Lung Mechanics

With mathematical and computational models furthering our understanding of lung mechanics, function, and disease, this book provides an all-inclusive introduction to the topic from a quantitative standpoint. Focusing on inverse modeling, the reader is guided through the theory in a logical progression, from the simplest models up to state-of-the-art models that are both dynamic and nonlinear.

Key tools used in biomedical engineering research, such as regression theory, linear and nonlinear systems theory, and the Fourier transform, are explained. Derivations of important physical relationships, such as the Poiseuille equation and the wave speed equation, from first principles are also provided. Examples of applications to experimental data illustrate physiological relevance throughout, whilst problem sets at the end of each chapter provide practice and test reader comprehension. This book is ideal for biomedical engineering and biophysics graduate students and researchers wishing to understand this emerging field.

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Lung Mechanics

An Inverse Modeling Approach

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CAMBRIDGE
UNIVERSITY PRESS

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Shaftesbury Road, Cambridge CB2 8EA, United Kingdom

One Liberty Plaza, 20th Floor, New York, NY 10006, USA

477 Williamstown Road, Port Melbourne, VIC 3207, Australia

314–321, 3rd Floor, Plot 3, Splendor Forum, Jasola District Centre, New Delhi – 110025, India

103 Penang Road, #05–06/07, Visioncrest Commercial, Singapore 238467

Cambridge University Press is part of Cambridge University Press & Assessment, a department of the University of Cambridge.

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www.cambridge.org
Information on this title: www.cambridge.org/9780521509602

First published 2009

A catalogue record for this publication is available from the British Library

Library of Congress Cataloging-in-Publication data
Bates, Jason H. T.
Lung mechanics / Jason H. T. Bates.
p. cm.
Includes bibliographical references and index.
ISBN 978-0-521-50960-2 (hardback)
1. Lungs. 2. Human mechanics. 3. Respiration. I. Title.
QP121.B35 2009
611′.24 – dc22 2009011365

ISBN 978-0-521-50960-2 Hardback

Dedicated with love to my wife, Nancy MacGregor, for her constant support.

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Preface

Viewing the lungs as a mechanical system has intrigued engineers, physicists, and mathematicians for decades. Indeed, the field of lung mechanics is now mature and highly quantitative, making wide use of sophisticated mathematical and computational methods. Nevertheless, most books on lung mechanics are aimed primarily at physiologists and medical professionals, and are therefore somewhat lacking in the mathematical treatment necessary for a rigorous scientific introduction to the subject. This book attempts to fill that gap. Accordingly, some familiarity with the methods of applied mathematics, including basic calculus and differential equations, is assumed. The material covered is suitable for a first-year graduate course in bioengineering. I hope, however, it will also be accessible to motivated biologists and physiologists.

This book focuses on inverse models of lung mechanics, and is organized around the principle that these models can be arranged in a hierarchy of complexity. Chapter 1 expands on this concept and introduces the adjunct notion of forward modeling. It also sets the scene with a brief overview of pulmonary physiology in general. Chapter 2 attends to the fact that all the mathematical modeling skill in the world is for nought without good experimental data. Accordingly, this chapter is devoted to the key experimental methodologies that have provided the data on which the models described in subsequent chapters are based. It can thus be skipped without loss of continuity and referred back to when issues related to experimental validation of models arise. The discussion of inverse lung models begins in earnest in Chapter 3, which develops the theory behind the simplest plausible physiological model of all – a single elastic compartment served by a single flow-resistive airway. This represents the most basic level of inverse-model complexity, but one which still has a very useful physiological interpretation, discussed in Chapter 4. In proceeding to the second level of model complexity, we have a choice to make; is it more appropriate to require the elements of the simple model to be nonlinear, or should we add a second linear compartment? There is no simple answer to this question, so we proceed by examining nonlinear extensions of the basic model in Chapter 5 and go specifically into the nonlinear phenomenon of expiratory flow limitation in Chapter 6. The alternative to introducing nonlinearity, namely adding a second linear compartment, is developed in Chapter 7. This segues into the third level of complexity represented by the general linear dynamic model and the concept of impedance, discussed in Chapter 8. Various models of lung impedance are discussed in Chapter 9, while Chapter 10 is devoted to a particular example currently in widespread use, known as the constant phase model. Chapter 11 deals with the fourth and final level of complexity, that of the nonlinear dynamic model. Chapter 12 concludes the book with a brief overview in which the various inverse models considered in previous chapters are brought together into a unified picture.

In addition to covering the field of lung mechanics, this book also has a second goal. This is to exemplify how quantitative methods from the physical sciences can be used to advance knowledge in a biomedical subject of significant practical importance for human health. Lung mechanics is a prime example of this because it is so well suited to quantitative investigation, being essentially a manifestation of classical Newtonian physics in the body. However, there are many other areas of biomedical research that benefit from use of the same methods, which therefore have wide applicability. Accordingly, significant attention is paid to the explanation of these methods, which include multiple linear regression and its recursive formulation, statistical tests of model order, linear and nonlinear system identification, and the Fourier transform. Also, when the physiological interpretation of lung models is discussed, formulae encapsulating relevant physical processes are derived from first principles where possible. This is to try to minimize the uncomfortable sense of mystery that inevitably arises when any mathematical formula has to be taken on trust.

The material presented in this book stems from work carried out in numerous laboratories around the world, as well as research from my own laboratory over the past 25 years both at the Meakins-Christie Laboratories of McGill University and subsequently at the Vermont Lung Center of the University of Vermont College of Medicine. Some of what appears is thus the result of interactions I have had the privilege to enjoy with countless mentors, colleagues, and students. Space does not permit me to list everyone, much as I would like to. However, several friends and associates graciously read through drafts of this book and gave me their invaluable comments. On this account, my thanks go to (in alphabetical order) Gil Allen, Sharon Bullimore, Anne Dixon, Charlie Irvin, David Kaminsky, Anne-Marie Lauzon, and Bela Suki.

Cambridge University Press & Assessment
978-0-521-50960-2 — Lung Mechanics
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Notation

A	1) parameter in exponential pressure-volume relationship of lung 2) area 3) amplitude
A_0	equilibrium area of elastic tube
A_i	1) coefficient of exponential term 2) coefficient of term in general second-order equation of motion
A	vector of parameter values
$\underline{\hat{A}}$	estimate of parameter vector
A-D	analog to digital
AICc	corrected Akaike criterion
ΔA_i	change in the *i*th parameter value
a	parameter in sigmoidal pressure-volume relationship of lung
a_i	parameters in a series
B	parameter of exponential pressure-volume relationship of lung
B_i	coefficient of general second-order equation of motion
b	parameter in sigmoidal pressure-volume relationship of lung
b_i	parameter in a general linear differential equation
C	constant of integration
$C_{P,\dot{V}}$	cross-spectral density between pressure and flow
$C_{P,P}$	auto-spectral density of pressure
CD	coefficient of determination
c	parameter in sigmoidal pressure-volume relationship of lung
D	length of dashpot in tissue model
E	elastance
E_A	elastance of lung region under an alveolar capsule
E_{cw}	chest wall elastance
E_L	lung elastance
E_{rs}	respiratory system elastance
E_t	elastance of lung tissue
E_0	elastance of homogeneous lung model
E_1	volume-independent term in P_{el}
E_2	volume-dependent term in P_{el}
E_i, $i = 1,2\ldots$	elastance of *i*th compartment
ΔE	increase in elastance due to mechanical heterogeneity

$F\{\}$	operation of Fourier transformation on bracketed quantity
f	frequency (Hz)
$f(x)$	general nonlinear function of x
FEV_1	volume of air exhaled in the first second of a forced expiration
FVC	forced vital capacity
G	tissue damping in the constant phase model
H	tissue elastance in the constant phase model
H	Heaviside step function
$H_{\min}$	minimum value of H in the distributed constant phase model
$H_{\max}$	maximum value of H in the distributed constant phase model
h	impulse response function
h_i	kernels in the Volterra series
I	inertance
I_{aw}	inertance of airway gas
I_t	inertance of lung tissue
$\underline{\underline{I}}$	identity matrix
J	cost function for Poiseuille flow formula
K	parameter in exponential pressure-volume relationship of lung
K_1	flow-independent term of the Rohrer equation for flow resistance
K_2	flow-dependent term of the Rohrer equation for flow resistance
k	1) spring constant in model of lung tissue strip 2) power-law exponent
L	total length of model of lung tissue strip
l	length
M	mass
$\underline{\underline{M}}$	covariance matrix for recursive multiple linear regression
MSR	mean squared residual
m	number of model parameters
N	1) distribution of string lengths in model of lung tissue strip 2) number of series springs in tissue model
$\underline{\underline{N}}$	vector of noise values in dependent variable
n	number of data points
P	pressure
$\bar{p}$	mean pressure
$\underline{P}$	vector of pressure measurements
P_A	alveolar pressure
P_{ao}	airway opening pressure
P_b	Bernoulli pressure
P_{box}	plethysmographic pressure
P_{el}	elastic pressure
P_{es}	esophageal pressure
$P_{impulse}$	impulse response in pressure
P_j	pressure at airway junction
P_{pl}	pleural pressure

P_{step}	step response in pressure
P_{tm}	airway transmural pressure
P_{tp}	transpulmonary pressure
P_0	1) baseline pressure 2) initial pressure
P_i	pressure in ith compartment
PEEP	positive end-expiratory pressure
ΔP	change in pressure
ΔP_d	pressure drop across daughter airway
ΔP_{dif}	pressure change due to stress adaptation
ΔP_{init}	initial pressure change following flow interruption
ΔP_p	pressure drop across parent airway
p	dummy variable of integration
$\underline{\underline{Q}}$	matrix of noise values in independent variables
R	1) resistance 2) real part of impedance
R_A	airway resistance leading into the lung from under an alveolar capsule
R_{aw}	airway resistance
R_c	resistance of common airway
R_{cw}	chest wall resistance
R_d	resistance of daughter airway
R_g	real part of thoracic gas impedance
R_{hole}	resistance of hole in pleural surface
R_L	lung resistance
R_N	Newtonian resistance of the constant phase model
R_p	resistance of parent airway
R_{rs}	respiratory system resistance
R_t	tissue resistance
R_0	resistance of homogeneous lung model
$R_i, i = 1, 2 \ldots$	resistance of ith compartment
Re	Reynolds number
ΔR	increase in resistance due to mechanical heterogeneity
r	radius
r_0	equilibrium radius of elastic tube
S	stress in viscoelastic tissue model
SSR	sum of squared residuals
T	tension
t	time
Δt	time step
u	dummy variable of integration representing time
V	volume
V_i	volume of ith compartment

v	1) velocity
	2) voltage
$\dot{V}$	flow
$\dot{V}_{\max}$	maximal expiratory flow
$\ddot{V}$	rate of change of flow
ΔV	change in volume
V_{TG}	thoracic gas volume
$\dot{W}$	rate of energy dissipation in laminar flow of fluid
X	imaginary part of impedance
X_{aw}	imaginary part of airway impedance
X_g	imaginary part of thoracic gas impedance
X_t	imaginary part of tissue impedance
$\underline{\underline{X}}$	matrix of independent variables
x	extension of spring in Maxwell body
Z	impedance
Z_{aw}	impedance of airways
Z_g	impedance of thoracic gas
Z_{in}	input impedance
Z_t	impedance of tissues
Z_{tr}	transfer impedance
Φ	coherence
α	1) Womersley number
	2) coefficient of exponential force-length relationship of lung tissue
	3) width of axial strip of airway wall
	4) sinusoidal coefficient
	5) exponent of frequency in the constant phase model
	6) exponent of elastic force in tissue
β	1) coefficient of exponential force-length relationship of lung tissue
	2) sinusoidal coefficient
	3) exponent of resistive force in tissue model
δ	1) asymmetry index in orders of the airway tree
	2) Dirac delta-function
ε	strain
λ	forgetting factor for recursive algorithms
σ	stress
σ^2	variance
$\hat{\sigma}^2$	estimate of variance
ϕ	phase
η	hysteresivity
μ	viscosity
ρ	density
τ	time-constant
ω	angular frequency