Applied Numerical Computing for Scientists and Engineers

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Weighted Sum of Squared Residuals Example

1. Weighted least squares

Weighted least squares (WLS) minimizes the weighted sum of squared residuals (WSSR or WRSS). This is used to take errors in the data explicitly into account through the weights [1, p. 204]:

$$WLS(p) = \sum_{i=1}^{N} w(t_i)[y(t_i, p) - z(t_i)]^2 = \sum_{i=1}^{N} \frac{1}{\sigma^2(t_i)}[y(t_i, p) - z_i]^2 \tag{1}$$

where i is the index of data points, t_i are the measured time points when data is collected, z_i are the measured output values, $y(t_i, p)$ are the model output calculated values at each time point and with the parameter set p, and $w(t_i) = 1/\sigma^2(t_i)$ are the weights with respect to the standard deviations σ of the output at each time point.

2. Weighted least squares for more than one output

For M outputs, (1) becomes [2, p. 534]

$$WLS(p) = \sum_{i=1}^{N} \sum_{k=1}^{M} w_k(t_i)[y_k(t_i, p) - z_k(t_i)]^2 = \sum_{i=1}^{N} \sum_{k=1}^{M} \frac{1}{\sigma_k^2(t_i)}[y_k(t_i, p) - z_k(t_i)]^2 \tag{2}$$

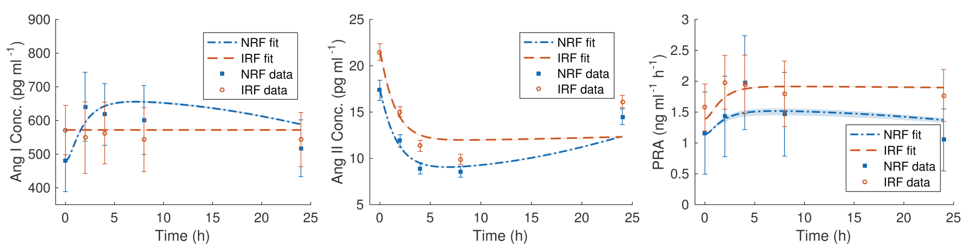
where i is the index of data points, k is the index of the outputs, t_i are the measured time points when data is collected, $z_k(t_i)$ are the measured values of output k, $y_k(t_i, p)$ are the model calculated values of output k at each time point and with the parameter set p, and $w_k(t_i) = 1/\sigma_k^2(t_i)$ are the weights with respect to the standard deviations σ of output k at each time point. Example: `WSSR_Example.m`

```
%% Parameter estimation function for PK-PD model for ACE ...
    inhibition

function param_estimation
format long e
close all
%% Take data from plots
% X is a vector of time points. Ydata is a matrix of Ang ...
    I, Ang II, and
% PRA values at each of the time points estimated from ...
    Shionori data during
% inhibition by ACE inhibitor drugs
paramsfile = strcat('params_',drugname,renalfunction,'.mat');
params = matfile(paramsfile);
%PK_params = matfile(strcat('PK_',paramsfile));
AngIIvalue = params.AngIIvalue;
PRAvalue = params.PRAvalue;
Xdata = params.Xdata; % row vector for measurement time points
sim_time_end = 24;
Ydata = [AngIvalue;...% AngII row vector for measured values
    AngIIvalue;%...%ANGI row vector for measured values
    PRAvalue];% PRA row vector for measured values
sigma = [AngIerror;...% AngII row vector for stddev values
    AngIIerror;%...%ANGI row vector for stddev values
    PRAerror]; % PRA row vector for stddev values
Ydata_weighted = Ydata./sigma;
% Guesses for coefficients
VmaxoverKm = 1;
k_cat_Renin = 1;
k_feedback =  1;
feedback_capacity = 250;
k_cons_AngII = 1;
% package the coefficients
coefficientsguess(1) = VmaxoverKm;
coefficientsguess(2) = k_cat_Renin;
coefficientsguess(3) = k_feedback;
```

```
coefficientsguess(4) = feedback_capacity;
coefficientsguess(5) = k_cons_AngII;
LB = [0,0,0,250,0]; % lower bound %feedback lower bound
UB = []; % upper bound
OPTIONS = ...
    optimoptions(@lsqcurvefit,'Algorithm','trust-region-reflective',...
     'TolX', 1e-6, 'TolFun', 1e-6, 'StepTolerance', 1e-13, ...
         'MaxFunEvals', 1000, 'MaxIter', 3000); % use ...
         default for first guess
tic
[coefficients, resnorm_fitted] = ...
    lsqcurvefit(@(coefficients,Xdata) model(coefficients, ...
    Xdata, sigma), coefficientsguess, Xdata, ...
    Ydata_weighted, LB, UB, OPTIONS)
toc

%% Create Ycalc matrix for model output at Xdata values
Ycalc_weighted = model(coefficients,Xdata,sigma);
Ycalc = Ycalc_weighted.*sigma;
resnorm = sum((Ycalc(1,:)-Ydata(1,:)).^2 + ...
    (Ycalc(2,:)-Ydata(2,:)).^2 + (Ycalc(3,:)-Ydata(3,:)).^2)
resnorm_weighted = ...
    sum((Ycalc_weighted(1,:)-Ydata_weighted(1,:)).^2 + ...
    (Ycalc_weighted(2,:)-Ydata_weighted(2,:)).^2 + ...
    (Ycalc_weighted(3,:)-Ydata_weighted(3,:)).^2)
for i = 1:3
     residual(i,:) = Ydata(i,:) - Ycalc(i,:);
     RMSE(i) = sqrt(mean(residual(i,:).^2));
end
```



(a) Ang I, Ydata(1,:) (b) Ang II, Ydata(2,:) (c) PRA, Ydata(3,:)

Figure 1: WSSR results from [3] for parameter estimation with three vectors of Ydata vs. time simultaneously for `WSSR_Example.m`

References

[1] C. Cobelli and E. Carson. *Introduction to Modeling in Physiology and Medicine*. Academic Press, New York, 2008.

[2] DiStefano III, J. *Dynamic Systems Biology Modeling and Simulation*. Academic Press, New York, 2014.

[3] A. N. Ford Versypt, G. K. Harrell, and A. N. McPeak. A pharmacokinetic/pharmacodynamic model of ACE inhibition of the renin-angiotensin system for normal and impaired renal function. *Comput Chem Eng*, 104:311–322, 2017.