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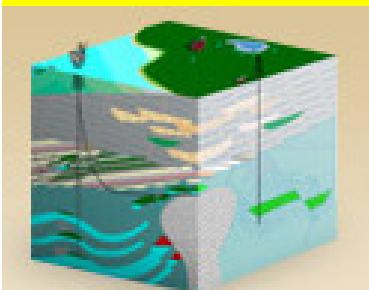


Department of Computer Engineering  
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# Fast Processing of Data in Imaging Methods Based on Relaxation Processes

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Based on geological application developed for KMS  
Technologies, Houston, Texas, U.S.A.



# Summary

**Imaging methods of fluorescence and nuclear magnetic resonance are based on characterization of relaxation processes from excited state. Typical signal coming from such processes is a sum of exponential functions. This type of signal is also characteristic for decay of mixture of radionuclides, parallel chemical reactions, pharmacological modelling, etc.**



## Summary:

**This is important and difficult problem.  
Often the techniques are chosen that are  
noise sensitive and their error poorly  
understood. We present general, numerically  
robust and fast (real time) solution method.  
Noise attenuation and flexibility of the  
method are analyzed in detail. Its relevance  
for signal analysis for different instruments is  
discussed.**



## The major steps in our methodology

- Linearization by numerical integration method
- Solution of linear system of equations with or without non-negativity constraints
- Determining coefficients and roots of polynomial equation(s) based on linear system solutions. This step yields non-linear parameters, i.e. decay constants.
- Reformulating original problem using now known decay constants in order to compute pre-exponential terms.
- Testing and verifying the results by detailed error analysis.



(12) **United States Patent**  
**Jeričević**

(54) **METHOD FOR FITTING A SUM OF EXPONENTIALS TO EXPERIMENTAL DATA BY LINEARIZATION USING A NUMERICAL INTEGRATION APPROXIMATION, AND ITS APPLICATION TO WELL LOG DATA**

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**G01V 3/00** (2006.01)

(52) **U.S. Cl.** ..... 324/303; 324/323

(58) **Field of Classification Search** ..... 324/303, 324/323, 332; 250/296.6

See application file for complete search history.

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(57) **ABSTRACT**

A method for analyzing formations using measurements from a detector in response to energy imparted therein. The measurements have characteristics which exponentially reduce in magnitude with time. The method includes (a) determining, an N-th order integral of the value of each measurement from an initial time to the time of each measurement, wherein N represents a number of exponentially decaying characteristics; b) determining a solution to a system of linear equations relating the measurements to the integrals, the solution representing polynomials of order N related to a decay rate and an initial measurement amplitude for each component; (c) solving the polynomials to determine the decay rate and the initial amplitude for each component; (d) determining if the decay rates and initial amplitudes are within possible limits; and (e) incrementing N and repeating (a) through (d) until the decay rates or the initial amplitudes are not within possible limits.



# Mono-exponential function with background term

$$\int y \, dt = A \int e^{-kt} \, dt + b \int dt$$

$$y = Ae^{-kt} + b$$

$$\int y \, dt = \frac{A}{k} (1.0 - e^{-kt}) + bt$$

$$k \int y \, dt = -Ae^{-kt} - b + b + A + kbt$$

Substitute:  $-y \approx -Ae^{-kt} - b$

$$y \approx -k \int y \, dt + kbt + A + b$$



$$y = Ae^{-kt} + b$$

$$y \approx -k \int y dt + kbt + A + b$$

$$y(t_j) \approx -k \int_{t=0}^{t=t_j} y(t)dt + kbt_j + A + b$$

$$p_1 = -k$$

$$p_2 = kb$$

$$p_3 = A + b$$



## Bi-exponential function with background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + b$$

$$\int y dt = A_1 \int e^{-k_1 t} dt + A_2 \int e^{-k_2 t} dt + b \int dt$$

$$\int y dt = \frac{A_1}{k_1} (1.0 - e^{-k_1 t}) + \frac{A_2}{k_2} (1.0 - e^{-k_2 t}) + bt$$

$$k_1 k_2 \int y dt = k_2 A_1 - k_2 A_1 e^{-k_1 t} + k_1 A_2 - k_1 A_2 e^{-k_2 t} + k_1 k_2 b t$$

$$\begin{aligned} k_1 k_2 \int y dt &= k_2 (A_1 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t}) \\ &\quad + k_1 (A_2 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} + A_1 e^{-k_1 t}) + k_1 k_2 b t \end{aligned}$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - b$



$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + b$$

$$k_1 k_2 \int y dt \approx k_2 (A_1 + b - y) + k_2 A_2 e^{-k_2 t} + k_1 (A_2 + b - y) + k_1 A_1 e^{-k_1 t} + k_1 k_2 b t$$

Second integration yields:

$$\begin{aligned} k_1 k_2 \iint y dt dt &\approx k_2 (A_1 + b) \int dt - k_2 \int y dt + A_2 (1.0 - e^{-k_2 t}) + \\ & k_1 (A_2 + b) \int dt - k_1 \int y dt + A_1 (1.0 - e^{-k_1 t}) + k_1 k_2 b \int t dt \end{aligned}$$

Second substitution of:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - b$

$$\begin{aligned} k_1 k_2 \iint y dt dt &\approx t [k_2 (A_1 + b) + k_1 (A_2 + b)] - (k_1 + k_2) \int y dt + \frac{k_1 k_2 b t^2}{2} \\ & - y + A_1 + A_2 + b \end{aligned}$$

$$\begin{aligned} y &\approx -(k_1 + k_2) \int y dt - k_1 k_2 \iint y dt dt + A_1 + A_2 + b \\ & + t [k_2 (A_1 + b) + k_1 (A_2 + b)] + \frac{k_1 k_2 b t^2}{2} \end{aligned}$$



$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + b$$

$$y \approx -(k_1 + k_2) \int y dt - k_1 k_2 \int \int y dt dt + A_1 + A_2 + b$$

$$+ t [k_2(A_1 + b) - k_1(A_2 + b)] + \frac{k_1 k_2 b t^2}{2}$$

$$p_1 = -k_1 - k_2$$

$$p_2 = -k_1 k_2$$

$$p_3 = b + A_1 + A_2$$

$$p_4 = b(k_1 + k_2) + A_1 k_2 + A_2 k_1$$

$$p_5 = \frac{b k_1 k_2}{2}$$



# Tri-exponential function with background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + b$$

$$\int y dt = A_1 \int e^{-k_1 t} dt + A_2 \int e^{-k_2 t} dt + A_3 \int e^{-k_3 t} dt + b \int dt$$

$$\int y dt = \frac{A_1}{k_1} (1.0 - e^{-k_1 t}) + \frac{A_2}{k_2} (1.0 - e^{-k_2 t}) + \frac{A_3}{k_3} (1.0 - e^{-k_3 t}) + bt$$

$$k_1 k_2 k_3 \int y dt dt = k_1 k_3 A_1 - k_1 k_3 A_1 e^{-k_1 t} + k_1 k_3 A_2 - k_1 k_3 A_2 e^{-k_1 t} + k_1 k_3 A_3 - k_1 k_3 A_3 e^{-k_1 t} + k_1 k_3 b t$$

$$k_1 k_2 k_3 \int y dt = k_1 k_3 (A_1 + b - b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t})$$

$$+ k_1 k_3 (A_2 + b - b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t})$$

$$+ k_1 k_2 (A_3 + b - b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t}) + k_1 k_2 k_3 b t$$

$$\text{Substitute: } -y \approx -b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t}$$

$$k_1 k_2 k_3 \int y dt = k_1 k_3 (A_1 + b - y) + k_1 k_3 A_2 e^{-k_1 t} + k_1 k_3 A_3 e^{-k_1 t}$$

$$+ k_1 k_3 (A_2 + b - y) + k_1 k_3 A_1 e^{-k_2 t} + k_1 k_3 A_3 e^{-k_2 t}$$

$$+ k_1 k_2 (A_3 + b - y) + k_1 k_2 A_1 e^{-k_3 t} + k_1 k_2 A_2 e^{-k_3 t} + k_1 k_2 k_3 b t$$

Second integration yields:

$$k_1 k_2 k_3 \int \int y dt dt = k_2 k_3 (A_1 + b) \int dt - k_2 k_3 \int y dt dt + k_3 A_2 (1.0 - e^{-k_2 t}) + k_2 A_3 (1.0 - e^{-k_3 t})$$

$$+ k_1 k_3 (A_2 + b) \int dt - k_1 k_3 \int y dt dt + k_3 A_1 (1.0 - e^{-k_3 t}) + k_1 A_2 (1.0 - e^{-k_1 t})$$

$$+ k_1 k_2 (A_3 + b) \int dt - k_1 k_2 \int y dt dt + k_2 A_1 (1.0 - e^{-k_1 t}) + k_1 A_3 (1.0 - e^{-k_3 t}) + k_1 k_2 k_3 b \int dt$$

$$k_1 k_2 k_3 \int \int y dt dt = [k_1 k_3 A_1 + k_1 k_3 A_2 + k_1 k_2 A_3 + (k_2 k_3 + k_1 k_3 + k_1 k_2) b] t + \frac{k_1 k_2 k_3 b t^2}{2}$$

$$+ A_1 (k_2 + k_3) + A_2 (k_1 + k_3) + A_3 (k_1 + k_2)$$

$$- (k_2 k_3 + k_1 k_3 + k_1 k_2) \int y dt$$

$$+ k_1 (-A_2 e^{-k_1 t} - A_3 e^{-k_1 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - b + b)$$

$$+ k_2 (-A_1 e^{-k_2 t} - A_3 e^{-k_2 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - b + b)$$

$$+ k_3 (-A_1 e^{-k_3 t} - A_2 e^{-k_3 t} - A_3 e^{-k_3 t} - A_3 e^{-k_3 t} - b + b)$$

$$\text{Substitute: } -y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - b$$

$$k_1 k_2 k_3 \int \int y dt dt = [k_1 k_3 A_1 + k_1 k_3 A_2 + k_1 k_2 A_3 + (k_2 k_3 + k_1 k_3 + k_1 k_2) b] t + \frac{k_1 k_2 k_3 b t^2}{2}$$

$$+ A_1 (k_2 + k_3) + A_2 (k_1 + k_3) + A_3 (k_1 + k_2)$$

$$- (k_2 k_3 + k_1 k_3 + k_1 k_2) \int y dt$$

$$+ k_1 (A_1 e^{-k_1 t} + b - y) + k_2 (A_2 e^{-k_2 t} + b - y) + k_3 (A_3 e^{-k_3 t} + b - y)$$

Third integration yields:

$$k_1 k_2 k_3 \int \int \int y dt dt dt = [k_2 k_3 A_1 + k_1 k_3 A_2 + k_1 k_2 A_3 + (k_2 k_3 + k_1 k_3 + k_1 k_2) b] \int dt + \frac{k_1 k_2 k_3 b}{2} \int t^2 dt$$

$$+ [A_1 (k_2 + k_3) + A_2 (k_1 + k_3) + A_3 (k_1 + k_2)] \int dt + (k_1 + k_2 + k_3) b \int dt$$

$$- (k_2 k_3 + k_1 k_3 + k_1 k_2) \int \int y dt dt$$

$$- (k_1 + k_2 + k_3) \int y dt$$

$$+ A_1 (1 - e^{-k_1 t}) + A_2 (1 - e^{-k_2 t}) + A_3 (1 - e^{-k_3 t}) - b + b$$

After substitution of:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - b$

$$y \approx -(k_1 + k_2 + k_3) \int y dt dt - (k_1 k_2 + k_1 k_3 + k_2 k_3) \int \int y dt dt - k_1 k_2 k_3 \int \int \int y dt dt dt$$

$$+ b + A_1 + A_2 + A_3$$

$$+ [(k_1 + k_2 + k_3) b + A_1 (k_2 + k_3) + A_2 (k_1 + k_3) + A_3 (k_1 + k_2)] t$$

$$+ [(k_1 k_2 + k_1 k_3 + k_2 k_3) b + k_2 k_3 A_1 + k_1 k_3 A_2 + k_1 k_2 A_3] \frac{t^2}{2} + k_1 k_2 k_3 b \frac{t^3}{6}$$

Solution of linear system of equations:

$$p_1 = -k_1 - k_2 - k_3$$

$$p_2 = -k_1 k_2 - k_1 k_3 - k_2 k_3$$

$$p_3 = -k_1 k_2 k_3$$

$$p_4 = b + A_1 + A_2 + A_3$$

$$p_5 = b(k_1 + k_2 + k_3) + A_1(k_2 + k_3) + A_2(k_1 + k_3) + A_3(k_1 + k_2)$$

$$p_6 = \frac{1}{2} \{b(k_1 k_2 + k_1 k_3 + k_2 k_3) + A_1 k_2 k_3 + A_2 k_1 k_3 + A_3 k_1 k_2\}$$

$$p_7 = \frac{b k_1 k_2 k_3}{6}$$



## Tri-exponential function with background term

$$y = A_1 e^{-k_1 t} +$$

$$\begin{aligned} p_1 &= -k_1 - k_2 - k_3 \\ p_2 &= -k_1 k_2 - k_1 k_3 - k_2 k_3 \\ p_3 &= -k_1 k_2 k_3 \\ p_4 &= b + A_1 + A_2 + A_3 \\ p_5 &= b(k_1 + k_2 + k_3) + A_1(k_2 + k_3) + A_2(k_1 + k_3) + A_3(k_1 + k_2) \\ p_6 &= \frac{1}{2} [b(k_1 k_2 + k_1 k_3 + k_2 k_3) + A_1 k_2 k_3 + A_2 k_1 k_3 + A_3 k_1 k_2] \\ p_7 &= \frac{b k_1 k_2 k_3}{6} \end{aligned}$$



## Quartic-exponential with background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t} + b$$

$$p_1 = -k_1 - k_2 - k_3 - k_4$$

$$p_2 = -k_1 k_2 - k_1 k_3 - k_1 k_4 - k_2 k_3 - k_2 k_4 - k_3 k_4$$

$$p_3 = -k_1 k_2 k_3 - k_1 k_2 k_4 - k_1 k_3 k_4 - k_2 k_3 k_4$$

$$p_4 = -k_1 k_2 k_3 k_4$$

$$p_5 = b + A_1 + A_2 + A_3 + A_4$$

$$p_6 = b(k_1 + k_2 + k_3 + k_4) + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3)$$

$$p_7 = \frac{1}{2} \left[ b(k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) + A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \right. \\ \left. + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \right]$$

$$p_8 = \frac{1}{6} [b(k_1 k_2 k_3 + k_1 k_2 k_4 + k_1 k_3 k_4 + k_2 k_3 k_4) + A_1 k_2 k_3 k_4 + A_2 k_1 k_3 k_4 + A_3 k_1 k_2 k_4 + A_4 k_1 k_2 k_3]$$

$$p_9 = \frac{b k_1 k_2 k_3 k_4}{24}$$



# General solution (by inference)

$$p_1 = - \sum_{i=1}^N k_i$$

$$p_n = - \sum_{i=1}^{\frac{N!}{(N-n)!n!}} \prod_{l=1}^n k_m \quad m \in (^N C_n)$$

$$p_N = - \prod_{i=1}^N k_i$$

$${}^n C_k = \frac{n!}{(n-k)!k!}$$

$$p_{N+1} = b + \sum_{i=1}^N A_i$$

$$p_{N+2} = b \sum_{i=1}^{i=N} k_i + \sum_{i=1}^{i=N} A_i \sum_{j=1; j \neq i}^N k_j$$

$$p_{N+n} = \frac{1}{(n-1)!} \left\{ b \sum_{j=1}^{\frac{N!}{(N-n)!n!}} \prod_{l=1}^{n-1} k_l + \sum_{i=1}^N A_i \sum_{j=1; j \neq i}^{\frac{(N-1)!}{(N-n)!(n-1)!}} \prod_{l=1}^{n-1} k_m \right\} \quad l \in (^N C_n) \quad m \in (^{N-1} C_{n-1}; m \neq i)$$

$$p_{2N} = \frac{1}{(N-1)!} \left\{ b \sum_{l=1}^{\frac{N!}{(N-1)!}} \prod_{m=1}^{N-1} k_m + \sum_{i=1}^N A_i \sum_{j=1; j \neq i}^N k_j \right\} \quad m \in (^N C_{N-1})$$

$$p_{2N+1} = - \frac{b}{N!} \prod_{i=1}^N k_i$$

$$y = b + \sum_{i=1}^N A_i e^{-k_i t}$$



System of linear equations for  $y = b + \sum_{i=1}^N e^{-k_i t}$

$$\int y dt \quad \int \int y dt dt \quad \int \int \int y dt dt dt \quad \dots, Nth order \int \quad 1.0 \quad t \quad t^2 \quad \dots \quad t^{N-1} \quad t^N$$

$$\begin{pmatrix} y_1 \\ y_2 \\ \dots \\ y_M \end{pmatrix} = \begin{pmatrix} 0 & 0 & 0 & \dots & 0 & 1.0 & t_1 & t_1^2 & \dots & t_1^{N-1} & t_1^N \\ \int_{t_1}^{t_2} y dt & \int \int y dt dt & \int \int \int y dt dt dt & \dots & Nth order \int & 1.0 & t_2 & t_2^2 & \dots & t_2^{N-1} & t_2^N \\ \dots & \dots \\ \int_{t_1}^{t_M} y dt & \int \int y dt dt & \int \int \int y dt dt dt & \dots & Nth order \int & 1.0 & t_M & t_M^2 & \dots & t_M^{N-1} & t_M^N \end{pmatrix} \begin{pmatrix} p_1 \\ p_2 \\ p_3 \\ \dots \\ p_N \\ p_{N+1} \\ p_{N+2} \\ p_{N+3} \\ \dots \\ p_{2N} \\ p_{2N+1} \end{pmatrix}$$



# General solution (by inference)

$$p_1 = - \sum_{i=1}^N k_i$$

$$p_n = - \sum_{i=1}^{\frac{N!}{(N-n)!n!}} \prod_{m=1}^n k_m$$

$$m \in (^N C_n)$$

$$p_N = - \prod_{i=1}^N k_i$$

$${}^n C_k = \frac{n!}{(n-k)!k!}$$

$$p_{N+1} = \sum_{i=1}^N A_i$$

$$p_{N+2} = \sum_{i=1}^{i=N} A_i \sum_{j=1; j \neq i}^N k_j$$

$$p_{N+n} = \frac{1}{(n-1)!} \sum_{i=1}^N A_i \sum_{j=1; j \neq i}^{\frac{(N-1)!}{(N-n)!(n-1)!}} \prod_{m=1}^{n-1} k_m$$

$$m \in (^{N-1} C_{n-1}; m \neq i)$$

$$p_{2N} = \frac{1}{(N-1)!} \sum_{i=1}^N A_i \prod_{j=1; j \neq i}^N k_j$$

$$m \in (^N C_{N-1})$$

$$y = \sum_{i=1}^N A_i e^{-k_i t}$$



# Triexponential function without background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t}$$

$$p_1 = -k_1 - k_2 - k_3$$

$$p_2 = -k_1 k_2 - k_1 k_3 - k_2 k_3$$

$$p_3 = -k_1 k_2 k_3$$

$$p_4 = A_1 + A_2 + A_3$$

$$p_5 = A_1(k_2 + k_3) + A_2(k_1 + k_3) + A_3(k_1 + k_2)$$

$$p_6 = \frac{1}{2}(A_1 k_2 k_3 + A_2 k_1 k_3 + A_3 k_1 k_2)$$

Compute nonlinear parameters (k's) first



# Computing linear parameters I

$$p_4 = A_1 + A_2 + A_3$$

$$p_5 = A_1(k_2 + k_3) + A_2(k_1 + k_3) + A_3(k_1 + k_2)$$

$$p_6 = \frac{1}{2}(A_1k_2k_3 + A_2k_1k_3 + A_3k_1k_2)$$

$$\begin{pmatrix} p_4 \\ p_5 \\ 2p_6 \end{pmatrix} = \begin{pmatrix} 1 & 1 & 1 \\ k_2 + k_3 & k_1 + k_3 & k_1 + k_2 \\ k_2k_3 & k_1k_3 & k_1k_2 \end{pmatrix} \begin{pmatrix} A_1 \\ A_2 \\ A_3 \end{pmatrix}$$



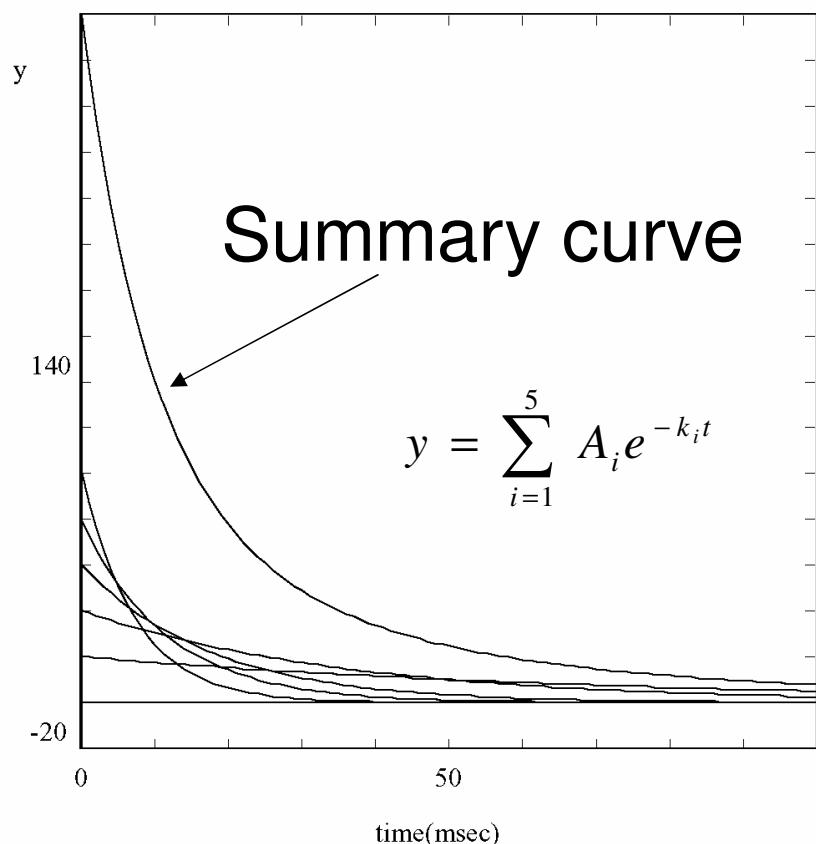
# Computing linear parameters II

Recasting normal equations

$$\begin{pmatrix} y_1 \\ y_2 \\ \dots \\ y_M \end{pmatrix} = \begin{pmatrix} e^{-k_1 t_1} & e^{-k_2 t_1} & \dots & e^{-k_N t_1} \\ e^{-k_1 t_2} & e^{-k_2 t_2} & \dots & e^{-k_N t_2} \\ \dots & \dots & \dots & \dots \\ e^{-k_1 t_M} & e^{-k_2 t_M} & \dots & e^{-k_N t_M} \end{pmatrix} \begin{pmatrix} A_1 \\ A_2 \\ \dots \\ A_N \end{pmatrix}$$



## Syntetic example (5 exponentials)



$$A_1 = 0.100E+03$$

$$k_1 = 0.138629436E+00 \quad \text{half life=} \ 0.50E+01$$

$$A_2 = 0.800 E+02$$

$$k_2 = 0.866433976E-01 \quad \text{half life=} \ 0.80E+01$$

$$A_3 = 0.600E+02$$

$$k_3 = 0.577762265E-01 \quad \text{half life=} \ 0.12E+02$$

$$A_4 = 0.400 E+02$$

$$k_4 = 0.277258872E-01 \quad \text{half life=} \ 0.25E+02$$

$$A_5 = 0.200E+02$$

$$k_5 = 0.138629436E-01 \quad \text{half life=} \ 0.50E+02$$

Optimized values:

$$A_1 = 0.10051341E+03$$

$$k_1 = 0.13840872E+00 \quad \text{half life=} \ 0.5007973E+01$$

$$A_2 = 0.79254406E+02$$

$$k_2 = 0.86603987E-01 \quad \text{half life=} \ 0.8003641E+01$$

$$A_3 = 0.60246423E+02$$

$$k_3 = 0.57773666E-01 \quad \text{half life=} \ 0.1199763E+02$$

$$A_4 = 0.39947621E+02$$

$$k_4 = 0.27738458E-01 \quad \text{half life=} \ 0.2498867E+02$$

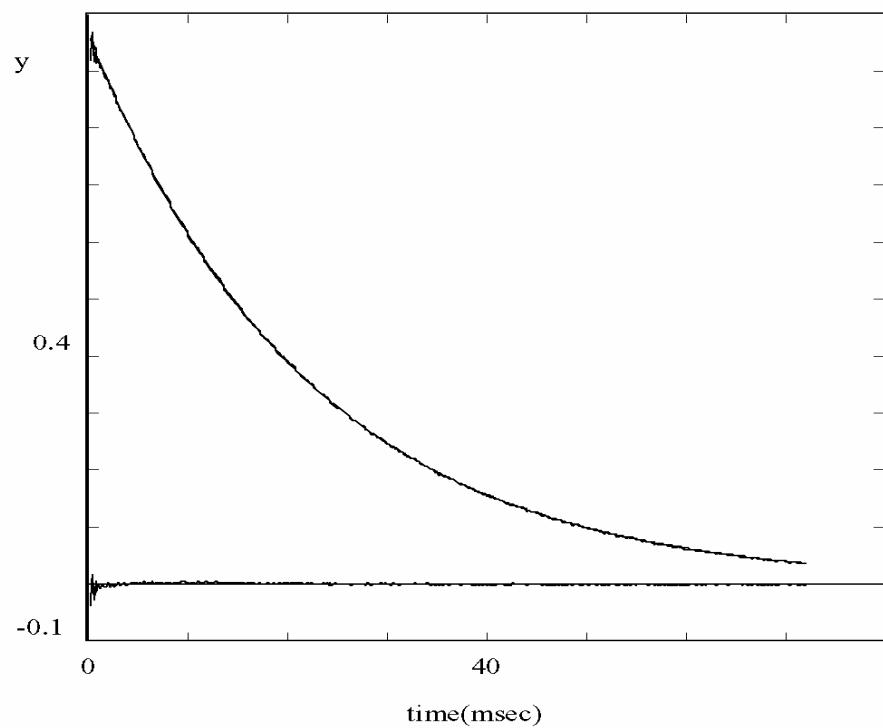
$$A_5 = 0.20031300E+02$$

$$k_5 = 0.13866377E-01 \quad \text{half life=} \ 0.4998762E+02$$

$$\text{lstsqsum=} \ 8.79827459E-05 \quad \text{correlation_index=} \ 1.0$$



# Liquid water sample



$A = 0.96582002E+00 \pm 0.58947868E-03$

$k = 0.45511752E-01 \pm 0.39924135E-04 \text{ ms}^{-1}$

half life =  $0.1523007E+02 \text{ ms}$

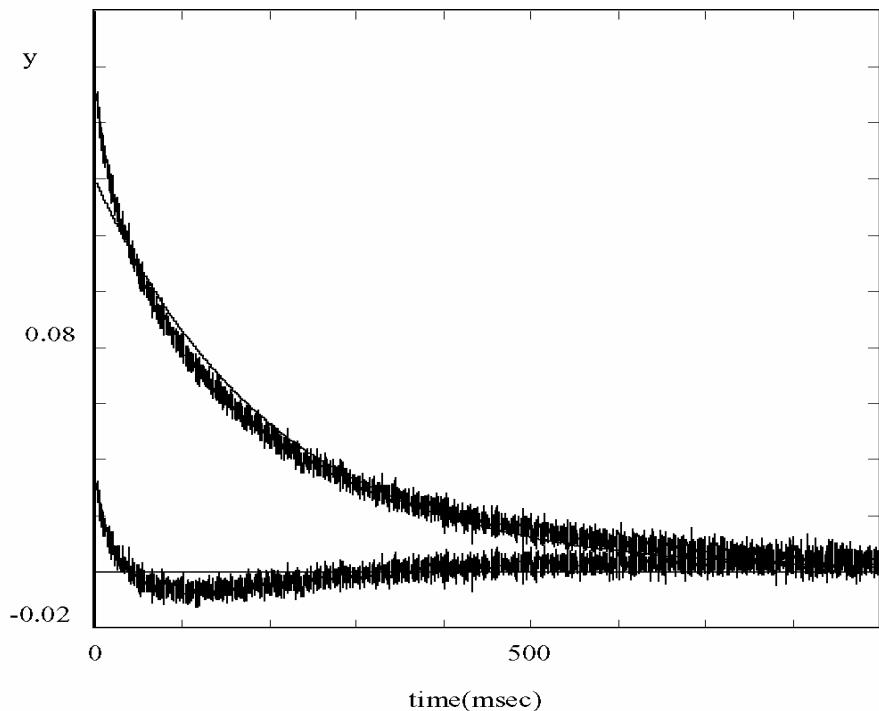
relaxation time =  $0.2197235E+02 \text{ ms}$

Istsqsum= 0.0040524169

correlation index= 0.999917564



# Mono-exponential (water saturated sandstone)



$A = 0.13949057E+00 \pm 0.29125569E-03$

$k = 0.48606613E-02 \pm 0.14400395E-04$

half life=  $0.1426035E+03$

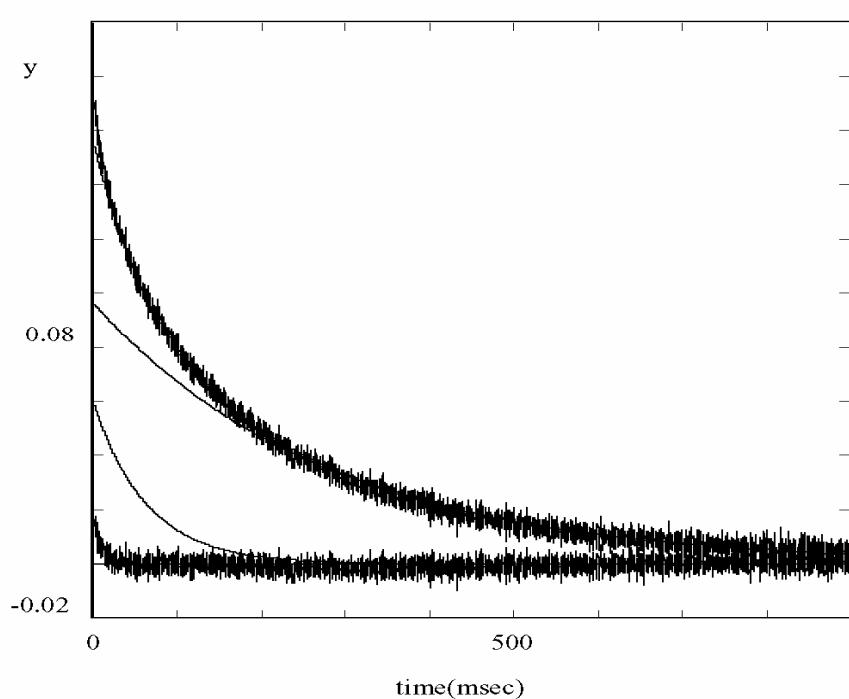
relaxation time=  $0.2057333E+03$

Istsqsum= 0.120345826

correlation index= 0.989756773



# Bi-exponential (water saturated sandstone)



$$A_1 = 0.59319738E-01 \pm 0.79078679E-03$$

$$k_1 = 0.15693409E-01 \pm 0.29413902E-03$$

$$\text{half life} = 0.4416804E+02$$

$$\text{relaxation time} = 0.6372102E+02$$

$$A_2 = 0.96319818E-01 \pm 0.86393897E-03$$

$$k_2 = 0.36296576E-02 \pm 0.21384621E-04$$

$$\text{half life} = 0.1909676E+03$$

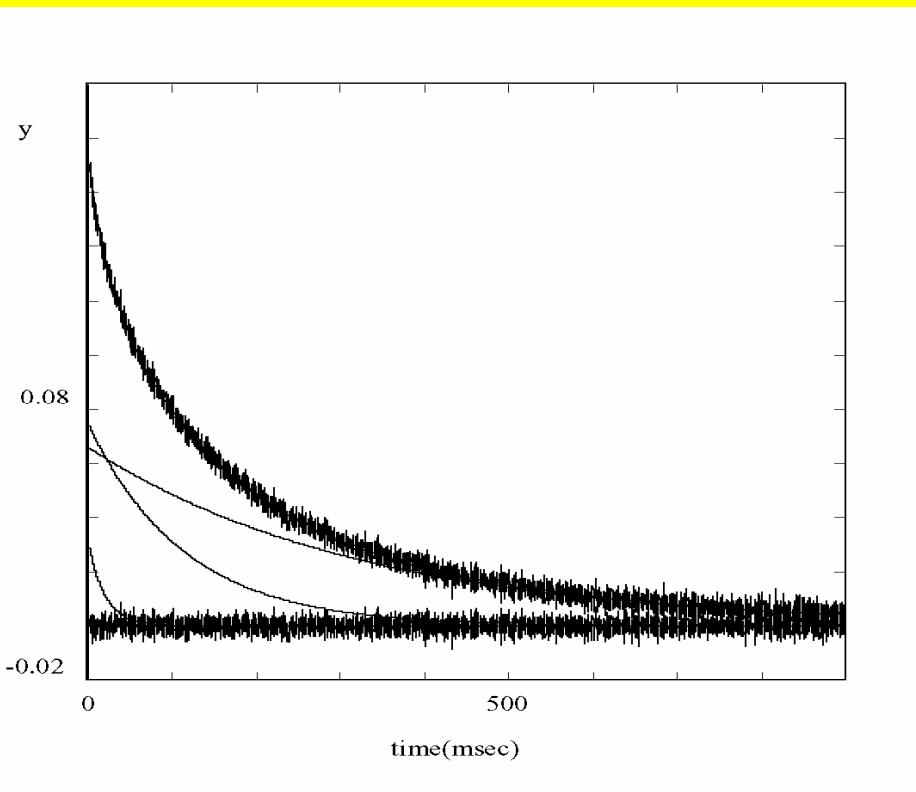
$$\text{relaxation time} = 0.2755081E+03$$

$$\text{lstsqsum} = 0.0368186046$$

$$\text{correlation index} = 0.996875668$$



# Tri-exponential (water saturated sandstone)



$$A_1 = 0.30407613E-01 \pm 0.12788985E-02$$

$$k_1 = 0.50342595E-01 \pm 0.29138408E-02$$

$$\text{half life} = 0.1376860E+02$$

$$\text{relaxation time} = 0.1986389E+02$$

$$A_2 = 0.74244158E-01 \pm 0.22410786E-02$$

$$k_2 = 0.87824596E-02 \pm 0.37225783E-03$$

$$\text{half life} = 0.7892404E+02$$

$$\text{relaxation time} = 0.1138633E+03$$

$$A_3 = 0.65767841E-01 \pm 0.31735761E-02$$

$$k_3 = 0.30752393E-02 \pm 0.66313207E-04$$

$$\text{half life} = 0.2253962E+03$$

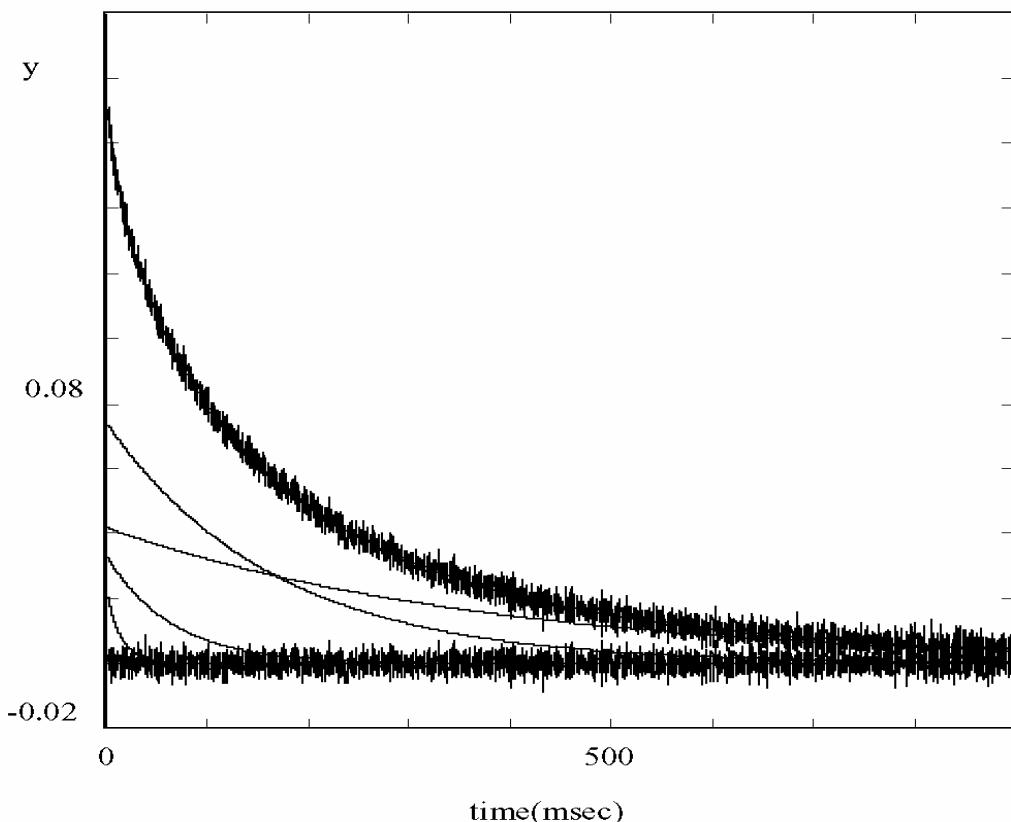
$$\text{relaxation time} = 0.3251779E+03$$

$$\text{Istsqsum} = 0.0271196126$$

$$\text{correlation index} = 0.997699536$$



# Quartic-exponential (water saturated sandstone)



$$A_1 = 0.21951913E-01 \pm 0.29337615E-02$$

$$k_1 = 0.68884024E-01 \pm 0.90549317E-02$$

half life= 0.1006252E+02

relaxation time= 0.1451715E+02

$$A_2 = 0.32980727E-01 \pm 0.56601136E-02$$

$$k_2 = 0.15413767E-01 \pm 0.31277764E-02$$

half life= 0.4496936E+02

relaxation time= 0.6487707E+02

$$A_3 = 0.73851740E-01 \pm 0.92488193E-02$$

$$k_3 = 0.60243592E-02 \pm 0.24350045E-03$$

half life= 0.1150574E+03

relaxation time= 0.1659928E+03

$$A_4 = 0.41678145E-01 \pm 0.12277373E-02$$

$$k_4 = 0.26144138E-02 \pm 0.60907306E-04$$

half life= 0.2651253E+03

relaxation time= 0.3824949E+03

$$\text{Istsqsum}= 0.026920193$$

25

$$\text{correlation index}= 0.997716472$$



# What is Global Analysis Method?

- The idea was to combine multiple realizations of the same experiment into one optimization in order to improve ill conditioning in separation of exponentials. Method works for different pre-exponential terms in each realization, as in fluorescence relaxation monitored at different wavelengths.
- Based on work of Beechem, Knutson and Brant. For example see Knutson, J.R. et al, Chem. Phys. Lett., 102 (1983) 501-507.

CCVW 2012.09.20

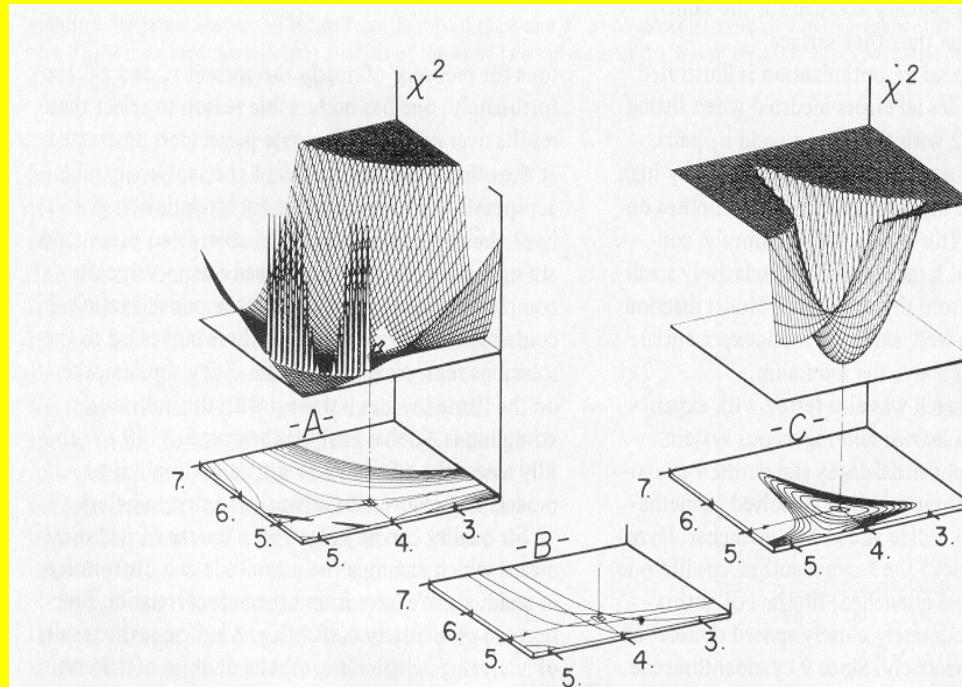


Fig. 1. Three-dimensional and contour map representations of the variation in fitting error ( $\chi^2$ ) with respect to the lifetimes  $\tau_1$  and  $\tau_2$ , fitting biexponential decays of 4.0 and 5.0 ns. The pre-exponential factors were allowed to vary to minimize  $\chi^2$  at any given  $\tau_1, \tau_2$  location. (A) The  $\chi^2$  surface (from 1.18 to 8.0) for single decay curve analysis. The penalty incurred for monoexponential modeling can be seen as the saddle point along the diagonal wall where  $\tau_1 = \tau_2$ . Contours are spaced 0.05 from the minimum with subsequent spacings of 0.75. (B) The first 0.1  $\chi^2$  contours are used here to show how curves showing identical (4 and 5 ns) lifetimes but differing in amplitude mixture (1 : 3 and 3 : 1) have different loci of covariance. In particular, a penalty-free motion in one curve may be blocked by  $\chi^2$  penalties in the other. (C)  $\chi^2$  surface from 1.18 to 3.5 for the superimposition of the two curves described in B. Contours being 0.05 above the minimum and are spaced 0.5 thereafter.



# Global method with background

$$\begin{pmatrix} \boxed{y_1} \\ \boxed{y_2} \\ \dots \\ \boxed{y_L} \end{pmatrix} = \begin{pmatrix} \boxed{\square_1} & \boxed{g_1} & 0 & \dots & 0 & \boxed{t_1^N} \\ \boxed{\square_2} & \text{go} & \boxed{t_2} & \dots & 0 & \boxed{t_2^N} \\ \dots & \dots & \dots & \dots & \dots & \dots \\ \boxed{\square_L} & \text{go} & 0 & \dots & \boxed{t_L} & \boxed{t_L^N} \end{pmatrix} \begin{pmatrix} p_k \\ p_{1,A} \\ p_{2,A} \\ \dots \\ p_{L,A} \\ b \end{pmatrix}$$

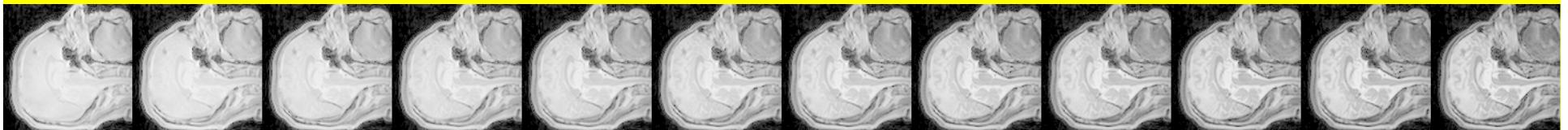
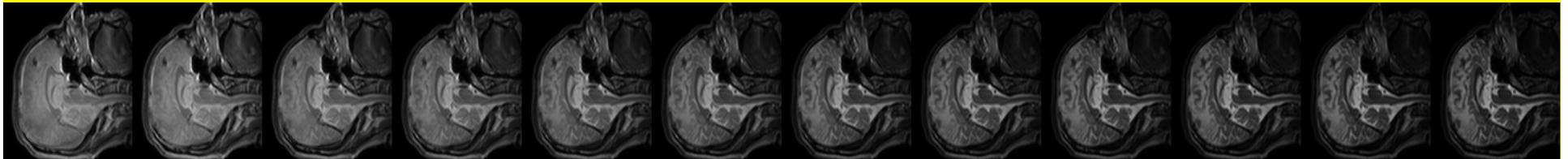


## Global method without background

$$\begin{pmatrix} y_1 \\ y_2 \\ \dots \\ y_L \end{pmatrix} = \begin{pmatrix} \square_1 & \mathbf{t}\mathbf{C} & 0 & \dots & 0 \\ \square_2 & \mathbf{C} & t_2 & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots \\ \square_L & \mathbf{C} & 0 & \dots & t_L \end{pmatrix} \begin{pmatrix} p_k \\ p_{1,A} \\ p_{2,A} \\ \dots \\ p_{L,A} \end{pmatrix}$$



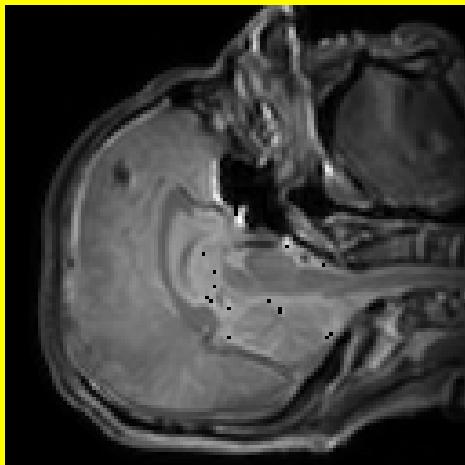
# Medical NMR imaging?



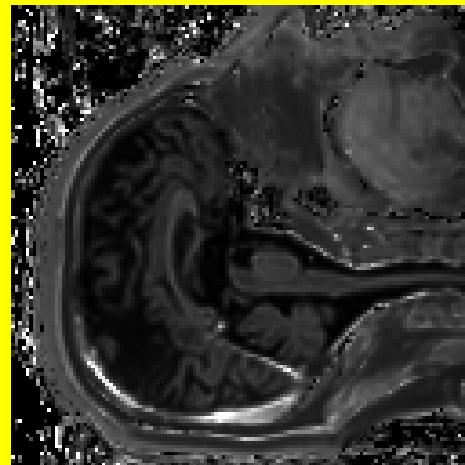


# Mono-exponential fit

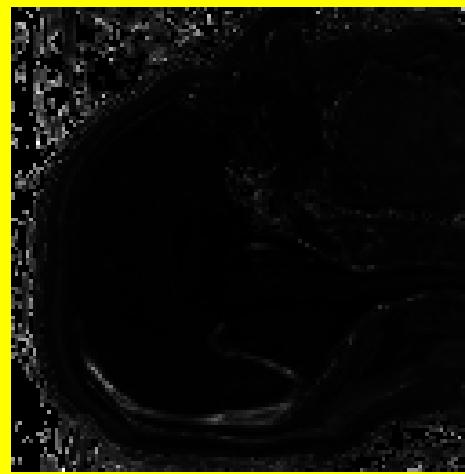
A & A error



k & k error



CI & error flag





## Plans:

- Improve resolution of the instruments by increasing sampling resolution in time domain during the relaxation process and perform new, superior processing of such collected data. Increasing the sampling in time domain (faster electronics) is much more economical then increasing sampling in space (stronger magnets).



## Plans:

- Our method of **data collection and processing** allows for determining more than one relaxation component inside each voxel (volumetric pixel). The result is a better diagnostics in new instruments and prolonged useful life of older instruments, giving better return on investment for the very expensive instrumentation.

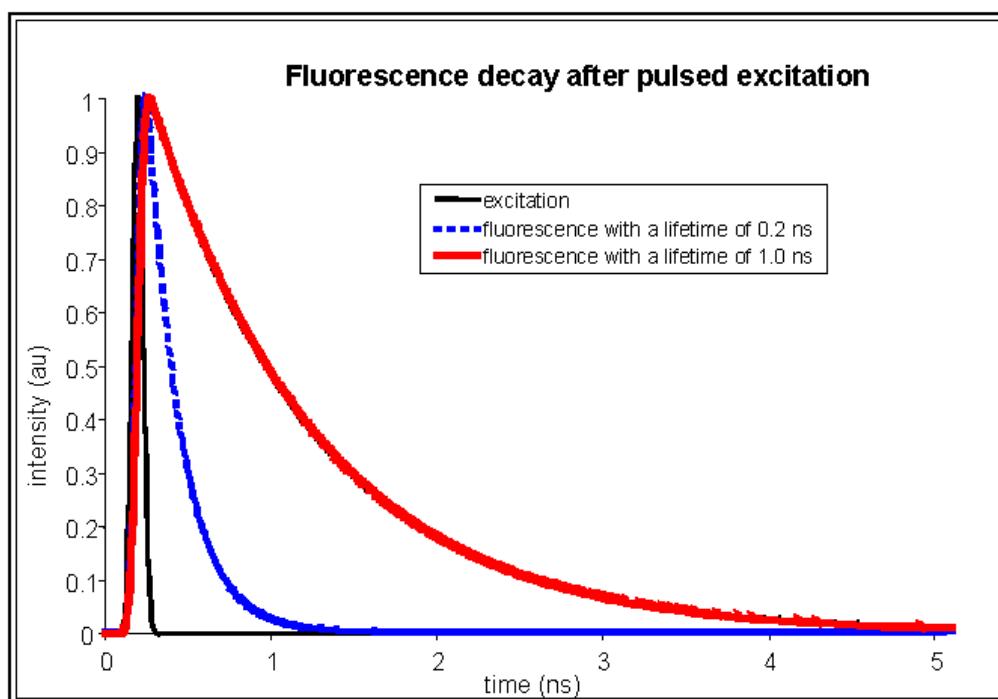


# FLIM (Fluorescence Lifetime Imaging)

Time series of images captured to characterize fluorescence decay (sampling ~100ps pico=10<sup>-12</sup>)  
Fluorescence relaxation lasts 10<sup>-9</sup>-10<sup>-7</sup>s.



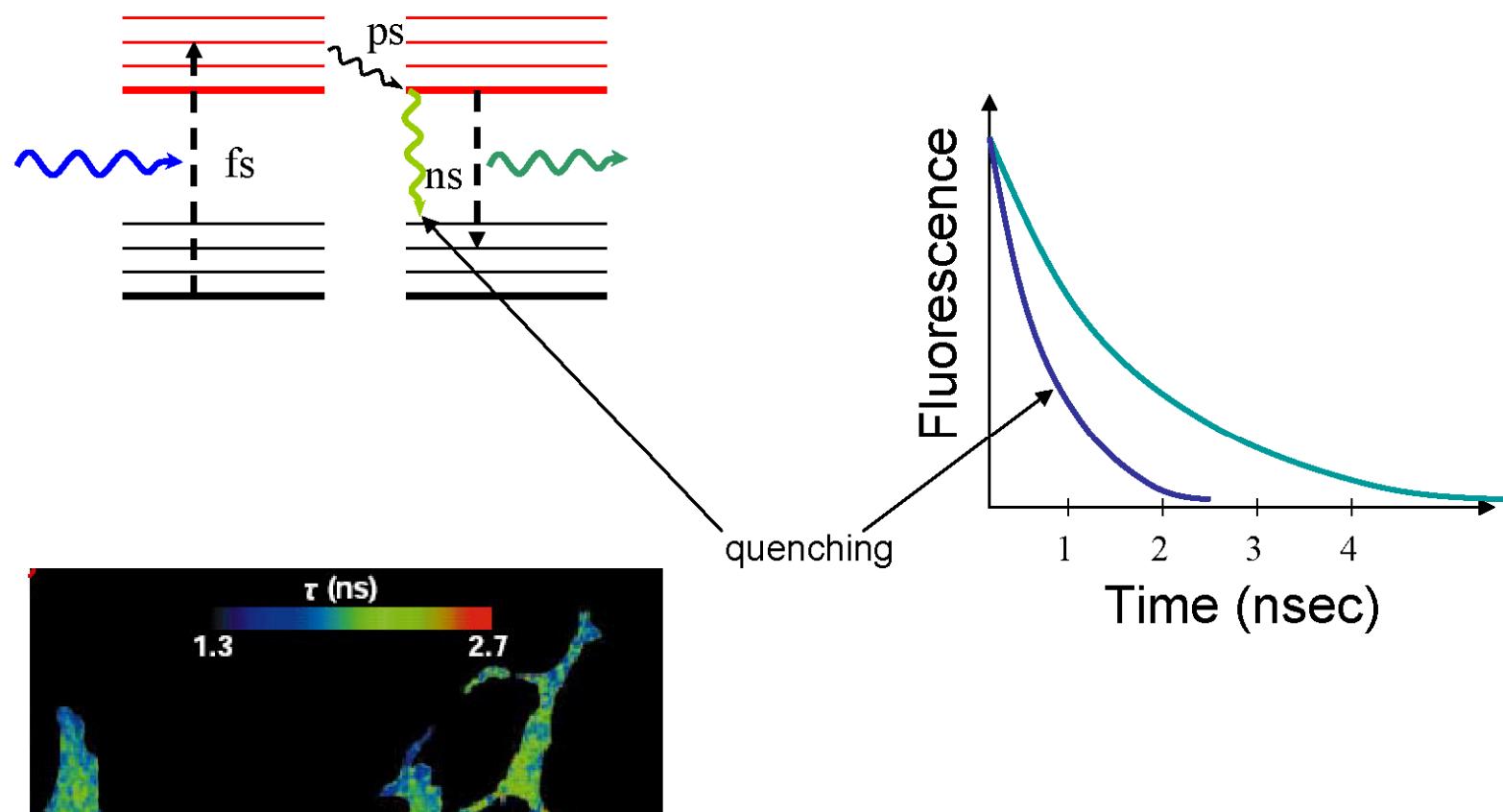
# FLIM (Fluorescence Lifetime IMaging)



*Fig.4. Upon excitation with a short light pulse (black line) of fluorescent molecules the time-course of the emission intensity shows an exponential decay.*



# FLIM (Fluorescence Lifetime IMaging)



Phizicky et al., Nature. 2003 422:208-15



## Recent activities

- **Graphical interface for stand-alone Linux version of the program (student Rene Barak)**
- **Web server (student Alan Martinović with help from doctoral student Damir Arbula)**



# Web Server

## Exponential fitting

Web service for nonlinear exponential fitting.

Welcome to the web service for nonlinear exponential fitting provided freely by the Technical Faculty Rijeka.

Anonymous usage is for users who have small numbers of data points which need to be fitted. In that case the results can quickly be computed and showed. No information need to be submitted.

[Anonymous usage](#)

Registered usage is for users who wish to have the results emailed. A simple registration is required which include a mandatory email address and optional name and company name.

[Registered usage](#)



## Parameter input

[Download pdf manual](#)

Upload the file containing the data which should be fitted and select the fitting parameters.

**Input file**

**Input type**

**Task**

**NNLSTSQ**  False  True

**Weight flag**  False  True

**Norm col**  False  True

**Norm row**  False  True

**Compute errors**  False  True

**Time scale**

**Print flag**  False  True

**Grh out**  False  True



# Web server

Number of exponentials: 2

[Start new fitting](#)

Function:  $y = a_0 e^{-k_0 t} + a_1 e^{-k_1 t}$

Parameters of exponentials:

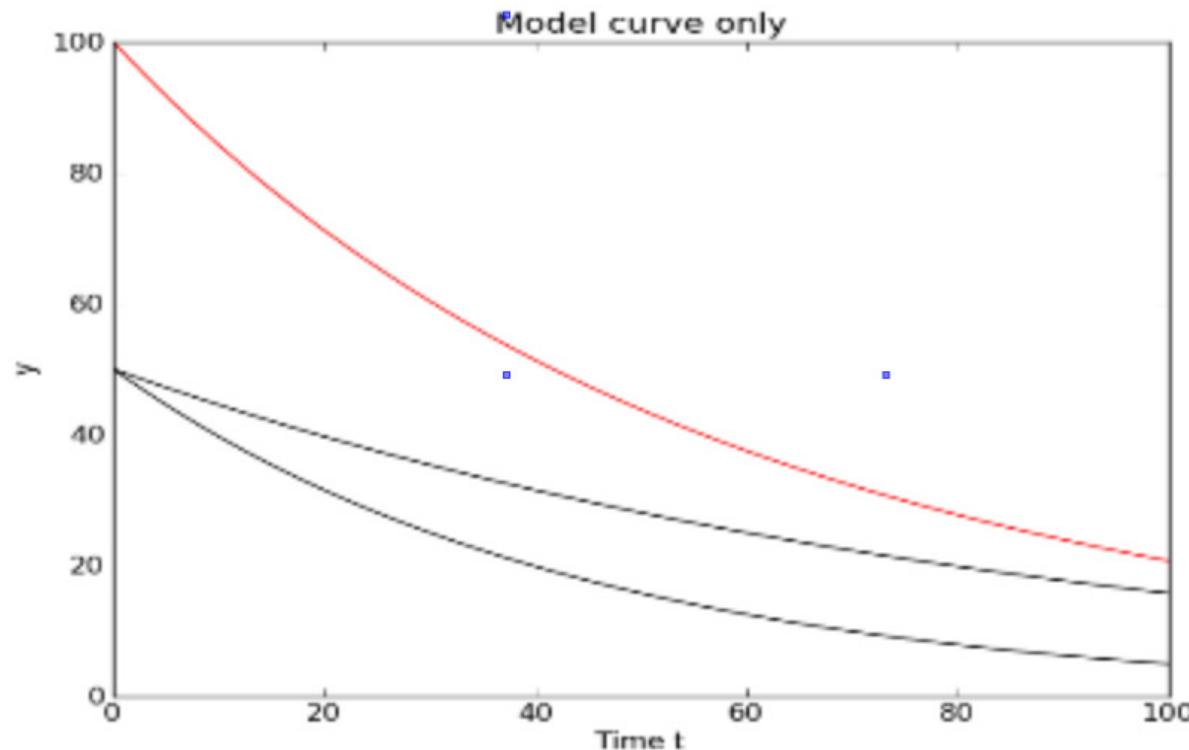
$a_0: 49.99999$

$k_0: 0.023103878$  Half life: 30.00133 Relax time: 43.28278

$a_1: 50.000001$

$k_1: 0.011552325$  Half life: 60.00067 Relax time: 86.56266

Non physical solution: False



[Download pdf](#)



## References:

- [1] Foss, S.D., Biometrics, 26 (1970) 815-821.
- [2] Matheson, I.B.C., Anal. Instr., 16 (1987) 345-373.
- [3] Jericevic, Z. et al., Adv. Cell Biol., 3 (1990) 111-151.
- [4] Knutson, J.R. et al, Chem. Phys. Lett., 102 (1983) 501-507.
- [5] Lawson, C.L. and Hanson, R.J. “Solving Least Squares Problems”, 1974, Prentice-Hall, Englewood Cliffs, 340p
- [6] Jericevic, Z., (08 Aug. 2006)  
**Patent # US 7,088,097 issued to KMS Technologies**



# Thank you for your attention

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[http://www.riteh.uniri.hr/~zeljkoj/Zeljko\\_Jericevic.html](http://www.riteh.uniri.hr/~zeljkoj/Zeljko_Jericevic.html)

**(011.385.51) 651.594**



# doc.dr.sc Kristijan Lenac

Zainteresiran za primjenu i razvoj algoritama racunalnogvida i obrade slika u mobilnoj robotici:

- blob tracking
- face recognition
- visual odometry
- object recognition
- head/eye tracking
- ...

U laboratoriju također aktivno koriste i razvijaju algoritme sa 3D oblacima točaka (Kinect sensor).

Spremnost za suradnju, testiranje, primjenu.



**UNIVERSITY OF RIJEKA**  
Faculty of Engineering



**Department of Computer Engineering**  
Faculty of Engineering - University of Rijeka



# All questions welcome





## Monoexponential function without background term

$$y = A e^{-kt}$$

$$\int y \, dt = A \int e^{-kt} \, dt$$

$$\int y \, dt = \frac{A}{k} (1.0 - e^{-kt})$$

$$k \int y \, dt = -A e^{-kt} + A$$

Substitute:  $-y \approx -A e^{-kt}$

$$y \approx -k \int y \, dt + A$$



$$y \approx -k \int y dt + A$$

$$y = Ae^{-kt}$$

$$y(t_j) \approx -k \int_{t=0}^{t=t_j} y(t) dt + A$$

$$p_1 = -k$$

$$p_2 = A$$



# Triexponential function without background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t}$$

Computing decay constants ( $k_1, k_2, k_3$ )

$$p_1 = -k_1 - k_2 - k_3$$

$$p_2 = -k_1 k_2 - k_1 k_3 - k_2 k_3$$

$$p_3 = -k_1 k_2 k_3$$

$$P(x) = \prod_{i=1}^N (x - x_i) = 0$$

$$P(x) = (x - x_1)(x - x_2)(x - x_3) = x^3 - (x_1 + x_2 + x_3)x^2 + (x_1x_2 + x_1x_3 + x_2x_3)x - x_1x_2x_3 = 0$$

$P(x) = \sum_{i=0}^3 a_i x^i$  has the following companion matrix:

$$\begin{pmatrix} x_1 + x_2 + x_3 & -(x_1x_2 + x_1x_3 + x_2x_3) & x_1x_2x_3 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix} = \begin{pmatrix} -p_1 & p_2 & -p_3 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{pmatrix}$$



# Companion Matrix of a Polynomial

$$P(x) = \sum_{i=0}^N a_i x^i$$

$$\begin{pmatrix} \frac{-a_{N-1}}{a_N} & \frac{-a_{N-2}}{a_N} & \dots & \frac{-a_1}{a_N} & \frac{-a_0}{a_N} \\ 1 & 0 & \dots & 0 & 0 \\ 0 & 1 & \dots & 0 & 0 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & \dots & 1 & 0 \end{pmatrix}$$



# Quartic-exponential with background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t} + b$$

Integration yields:

$$\int y dt = A_1 \int e^{-k_1 t} dt + A_2 \int e^{-k_2 t} dt + A_3 \int e^{-k_3 t} dt + A_4 \int e^{-k_4 t} dt + b \int dt$$

$$\int y dt = \frac{A_1}{k_1} (1.0 - e^{-k_1 t}) + \frac{A_2}{k_2} (1.0 - e^{-k_2 t}) + \frac{A_3}{k_3} (1.0 - e^{-k_3 t}) + \frac{A_4}{k_4} (1.0 - e^{-k_4 t}) + bt$$

$$k_1 k_2 k_3 k_4 \int y dt = k_2 k_3 k_4 A_1 - k_2 k_3 k_4 A_1 e^{-k_1 t} + k_1 k_3 k_4 A_2 - k_1 k_3 k_4 A_2 e^{-k_2 t} \\ + k_1 k_2 k_4 A_3 - k_1 k_2 k_4 A_3 e^{-k_3 t} + k_1 k_2 k_3 A_4 - k_1 k_2 k_3 A_4 e^{-k_4 t} + k_1 k_2 k_3 k_4 b t$$

$$k_1 k_2 k_3 k_4 \int y dt = k_2 k_3 k_4 (A_1 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t}) \\ + k_1 k_3 k_4 (A_2 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t}) \\ + k_1 k_2 k_4 (A_3 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_4 e^{-k_4 t}) \\ + k_1 k_2 k_3 (A_4 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t}) \\ + k_1 k_2 k_3 k_4 b t$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

$$k_1 k_2 k_3 k_4 \int y dt \approx k_2 k_3 k_4 (A_1 + b - y) + k_2 k_3 k_4 A_2 e^{-k_2 t} + k_2 k_3 k_4 A_3 e^{-k_3 t} + k_1 k_2 k_3 A_4 e^{-k_4 t} \\ + k_1 k_3 k_4 (A_2 + b - y) + k_1 k_3 k_4 A_1 e^{-k_1 t} + k_1 k_3 k_4 A_3 e^{-k_3 t} + k_1 k_3 k_4 A_4 e^{-k_4 t} \\ + k_1 k_2 k_4 (A_3 + b - y) + k_1 k_2 k_4 A_1 e^{-k_1 t} + k_1 k_2 k_4 A_2 e^{-k_2 t} + k_1 k_2 k_4 A_4 e^{-k_4 t} \\ + k_1 k_2 k_3 (A_4 + b - y) + k_1 k_2 k_3 A_1 e^{-k_1 t} + k_1 k_2 k_3 A_2 e^{-k_2 t} + k_1 k_2 k_3 A_3 e^{-k_3 t} \\ + k_1 k_2 k_3 k_4 b t$$



$$k_1 k_2 k_3 k_4 \int \int y dt dt \approx k_2 k_3 k_4 (A_1 + b) \int dt - k_2 k_3 k_4 \int y dt$$

$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

$$\begin{aligned} &+ k_1 k_3 k_4 (A_2 + b) \int dt - k_1 k_3 k_4 \int y dt \\ &+ k_3 k_4 A_1 (1.0 - e^{-k_1 t}) + k_1 k_4 A_3 (1.0 - e^{-k_3 t}) + k_1 k_3 A_4 (1.0 - e^{-k_4 t}) \\ &+ k_1 k_2 k_4 (A_3 + b) \int dt - k_1 k_2 k_4 \int y dt \\ &+ k_2 k_4 A_1 (1.0 - e^{-k_1 t}) + k_1 k_4 A_2 (1.0 - e^{-k_2 t}) + k_1 k_2 A_4 (1.0 - e^{-k_4 t}) \\ &+ k_1 k_2 k_3 (A_4 + b) \int dt - k_1 k_2 k_3 \int y dt \\ &+ k_2 k_3 A_1 (1.0 - e^{-k_1 t}) + k_1 k_3 A_2 (1.0 - e^{-k_2 t}) + k_1 k_2 A_3 (1.0 - e^{-k_3 t}) + k_1 k_2 k_3 k_4 b \int t dt \end{aligned}$$

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int y dt dt \approx & \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] t + \frac{k_1 k_2 k_3 k_4 b}{2} t^2 \\ & + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \\ & + A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ & - (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int y dt \\ & + k_1 k_2 (-A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - b + b) \\ & + k_1 k_3 (-A_2 e^{-k_2 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ & + k_1 k_4 (-A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \\ & + k_2 k_3 (-A_1 e^{-k_1 t} - A_4 e^{-k_4 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ & + k_2 k_4 (-A_1 e^{-k_1 t} - A_3 e^{-k_3 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \\ & + k_3 k_4 (-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \end{aligned}$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

$$k_1 k_2 k_3 k_4 \int \int \int y dt dt dt$$

$$\approx \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_1 k_2 k_4 + k_1 k_3 k_4 + k_1 k_2 k_3 + k_1 k_2 k_4) b \\ + \frac{k_1 k_2 k_3 k_4 b}{2} t^2 \end{array} \right] t$$

$$\begin{aligned} &+ A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \\ &+ A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) y \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int y dt \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4) A_1 e^{-k_1 t} + (k_1 k_2 + k_2 k_3 + k_2 k_4) A_2 e^{-k_2 t} \\ &+ (k_1 k_3 + k_2 k_3 + k_3 k_4) A_3 e^{-k_3 t} + (k_1 k_4 + k_2 k_4 + k_3 k_4) A_4 e^{-k_4 t} \end{aligned}$$

Third integration yields:

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int \int y dt dt dt &\approx \left[ \begin{array}{l} A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \\ + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ + (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \end{array} \right] t \\ &\quad \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] \frac{t^2}{2} \\ &\quad + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int \int y dt dt \\ &+ A_1 (k_2 + k_3 + k_4) (1 - e^{-k_1 t}) + A_2 (k_1 + k_3 + k_4) (1 - e^{-k_2 t}) \\ &+ A_3 (k_1 + k_2 + k_4) (1 - e^{-k_3 t}) + A_4 (k_1 + k_2 + k_3) (1 - e^{-k_4 t}) \end{aligned}$$

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$$\begin{aligned} & A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \\ & + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) t \\ & + (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \end{aligned}$$

$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

$$\begin{aligned} & \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] t^2 + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ & - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt - (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int \int y dt dt \\ & + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ & - A_1 e^{-k_1 t} (k_2 + k_3 + k_4) - A_2 e^{-k_2 t} (k_1 + k_3 + k_4) - A_3 e^{-k_3 t} (k_1 + k_2 + k_4) - A_4 e^{-k_4 t} (k_1 + k_2 + k_3) \end{aligned}$$

$$\begin{aligned} & k_1 k_2 k_3 k_4 \int \int \int y dt dt dt \approx \left[ \begin{aligned} & A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \\ & + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \end{aligned} \right] t \\ & \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] t^2 + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ & - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt - (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int \int y dt dt \\ & + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ & + k_1 (-A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - b + b) \\ & + k_2 (-A_1 e^{-k_1 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - b + b) \\ & + k_3 (-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_4 e^{-k_4 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ & + k_4 (-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \end{aligned} \right]$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

Fourth integration yields:

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int \int y dt dt dt &\approx \left[ A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \right. \\ &+ A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \left. \right] t \\ &\quad \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] \frac{t^2}{2} + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt dt \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int \int y dt dt \\ &+ A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ &+ k_1(-y + A_1 e^{-k_1 t} + b) + k_2(-y + A_2 e^{-k_2 t} + b) \\ &+ k_3(-y + A_3 e^{-k_3 t} + b) + k_4(-y + A_4 e^{-k_4 t} + b) \end{aligned}$$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$



Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

$$\begin{aligned} y &\approx -(k_1 + k_2 + k_3 + k_4) \int y dt \\ &\quad - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \iint y dt dt \\ &\quad - (k_1 k_2 k_3 + k_1 k_2 k_4 + k_1 k_3 k_4 + k_2 k_3 k_4) \iiint y dt dt dt \\ &\quad - k_1 k_2 k_3 k_4 \square \ddot{\square} \ddot{\square} y d\ddot{\square} dt dt dt \\ &\quad + b + A_1 + A_2 + A_3 + A_4 \\ &\quad + \left[ (k_1 + k_2 + k_3 + k_4) b + \right. \\ &\quad \left. + \left[ A_1 (k_2 + k_3 + k_4) + A_2 (k_1 + k_3 + k_4) + A_3 (k_1 + k_2 + k_4) + A_4 (k_1 + k_2 + k_3) \right] t \right. \\ &\quad \left. + \left[ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \right. \right. \\ &\quad \left. \left. + \left[ A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \right] \frac{t^2}{2} \right. \\ &\quad \left. \left. + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \right] \right. \\ &\quad \left. + \left[ (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \right. \right. \\ &\quad \left. \left. + \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] \frac{t^3}{6} \right. \\ &\quad \left. + \frac{k_1 k_2 k_3 k_4 b}{24} t^4 \right] \end{aligned}$$



$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t} + b$$

$$p_1 = -k_1 - k_2 - k_3 - k_4$$

$$p_2 = -k_1 k_2 - k_1 k_3 - k_1 k_4 - k_2 k_3 - k_2 k_4 - k_3 k_4$$

$$p_3 = -k_1 k_2 k_3 - k_1 k_2 k_4 - k_1 k_3 k_4 - k_2 k_3 k_4$$

$$p_4 = -k_1 k_2 k_3 k_4$$

$$p_5 = b + A_1 + A_2 + A_3 + A_4$$

$$p_6 = b(k_1 + k_2 + k_3 + k_4) + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3)$$

$$p_7 = \frac{1}{2} \left[ b(k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) + A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \right. \\ \left. + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \right]$$

$$p_8 = \frac{1}{6} [b(k_1 k_2 k_3 + k_1 k_2 k_4 + k_1 k_3 k_4 + k_2 k_3 k_4) + A_1 k_2 k_3 k_4 + A_2 k_1 k_3 k_4 + A_3 k_1 k_2 k_4 + A_4 k_1 k_2 k_3]$$

$$p_9 = \frac{bk_1 k_2 k_3 k_4}{24}$$



# Quartic-exponential with background term

$$y = A_1 e^{-k_1 t} + A_2 e^{-k_2 t} +$$

Integration yields:

$$\int y dt = A_1 \int e^{-k_1 t} dt + A_2 \int e^{-k_2 t} dt + A_3 \int e^{-k_3 t} dt + A_4 \int e^{-k_4 t} dt + b \int dt$$

$$\int y dt = \frac{A_1}{k_1} (1.0 - e^{-k_1 t}) + \frac{A_2}{k_2} (1.0 - e^{-k_2 t}) + \frac{A_3}{k_3} (1.0 - e^{-k_3 t}) + \frac{A_4}{k_4} (1.0 - e^{-k_4 t}) + bt$$

$$k_1 k_2 k_3 k_4 \int y dt = k_2 k_3 k_4 A_1 - k_2 k_3 k_4 A_1 e^{-k_1 t} + k_1 k_3 k_4 A_2 - k_1 k_3 k_4 A_2 e^{-k_2 t} \\ + k_1 k_2 k_4 A_3 - k_1 k_2 k_4 A_3 e^{-k_3 t} + k_1 k_2 k_3 A_4 - k_1 k_2 k_3 A_4 e^{-k_4 t} + k_1 k_2 k_3 k_4 b t$$

$$k_1 k_2 k_3 k_4 \int y dt = k_2 k_3 k_4 (A_1 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t}) \\ + k_1 k_3 k_4 (A_2 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_3 e^{-k_3 t} + A_4 e^{-k_4 t}) \\ + k_1 k_2 k_4 (A_3 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_4 e^{-k_4 t}) \\ + k_1 k_2 k_3 (A_4 + b - A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_1 e^{-k_1 t} + A_2 e^{-k_2 t} + A_3 e^{-k_3 t}) \\ + k_1 k_2 k_3 k_4 b t$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

$$k_1 k_2 k_3 k_4 \int y dt \approx k_2 k_3 k_4 (A_1 + b - y) + k_2 k_3 k_4 A_2 e^{-k_2 t} + k_2 k_3 k_4 A_3 e^{-k_3 t} + k_1 k_2 k_3 A_4 e^{-k_4 t} \\ + k_1 k_3 k_4 (A_2 + b - y) + k_1 k_3 k_4 A_1 e^{-k_1 t} + k_1 k_3 k_4 A_3 e^{-k_3 t} + k_1 k_3 k_4 A_4 e^{-k_4 t} \\ + k_1 k_2 k_4 (A_3 + b - y) + k_1 k_2 k_4 A_1 e^{-k_1 t} + k_1 k_2 k_4 A_2 e^{-k_2 t} + k_1 k_2 k_4 A_4 e^{-k_4 t} \\ + k_1 k_2 k_3 (A_4 + b - y) + k_1 k_2 k_3 A_1 e^{-k_1 t} + k_1 k_2 k_3 A_2 e^{-k_2 t} + k_1 k_2 k_3 A_3 e^{-k_3 t} \\ + k_1 k_2 k_3 k_4 b t$$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

Second integration yields:

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int y dt dt &\approx k_2 k_3 k_4 (A_1 + b) \int dt - k_2 k_3 k_4 \int y dt \\ &+ k_3 k_4 A_2 (1.0 - e^{-k_2 t}) + k_2 k_4 A_3 (1.0 - e^{-k_3 t}) + k_2 k_3 A_4 (1.0 - e^{-k_4 t}) \\ &+ k_1 k_3 k_4 (A_2 + b) \int dt - k_1 k_3 k_4 \int y dt \\ &+ k_3 k_4 A_1 (1.0 - e^{-k_1 t}) + k_1 k_4 A_3 (1.0 - e^{-k_3 t}) + k_1 k_3 A_4 (1.0 - e^{-k_4 t}) \\ &+ k_1 k_2 k_4 (A_3 + b) \int dt - k_1 k_2 k_4 \int y dt \\ &+ k_2 k_4 A_1 (1.0 - e^{-k_1 t}) + k_1 k_4 A_2 (1.0 - e^{-k_2 t}) + k_1 k_2 A_4 (1.0 - e^{-k_4 t}) \\ &+ k_1 k_2 k_3 (A_4 + b) \int dt - k_1 k_2 k_3 \int y dt \\ &+ k_2 k_3 A_1 (1.0 - e^{-k_1 t}) + k_1 k_3 A_2 (1.0 - e^{-k_2 t}) + k_1 k_2 A_3 (1.0 - e^{-k_3 t}) + k_1 k_2 k_3 k_4 b \int t dt \\ k_1 k_2 k_3 k_4 \int \int y dt dt &\approx \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] t + \frac{k_1 k_2 k_3 k_4 b}{2} t^2 \\ &+ A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int y dt \\ &+ k_1 k_2 (-A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - b + b) \\ &+ k_1 k_3 (-A_2 e^{-k_2 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ &+ k_1 k_4 (-A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \\ &+ k_2 k_3 (-A_1 e^{-k_1 t} - A_4 e^{-k_4 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ &+ k_2 k_4 (-A_1 e^{-k_1 t} - A_3 e^{-k_3 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \\ &+ k_3 k_4 (-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \end{aligned}$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

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$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$



$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int \int y dt dt dt &\approx \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] t \\ &+ \frac{k_1 k_2 k_3 k_4 b}{2} t^2 \\ &+ A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \\ &+ A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) y \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int y dt \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4) A_1 e^{-k_1 t} + (k_1 k_2 + k_2 k_3 + k_2 k_4) A_2 e^{-k_2 t} \\ &+ (k_1 k_3 + k_2 k_3 + k_3 k_4) A_3 e^{-k_3 t} + (k_1 k_4 + k_2 k_4 + k_3 k_4) A_4 e^{-k_4 t} \end{aligned}$$

Third integration yields:

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int \int y dt dt dt &\approx \left[ \begin{array}{l} A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \\ + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3) \\ + (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \end{array} \right] t \\ &+ \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] \frac{t^2}{2} \\ &+ \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \int \int y dt dt \\ &+ A_1 (k_2 + k_3 + k_4) (1 - e^{-k_1 t}) + A_2 (k_1 + k_3 + k_4) (1 - e^{-k_2 t}) \\ &+ A_3 (k_1 + k_2 + k_4) (1 - e^{-k_3 t}) + A_4 (k_1 + k_2 + k_3) (1 - e^{-k_4 t}) \end{aligned}$$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

$$k_1 k_2 k_3 k_4 \iiint y \, dt \, dt \, dt \approx \begin{aligned} & \left[ A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \right. \\ & + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \Big] t \\ & + (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ & \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] \frac{t^2}{2} + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ & - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y \, dt - (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \iint y \, dt \, dt \\ & + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ & - A_1 e^{-k_1 t} (k_2 + k_3 + k_4) - A_2 e^{-k_2 t} (k_1 + k_3 + k_4) - A_3 e^{-k_3 t} (k_1 + k_2 + k_4) - A_4 e^{-k_4 t} (k_1 + k_2 + k_3) \end{aligned}$$

$$k_1 k_2 k_3 k_4 \iiint y \, dt \, dt \, dt \approx \begin{aligned} & \left[ A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \right] t \\ & + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \Big] t \\ & + (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ & \left[ k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] \frac{t^2}{2} + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ & - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y \, dt - (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \iint y \, dt \, dt \\ & + A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ & + k_1(-A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_1 e^{-k_1 t} + A_1 e^{-k_1 t} - b + b) \\ & + k_2(-A_1 e^{-k_1 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - A_2 e^{-k_2 t} + A_2 e^{-k_2 t} - b + b) \\ & + k_3(-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_4 e^{-k_4 t} - A_3 e^{-k_3 t} + A_3 e^{-k_3 t} - b + b) \\ & + k_4(-A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} + A_4 e^{-k_4 t} - b + b) \end{aligned}$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

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$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

$$\begin{aligned} k_1 k_2 k_3 k_4 \iiint y dt dt dt &\approx \left[ \begin{array}{l} A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \\ + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \end{array} \right] t \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ &\left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] \frac{t^2}{2} + \frac{k_1 k_2 k_3 k_4 b}{6} t^3 \\ &- (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int y dt \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \iint y dt dt \\ &+ A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ &+ k_1(-y + A_1 e^{-k_1 t} + b) + k_2(-y + A_2 e^{-k_2 t} + b) \\ &+ k_3(-y + A_3 e^{-k_3 t} + b) + k_4(-y + A_4 e^{-k_4 t} + b) \end{aligned}$$

Fourth integration yields:

$$\begin{aligned} k_1 k_2 k_3 k_4 \int \int \int y d\zeta dt dt dt &\approx \left[ \begin{array}{l} A_1(k_2 + k_3 + k_4) + A_2(k_1 + k_3 + k_4) + A_3(k_1 + k_2 + k_4) + A_4(k_1 + k_2 + k_3) \\ + (k_1 + k_2 + k_3 + k_4) b \end{array} \right] t \\ &+ \left[ \begin{array}{l} A_1(k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2(k_1 k_3 + k_1 k_4 + k_3 k_4) \\ + A_3(k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4(k_1 k_2 + k_1 k_3 + k_2 k_3) \end{array} \right] \frac{t^2}{2} \\ &+ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \\ &+ \left[ \begin{array}{l} k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \\ + (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \end{array} \right] \frac{t^3}{6} + \frac{k_1 k_2 k_3 k_4 b}{24} t^4 \\ &- (k_1 + k_2 + k_3 + k_4) \int y dt - (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \iint y dt dt \\ &- (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) \iiint y dt dt dt \\ &+ A_1(1 - e^{-k_1 t}) + A_2(1 - e^{-k_2 t}) + A_3(1 - e^{-k_3 t}) + A_4(1 - e^{-k_4 t}) \end{aligned}$$



$$y = b + \sum_{i=1}^4 A_i e^{-k_i t}$$

Substitute:  $-y \approx -A_1 e^{-k_1 t} - A_2 e^{-k_2 t} - A_3 e^{-k_3 t} - A_4 e^{-k_4 t} - b$

$$y \approx -(k_1 + k_2 + k_3 + k_4) \int y dt$$

$$-(k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) \int \int y dt dt$$

$$-(k_1 k_2 k_3 + k_1 k_2 k_4 + k_1 k_3 k_4 + k_2 k_3 k_4) \int \int \int y dt dt dt$$

$$-k_1 k_2 k_3 k_4 \square \ddot{y} dt dt dt$$

$$+b + A_1 + A_2 + A_3 + A_4$$

$$+ \left[ (k_1 + k_2 + k_3 + k_4) b + \right. \\ \left. A_1 (k_2 + k_3 + k_4) + A_2 (k_1 + k_3 + k_4) + A_3 (k_1 + k_2 + k_4) + A_4 (k_1 + k_2 + k_3) \right] t$$

$$+ \left[ (k_1 k_2 + k_1 k_3 + k_1 k_4 + k_2 k_3 + k_2 k_4 + k_3 k_4) b \right. \\ \left. + A_1 (k_2 k_3 + k_2 k_4 + k_3 k_4) + A_2 (k_1 k_3 + k_1 k_4 + k_3 k_4) \right] \frac{t^2}{2} \\ + A_3 (k_1 k_2 + k_1 k_4 + k_2 k_4) + A_4 (k_1 k_2 + k_1 k_3 + k_2 k_3)$$

$$+ \left[ (k_2 k_3 k_4 + k_1 k_3 k_4 + k_1 k_2 k_4 + k_1 k_2 k_3) b \right. \\ \left. + k_2 k_3 k_4 A_1 + k_1 k_3 k_4 A_2 + k_1 k_2 k_4 A_3 + k_1 k_2 k_3 A_4 \right] \frac{t^3}{6}$$

$$+ \frac{k_1 k_2 k_3 k_4 b}{24} t^4$$





System of linear equations for  $y = \sum_{i=1}^N e^{-k_i t}$

$$\int y dt \quad \int \int y dt dt \quad \int \int \int y dt dt dt \quad \dots, Nth order \int \quad 1.0 \quad t \quad t^2 \quad \dots \quad t^{N-1}$$

$$\begin{pmatrix} y_1 \\ y_2 \\ \dots \\ y_M \end{pmatrix} = \begin{pmatrix} 0 & 0 & 0 & \dots & 0 & 1.0 & t_1 & t_1^2 & \dots & t_1^{N-1} \\ \int_{t_1}^{t_2} y dt & \int \int y dt dt & \int \int \int y dt dt dt & \dots & Nth order \int & 1.0 & t_2 & t_2^2 & \dots & t_2^{N-1} \\ \dots & \dots \\ \int_{t_1}^{t_M} y dt & \int \int y dt dt & \int \int \int y dt dt dt & \dots & Nth order \int & 1.0 & t_M & t_M^2 & \dots & t_M^{N-1} \end{pmatrix} \begin{pmatrix} p_1 \\ p_2 \\ p_3 \\ \dots \\ p_N \\ p_{N+1} \\ p_{N+2} \\ p_{N+3} \\ \dots \\ p_{2N} \end{pmatrix}$$



# Global method implementation of biexponential with background (for the $L=3$ simultaneous data sets containing $M$ data points each)

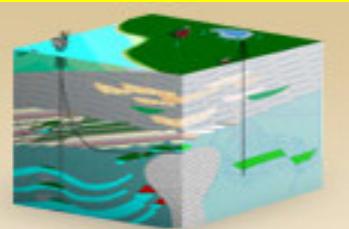
$$\begin{pmatrix} y_{1,1} \\ \dots \\ y_{1,M} \\ y_{2,1} \\ \dots \\ y_{2,M} \\ y_{L,1} \\ \dots \\ y_{L,M} \end{pmatrix} = \begin{pmatrix} \int_{t_{1,1}}^{t_{1,1}} y_{1,\cdot} dt & \int_{t_{1,1}}^{t_{1,1}} \int_{t_{1,1}}^{t_{1,1}} y_{1,\cdot} dt dt & 1 & t_{1,1} & 0 & 0 & 0 & 0 & t_{1,1}^2 \\ \dots & \dots \\ \int_{t_{1,1}}^{t_{1,M}} y_{1,\cdot} dt & \int_{t_{1,1}}^{t_{1,M}} \int_{t_{1,1}}^{t_{1,M}} y_{1,\cdot} dt dt & 1 & t_{1,M} & 0 & 0 & 0 & 0 & t_{1,M}^2 \\ \dots & \dots \\ \int_{t_{2,1}}^{t_{2,1}} y_{2,\cdot} dt & \int_{t_{2,1}}^{t_{2,1}} \int_{t_{2,1}}^{t_{2,1}} y_{2,\cdot} dt dt & 0 & 0 & 1 & t_{2,1} & 0 & 0 & t_{2,1}^2 \\ \dots & \dots \\ \int_{t_{2,1}}^{t_{2,M}} y_{2,\cdot} dt & \int_{t_{2,1}}^{t_{2,M}} \int_{t_{2,1}}^{t_{2,M}} y_{2,\cdot} dt dt & 0 & 0 & 1 & t_{2,M} & 0 & 0 & t_{2,M}^2 \\ \dots & \dots \\ \int_{t_{L,1}}^{t_{L,1}} y_{L,\cdot} dt & \int_{t_{L,1}}^{t_{L,1}} \int_{t_{L,1}}^{t_{L,1}} y_{L,\cdot} dt dt & 0 & 0 & 0 & 0 & 1 & t_{L,1} & t_{L,1}^2 \\ \dots & \dots \\ \int_{t_{L,1}}^{t_{L,M}} y_{L,\cdot} dt & \int_{t_{L,1}}^{t_{L,M}} \int_{t_{L,1}}^{t_{L,M}} y_{L,\cdot} dt dt & 0 & 0 & 0 & 0 & 1 & t_{L,M} & t_{L,M}^2 \end{pmatrix} \begin{pmatrix} -k_1 - k_2 \\ -k_1 k_2 \\ b + A_{1,1} + A_{1,2} \\ (k_1 + k_2)b + A_{1,1}k_2 + A_{1,2}k_1 \\ b + A_{2,1} + A_{2,2} \\ (k_1 + k_2)b + A_{2,1}k_2 + A_{2,2}k_1 \\ b + A_{L,1} + A_{L,2} \\ (k_1 + k_2)b + A_{L,1}k_2 + A_{L,2}k_1 \\ \frac{k_1 k_2 b}{2} \end{pmatrix}$$



# How about some other applications?

KMS

From



to

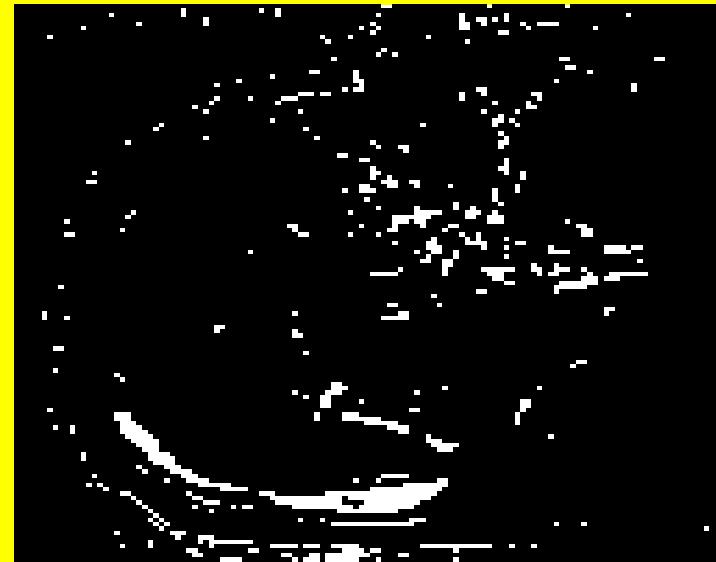
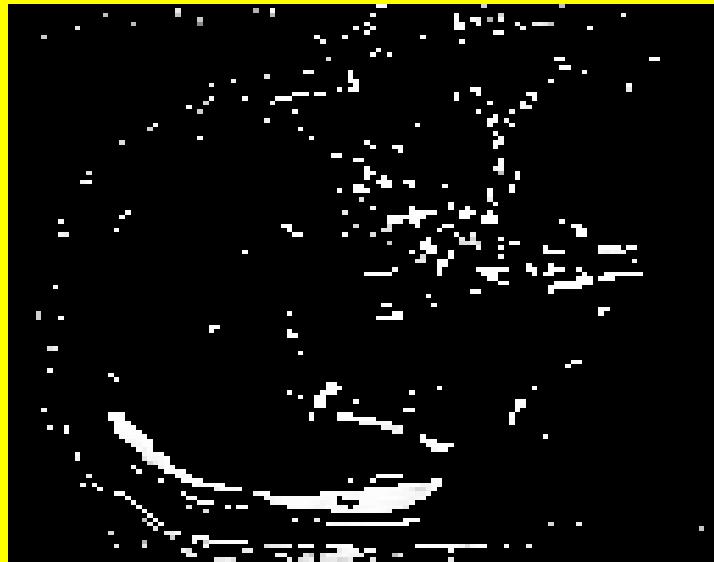




## Bi-exponential fit

Correlation index

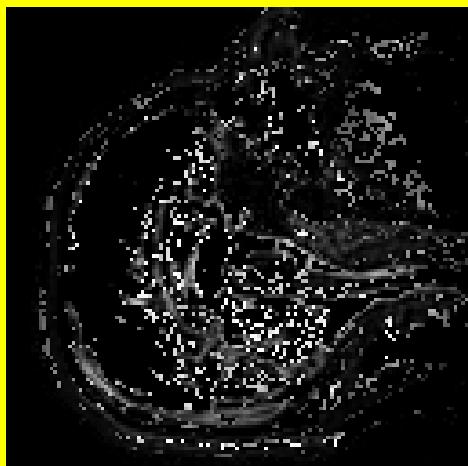
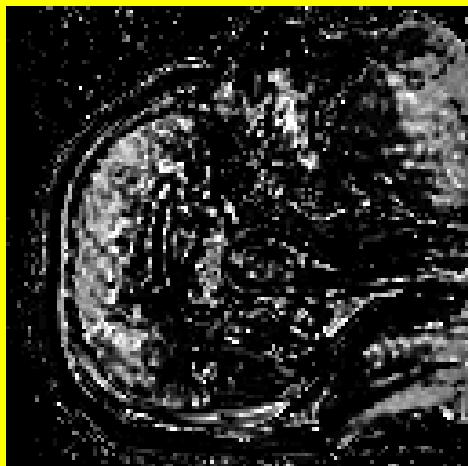
Error flag



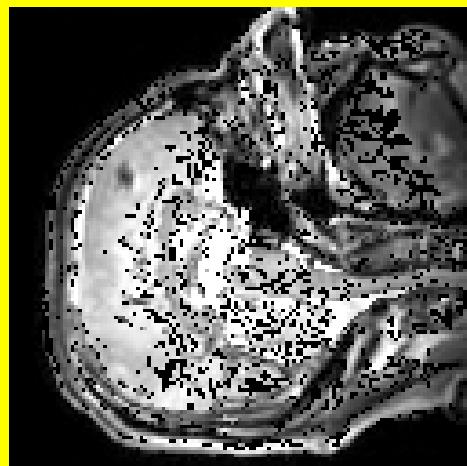
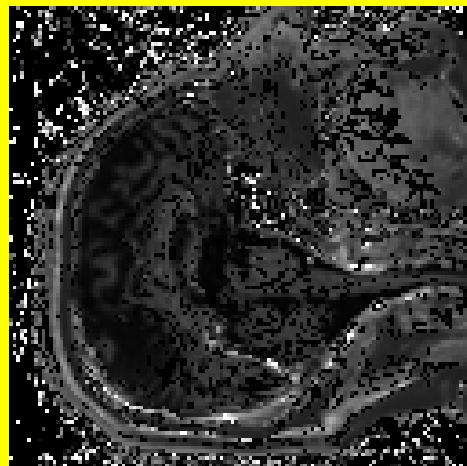


## Bi-exponential fit NNLS

K0 & A0



K1 & A1



CI & err\_flg

