /input/model/connections/switch_XXX group*

EXTFUN_TYPE = LINEAR_INTERP_DATA – Group /input/model/external/source_XXX					
Dataset	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 3.5.4: *Datasets in the /input/model/external/source_XXX group*

EXTFUN_TYPE = PIECEWISE_CUBIC_POLY – Group /input/model/external/source_XXX					
Dataset	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 3.5.5: *Datasets in the /input/model/external/source_XXX group*

Group /input/model/solver				
Dataset	Description	Type	Range	Length
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 GMRES 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 3.5.6: *Datasets in the /input/model/solver group*

3.5.2 Unit operation models

Inlet

UNIT_TYPE = INLET – Group /input/model/unit_XXX					
Dataset	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 3.5.7: *Datasets for the inlet unit operation (/input/model/unit_XXX group)*

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

Table 3.5.8: *Datasets in the /input/model/unit_XXX/sec_XXX groups*

Outlet

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

Table 3.5.9: *Datasets for the outlet unit operation (/input/model/unit_XXX group)*

General rate model

UNIT_TYPE = GENERAL_RATE_MODEL – Group /input/model/unit_XXX					
Dataset	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 3.5.4	1
INIT_C	Initial concentrations for each comp. in the bulk mobile phase	$\mathrm{mol\,m_{IV}^{-3}}$	double	≥ 0.0	NCOMP
INIT_CP	Initial concentrations for each comp. in the bead liquid phase (optional, INIT_C is used if left out)	$\mathrm{mol\,m_{MP}^{-3}}$	double	≥ 0.0	NCOMP
INIT_Q	Same as INIT_C but for the bound phase	$\mathrm{mol\,m_{SP}^{-3}}$	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 * $ NDOF, then the second half is used for time derivatives)	various	double	–	NDOF
COL_DISPERSION	Axial dispersion coefficient	$\mathrm{m_{IV}^2\,s^{-1}}$	double	≥ 0.0	1 / NSEC
COL_LENGTH	Column length	m	double	> 0.0	1
COL_POROSITY	Column porosity	–	double	$[0, 1]$	1
FILM_DIFFUSION	Film diffusion coefficients	$\mathrm{m\,s^{-1}}$	double	≥ 0.0	NCOMP / NCOMP $\times$ NSEC
PAR_POROSITY	Particle porosity	–	double	$[0, 1]$	1
PAR_RADIUS	Particle radius	m	double	> 0.0	1
PORE_ACCESSIBILITY	Pore accessibility factor (optional, defaults to all 1)	–	double	$(0, 1]$	NCOMP
PAR_DIFFUSION	Effective particle diffusion coefficients	$\mathrm{m_{MP}^2\,s^{-1}}$	double	≥ 0.0	NCOMP / NCOMP $\times$ NSEC
PAR_SURFDIFFUSION	Particle surface diffusion coefficients	$\mathrm{m_{SP}^2\,s^{-1}}$	double	≥ 0.0	NTOTALBND / NTOTALBND $\times$ NSEC
VELOCITY	Interstitial velocity of the mobile phase (optional if CROSS_SECTION_AREA is present, see Section 2.2.3)	$\mathrm{m\,s^{-1}}$	double		1 / NSEC
CROSS_SECTION_AREA	Cross section area of the column (optional if VELOCITY is present, see Section 2.2.3)	$\mathrm{m^2}$	double	> 0.0	1

Table 3.5.10: *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 GMRES 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 3.5.11: *Datasets for the discretization of the general rate model unit operation (/input/model/unit_XXX/discretization group)*

UNIT_TYPE = LUMPED_RATE_MODEL_WITH_PORES – Group /input/model/unit_XXX					
Dataset	Description	Unit	Type	Range	Length
UNIT_TYPE	Specifies the type of unit operation model	–	string	LUMPED_RATE_MODEL_WITH_PORES	1
NCOMP	Number of chemical components in the chromatographic media	–	int	≥ 1	1
ADSORPTION_MODEL	Specifies the type of adsorption model	–	string	See Section 3.5.4	1
INIT_C	Initial concentrations for each comp. in the bulk mobile phase	$\mathrm{mol\,m_{IV}^{-3}}$	double	≥ 0.0	NCOMP
INIT_CP	Initial concentrations for each comp. in the bead liquid phase (optional, INIT_C is used if left out)	$\mathrm{mol\,m_{MP}^{-3}}$	double	≥ 0.0	NCOMP
INIT_Q	Same as INIT_C but for the bound phase	$\mathrm{mol\,m_{SP}^{-3}}$	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 * $ NDOF, then the second half is used for time derivatives)	various	double	–	NDOF
COL_DISPERSION	Axial dispersion coefficient	$\mathrm{m_{IV}^{2}\,s^{-1}}$	double	≥ 0.0	1 / NSEC
COL_LENGTH	Column length	m	double	> 0.0	1
COL_POROSITY	Column porosity	–	double	$[0, 1]$	1
FILM_DIFFUSION	Film diffusion coefficients	$\mathrm{m\,s^{-1}}$	double	≥ 0.0	NCOMP / NCOMP $\times$ NSEC
PAR_POROSITY	Particle porosity	–	double	$[0, 1]$	1
PAR_RADIUS	Particle radius	m	double	> 0.0	1
PORE_ACCESSIBILITY	Pore accessibility factor (optional, defaults to all 1)	–	double	$(0, 1]$	NCOMP
VELOCITY	Interstitial velocity of the mobile phase (optional if CROSS_SECTION_AREA is present, see Section 2.2.3)	$\mathrm{m\,s^{-1}}$	double		1 / NSEC
CROSS_SECTION_AREA	Cross section area of the column (optional if VELOCITY is present, see Section 2.2.3)	$\mathrm{m^2}$	double	> 0.0	1

28

Table 3.5.12: *Datasets for the lumped rate model with pores unit operation (/input/model/unit_XXX group)*

UNIT_TYPE = LUMPED_RATE_MODEL_WITH_PORES – Group /input/model/unit_XXX/discretization					
Dataset	Description	Unit	Type	Range	Length
NCOL	Number of column (axial) discretization cells	–	int	≥ 1	1
NBOUND	Number of bound states for each component	–	int	≥ 0	NCOMP
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 GMRES 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 3.5.13: *Datasets for the discretization of the lumped rate model with pores unit operation (/input/model/unit_XXX/discretization group)*

Lumped rate model without pores

UNIT_TYPE = LUMPED_RATE_MODEL_WITHOUT_PORES – Group /input/model/unit_XXX					
Dataset	Description	Unit	Type	Range	Length
UNIT_TYPE	Specifies the type of unit operation model	–	string	LUMPED_RATE_MODEL_WITHOUT_PORES	1
NCOMP	Number of chemical components in the chromatographic media	–	int	≥ 1	1
ADSORPTION_MODEL	Specifies the type of adsorption model	–	string	See Section 3.5.4	1
INIT_C	Initial concentrations for each comp. in the bulk mobile phase	$\mathrm{mol\,m_{IV}^{-3}}$	double	≥ 0.0	NCOMP
INIT_Q	Same as INIT_C but for the bound phase	$\mathrm{mol\,m_{SP}^{-3}}$	double	≥ 0.0	NTOTALBND
INIT_STATE	Full state vector for initialization (optional, INIT_C and INIT_Q will be ignored; if length is $2 * $ NDOF, then the second half is used for time derivatives)	various	double	–	NDOF
COL_DISPERSION	Axial dispersion coefficient	$\mathrm{m_{IV}^2\,s^{-1}}$	double	≥ 0.0	1 / NSEC
COL_LENGTH	Column length	m	double	> 0.0	1
TOTAL_POROSITY	Total porosity	–	double	$[0, 1]$	1
VELOCITY	Interstitial velocity of the mobile phase (optional if CROSS_SECTION_AREA is present, see Section 2.2.3)	$\mathrm{m\,s^{-1}}$	double		1 / NSEC
CROSS_SECTION_AREA	Cross section area of the column (optional if VELOCITY is present, see Section 2.2.3)	$\mathrm{m^2}$	double	> 0.0	1

Table 3.5.14: *Datasets for the lumped rate model without pores unit operation (/input/model/unit_XXX group)*

UNIT_TYPE = LUMPED_RATE_MODEL_WITHOUT_PORES – Group /input/model/unit_XXX/discretization					
Dataset	Description	Unit	Type	Range	Length
NCOL	Number of column (axial) discretization cells	–	int	≥ 1	1
NBOUND	Number of bound states for each component	–	int	≥ 0	NCOMP
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

Table 3.5.15: *Datasets for the discretization of the lumped rate model without pores unit operation (/input/model/unit_XXX/discretization group)*

Continuously stirred tank reactor model

UNIT_TYPE = CSTR – Group /input/model/unit_XXX					
Dataset	Description	Unit	Type	Range	Length
UNIT_TYPE	Specifies the type of unit operation model	–	string	CSTR	1
NCOMP	Number of chemical components in the chromatographic media	–	int	≥ 1	1
NBOUND	Number of bound states for each component (optional, defaults to all 0)	–	int	≥ 0	NCOMP
USE_ANALYTIC_JACOBIAN	Use analytically computed Jacobian matrix (faster) instead of Jacobian generated by algorithmic differentiation (optional, defaults to 1)	–	int	0/1	1
ADSORPTION_MODEL	Specifies the type of adsorption model (optional, defaults to NONE)	–	string	See Section 3.5.4	1
INIT_C	Initial concentrations for each comp. in the mobile phase	$\mathrm{mol\,m_{IV}^{-3}}$	double	≥ 0.0	NCOMP
INIT_VOLUME	Initial tank volume	$\mathrm{m^3}$	double	≥ 0.0	1
INIT_Q	Same as INIT_C but for the bound phase (optional, defaults to all 0)	$\mathrm{mol\,m_{SP}^{-3}}$	double	≥ 0.0	NTOTALBND
INIT_STATE	Full state vector for initialization (optional, INIT_C, INIT_Q, and INIT_VOLUME will be ignored; if length is $2 * $ NDOF, then the second half is used for time derivatives)	various	double	–	NDOF
POROSITY	Porosity ε (defaults to 1)	–	double	$[0, 1]$	1
FLOWRATE_FILTER	Flow rate of pure liquid without components (optional, defaults to $0\,\mathrm{m^3\,s^{-1}}$)	$\mathrm{m^3\,s^{-1}}$	double	≥ 0.0	1 / NSEC

Table 3.5.16: *Datasets for the continuously stirred tank reactor unit operation (/input/model/unit_XXX group)*

3.5.3 Flux reconstruction methods

WENO parameters – Group /input/model/unit_XXX/discretization/weno			
Dataset	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 3.5.17: *Datasets for the WENO reconstruction (/input/model/unit_XXX/discretization/weno group)*

3.5.4 Adsorption models

Externally dependent binding models   Some binding models have a variant that can use external sources as specified in Section 3.5.1 (also see Section 2.3 and Table 2.3.1 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:

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

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.

Nonlinear consistency solver parameters – Group `/input/model/unit_XXX/adsorption/consistency_solver`				
Dataset	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 3.5.18: *Datasets for the nonlinear consistency solver (`/input/model/unit_XXX/adsorption/consistency_solver` group)*

ADSORPTION_MODEL = LINEAR – 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
`LIN_KA`	Adsorption rate constants	$\mathrm{m^3_{MP}\,m^{-3}_{SP}\,s^{-1}}$	double	≥ 0.0	NCOMP
`LIN_KD`	Desorption rate constants	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP

Table 3.5.19: *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	$\mathrm{m^3_{MP}\,mol^{-1}\,s^{-1}}$	double	≥ 0.0	NCOMP
`MCL_KD`	Desorption rate constants	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP
`MCL_QMAX`	Maximum adsorption capacities	$\mathrm{mol\,m^{-3}_{SP}}$	double	> 0.0	NCOMP

Table 3.5.20: *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	$\mathrm{m^3_{MP}\,mol^{-1}\,s^{-1}}$	double	≥ 0.0	NCOMP
`MCAL_KD`	Desorption rate constants	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP
`MCAL_QMAX`	Maximum adsorption capacities	$\mathrm{mol\,m^{-3}_{SP}}$	double	> 0.0	NCOMP
`MCAL_ANTILANGMUIR`	Anti-Langmuir coefficients (optional)	–	double	$\{-1, 1\}$	NCOMP

Table 3.5.21: *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	$\mathrm{m}^3_{\mathrm{MP}}\,\mathrm{mol}^{-1}\,\mathrm{s}^{-1}$	double	≥ 0.0	NCOMP
MPM_KD	Desorption rate constants	$\mathrm{m}^{3\beta}_{\mathrm{MP}}\,\mathrm{mol}^{-\beta}\,\mathrm{s}^{-1}$	double	≥ 0.0	NCOMP
MPM_QMAX	Maximum adsorption capacities	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{SP}}$	double	≥ 0.0	NCOMP
MPM_BETA	Parameters describing the ion-exchange characteristics (IEX)	–	double	≥ 0.0	NCOMP
MPM_GAMMA	Parameters describing the hydrophobicity (HIC)	$\mathrm{m}^3_{\mathrm{MP}}\,\mathrm{mol}^{-1}$	double	≥ 0.0	NCOMP

Table 3.5.22: *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	$\mathrm{m}^3_{\mathrm{MP}}\,\mathrm{m}^{-3}_{\mathrm{SP}}\,\mathrm{s}^{-1}$	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	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{SP}}$	double	≥ 0.0	1
SMA_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{MP}}$	double	> 0.0	1
SMA_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{SP}}$	double	> 0.0	1

Table 3.5.23: *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	$\mathrm{m}^3_{\mathrm{MP}}\,\mathrm{m}^{-3}_{\mathrm{SP}}\,\mathrm{s}^{-1}$	double	≥ 0.0	NCOMP
SAI_KA2	Adsorption rate constants of dimerization	$\mathrm{m}^6_{\mathrm{MP}}\,\mathrm{m}^{-6}_{\mathrm{SP}}\,\mathrm{s}^{-1}$	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	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{SP}}$	double	≥ 0.0	1
SAI_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{MP}}$	double	> 0.0	1
SAI_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$\mathrm{mol}\,\mathrm{m}^{-3}_{\mathrm{SP}}$	double	> 0.0	1

Table 3.5.24: *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	$\mathrm{m_{MP}^3\,m_{SP}^{-3}\,s^{-1}}$	double	$\mathbb{R}$	NCOMP
SASKA_K	Quadratic factors	$\mathrm{m_{MP}^6\,m_{SP}^{-3}\,mol^{-1}\,s^{-1}}$	double	$\mathbb{R}$	NCOMP^2

Table 3.5.25: *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	$\mathrm{m_{MP}^3\,mol^{-1}\,s^{-1}}$	double	≥ 0.0	NSTATES · NCOMP
MCBL_KD	Desorption rate constants in state-major ordering	$\mathrm{s^{-1}}$	double	≥ 0.0	NSTATES · NCOMP
MCBL_QMAX	Maximum adsorption capacities in state-major ordering	$\mathrm{mol\,m_{SP}^{-3}}$	double	> 0.0	NSTATES · NCOMP

Table 3.5.26: *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	$\mathrm{m_{MP}^3\,mol^{-1}\,s^{-1}}$	double	≥ 0.0	NCOMP
KMCL_KD	Desorption rate	$\mathrm{m_{MP}^{3\nu_i}\,mol^{-\nu_i}\,s^{-1}}$	double	≥ 0.0	NCOMP
KMCL_KACT	Activation temperatures	K	double	≥ 0.0	NCOMP
KMCL_QMAX	Maximum adsorption capacities	$\mathrm{mol\,m_{SP}^{-3}}$	double	> 0.0	NCOMP
KMCL_NU	Salt exponents / characteristic charges	–	double	> 0.0	NCOMP
KMCL_TEMP	Temperature	K	double	≥ 0	1

Table 3.5.27: *Datasets for the Kumar-Langmuir adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = MULTI_COMPONENT_SPREADING – 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
MCSPR_KA	Adsorption rate constants in state-major ordering	$\mathrm{m_{MP}^3\,mol^{-1}\,s^{-1}}$	double	≥ 0.0	NTOTALBND
MCSPR_KD	Desorption rate constants in state-major ordering	$\mathrm{s^{-1}}$	double	≥ 0.0	NTOTALBND
MCSPR_QMAX	Maximum adsorption capacities in state-major ordering	$\mathrm{mol\,m_{SP}^{-3}}$	double	> 0.0	NTOTALBND
MCSPR_K12	Exchange rates from the first to the second bound state	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP
MCSPR_K21	Exchange rates from the second to the first bound state	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP

Table 3.5.28: *Datasets for the multi component spreading adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = MULTISTATE_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
MSSMA_KA	Adsorption rate constants of the components to the different bound states in component-major ordering	$\mathrm{m^3_{MP}\,m^{-3}_{SP}\,s^{-1}}$	double	≥ 0.0	NTOTALBND
MSSMA_KD	Desorption rate constants of the components in the different bound states in component-major ordering	$\mathrm{s^{-1}}$	double	≥ 0.0	NTOTALBND
MSSMA_NU	Characteristic charges of the components in the different bound states in component-major ordering	–	double	≥ 0.0	NTOTALBND
MSSMA_SIGMA	Steric factors of the components in the different bound states in component-major ordering	–	double	≥ 0.0	NTOTALBND
MSSMA_RATES	Conversion rates between different bound states in component-row-major ordering	$\mathrm{s^{-1}}$	double	≥ 0.0	$\sum_{i=0}^{\mathrm{NCOMP}-1}\mathrm{NBND}_i^2$
MSSMA_LAMBDA	Stationary phase capacity (monovalent salt counterions); The total number of binding sites available on the resin surface	$\mathrm{mol\,m^{-3}_{SP}}$	double	≥ 0.0	1
MSSMA_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$\mathrm{mol\,m^{-3}_{MP}}$	double	> 0.0	1
MSSMA_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$\mathrm{mol\,m^{-3}_{SP}}$	double	> 0.0	1

Table 3.5.29: *Datasets for the multi state steric mass action adsorption model (/input/model/unit_XXX/adsorption group)*

ADSORPTION_MODEL = SIMPLE_MULTISTATE_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
SMSSMA_LAMBDA	Stationary phase capacity (monovalent salt counterions); The total number of binding sites available on the resin surface	$\mathrm{mol\,m_{SP}^{-3}}$	double	≥ 0.0	1
SMSSMA_KA	Adsorption rate constants of the components to the different bound states in component-major ordering	$\mathrm{m_{MP}^{3}\,m_{SP}^{-3}\,s^{-1}}$	double	≥ 0.0	NTOTALBND
SMSSMA_KD	Desorption rate constants of the components to the different bound states in component-major ordering	$\mathrm{s^{-1}}$	double	≥ 0.0	NTOTALBND
SMSSMA_NU_MIN	Characteristic charges of the components in the first (weakest) bound state	–	double	≥ 0.0	NCOMP
SMSSMA_NU_MAX	Characteristic charges of the components in the last (strongest) bound state	–	double	≥ 0.0	NCOMP
SMSSMA_NU_QUAD	Quadratic modifiers of the characteristic charges of the different components depending on the index of the bound state	–	double	$\mathbb{R}$	NCOMP
SMSSMA_SIGMA_MIN	Steric factors of the components in the first (weakest) bound state	–	double	≥ 0.0	NCOMP
SMSSMA_SIGMA_MAX	Steric factors of the components in the last (strongest) bound state	–	double	≥ 0.0	NCOMP
SMSSMA_SIGMA_QUAD	Quadratic modifiers of steric factors of the different components depending on the index of the bound state	–	double	$\mathbb{R}$	NCOMP
SMSSMA_KWS	Exchange rates from a weakly bound state to the next stronger bound state	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP
SMSSMA_KWS_LIN	Linear exchange rate coefficients from a weakly bound state to the next stronger bound state	$\mathrm{s^{-1}}$	double	$\mathbb{R}$	NCOMP
SMSSMA_KWS_QUAD	Quadratic exchange rate coefficients from a weakly bound state to the next stronger bound state	$\mathrm{s^{-1}}$	double	$\mathbb{R}$	NCOMP
SMSSMA_KSW	Exchange rates from a strongly bound state to the next weaker bound state	$\mathrm{s^{-1}}$	double	≥ 0.0	NCOMP
SMSSMA_KSW_LIN	Linear exchange rate coefficients from a strongly bound state to the next weaker bound state	$\mathrm{s^{-1}}$	double	$\mathbb{R}$	NCOMP
SMSSMA_KSW_QUAD	Quadratic exchange rate coefficients from a strongly bound state to the next weaker bound state	$\mathrm{s^{-1}}$	double	$\mathbb{R}$	NCOMP
SMSSMA_REFC0	Reference liquid phase concentration (optional, defaults to 1.0)	$\mathrm{mol\,m_{MP}^{-3}}$	double	> 0.0	1
SMSSMA_REFQ	Reference solid phase concentration (optional, defaults to 1.0)	$\mathrm{mol\,m_{SP}^{-3}}$	double	> 0.0	1

Table 3.5.30: *Datasets for the simplified multi state steric mass action 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	$\mathrm{m}_{\mathrm{MP}}^3\,\mathrm{m}_{\mathrm{SP}}^{-3}\,\mathrm{s}^{-1}$	double	≥ 0.0	NSTATES · NCOMP
BISMA_KD	Desorption rate constants in state-major ordering	s^{-1}	double	≥ 0.0	NSTATES · NCOMP
BISMA_NU	Characteristic charges $\nu_{i,j}$ of the ith protein with respect to the jth binding site type in state-major ordering	–	double	≥ 0.0	NSTATES · NCOMP
BISMA_SIGMA	Steric factors $\sigma_{i,j}$ of the ith protein with respect to the jth binding site type in state-major ordering	–	double	≥ 0.0	NSTATES · NCOMP
BISMA_LAMBDA	Stationary phase capacity (monovalent salt counterions) of the different binding site types λ_j	$\mathrm{mol}\,\mathrm{m}_{\mathrm{SP}}^{-3}$	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)	$\mathrm{mol}\,\mathrm{m}_{\mathrm{MP}}^{-3}$	double	> 0.0	1/NSTATES
BISMA_REFQ	Reference solid phase concentration for each binding site type or one value for all types (optional, defaults to 1.0)	$\mathrm{mol}\,\mathrm{m}_{\mathrm{SP}}^{-3}$	double	> 0.0	1/NSTATES

Table 3.5.31: *Datasets for the bi steric mass action adsorption model (`/input/model/unit_XXX/adsorption` group)*

3.5.5 Return data

	Group `/input/return`		
Dataset	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 3.5.32: *Datasets in the `/input/model/return` group*

	Group `/input/return/unit_XXX`		
Dataset	Description	Type	Range
WRITE_SOLUTION_INLET	Write solutions at unit operation inlet $c_i(t,0)$	int	0/1
WRITE_SOLUTION_OUTLET	Write solutions at unit operation outlet (chromatograms) $c_i(t,L)$	int	0/1
WRITE_SOLUTION_BULK	Write solutions of the bulk volume c_i	int	0/1
WRITE_SOLUTION_PARTICLE	Write solutions of the particle mobile phase $c_{p,i}$	int	0/1
WRITE_SOLUTION_SOLID	Write solutions of the solid phase $q_{i,j}$	int	0/1
WRITE_SOLUTION_FLUX	Write solutions of the bead fluxes $j_{f,i}$	int	0/1
WRITE_SOLUTION_VOLUME	Write solutions of the volume V	int	0/1
WRITE_SOLDOT_INLET	Write solution time derivatives at unit operation inlet $\partial c_i(t,0)/\partial t$	int	0/1
WRITE_SOLDOT_OUTLET	Write solution time derivatives at unit operation outlet (chromatograms) $\partial c_i(t,L)/\partial t$	int	0/1
WRITE_SOLDOT_BULK	Write solution time derivatives of the bulk volume $\partial c_i/\partial t$	int	0/1
WRITE_SOLDOT_PARTICLE	Write solution time derivatives of the particle mobile phase $\partial c_{p,i}/\partial t$	int	0/1
WRITE_SOLDOT_SOLID	Write solution time derivatives of the solid phase $\partial q_{i,j}/\partial t$	int	0/1
WRITE_SOLDOT_FLUX	Write solution time derivatives of the bead fluxes $\partial j_{f,i}/\partial t$	int	0/1
WRITE_SOLDOT_VOLUME	Write solution time derivatives of the volume $\partial V/\partial t$	int	0/1
WRITE_SENS_INLET	Write sensitivities at unit operation inlet $\partial c_i(t,0)/\partial p$	int	0/1
WRITE_SENS_OUTLET	Write sensitivities at unit operation outlet (chromatograms) $\partial c_i(t,L)/\partial p$	int	0/1
WRITE_SENS_BULK	Write sensitivities of the bulk volume $\partial c_i/\partial p$	int	0/1
WRITE_SENS_PARTICLE	Write sensitivities of the particle mobile phase $\partial c_{p,i}/\partial p$	int	0/1
WRITE_SENS_SOLID	Write sensitivities of the solid phase $\partial q_{i,j}/\partial p$	int	0/1
WRITE_SENS_FLUX	Write sensitivities of the bead fluxes $\partial j_{f,i}/\partial p$	int	0/1
WRITE_SENS_VOLUME	Write sensitivities of the volume $\partial V/\partial p$	int	0/1
WRITE_SENSDOT_INLET	Write sensitivity time derivatives at unit operation inlet $\partial^2 c_i(t,0)/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_OUTLET	Write sensitivity time derivatives at unit operation outlet (chromatograms) $\partial^2 c_i(t,L)/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_BULK	Write sensitivity time derivatives of the bulk volume $\partial^2 c_i/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_PARTICLE	Write sensitivity time derivatives of the particle mobile phase $\partial^2 c_{p,i}/(\partial p, \partial t)$	int	0/1
WRITE_SENSDOT_SOLID	Write sensitivity time derivatives of the solid phase $\partial^2 q_{i,j}/(\partial p, \partial t)$	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
WRITE_SENSDOT_VOLUME	Write sensitivity time derivatives of the volume $\partial^2 V/(\partial p, \partial t)$	int	0/1

Table 3.5.33: *Datasets in the `/input/model/return/unit_XXX` group*

3.5.6 Parameter sensitivities

	Group /input/sensitivity		
Dataset	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 3.5.34: *Datasets in the /input/sensitivity group*

	Group /input/sensitivity/param_XXX			
Dataset	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 3.5.35: *Datasets in the /input/sensitivity/param_XXX groups*

3.5.7 Solver configuration

	Group /input/solver				
Dataset	Description	Unit	Type	Range	Length
NTHREADS	Number of used 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) 5 (full once, then lean) 6 (none once, then full) 7 (none once, then 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) 5 (full once, then lean) 6 (none once, then full) 7 (none once, then lean)	1

Table 3.5.36: *Datasets in the /input/solver group*

Group /input/solver/time_integrator				
Dataset	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
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 Sec. 4.5	int	≥ 0.0	1
MAX_STEP_SIZE	Maximum size of timesteps taken by IDAS (optional, defaults to unlimited 0.0), see IDAS guide Sec. 4.5	double	≥ 0	1
ERRORTEST_SENS	Determines whether (forward) sensitivities take part in local error test (optional, defaults to 1)	int	0/1	1
MAX_NEWTON_ITER	Maximum number of Newton iterations in time step (optional, defaults to 3)	int	≥ 0	1
MAX_ERRTEST_FAIL	Maximum number of local error test failures in time step (optional, defaults to 7)	int	≥ 0	1
MAX_CONVTEST_FAIL	Maximum number of Newton convergence test failures (optional, defaults to 10)	int	≥ 0	1
MAX_NEWTON_ITER_SENS	Maximum number of Newton iterations in forward sensitivity time step (optional, defaults to 3)	int	≥ 0	1

Table 3.5.37: *Datasets in the /input/solver/time_integrator group*

Group /input/solver/sections					
Dataset	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 3.5.38: *Datasets in the /input/solver/sections group*

3.6 Output group

Group /output/solution			
Dataset	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 3.6.1: *Datasets in the /output group*

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

Table 3.6.2: *Datasets in the /output/solution group*

Group /output/solution/unit_XXX			
Dataset	Description	Unit	Type
SOLUTION_BULK	Interstitial solution as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{IV}^{-3}}$	double
SOLUTION_PARTICLE	Mobile phase solution inside the beads as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{MP}^{-3}}$	double
SOLUTION_SOLID	Solid phase solution as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{SP}^{-3}}$	double
SOLUTION_FLUX	Flux solution as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m^{-2}\,s^{-1}}$	double
SOLUTION_VOLUME	Volume solution	$\mathrm{m^3}$	double
SOLUTION_OUTLET	Matrix of solutions at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\mathrm{mol\,m_{IV}^{-3}}$	double
SOLUTION_INLET	Matrix of solutions at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\mathrm{mol\,m_{IV}^{-3}}$	double
SOLUTION_OUTLET_COMP_XXX	Component XXX of the solution at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\mathrm{mol\,m_{IV}^{-3}}$	double
SOLUTION_INLET_COMP_XXX	Component XXX of the solution at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\mathrm{mol\,m_{IV}^{-3}}$	double
SOLDOT_BULK	Interstitial solution time derivative as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{IV}^{-3}\,s^{-1}}$	double
SOLDOT_PARTICLE	Mobile phase solution time derivative inside the beads as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{MP}^{-3}\,s^{-1}}$	double
SOLDOT_SOLID	Solid phase solution time derivative as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m_{SP}^{-3}\,s^{-1}}$	double
SOLDOT_FLUX	Flux solution time derivative as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\mathrm{mol\,m^{-2}\,s^{-2}}$	double
SOLDOT_VOLUME	Volume time derivatives	$\mathrm{m^3\,s^{-1}}$	double
SOLDOT_OUTLET	Matrix of solution time derivatives at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\mathrm{mol\,m_{IV}^{-3}\,s^{-1}}$	double
SOLDOT_INLET	Matrix of solution time derivatives at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\mathrm{mol\,m_{IV}^{-3}\,s^{-1}}$	double
SOLDOT_OUTLET_COMP_XXX	Component XXX of the solution time derivative at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\mathrm{mol\,m_{IV}^{-3}\,s^{-1}}$	double
SOLDOT_INLET_COMP_XXX	Component XXX of the solution time derivative at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\mathrm{mol\,m_{IV}^{-3}\,s^{-1}}$	double

Table 3.6.3: *Datasets in the /output/solution/unit_XXX group*

Group /output/sensitivity/param_XXX/unit_YYY			
Dataset	Description	Unit	Type
SENS_BULK	Interstitial sensitivity as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_PARTICLE	Mobile phase sensitivity inside the beads as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{MP}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_SOLID	Solid phase sensitivity as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{SP}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_FLUX	Flux sensitivity as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}^{-2}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENS_VOLUME	Volume sensitivity	$\text{m}^3\,[\text{Param}]^{-1}$	double
SENS_OUTLET	Matrix of sensitivities at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_INLET	Matrix of sensitivities at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_OUTLET_COMP_XXX	Component XXX of the sensitivity at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,[\text{Param}]^{-1}$	double
SENS_INLET_COMP_XXX	Component XXX of the sensitivity at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,[\text{Param}]^{-1}$	double
SENSDOT_BULK	Interstitial sensitivity time derivative as n_{Time}UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_PARTICLE	Mobile phase sensitivity time derivative inside the beads as n_{Time}UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{MP}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_SOLID	Solid phase sensitivity time derivative as n_{Time}UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}_{\text{SP}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_FLUX	Flux sensitivity time derivative as $n_{\text{Time}} \times$ UNITOPORDERING tensor in row-major storage	$\text{mol}\,\text{m}^{-2}\,\text{s}^{-2}\,[\text{Param}]^{-1}$	double
SENSDOT_VOLUME	Volume sensitivity time derivatives	$\text{m}^3\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_OUTLET	Matrix of sensitivity time derivatives at the unit operation outlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_INLET	Matrix of sensitivity time derivatives at the unit operation inlet with components as columns (only present if SPLIT_COMPONENTS_DATA is disabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_OUTLET_COMP_XXX	Component XXX of the sensitivity time derivative at the unit operation outlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double
SENSDOT_INLET_COMP_XXX	Component XXX of the sensitivity time derivative at the unit operation inlet (only present if SPLIT_COMPONENTS_DATA is enabled)	$\text{mol}\,\text{m}_{\text{IV}}^{-3}\,\text{s}^{-1}\,[\text{Param}]^{-1}$	double

Table 3.6.4: *Datasets in the /output/sensitivity/param_XXX/unit_YYY groups*

3.7 Meta group

Dataset	Group /meta Description	In / out	Type
FILE_FORMAT	Version of the file format (defaults to 030102 = 3.1.2 if omitted) with two digits per part (Major.Minor.Patch)	In	int
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 3.7.1: *Datasets in the /meta group*

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Index