What does a typical analys scheme look like ?

5 Programming the PSE elements

We would like to program: (i) the least squares criterion (consisting of weighted residuals and penalties), (ii) the parameter vector (enabling fixed/free parameters, relations, functional description with higher level parameters, e.g. thermodynamic parameters), (iii) the weighted data, which means compiling the data (e.g. linking) and programming the weights. Special data can be added (with weights) to include apriori knowledge e.g. candidate SAS shapes. The weighted data can be decomposed into P parts:

$$\psi_p = X_p(\theta)\beta_p \qquad p = 1, \ldots, P \tag{107}$$

where each part ψ_p contains n_p observations, with weight w_p, which can be either a scalar or a vector of length n_p. (iv) the matrices $X_p(\theta)$ using hierarchical models.

overhead of using a function?

5.1 Programming the least squares criterion

The weighted residuals are defined as: how calculated varpro nnLS

$$z_p = w_p(\psi_p - X_p(\theta)\hat{\beta}_p) \tag{108}$$

Their sum of squares gives

$$SSE(\theta) = \sum_{p=1}^{P} z_p^T z_p \tag{109}$$

The conditionally linear parameters β_p can be solved for using the variable projection algorithm, possibly with constraints (e.g. non-negative least squares when the β_p represent non-negative SAS). The penalties from (i) are derived from e.g. the spectra. Thus when spectral constraints (zero, or equality) are used, first the *SAS* must be resolved from all β_p. how

Then the area constraint penalty can be computed

Removing collums of X OR setting $X_{p5} = X_{p6}$ thus removing X_{p6} OR $X_{p5,d1} = X_{p5,d2}$ rem $X_{p5,d2}$

$$penalty_{ij} = weight_{ij}\int_{\lambda_{min}}^{\lambda_{max}} |SAS_i(\lambda) - \alpha_{ij}SAS_j(\lambda)|\,d\lambda \tag{110}$$

In practice, with emission SAS, the proportionality factor α_{ij} (which is not a parameter) equals one 1.0 for species with (approximately) equal oscillator strength. The weight is adjusted such that the relative importance of the penalties is not too large, e.g. about 1% of the $SSE(\theta)$. The sum of all penalties and $SSE(\theta)$ is called $\Upsilon(\theta)$.

can this be computed ?

5.2 Programming the parameter vector

In Kate's thesis the hierarchical modelling of the parameter vector is explained. The user specifies the models and the necessary intrinsically nonlinear parameters. Further specifications are fixed/free parameters, relations between parameters, functional description with higher level parameters (e.g. thermodynamic parameters), detailed balance relations between microscopic rates for a clockwise or anticlockwise traversal of a cycle, constraints on parameters, etc. The optimizer only sees a subset of free parameters $\tilde{\theta}$, and minimizes $\Upsilon(\tilde{\theta})$. In the function that computes $\Upsilon(\tilde{\theta})$ (the functor?) this $\tilde{\theta}$ is then translated to the full parameter vector Θ (thereby resolving all the constraints and relations). From Θ all sorts of subsets for different aspects of the kinetic model are then extracted, such as microscopic rates, IRF, linking, scaling, inputs or absorptions, fractions, anisotropy, dumping, frequency and damping rate of damped oscillations, etc. With spectral models a parametric description is sought of spectral shape, Stark effect, time or temperature dependence, etc.

5.3 Programming the weighted data

Each part consists of subparts, which are the experiments. Each experiment has its own IRF, which in general is wavelength dependent (thus differs for all parts). Weight w_p can be either a scalar or a vector of length n_p. The programming of w_p is possible both at the part level or at the subpart level. Special data that represent apriori knowledge on candidate SAS shapes are a special subpart with a single data point (the value at the wavelength of the part). The linkclp mechanism links those wavelengths in different experiments whose difference is less than a tolerance *linktol*. Typically, *linktol* must be smaller than the smallest wavelength step divided by 2, to avoid linking all data. Most often all experiments are linked (because the spectra can be assumed to be equal), although it is possible to specify a linkage scheme (which would be appropriate when analysing multiple experiments at different temperatures, where the spectra differ for with temperature).

5.4 Programming the matrices $X_p(\theta)$ using hierarchical models

An example was given in Hierarchical modelling of time-resolved polarized difference absorption on page 79. Here we describe two new developments: usage of megacomplexes and damped oscillations (for now, see separate pdf).

Partitioned residual vector

- Ragged matrix

λ	t
10	100
10	150
10	1

scal

2X

100

70% m2
30% m1

150

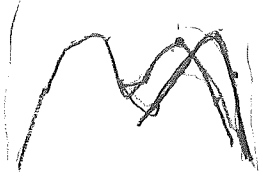
20% m2
80% m1

1X scal

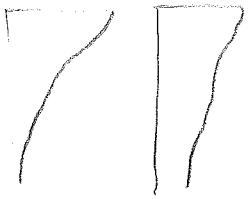
100% m1

10 — 1 ← SSspectra OR (better) SASspectra

pH 11 | pH 7 | ml:2 pH 4



C1 C2



case study #1

pH

megacompex 1

1 → 2 →

↳ ss-spectrum

megacomplex 2

1 ⇄ 2 ⇄ 3 →

dark

linked

#compartments: 2+3=5

#distinct spectra: 3
estimated spectra: 2

case study # 2

temperature ?

5.4.1 Megacomplexes

Assume that we have M megacomplexes. Each megacomplex m is described by a linear compartmental model with n_m compartments. The differential equation for the concentrations of megacomplex m is:

solution?

$$\frac{d}{dt}c_m(t) = K_m c_m(t) + j_m(t) \qquad (111)$$

where the input to the system is described by a vector $j_m(t) = i(t)\left[x_1\ x_2\ \ldots\ x_{n_m}\right]^T$, with $i(t)$ the IRF (§2.1.1) and x_l representing the input to compartment l. Note that each megacomplex can contain only a *subset* of all the species present in the system. An extreme case are special data that represent apriori knowledge on candidate SAS shapes. In that case the full c vector contains only one non-zero element for the index of the candidate SAS. In addition a scaling parameter is still necessary. The amount of megacomplex m present in an experiment is determined by the parameters that describe the inputs x_l. The inputs x_l contains two elements: the absorption and the amount present of species l. The absorption is dependent upon the excitation wavelength, and is common for all equivalent experiments.

how is it implemented

pH dependent

for instance

The modelling is summarized in Table 5. Note the intricate summations needed for $X_p(\theta)$, for

Table 5 Hierarchical modelling of time-resolved emission with megacomplexes

level of modelling	parametric description of	
linking of experiments, resolving the parts, computation of $X_p(\theta)$	relative scaling, linkage schemes	§2.7.5.2
resolving the spectral constraints, $c_l(t)\varepsilon_l(\lambda)$	spectral constraints for component l, $\varepsilon_l(\lambda)$	§2.7.2
summation over all complexes containing component l: $c_l(t) = \sum_{m=1}^{M} c_{l \in m}(t)$		
convolution $c_m(t) = c_m^{\delta}(t) \otimes i(t)$	Instrument Response Function $i(t)$	§2.4.2
MA concentration $c_m^{\delta}(t)$ with δ-input	compartmental scheme for megacomplex m with microscopic rates for n_m compartments	§2.4.3

each experiment all $c_m(t)$ have to be computed for those megacomplexes that are present in that experiment, taking into account the appropriate inputs $\left[x_1\ x_2\ \ldots\ x_{n_m}\right]^T$. Furthermore, keeping track of the indices is essential.