Lung Modeling Based on Multiscale Data

Andres Kriete
School of Biomedical Engineering, Science and Health Systems
Drexel University, Philadelphia
10/2007

Collaborators: Robert Kunz and team (Penn State), Viraj Shah (Drexel Biomed), Uday Kiran Thummalapalli (Drexel Biomed) Andreas Schmidt (Medical School, Giessen), Andreas Zidowitz (Mevis, Bremen)

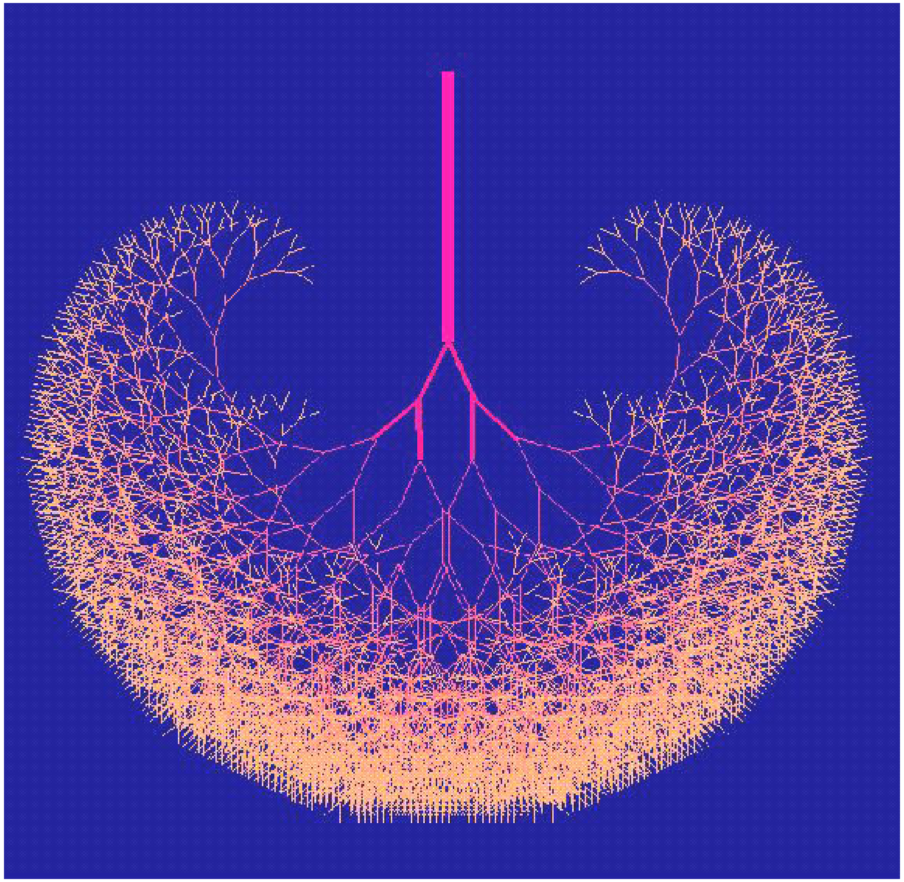
Content

- Introduction

- Structural modeling of mammalian lung
- Functional simulation
- Results and interpretation

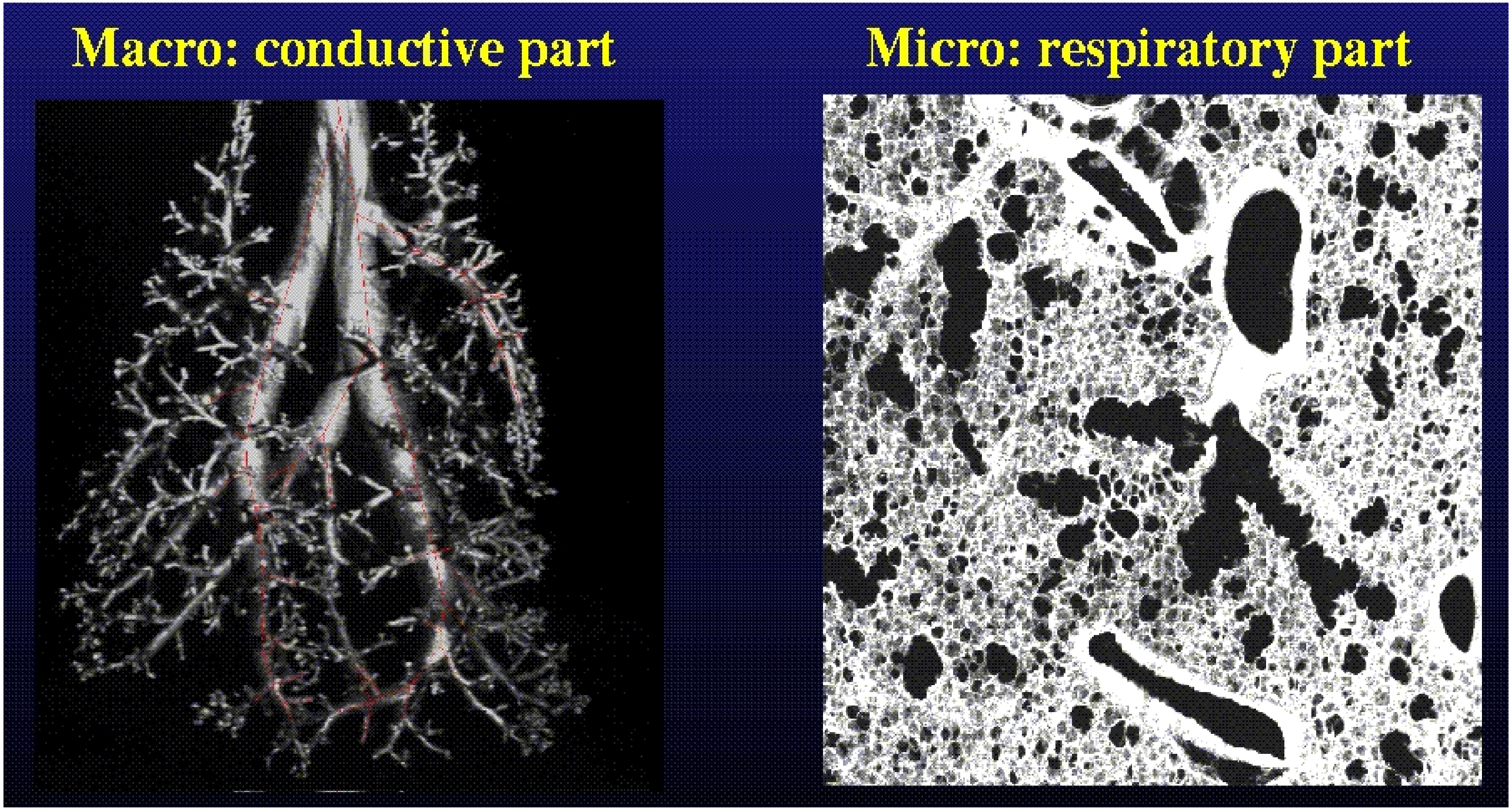
- Human lung
- Special Preparations and HRCT imaging
- Towards disease models

Lung Model with Dichotomous Branching



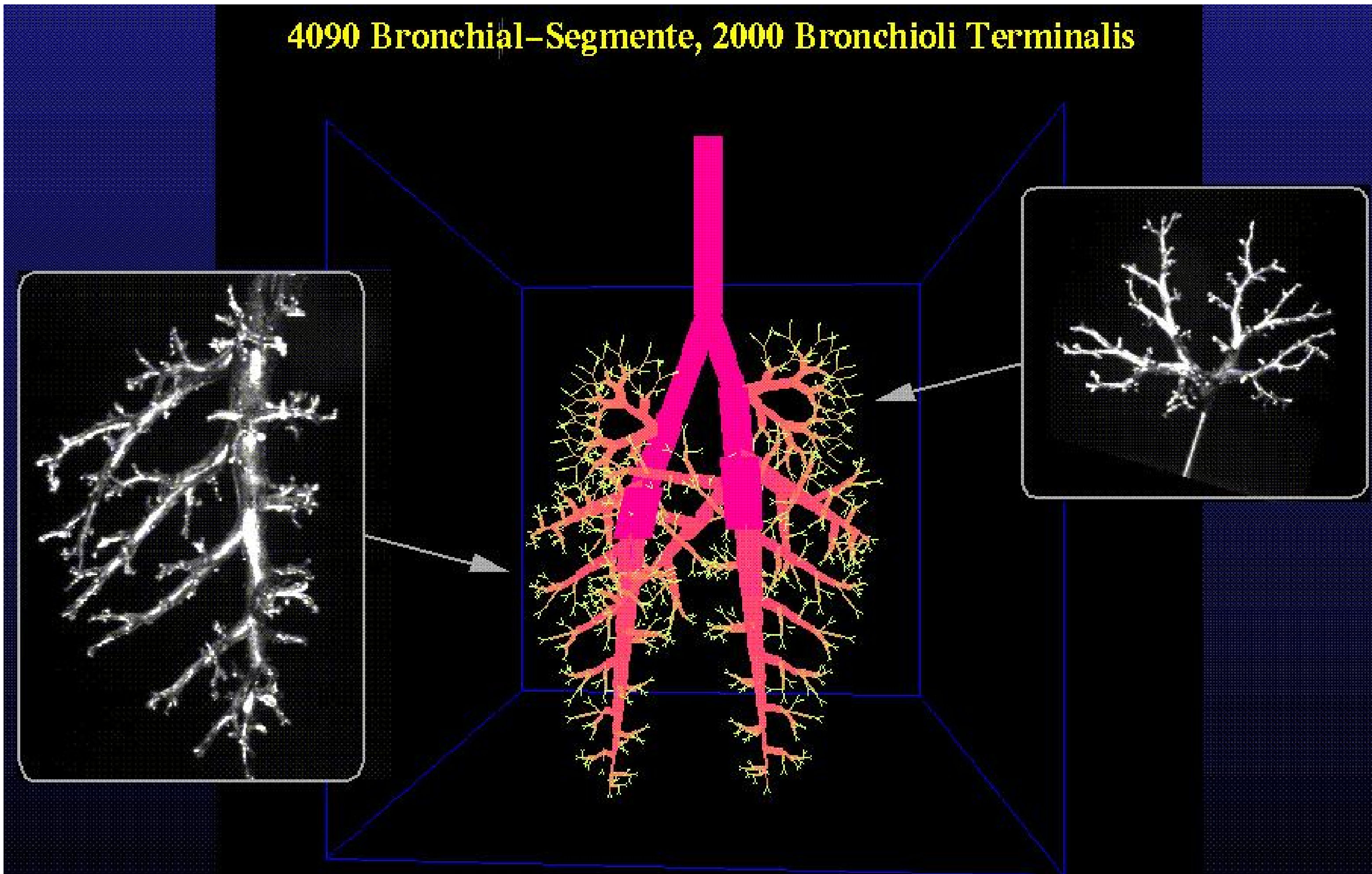
- 12 branching generations
- Resembles trumpet model by Weibel
- Function?
- Goal is to develop more realistic multiscale models
- We started with a (less complex) rat lung, developed key concepts and implement them for the development of a human lung model.

2-Level Structural Hierarchy of Bronchial Tree



Conductive 3D Model based on Casts

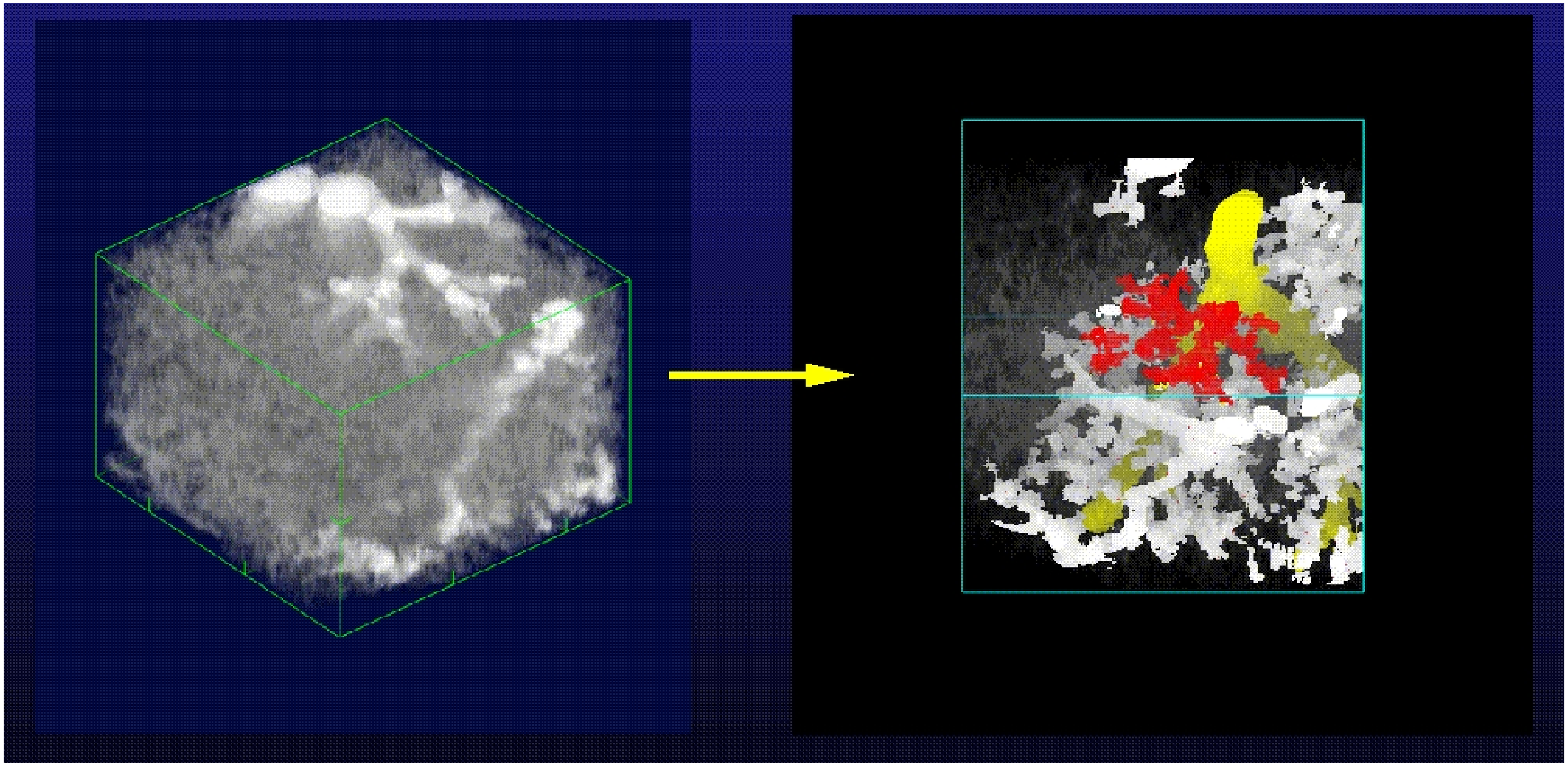
This model of rat lung has 2000 bronchioli terminalis, to which respiratory units need to be attached



med

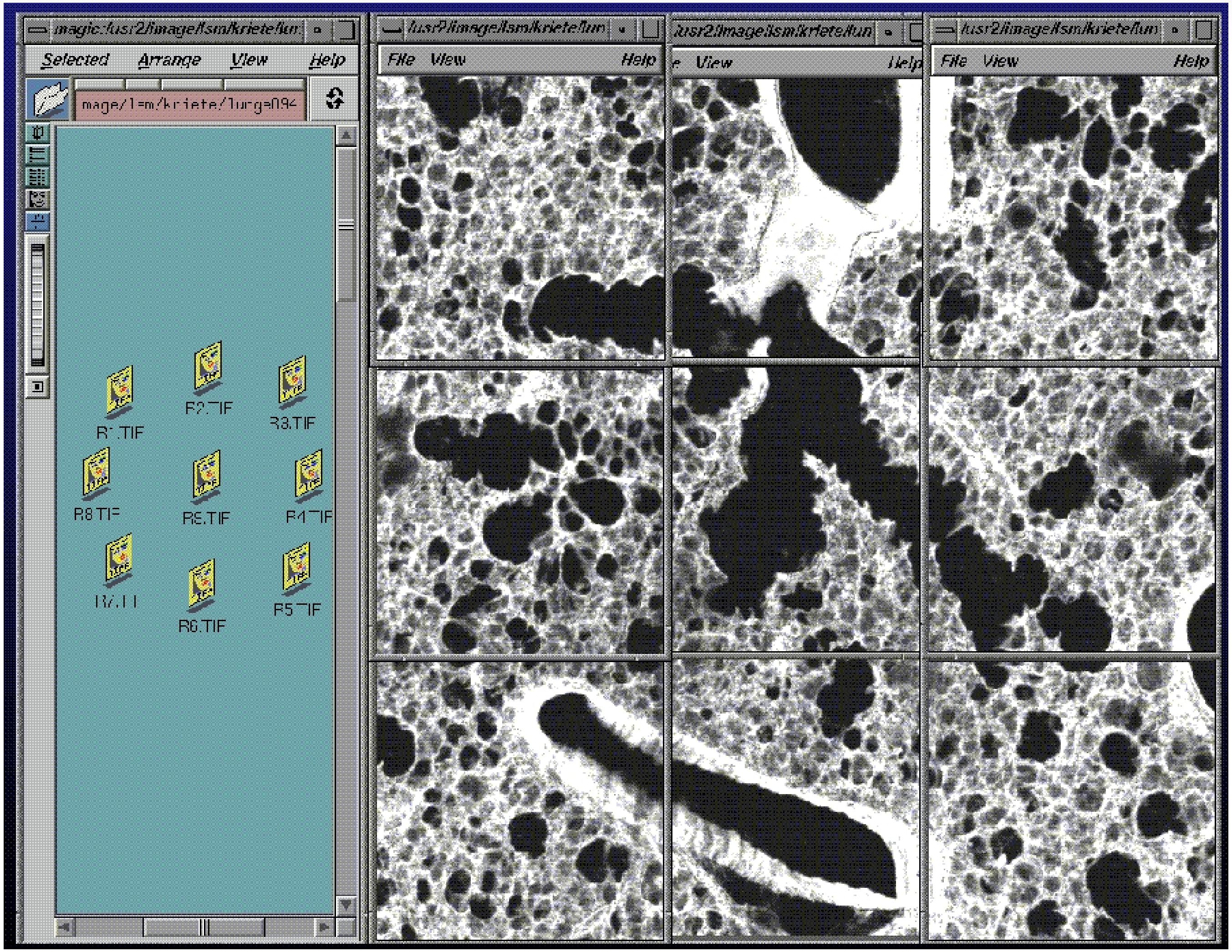
Visualization of Respiratory Units (Acini):

Definition of ROIs based on serial histological sections



Confocal Imaging

Problems: High Resolution brings along narrows field of view, solution is in the image fusion of adjacent field of views. Dense, sponge-like packed respiratory units make it difficult to outline boundaries.

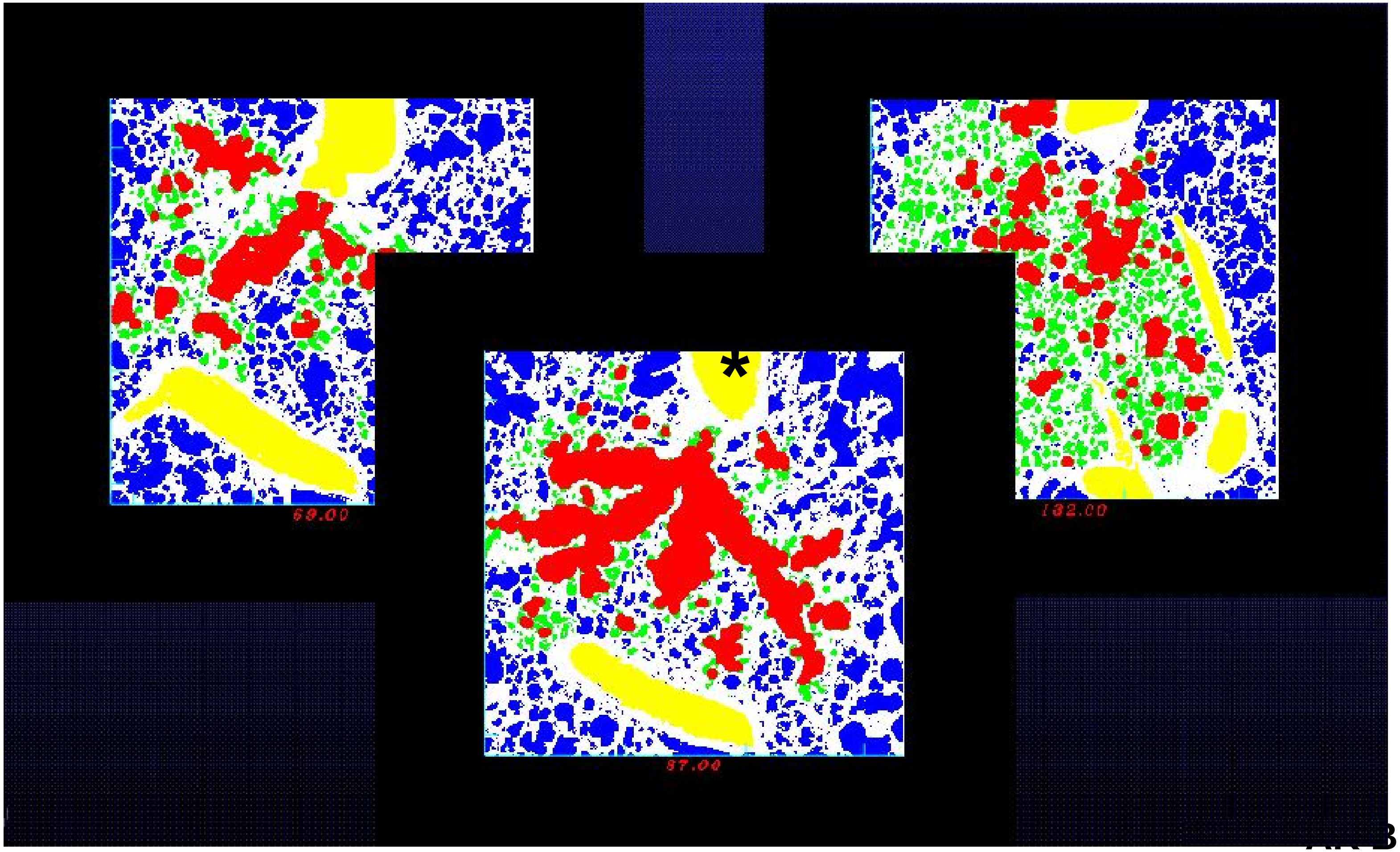


250 um

AK Biomed

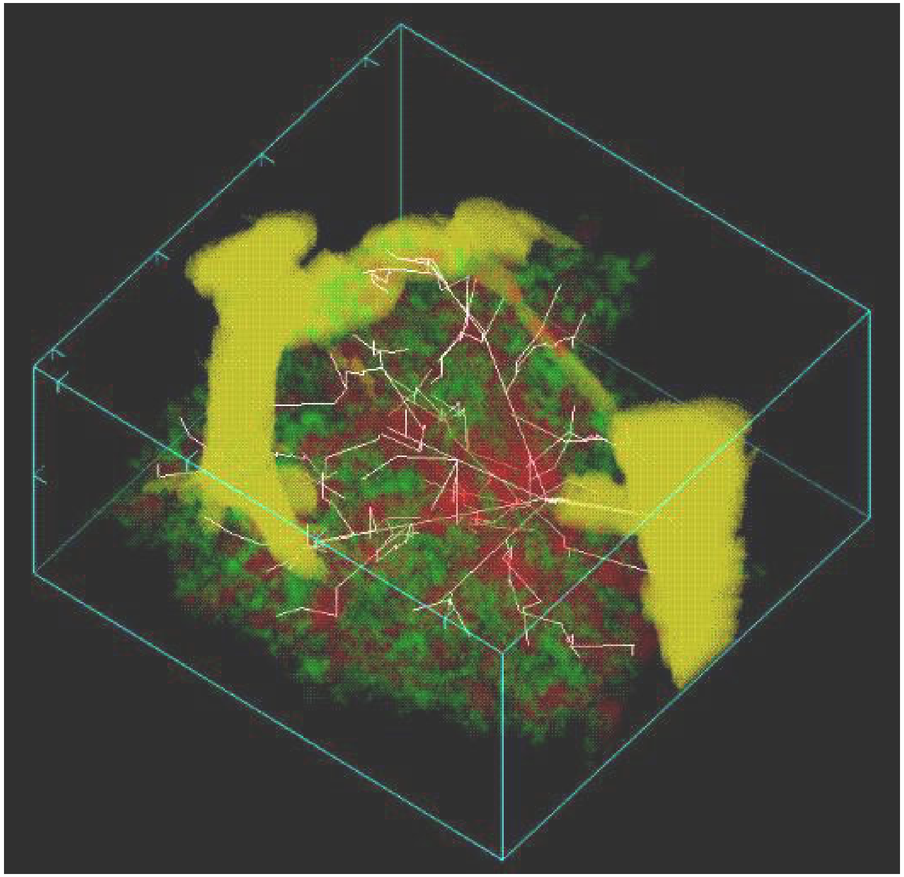
Image Segmentation, Region Growing

To identify the internal structure and boundary of respiratory units a 3D region-growing method is implemented, seed point is the bronchiolus terminalis (*). Misalignement can easily attach wrong structures, such as from adjacent units. Red = ducts, green = alveoli



AR Biomed

3-D Reconstruction of a Respiratory Unit

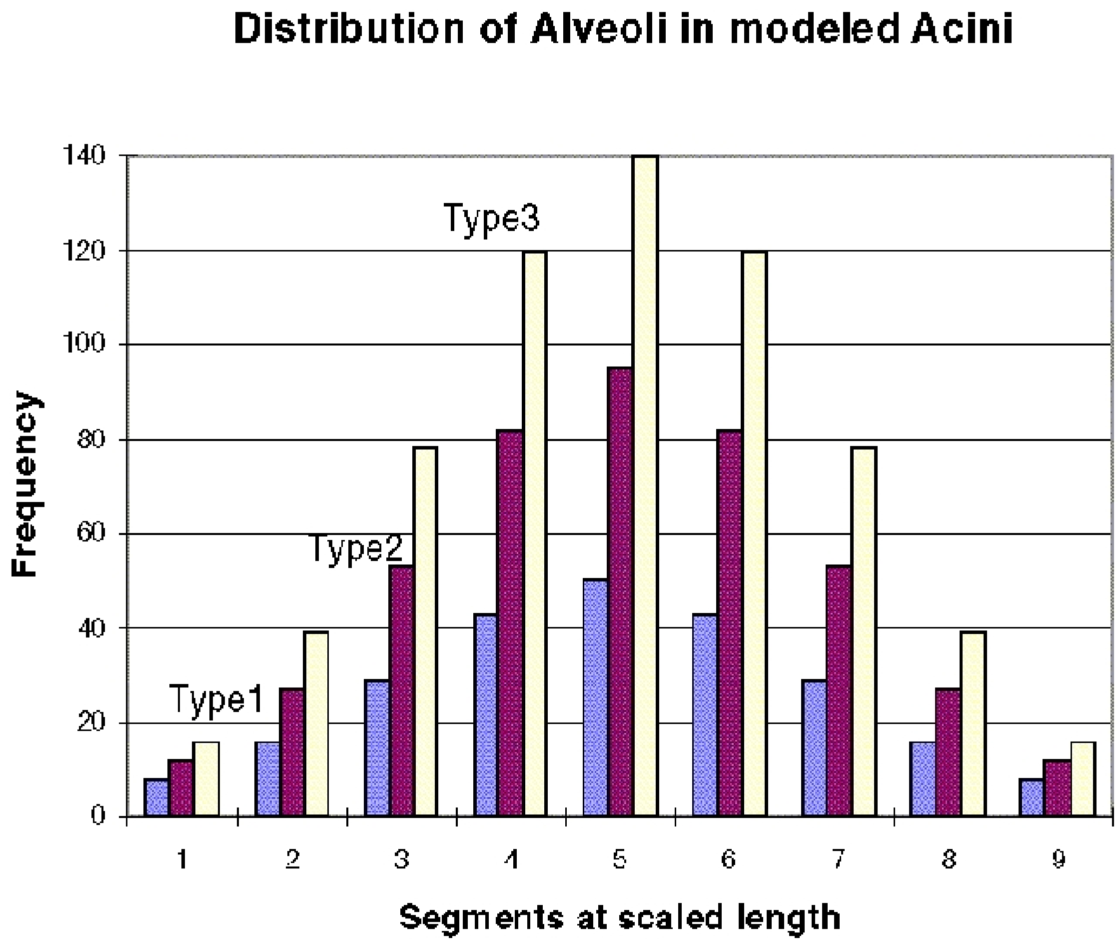


Based on:

- **13 thick serial sections**
- **7 confocal sections**
- **montage 3x3 images**
- **total of 819 images**
- **analytical volume rendition with embedded geometry**

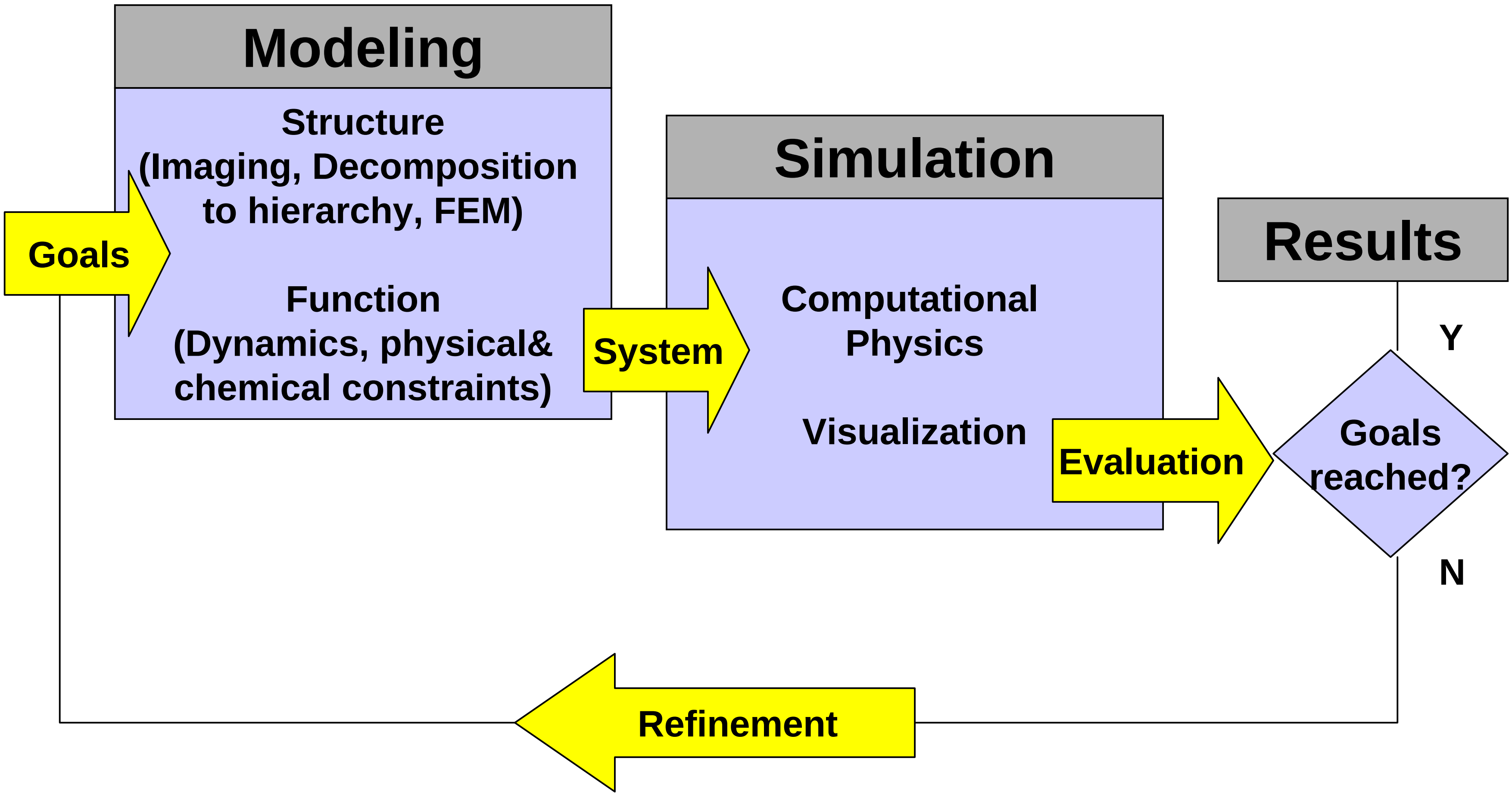
Volume Distribution of Alveoli in Respiratory Units:

variability in size is considered by different types



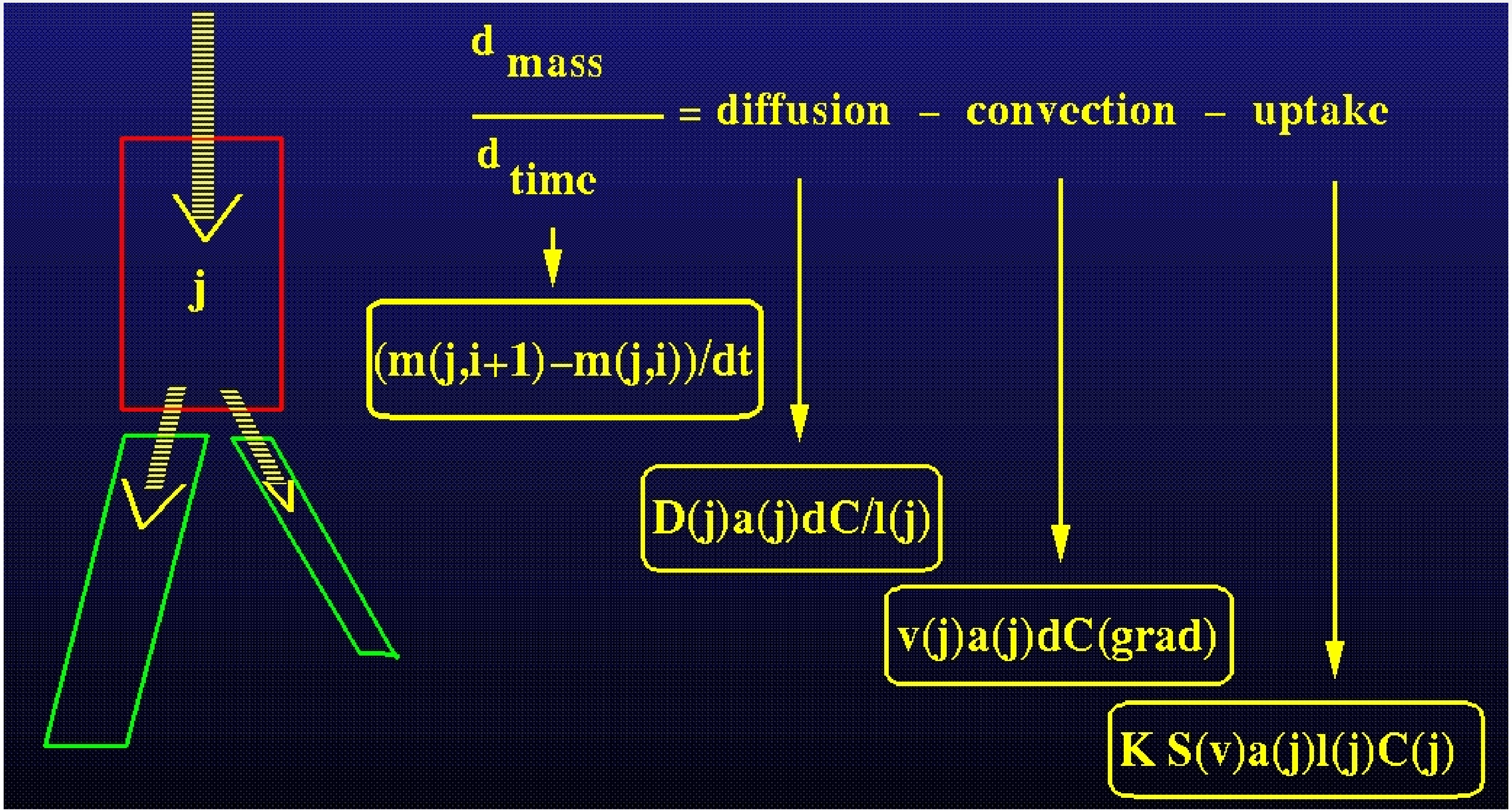
AK Biomed

Workflow Overview



AK Biomed

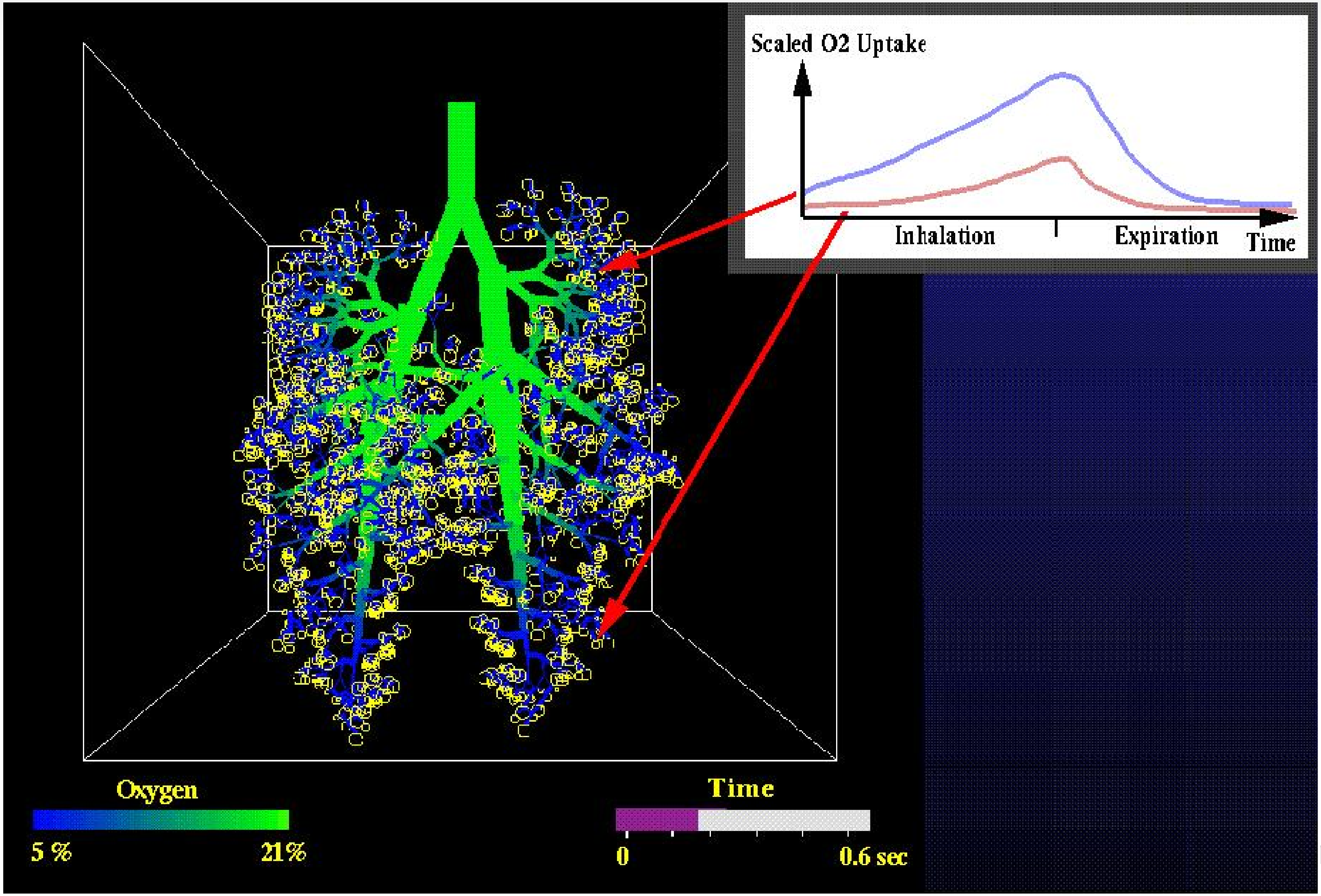
Factors Contributing to Mass Transport



l(j) = length of segment j, a = area, S(v) = surface-to-volume ratio, K = mass transport coefficient, C = average gas concentration

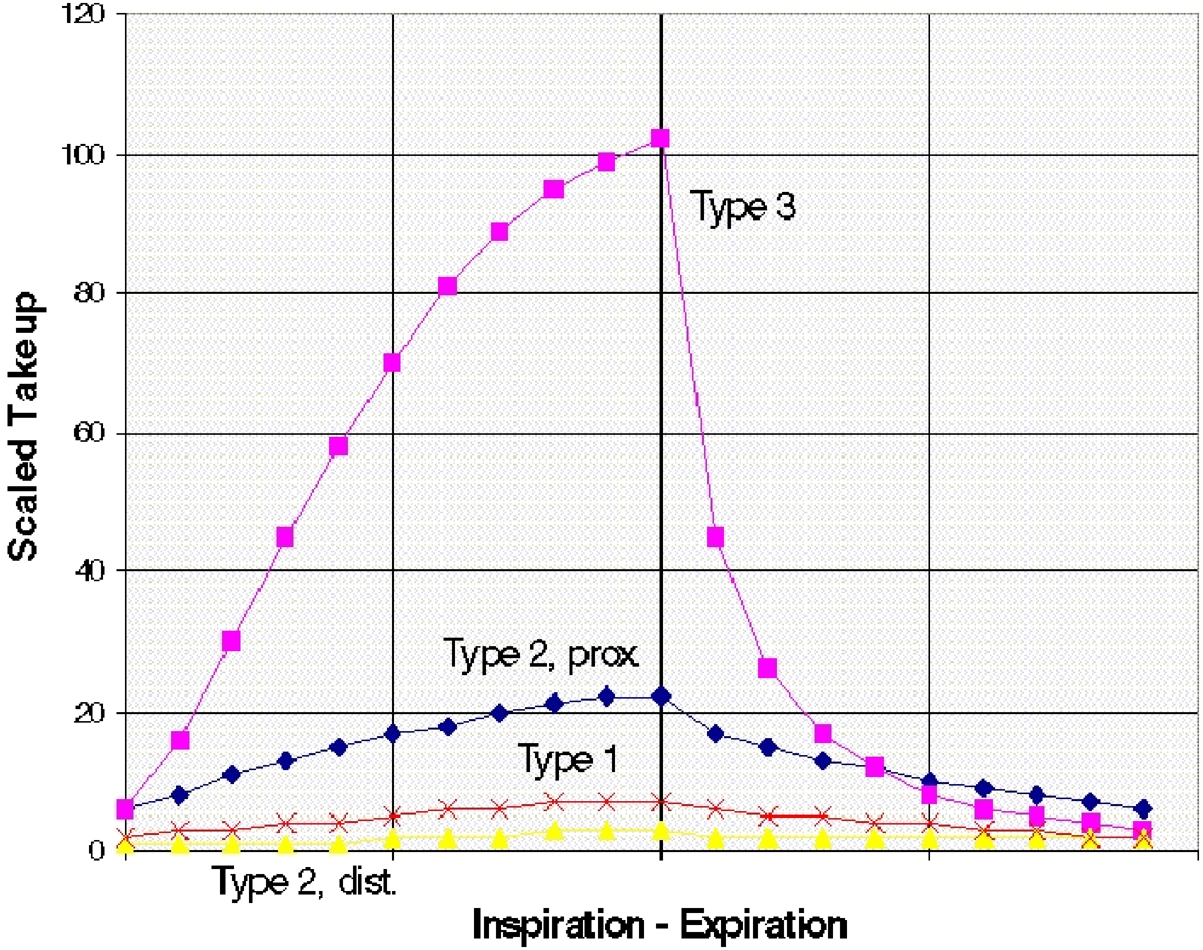
AK Biomed

Functional Simulation



med

Oxygen Uptake of Specific Acini



AK Biomed

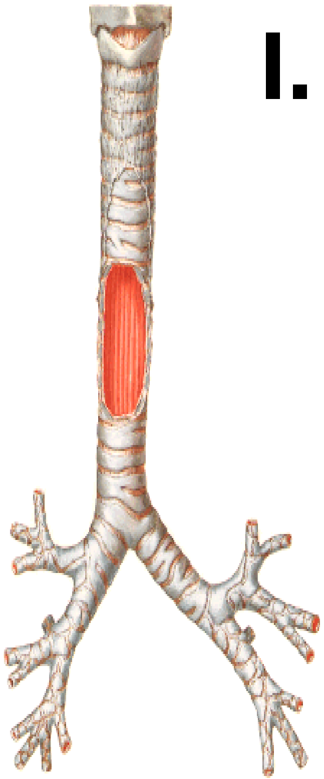
Summary

- **Each breathing amplitude generates a typical pattern of gas distribution**

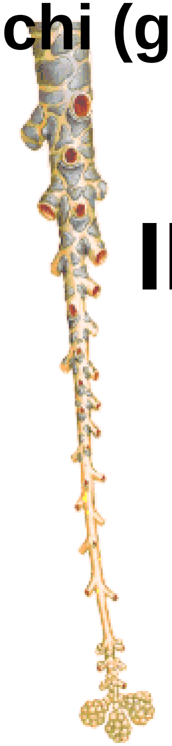
- **Each respiratory unit receives the same amount of ventilation, but the effective ventilation (O2 uptake) is different for each unit**

- **The difference in O2 uptake solves the paradoxon of Weibel, which predicts a morphometrically determined diffusion capacity to be 3-4 times higher than the physiologically required capacity**

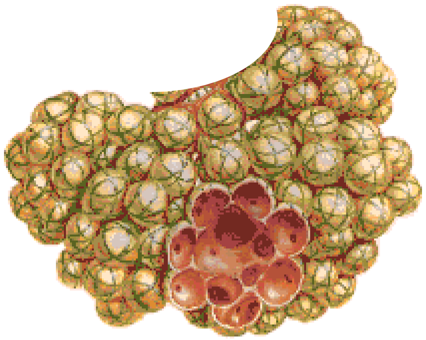
3 Structural Levels for a Hybrid Human Model



I. Main Bronchi (generations 1-5)



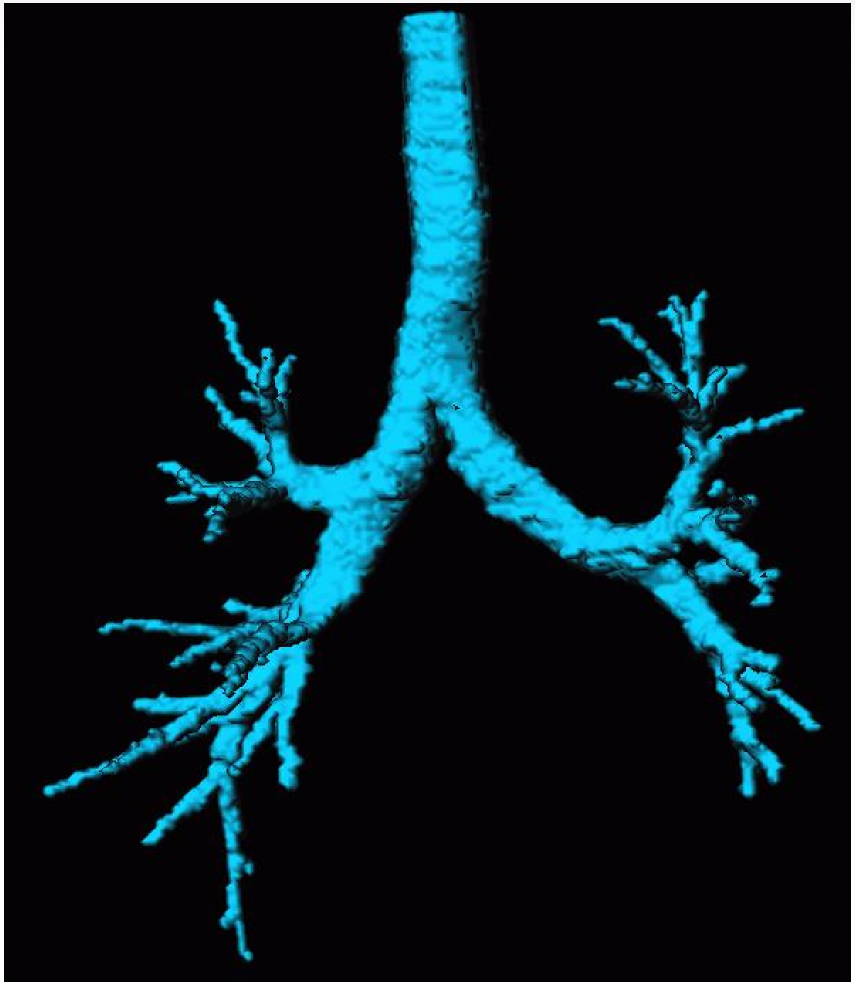
II. Bronchioli



III. Respiratory units

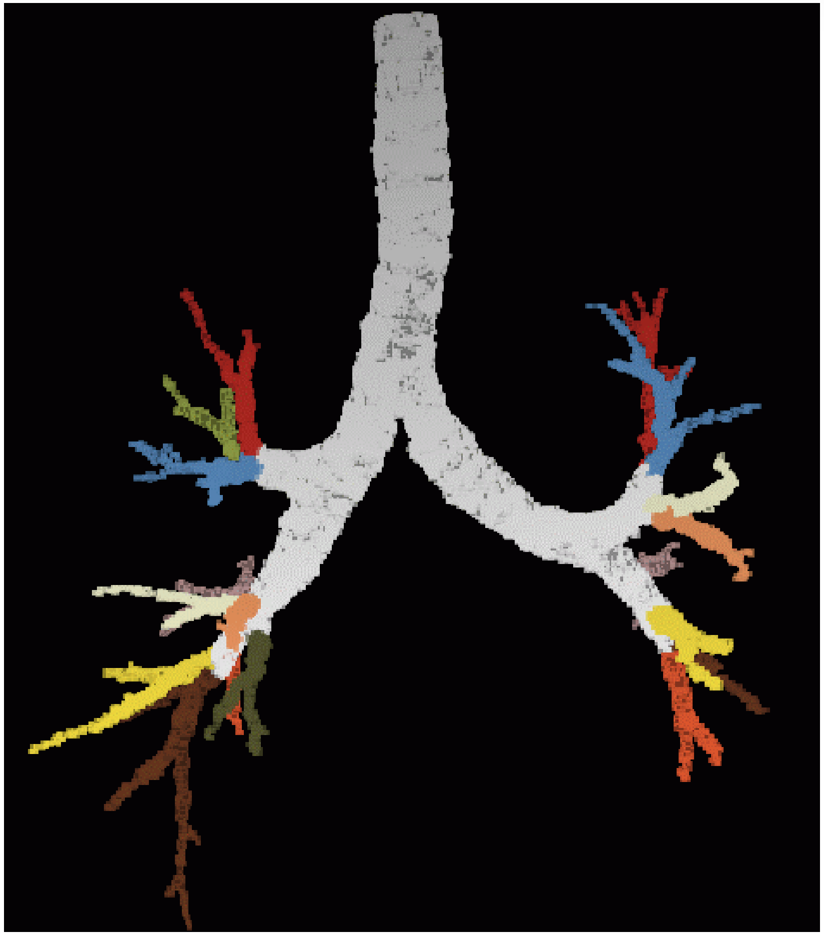
AK Biomed

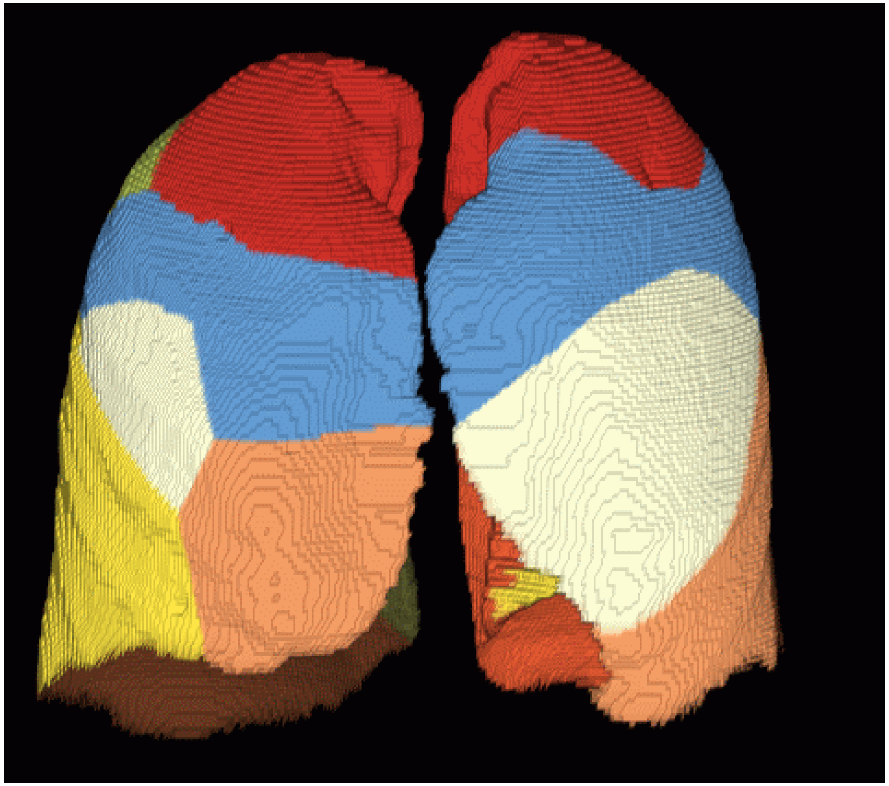
CT Imagery and Sceletonization



AK Biomed

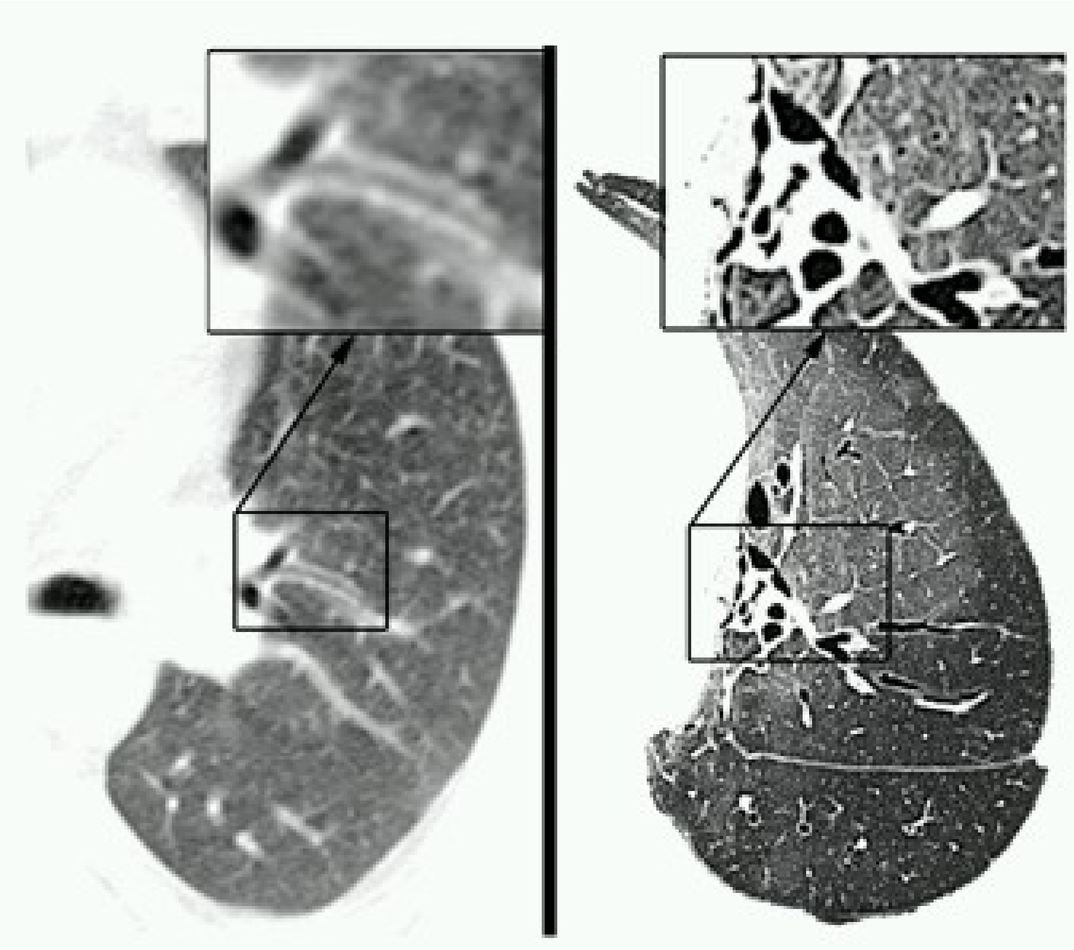
Segmentation and 3D Region-Growing

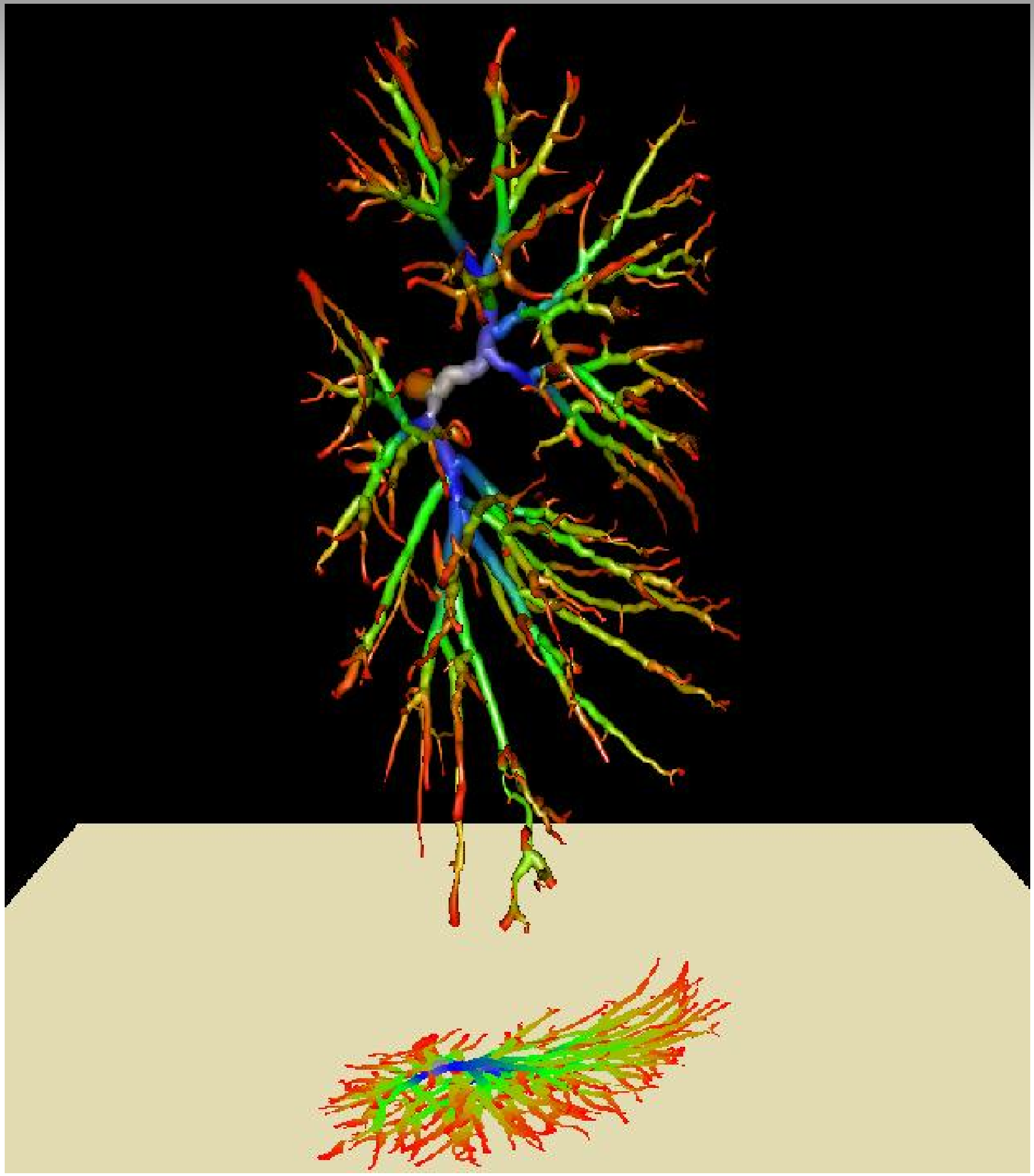




AK Biomed

CT vs HRCT

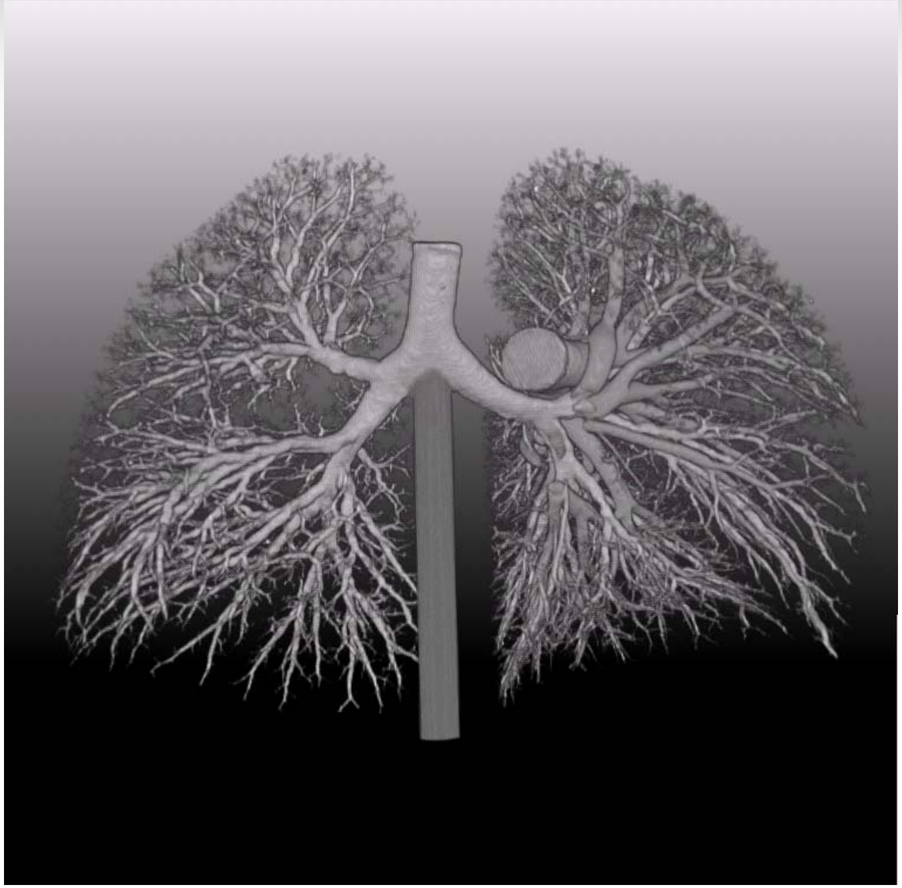


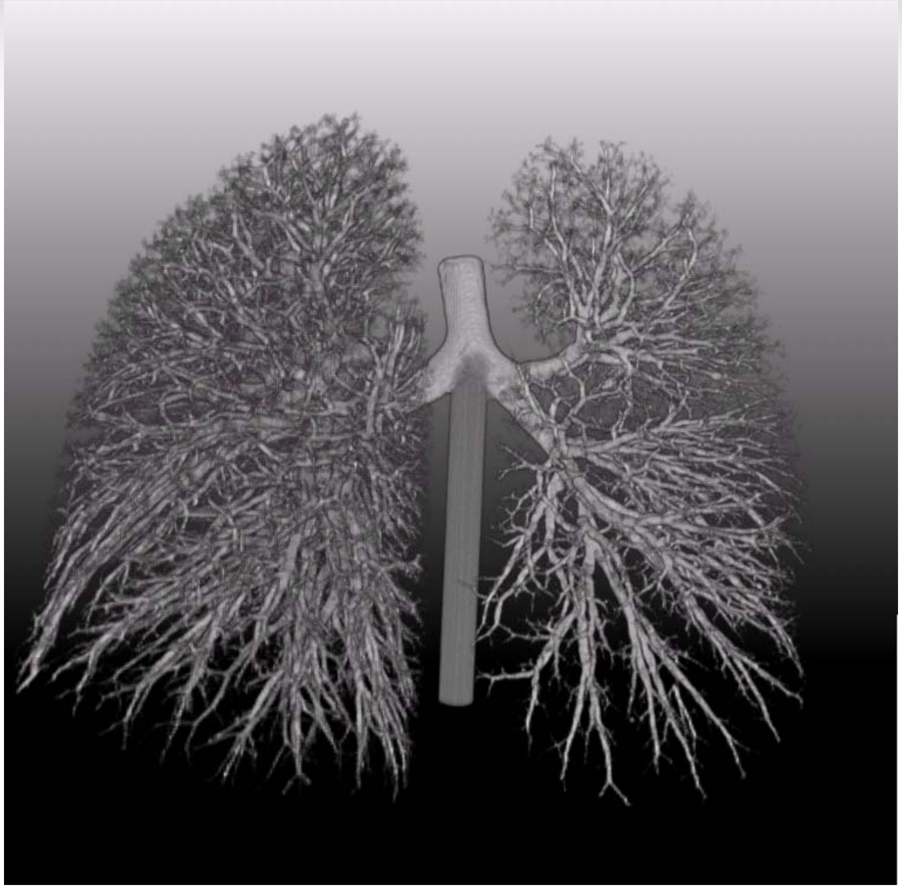


HRCT of fixed lung

AK Biomed

Volume Rendering of Cast (0.35 mm resolution)



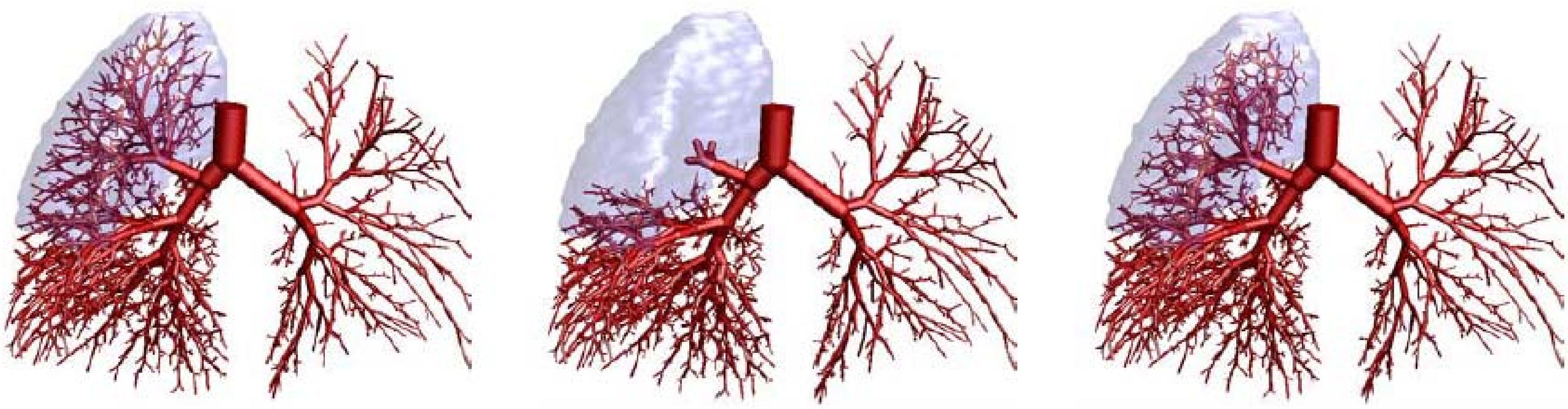


There are 1453 bronchi at the 17th order.

We statistically analyzed 726 branches, the results allow us to define branching patterns depending on branching order.

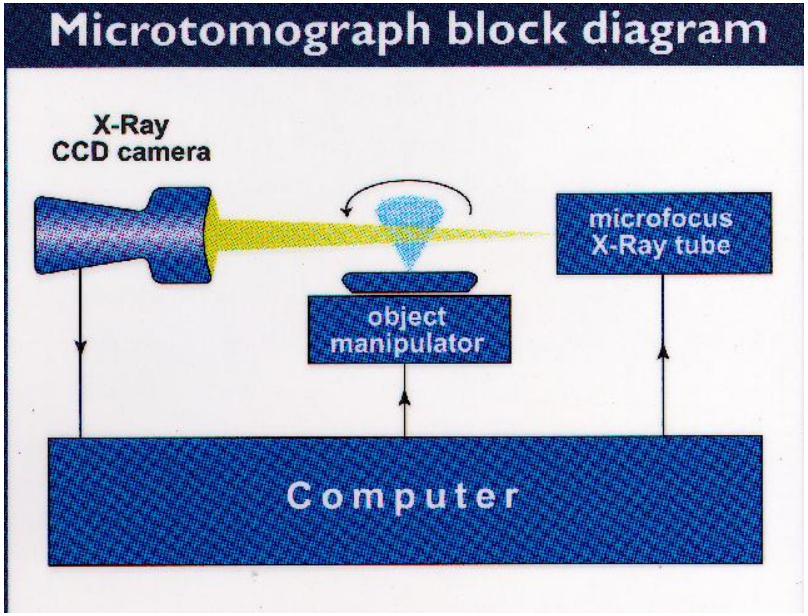
AK Biomed

Modeling using a space-filling algorithm



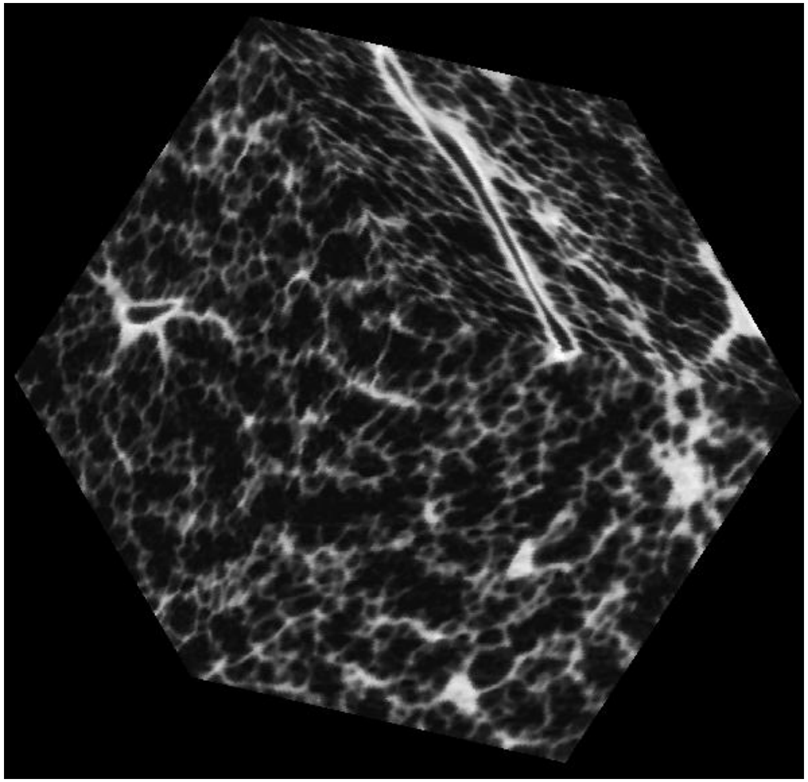
Artifically pruned branch is regrown to test algorithm

Micro-CT for High-Resolution Imaging of Lung Tissue

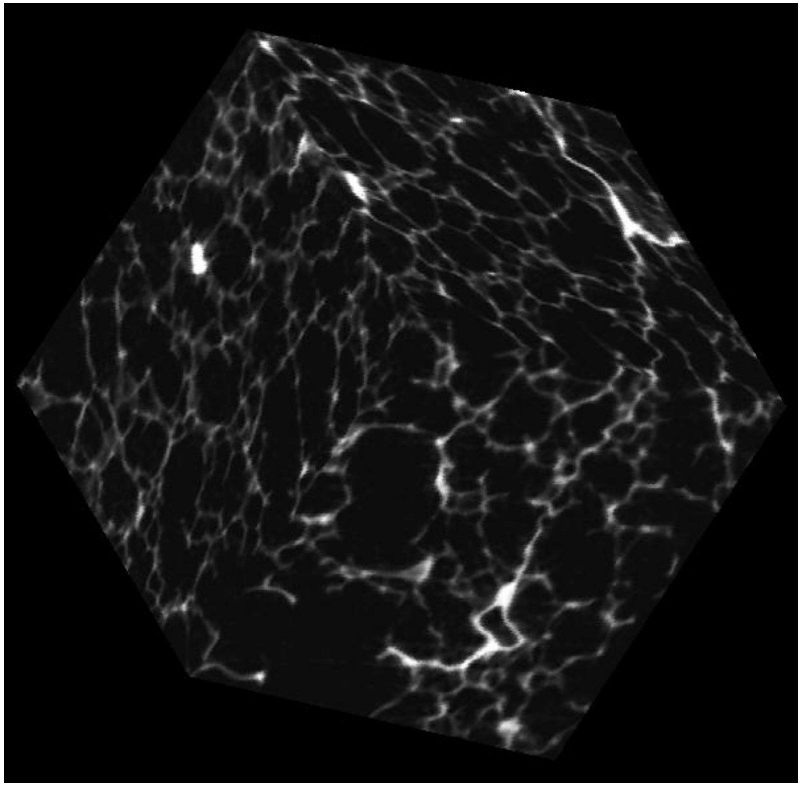


- microfocus tube with 5-8 micrometer diameter
- object is rotated
- reconstructions from projections
- Used to analyze the architecture of respiratory units

Imaging Lung Parenchyma with Micro-CT



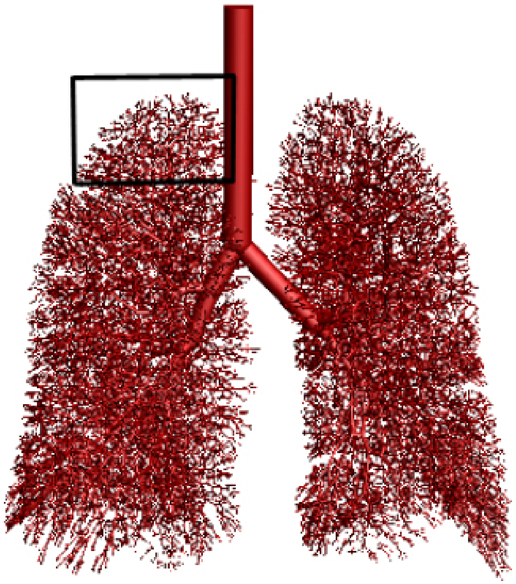
Size about 5x5x5 mm

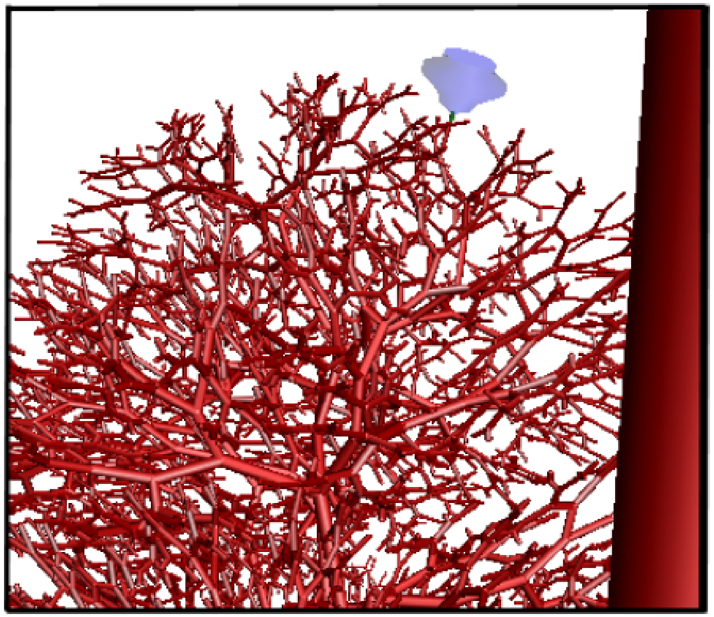


Lung tissue of an “old” person, with aging emphysema   AK Biomed

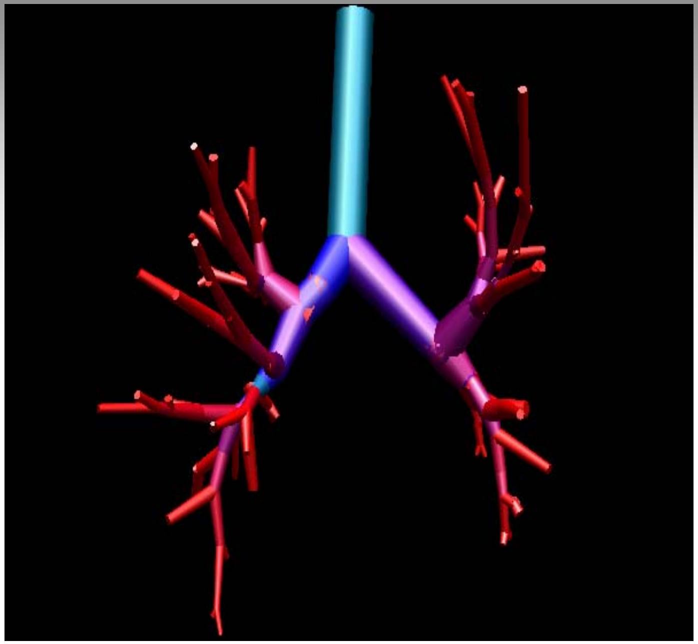
Hybrid Multiscale Model

1) CT for main bronchi
2) CT defines geometry and outer shape of lung boundaries are defined to model intermediate branches properly with a space-filling algorithm
3) Addition of respiratory units, replicated throughout



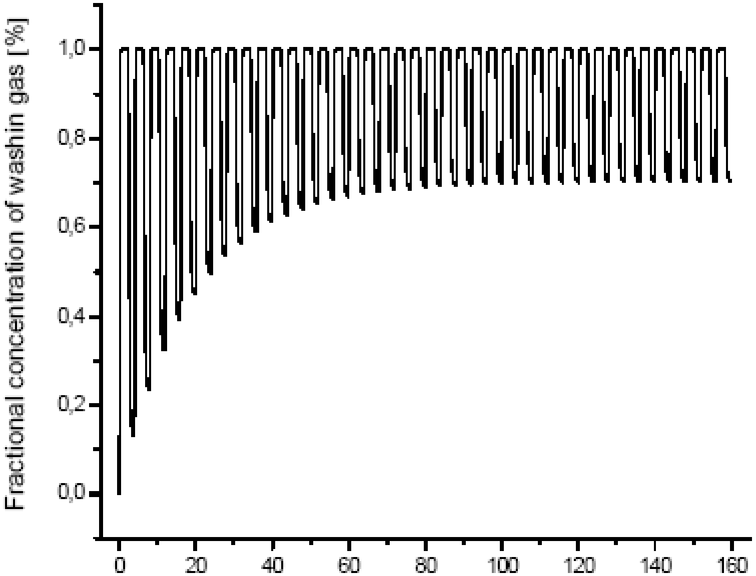


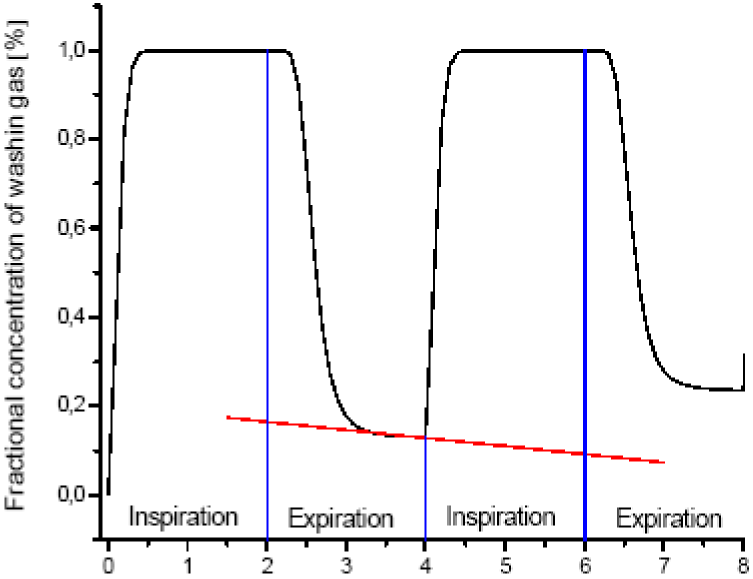
AK Biomed



Simulation of Gas Transport

Model reaches stable conditions after 20 breathing cycles

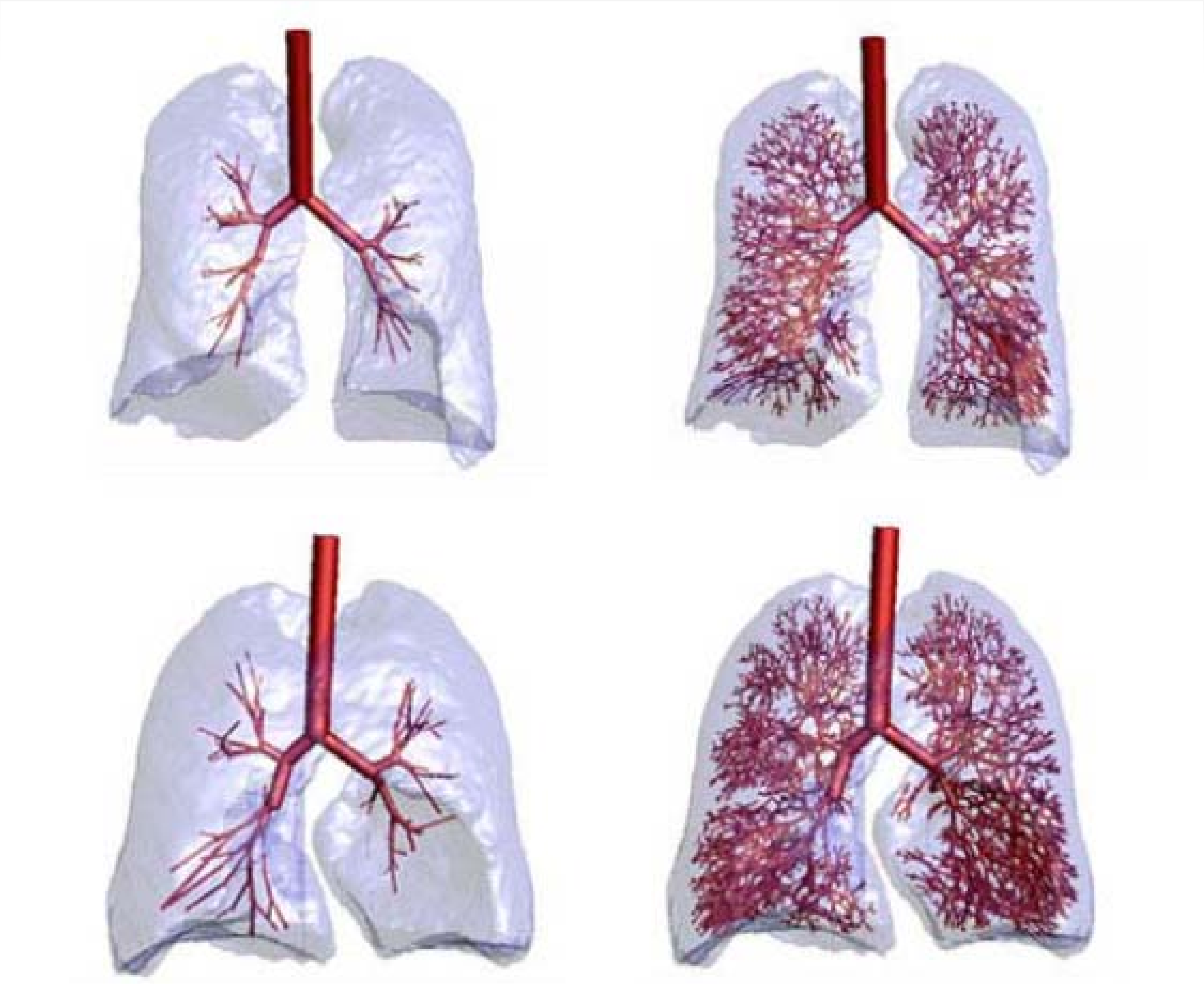




d

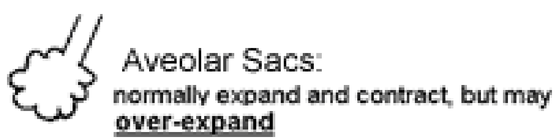
Patient-Individual Modeling

left: Clinical Imaging, right: Simulated



AK Biomed

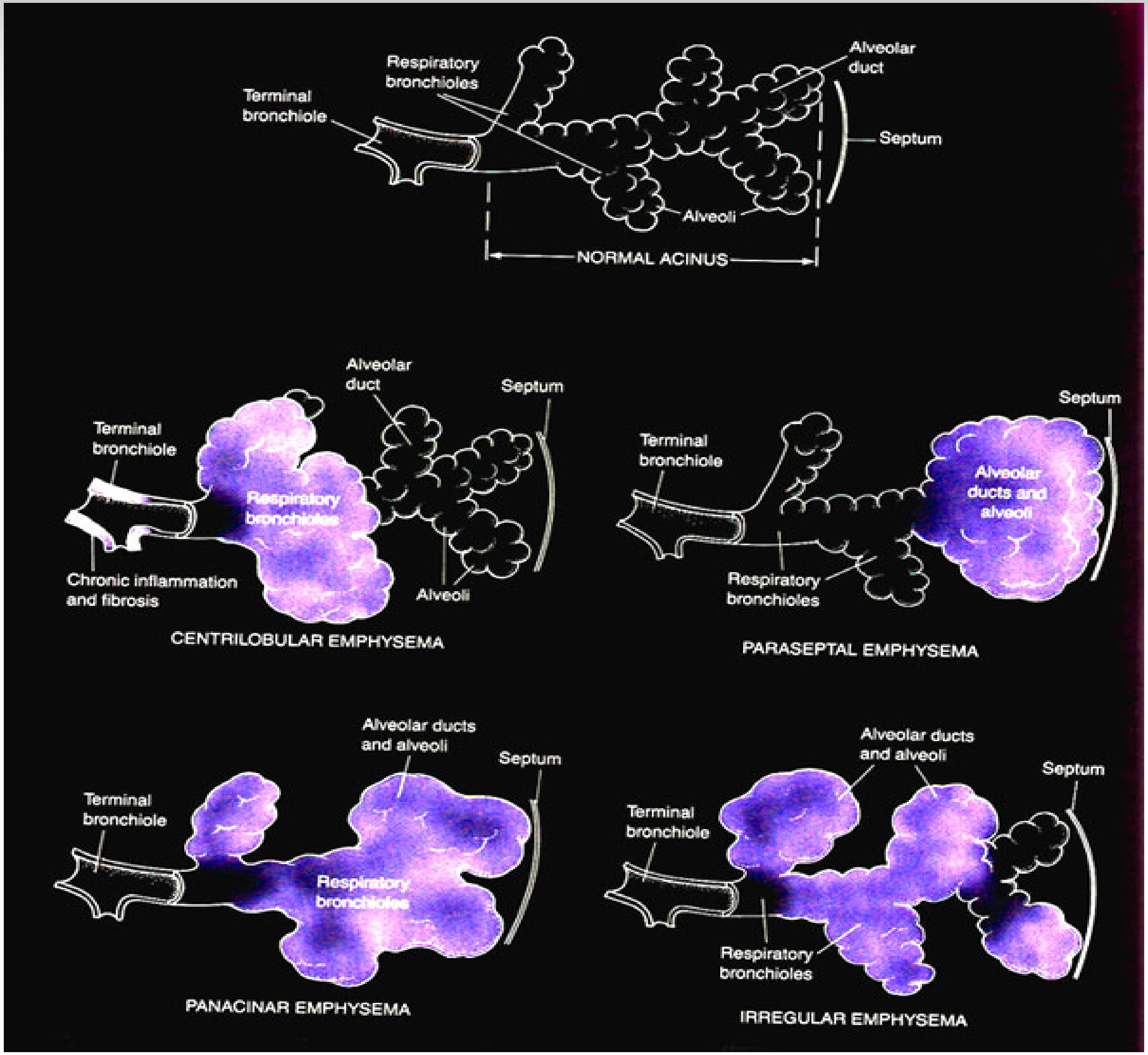
Emphesymatic conditions of the respiratory system

	Definition	Cause	Effects
EMPHYSEMA	**Pulmonary emphysema:** The air sacs (alveoli) of the lungs are enlarged and damaged, which reduces the surface area for the exchange of oxygen and carbon dioxide.	Normal lung tissue contains: Over-expansion of alveolar sacs leads to: •Loss of elasticity •Loss of surface area •Loss of lung capacity •Insufficient take-up of oxygen •It is particularly common in men in Britain and is associated with chronic bronchitis, smoking, and advancing age. 	Severe emphysema causes breathlessness/severe breathing difficulty, which is made worse by infections.

Ref: http://www.ivy-rose.co.uk/Topics/Respiratory_Conditions.htm

AK Biomed

Different types of Emphysema



AK Biomed

Multiscale Modeling Goals

- **Development of a complete geometrical model of (normal) lung at different levels of resolution**
  - completed

- **Optimization of functional simulation for gas distribution/uptake – comparing CFD, PDE for mass transport explicit and implicit**
  – work in progress

- **Modeling of disease/aging lungs, prediction of physiological function**
  - work in progress

References:
Schmidt, A: Human Lung Modeling. Thesis, Giessen Medical School, 2006
Schmidt A, Zidowitz S, Kriete A, Denhard T, Krass S, Peitgen HO.
A digital reference model of the human bronchial tree.
Comput Med Imaging Graph. 2004 Jun;28(4):203-11.
Kriete, A: Form and function of mammalian lung: analysis by scientific computing.Adv Anat Embryol Cell Biol. 1998;145:III-IX, 1-105.