New Classes of Interconnected Compartmental DCS Models

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Overview

- Study objectives.
- What is multi-exponential tissue kinetics?
- Prior work with multi-exponential tissue kinetics.
- Problem statement.
- Method of solution.
- Model optimization.
- Model extrapolation.
- Conclusions.

Study objectives

- Develop a general, fast solution method for optimizing and testing interconnected compartmental (multi-exponential) probabilistic decompression models.
- Test the fitting quality of 4 new interconnected models.
- Test the extrapolation quality of 4 new interconnected models.

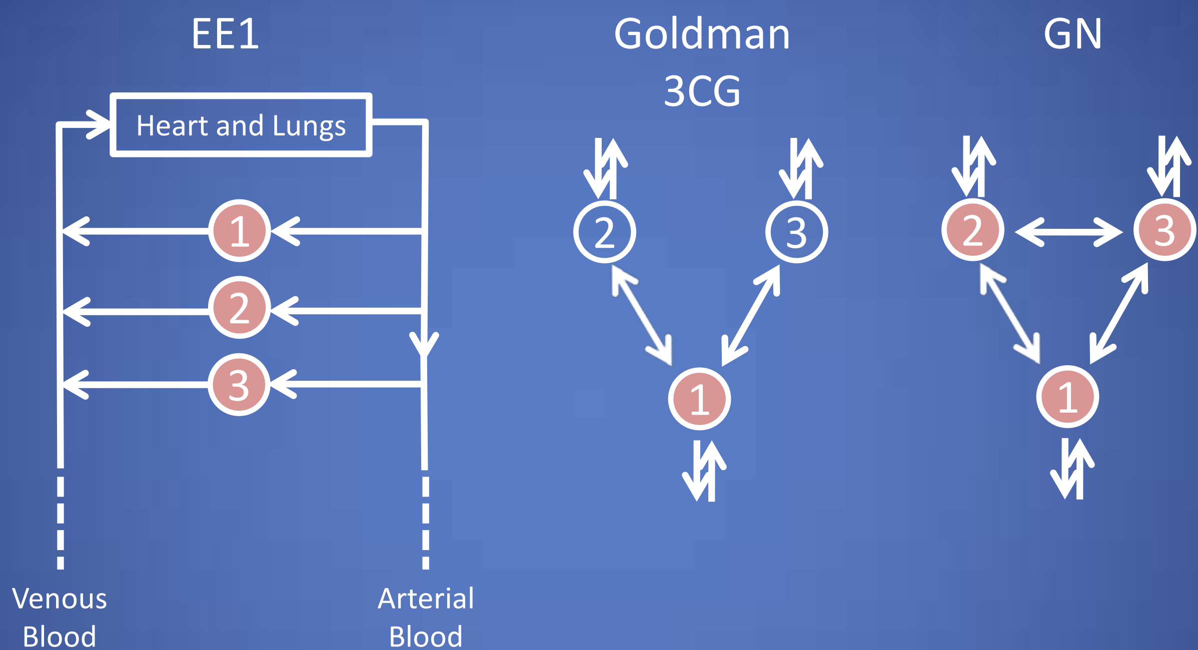
Multi-exponential kinetics

- Parallel, well perfused decompression models contain multiple *mono-exponential* tissues.
- *Multi-exponential* (within an individual tissue) kinetics can occur in tissues described with higher-order differential equations.
- *Multi-exponential* gas kinetics can also result from interconnections between first-order tissues.

Prior multi-exponential kinetics work

- Weathersby *et al.* J. Appl. Phys. 1979.
- Weathersby *et al*. J. Appl. Phys. 1981.
- Tikuisis *et al.* Und. Biomed. Res. 1988.
- Novatny *et al.* J. Appl. Phys. 1990.
- Doolette *et al.* J. Pharm. Bioph. 1998.
- Doolette *et al*. Acta Phys. Scand. 2001.
- Doolette *et al.* Acta Phys. Scand. 2005.
- Goldman J. Appl. Phys. 2007.

Problem statement



Red tissues are risk-bearing.
Arrows denote gas transfer.

Method of solution

$$\frac{d\mathbf{p}}{dt} = \mathbf{Ap} + \mathbf{f} \cdot p_{N_2}\left(t\right), \quad \mathbf{p} \in \Re^{n}, \quad \mathbf{A} \in \Re^{n \times n} \quad (1)$$

Let $\mathbf{A} = \mathbf{SDS}^{-1}$ be the spectral decompostion of $\mathbf{A}$

where $\mathbf{S}$ is an eigenvector matrix

and $\mathbf{D}$ is the diagonal eigenvalue matrix.

Now, define the tranformation $\mathbf{p} = \text{Æ}\mathbf{S}$ so thaÆ $\mathbf{S} = \mathbf{p}^{-1}$.

Then, equation (1) becomes

$$\frac{d\text{Æ}}{dt} = \mathbf{D}\text{Æ} + \mathbf{S}^{-1}\mathbf{f}\; p_{N_2}\left(0\right) + \mathbf{S}^{-1}\mathbf{f}\; r_{N_2} \cdot t$$

New models studied

- Upper triangular (UT)
- Symmetric (SY)
- Skew symmetric (SK)
- General (GN)

$$\mathbf{S} = \begin{bmatrix} 1 & s_{12} & s_{13} \\ s_{21} & 1 & s_{23} \\ s_{13} & s_{32} & 1 \end{bmatrix}$$

- Restricted to orthogonal eigenvectors through Gram-Schmidt orthogonalization.

$$\mathbf{A} = \mathbf{SDS}^{-1} = \mathbf{SDS}^{T}$$

Model optimization

- EE1 model used a null model.
- EE1, GN, SY, SK, and UT models trained on Big292 data set (3322 exposures, 190 DCS, 110 marginal DCS).
- Parameters optimized in parallel by maximum likelihood.
- Marginal DCS weighted as 0.1.
- Failure times not used.

Model Parameters

Parameters	EE1	UT	SK	SY	GN
$\lambda_1\left[\text{min}^{-1}\right]$	$-0.424^{+0.078}_{-0.084}$	$-0.917^{+0.306}_{-0.467}$	$-0.320^{+0.032}_{-0.042}$	$-0.317^{+0.056}_{-0.087}$	$-0.317^{+0.052}_{-0.084}$
$\lambda_2\cdot 10\left[\text{min}^{-1}\right]$	$-0.214^{+0.032}_{-0.043}$	$-0.084^{+0.009}_{-0.006}$	$-0.135^{+0.008}_{-0.002}$	$-0.167^{+0.017}_{-0.011}$	$-0.167^{+0.013}_{-0.010}$
$\lambda_3\cdot 10^2\left[\text{min}^{-1}\right]$	$-0.217^{+0.015}_{-0.013}$	$-0.221^{+0.011}_{-0.015}$	$-0.221^{+0.004}_{-0.007}$	$-0.229^{+0.013}_{-0.012}$	$-0.229^{+0.011}_{-0.011}$
S_{12}		$-0.066^{+0.010}_{-0.015}$	$-1.266^{+0.105}_{-0.034}$	$-0.397^{+0.001}_{-0.002}$	$-0.397^{+0.001}_{-0.001}$
S_{13}		$-0.572^{+0.021}_{-0.028}$	$-1.099^{+0.007}_{-0.024}$	$0.953^{+0.002}_{-0.002}$	$0.953^{+0.001}_{-0.002}$
S_{21}					$-0.397^{+0.075}_{-0.067}$
S_{23}		$-2.899^{+0.245}_{-0.311}$	$-0.503^{+0.020}_{-0.042}$	$-0.413^{+0.001}_{-0.001}$	$-0.413^{+0.038}_{-0.036}$
S_{31}					$0.953^{+0.003}_{-0.002}$
S_{32}					$-0.413^{+0.001}_{-0.001}$
α_1	$0.219^{+0.223}_{-0.132}$	$0.024^{+0.012}_{-0.010}$	$3.540^{+3.009}_{-2.270}$	$0.960^{+1.068}_{-0.524}$	$1.070^{+0.948}_{-0.625}$
$\alpha_2\cdot 10^2$	$0.670^{+0.210}_{-0.180}$	$0.0652^{+0.013}_{-0.011}$	$0.182^{+0.077}_{-0.072}$	$0.186^{+0.049}_{-0.044}$	$0.192^{+0.048}_{-0.042}$
$\alpha_3\cdot 10^2$	$0.186^{+0.037}_{-0.035}$	$0.046^{+0.040}_{-0.035}$	$0.102^{+0.020}_{-0.019}$	$0.145^{+0.037}_{-0.003}$	$0.145^{+0.034}_{-0.030}$
$b_1\left[\text{atm}\right]$	$1.427^{+0.162}_{-0.165}$	$-0.076^{+0.014}_{-0.009}$	$0.879^{+0.027}_{-0.008}$	$0.662^{+0.051}_{-0.022}$	$0.662^{+0.058}_{-0.018}$
$b_2\left[\text{atm}\right]$	$0.370^{+0.049}_{-0.046}$	$0.435^{+0.099}_{-0.097}$	$0.040^{+0.099}_{-0.077}$	$0.383^{+0.084}_{-0.061}$	$0.395^{+0.079}_{-0.061}$
$b_3\cdot 10\left[\text{atm}\right]$	$-0.519^{+0.149}_{-0.151}$	$-0.367^{+1.047}_{-0.473}$	$0.355^{+0.267}_{-0.271}$	$-0.606^{+0.192}_{-0.177}$	$-0.606^{+0.200}_{-0.170}$
LL	−705.82	−697.33	−701.15	−692.11	−691.99
Predicted DCS	201.4	200.3	201.1	201.3	201.5

Optimization results (p<0.05)

	2 LL diff.	Added DOF	95% Limit	95% Test
UT/EE1	16.98	3	7.81	Pass
SK/EE1	9.33	3	7.81	Pass
SY/EE1	27.41	3	7.81	Pass
GN/EE1	27.65	6	12.59	Pass
GN/UT	10.67	3	7.81	Pass
GN/SK	18.32	3	7.81	Pass
GN/SY	0.24	3	7.81	Fail

Model extrapolation

- 5163 exposures not included in training set, 214 DCS, 329 marginal DCS.
- Single air, Repetitive air, Repetitive multilevel air, Air + O_2 decompression, Air + surface O_2 decompression, Surface decompression, Submarine escape.
- Model parameters from optimization on training set.
- Discrimination by group χ^2.

Extrapolation Results

	Obs DCS	EE1	UT	SK	SY	GN
Single Air	122.1	125.6	103.8	95.0	106.2	107.8
Group χ^2		0.0951	3.2401	7.7241	2.3957	1.9012
Repetitive Air	5	15.4	15.6	14.4	14.2	14.2
Group χ^2		7.0109	7.2430	6.1722	5.9404	5.9590
Repet/Multi Non-Air	2	13.4	12.5	13.6	17.5	17.5
Group χ^2		9.6936	8.7888	9.9010	13.7167	13.7276
Air + O2 Deco	24.2	9.7	12.7	13.6	15.1	15.1
Group χ^2		21.602	10.403	8.3270	5.4575	5.4637
O2 Surface Deco	55.4	88.5	56.7	61.3	65.9	66.6
Group χ^2		12.376	0.0293	0.5604	1.6639	1.8690
Surface Deco	34.2	24.2	22.8	20.9	22.9	23.0
Group χ^2		4.0954	5.7615	8.4771	5.6192	5.4830
Submarine Escape	4	29.5	11.3	65.8	38.3	41.8
All Categories	246.9	306.3	235.4	284.6	280.0	285.9
Group χ^2		76.890	40.204	99.209	65.523	68.595

Conclusions ($p<0.05$)

- Single-risk-tissue models failed training.
- GN, SY, SK, UT beat EE1 in training.
- GN,SY, UT beat EE1 in extrapolation.
- UT beat all other models in extrapolation.
- UT worked especially well on O_2 deco dives.
- Future work with NEDU colleagues on various physiologically-derived and other coupled and multi-gas models.

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