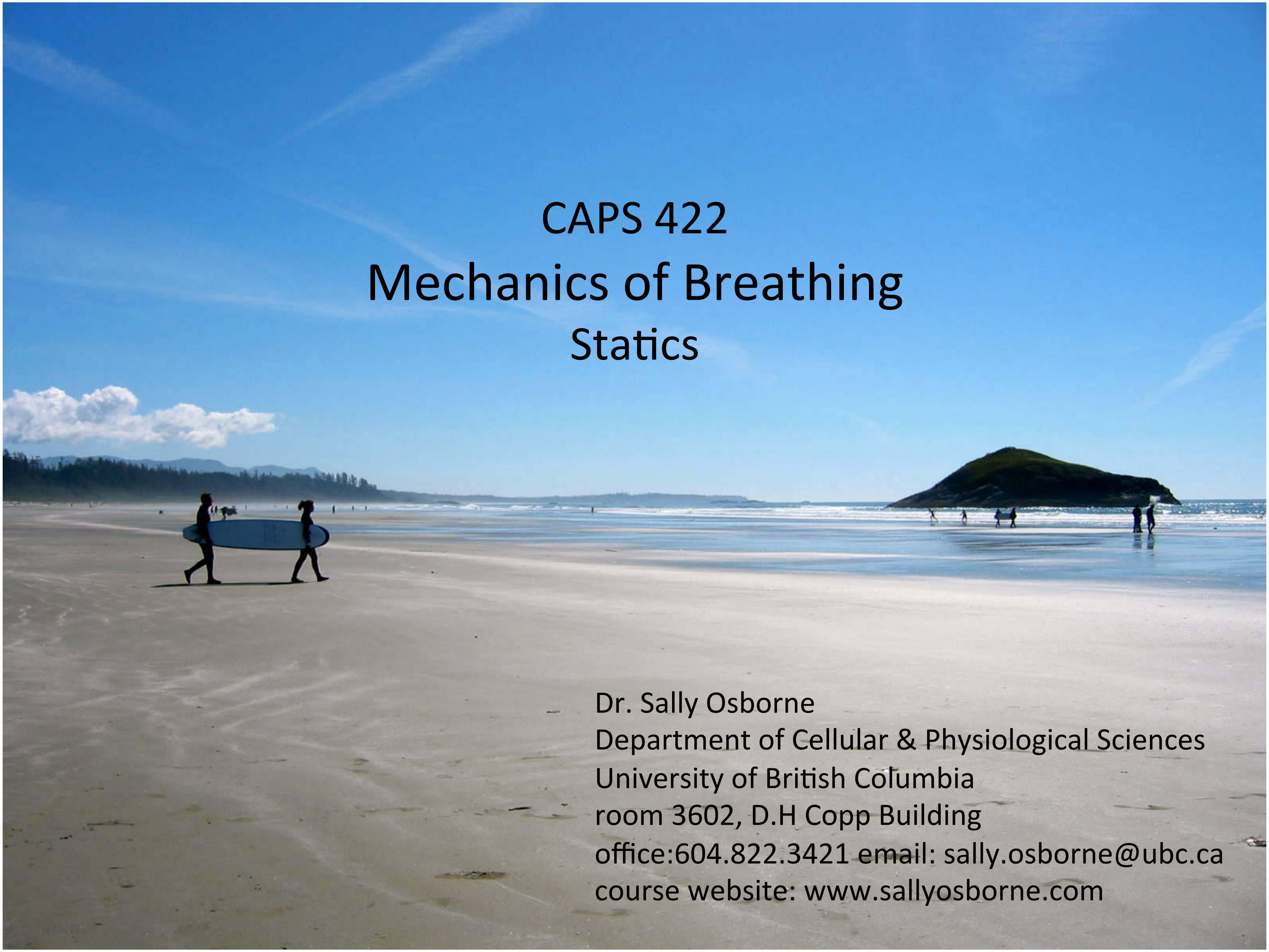

CAPS 422
Mechanics of Breathing
Statics

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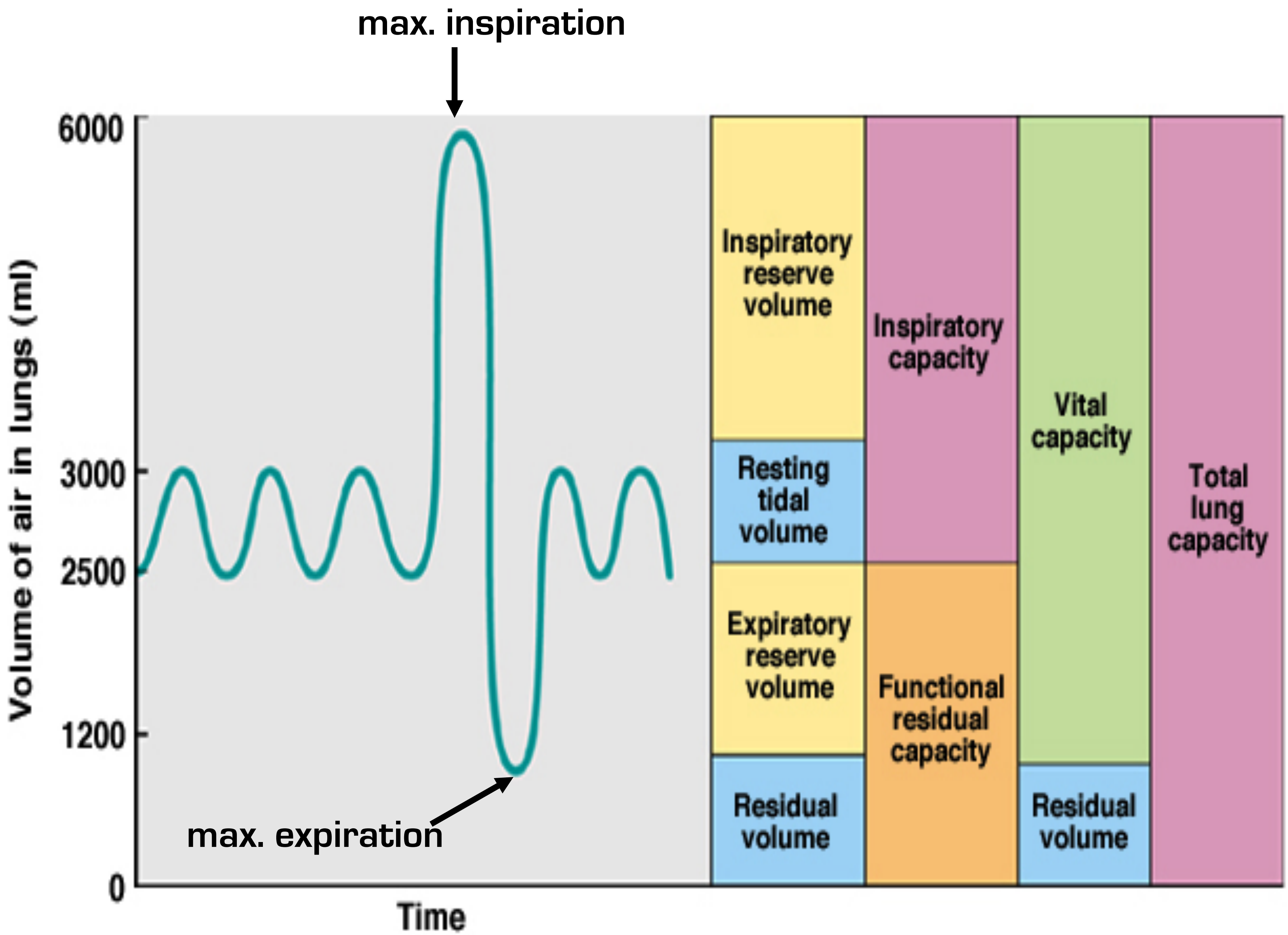
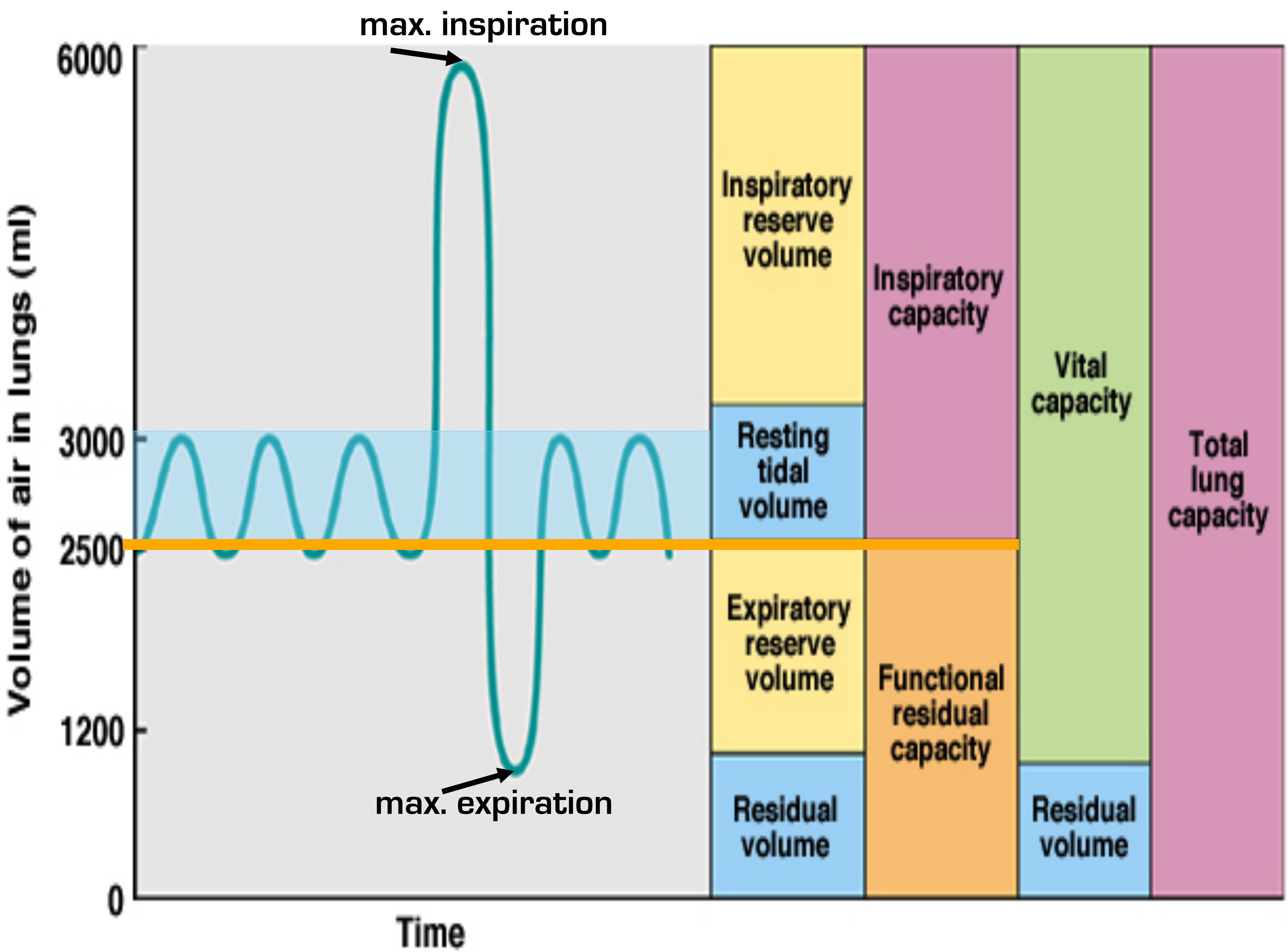

max. inspiration
6000
3000
2500
1200
0
Volume of air in lungs (ml)
max. expiration
Time
Inspiratory reserve volume
Resting tidal volume
Expiratory reserve volume
Residual volume
Inspiratory capacity
Functional residual capacity
Vital capacity
Residual volume
Total lung capacity

Maximum Inspiration

Maximum Expiration



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Inspiratory reserve volume
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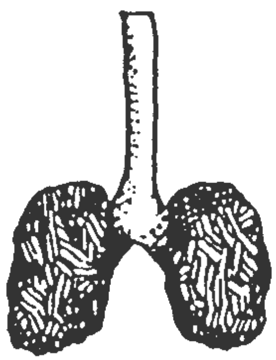
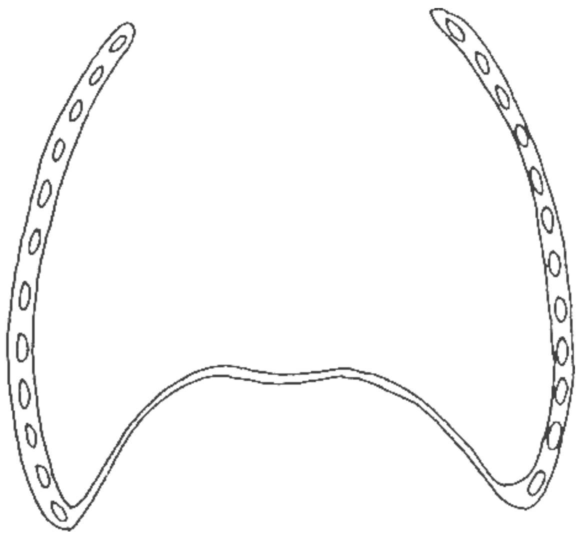
Residual volume
Total lung capacity

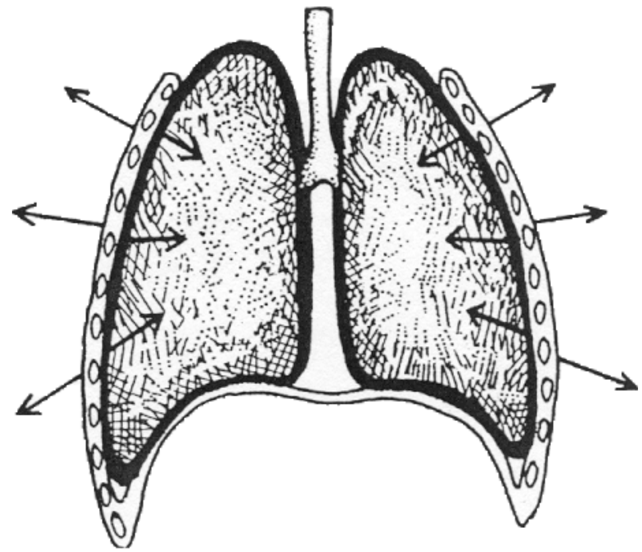
THE TWO COMPARTMENT MODEL

THE LUNGS & THE CHEST WALL

two mechanical structures with elastic recoil properties

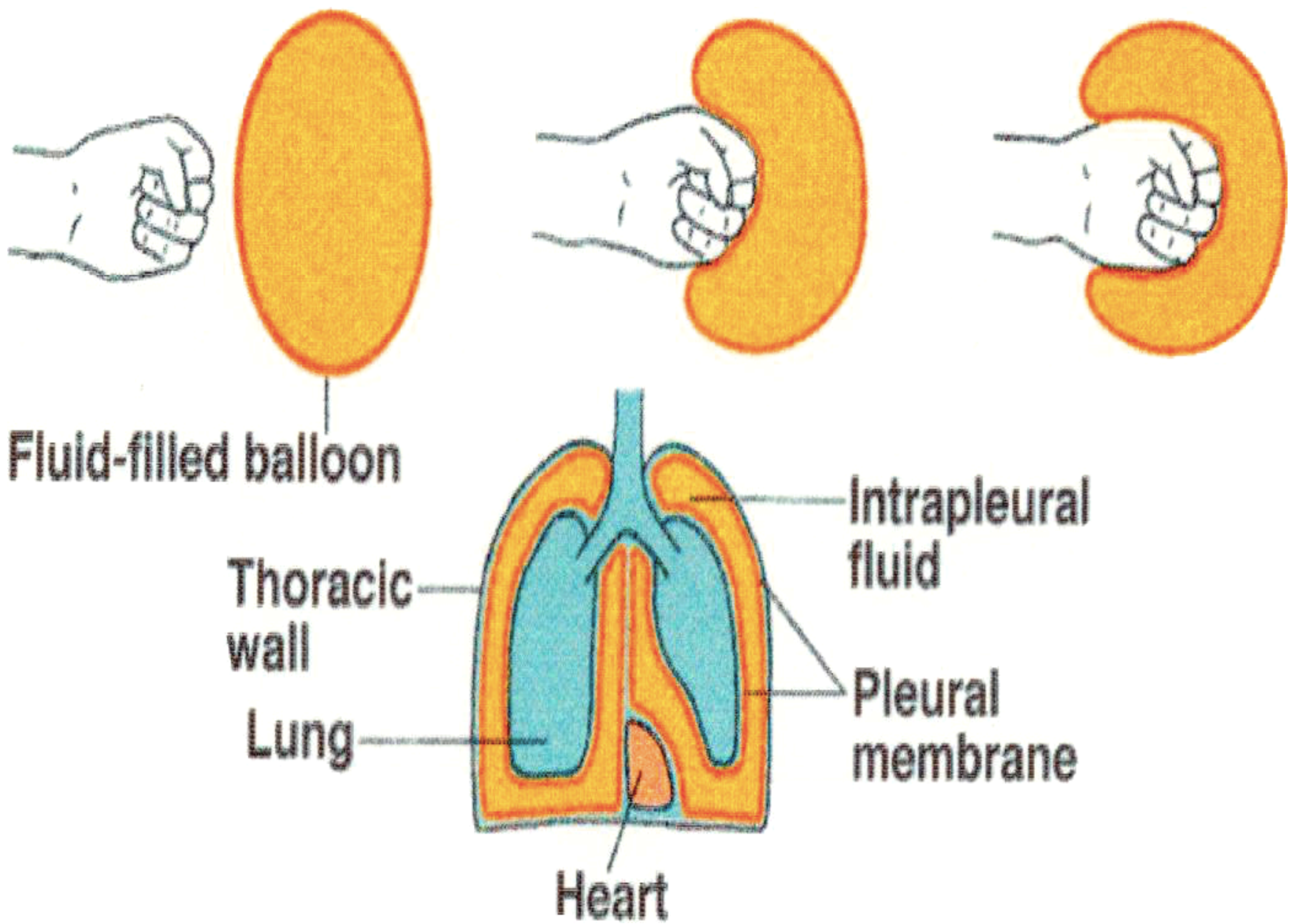




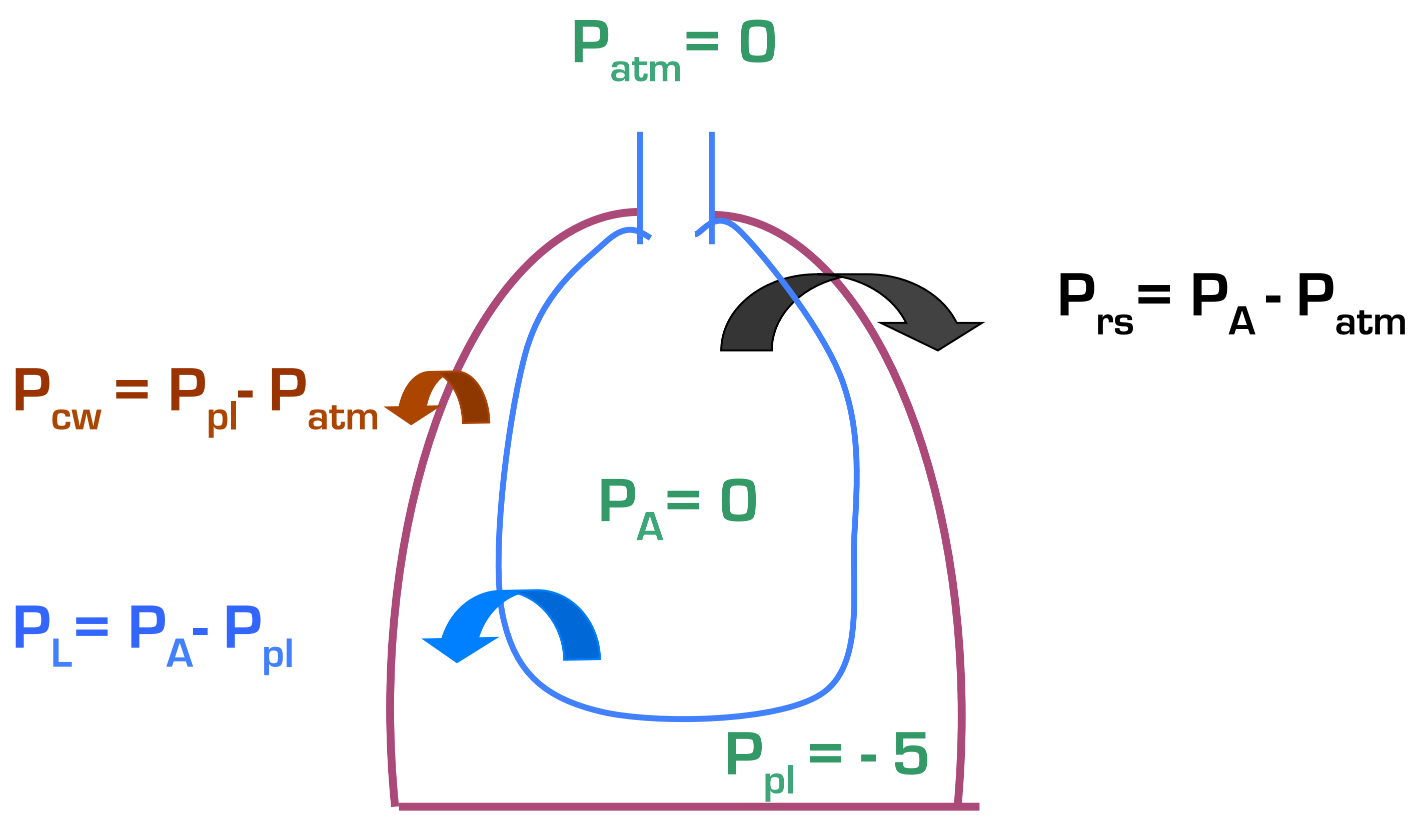


at FRC, the elastic recoil properties of the lungs are equal in magnitude but opposite in direction.

The Pleural Cavity or Space



Pressures Across the 2 Compartments at FRC

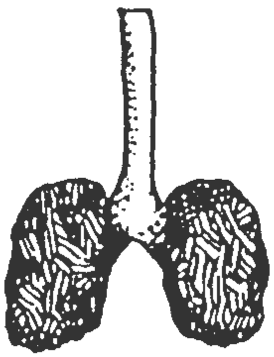


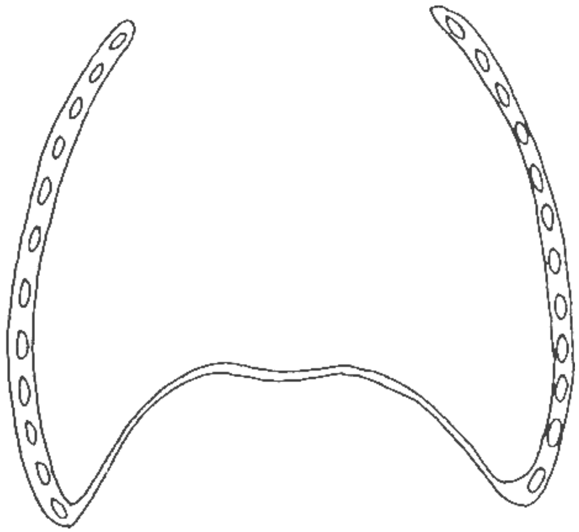
- all pressures are relative to atmosphere [by convention=zero]
- unit of pressure is cm H_2O
- transmural pressure is defined as $P_{in} - P_{out}$

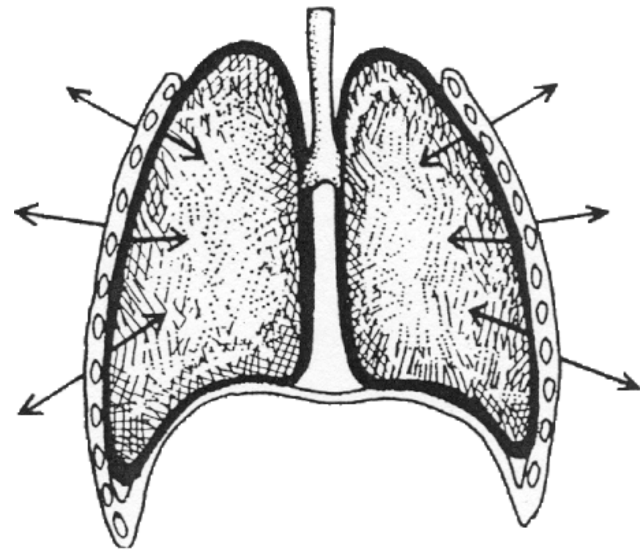
THE TWO COMPARTMENT MODEL

THE LUNGS & THE CHEST WALL

two mechanical structures with elastic recoil properties







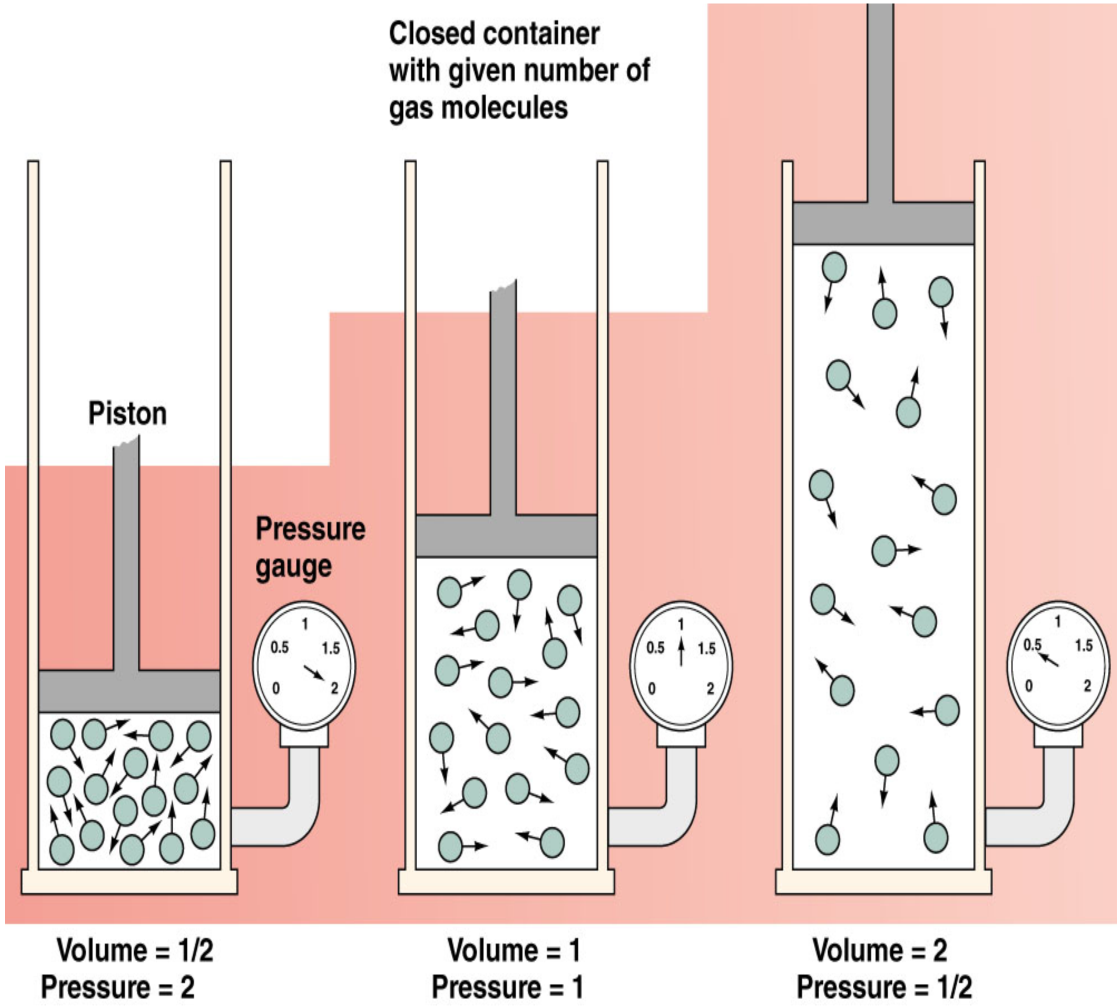
at FRC, the elastic recoil properties of the lungs are equal in magnitude but opposite in direction.

Boyle's Law: the relationship between pressure & volume

Pressure is caused by gas molecules striking walls of a container.

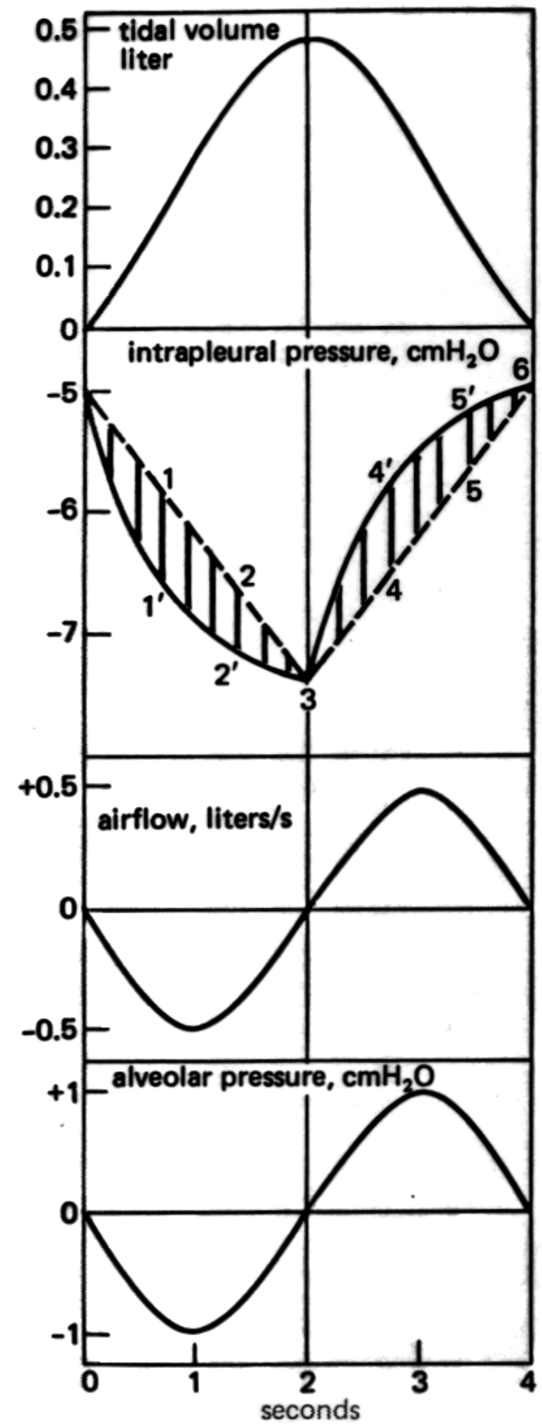
Pressure is related inversely to the volume of the container.

In a large volume, gas molecules strike the walls less frequently, exerting less pressure.

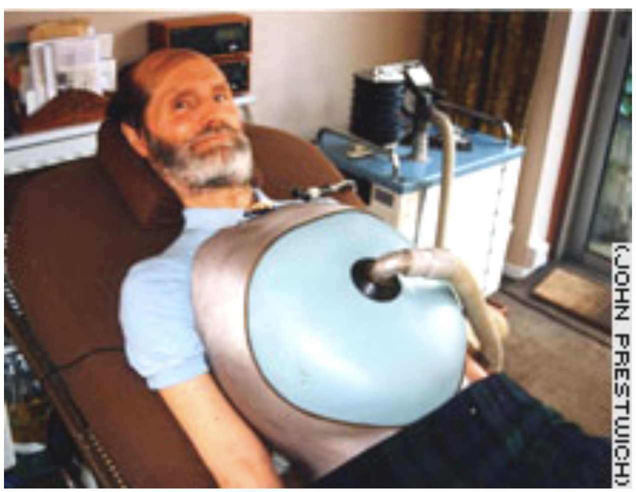


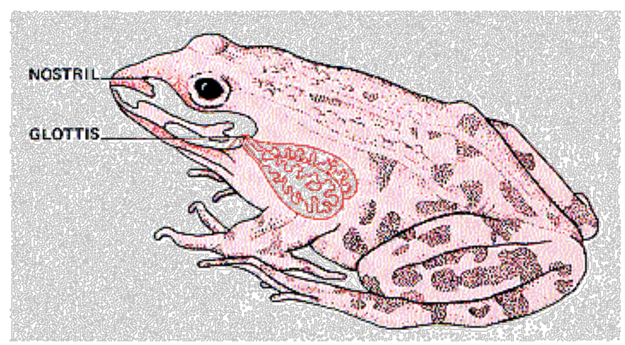
CHANGES IN VOLUME, PRESSURE & FLOW DURING A SINGLE IDEALIZED QUIET BREATH

Why does intrapleural pressure continuously decrease during inspiration whereas air flow and alveolar pressure swing down then up during this interval?



Negative versus Positive Pressure Breathing



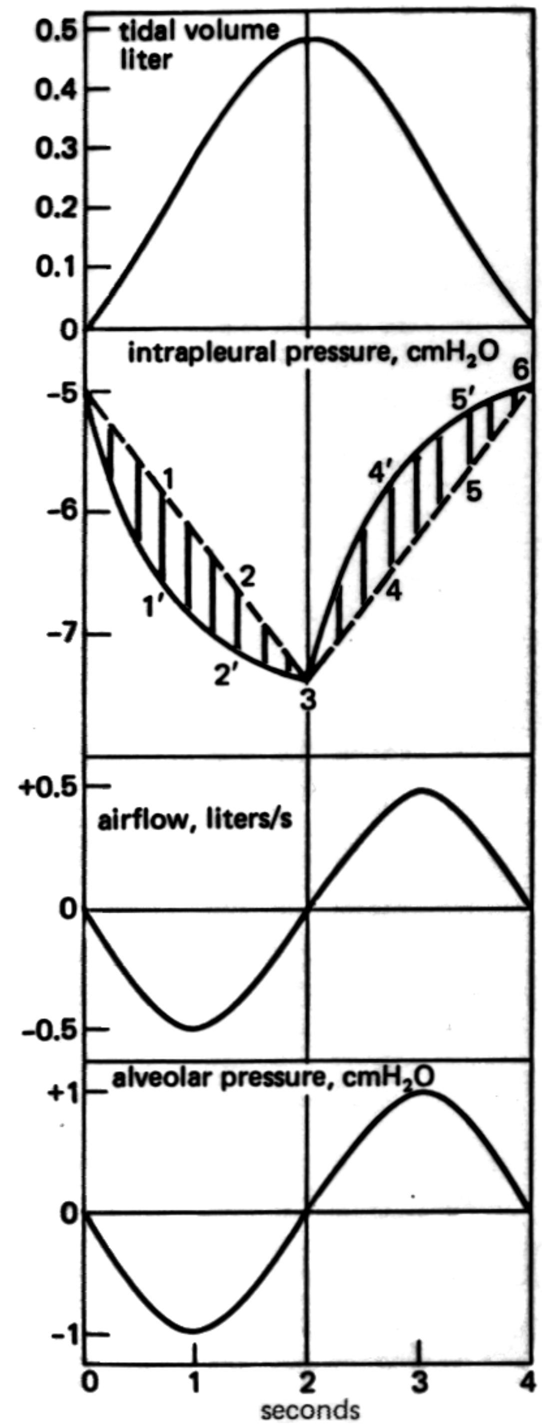


Read the Wikipedia article on course web page

CHANGES IN VOLUME, PRESSURE & FLOW DURING A SINGLE IDEALIZED QUIET BREATH

1-5 pressure required to overcome the elastic recoil of the lungs

1'-5' pressure required to overcome both the elastic recoil of the lungs and resistance to airflow



Lung Compliance & Airway Resistance

Key Factors in Movement of Air In & Out of the Lungs

Problems with airflow into the lungs have to do with an in ability to expand the lungs or the chest wall (low compliance) or alternatively, problems with airflow out of the lungs have to do with narrow airways (more airways resistance). Most patients in respiratory clinics show up with one or both of these problems.

Team work due next class--

In production of a documentary on lung diseases, experts in the field have suggested it best to categorize the diseases in terms of functional (physiologic) findings of obstructive or restrictive patterns of ventilatory failure or both. As science reporters your team is asked to explore the following diseases and provide the background information for the documentary. The key questions to ask are:

1) what is mechanically wrong with the lungs or chest wall? Which of the two patterns of obstructive or restrictive ventilatory abnormality is present?

Asthma - Emphysema, Chronic bronchitis, COPD, Cystic Fibrosis, Bronchioloitis, Respiratory Syncitial virus, ARDS (adult respiratory distress syndrome); Sarcoidosis. Pneumoconiosis, Hypersensitivity Pneumonitis, Lupus, Scleroderma, Obesity, Kyphoscoliosis & Scoliosis.

LUNG COMPLIANCE

A Key Factor in Movement of Air In & Out of the Lungs

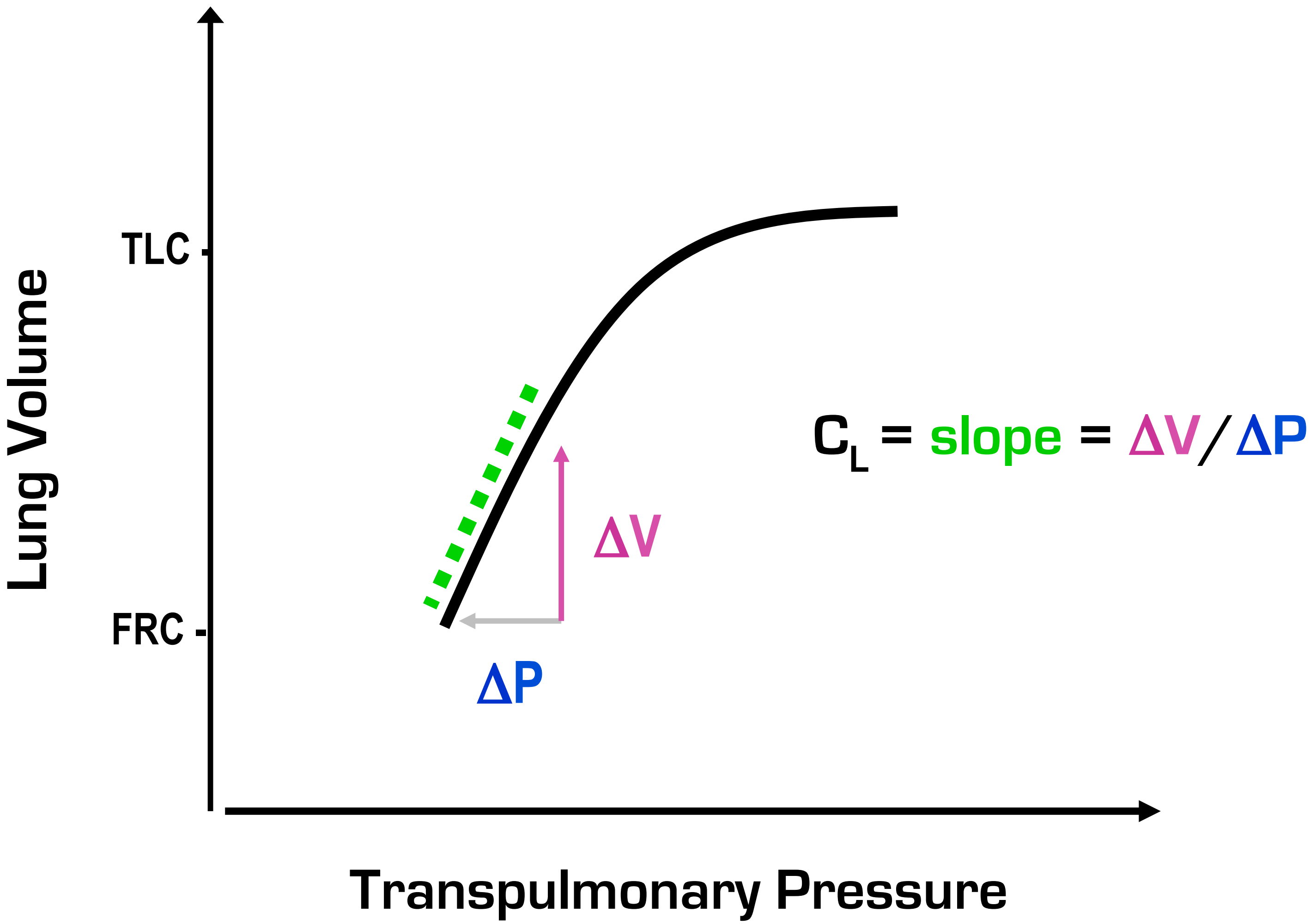
Compliance is a measure of distensibility of an object-how easily it can be stretched or deformed.

Elastance is the inverse of compliance. It refers to the tendency of an object to oppose stretch or distortion, as well as its ability to return to its original form after the distorting force is removed.

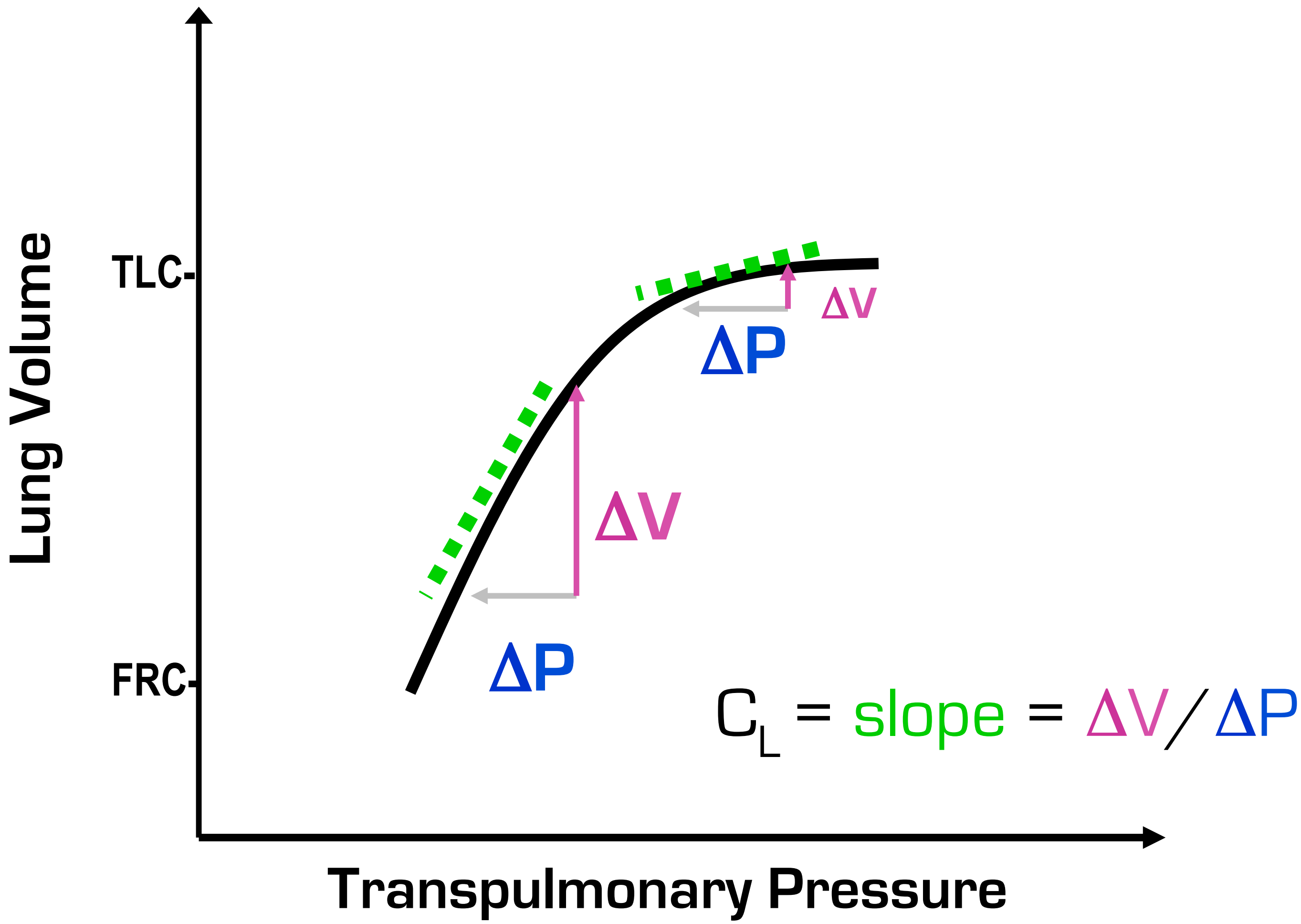
Compliance = 1/Elastance.

Static Compliance of the Lungs (C_L)

is obtained as the slope of the relaxation P-V curve of the lungs



The Static Compliance of the Lung Depends on Lung Volume



Key Factors that Affect Static Compliance [C_L]

1. Lung Volume
2. Tissue Elastic Recoil
3. Alveolar Surface Tension

Lung Tissue Elasticity

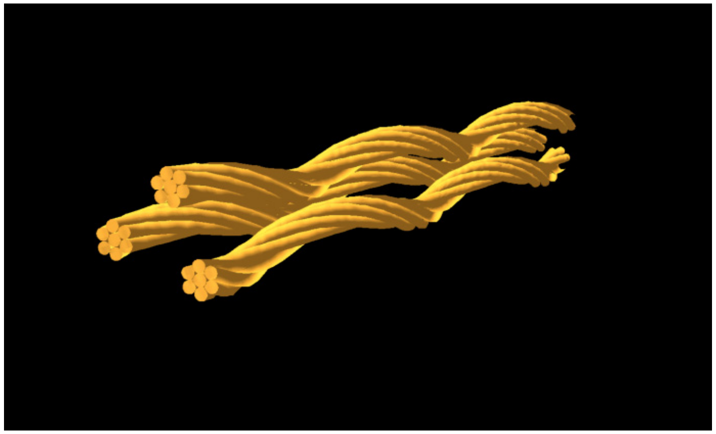
The lungs are embedded in connective tissue that surrounds the airways & the alveoli.

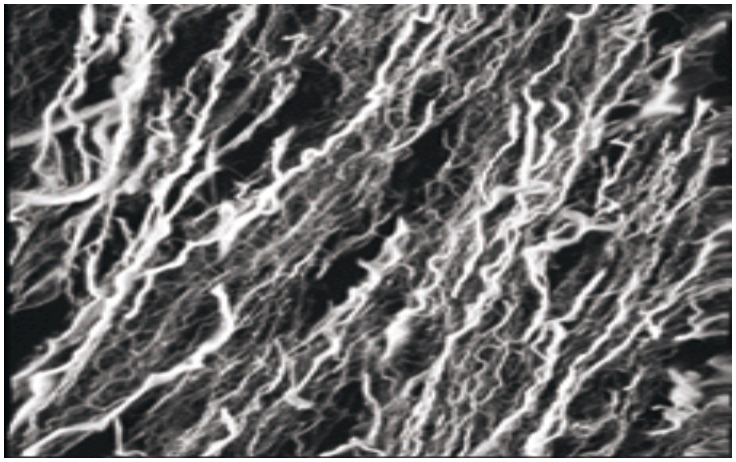
Two key connective tissue fibers are:

1) collagen fibers
2) elastin fibers

Collagen Fibers

- like a strong twine
- high tensile strength
- inextensible



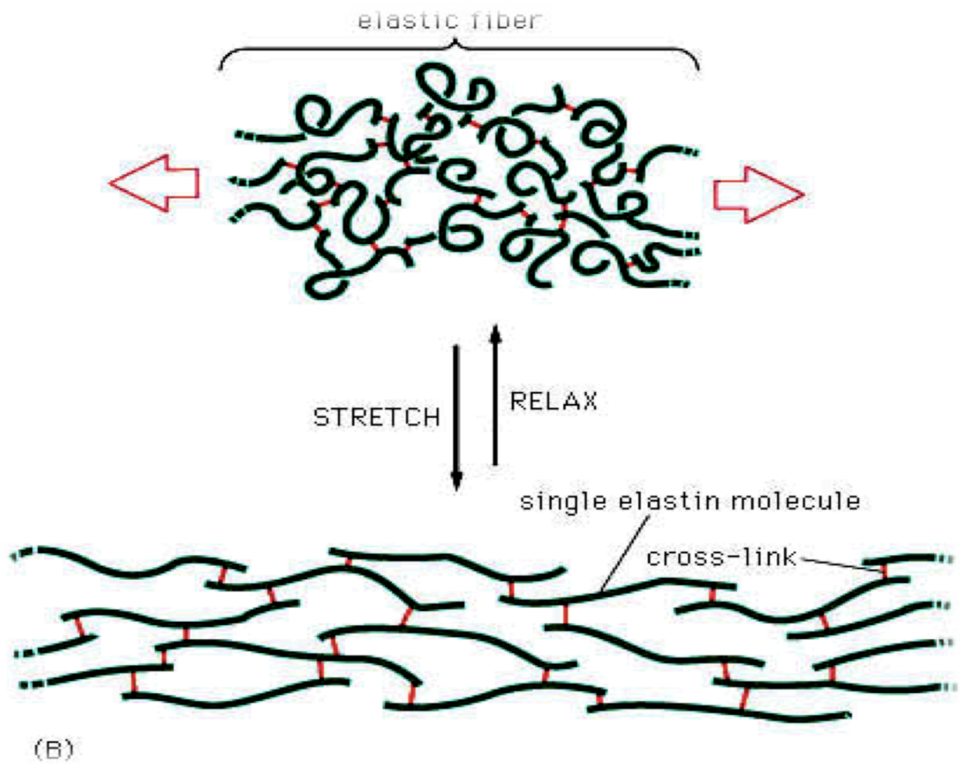


Elastin Fibers

- like a weak spring

- low tensile strength

- extensible



Change in Compliance of the Lungs due to Loss of Connective Tissue

aging

↓

loss of elastin

↓ ↓

wrinkled skin | floppy lungs ($\uparrow C_L$)

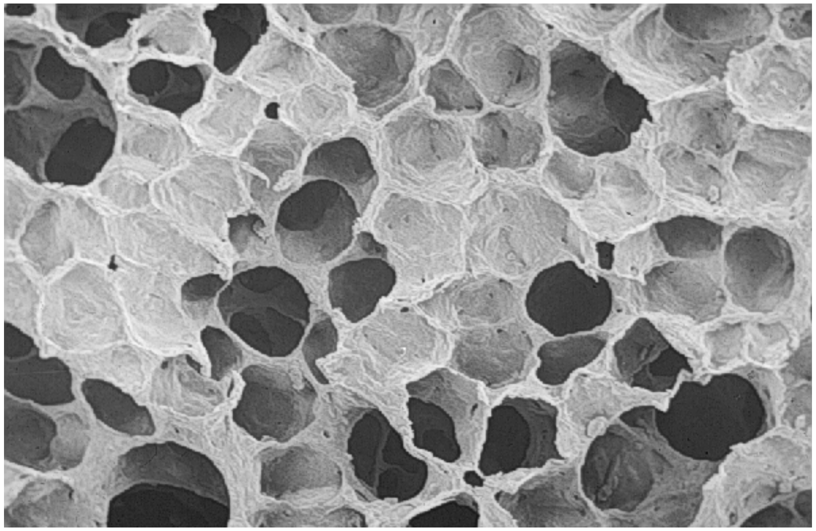
Emphysema
(the disappearing lung disease)

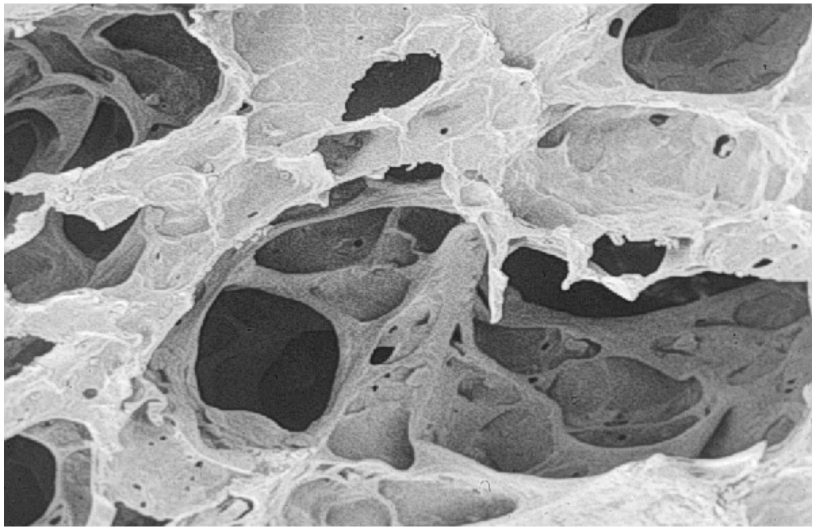
⬇

destruction of
alveolar walls
composed of
elastin & collagen fibers

⬇

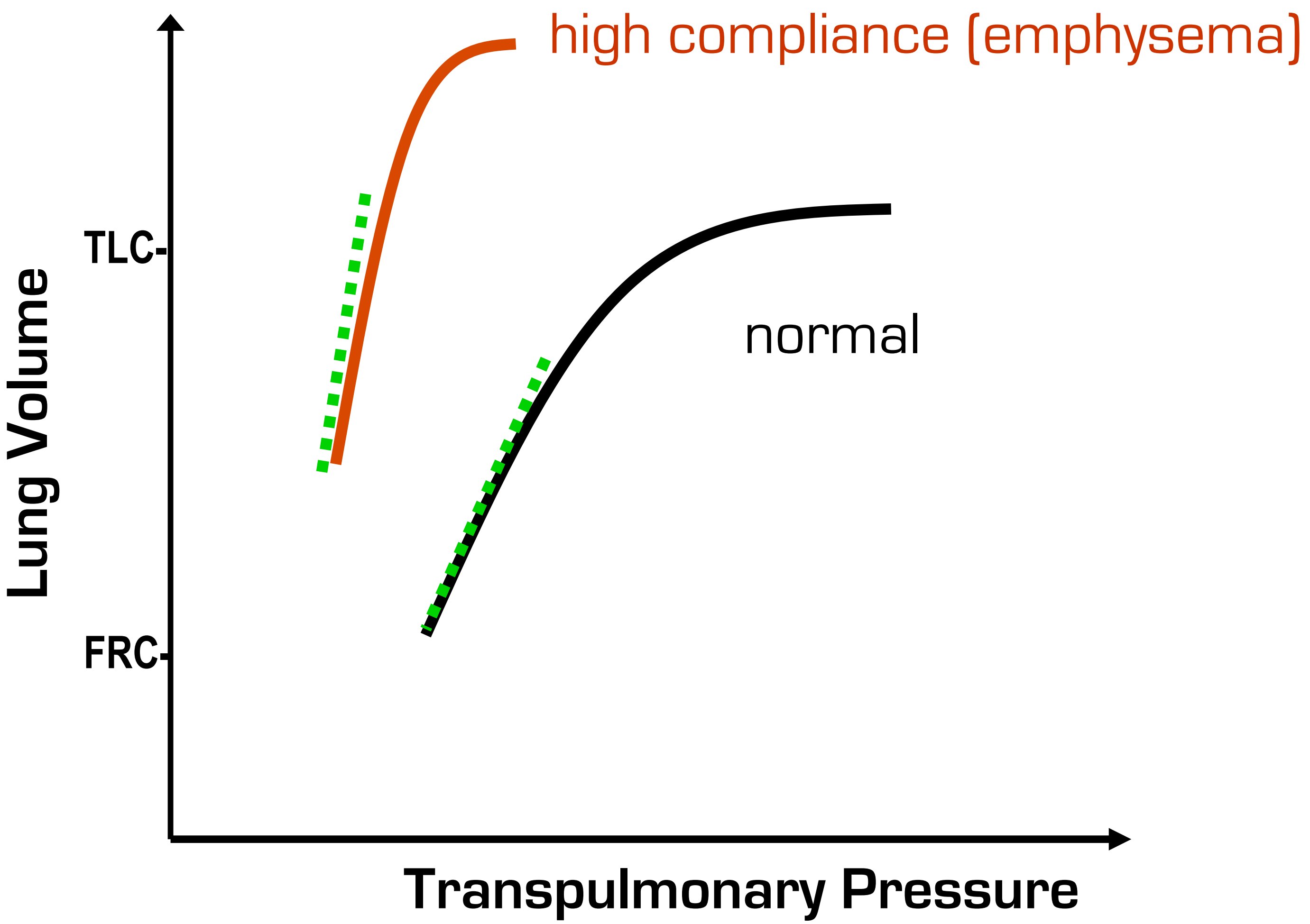
⬆ lung compliance
(floppy lungs)





Static Compliance of the Lungs (C_L)

is obtained as the slope of the relaxation P-V curve of the lungs



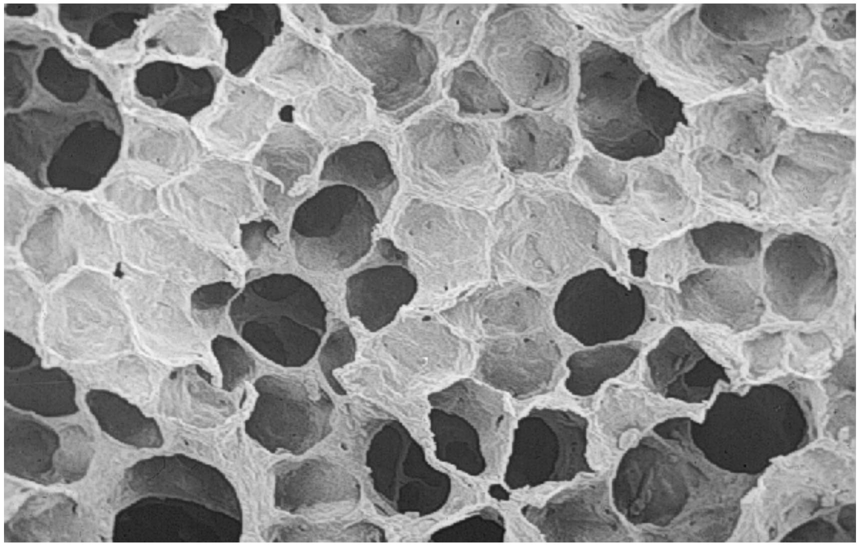
Pulmonary Fibrosis

⬇

collagen deposition in alveolar walls in response to lung injury (e.g. asbestosis)

⬇

↓ lung compliance
[stiff lungs]



Static Compliance of the Lungs (C_L)

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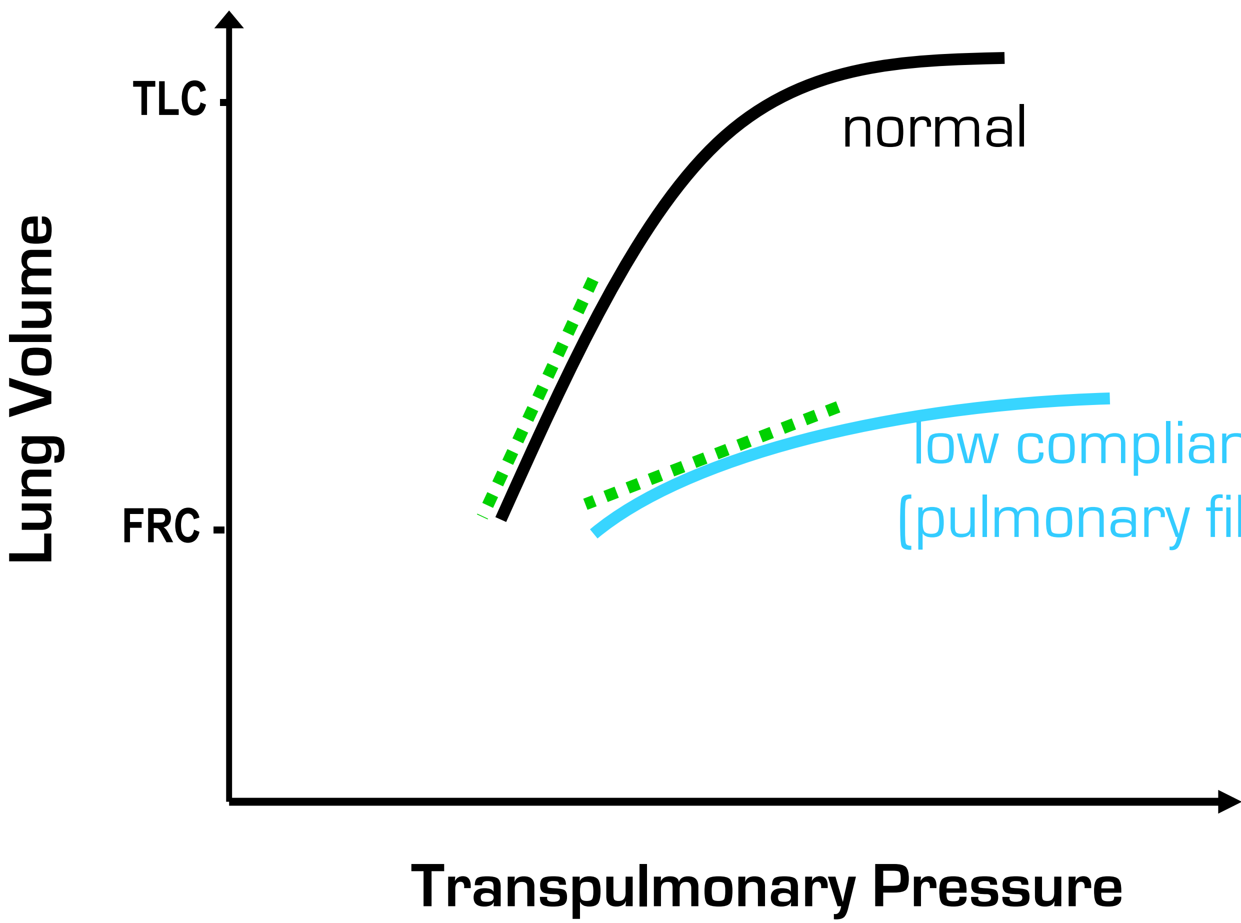
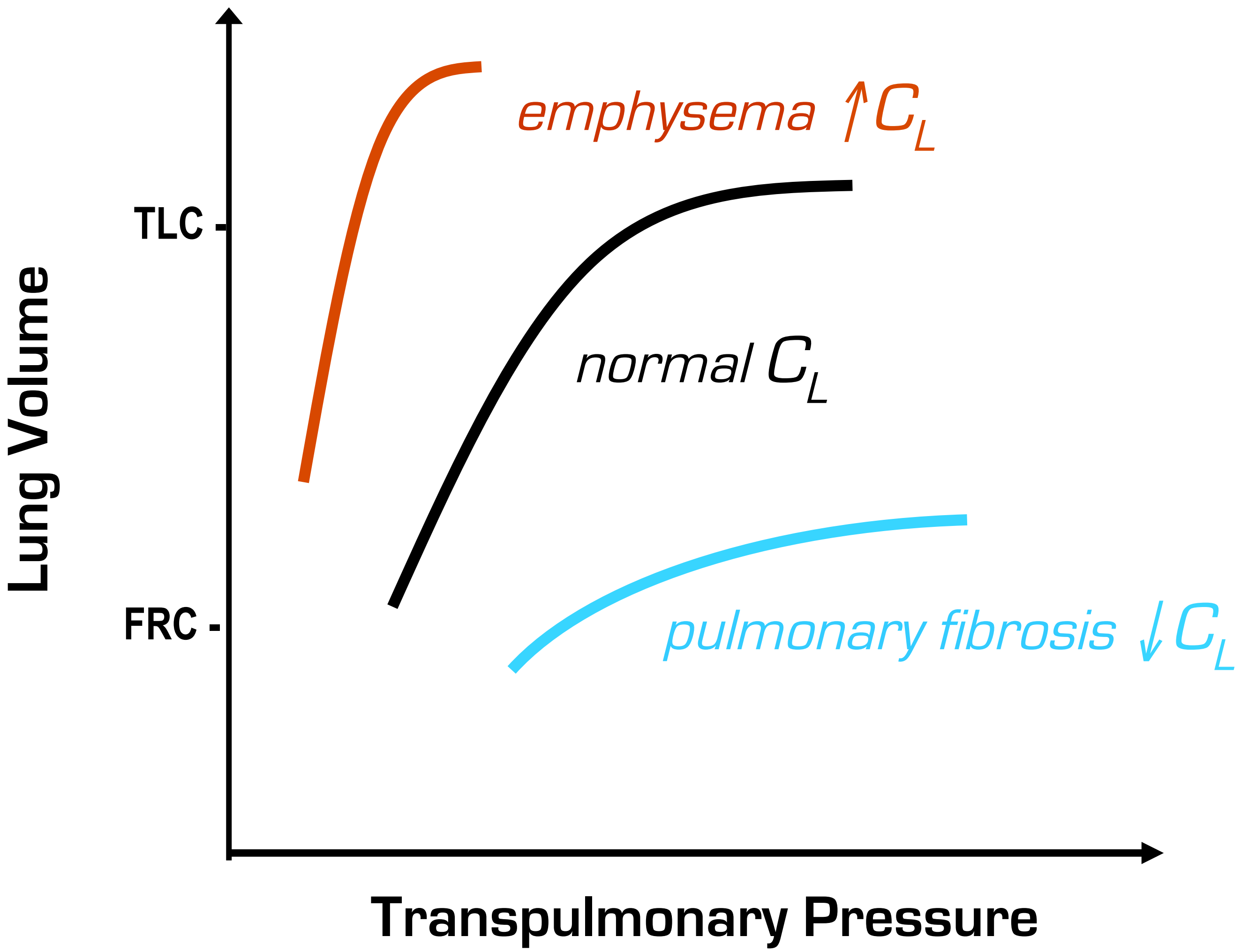
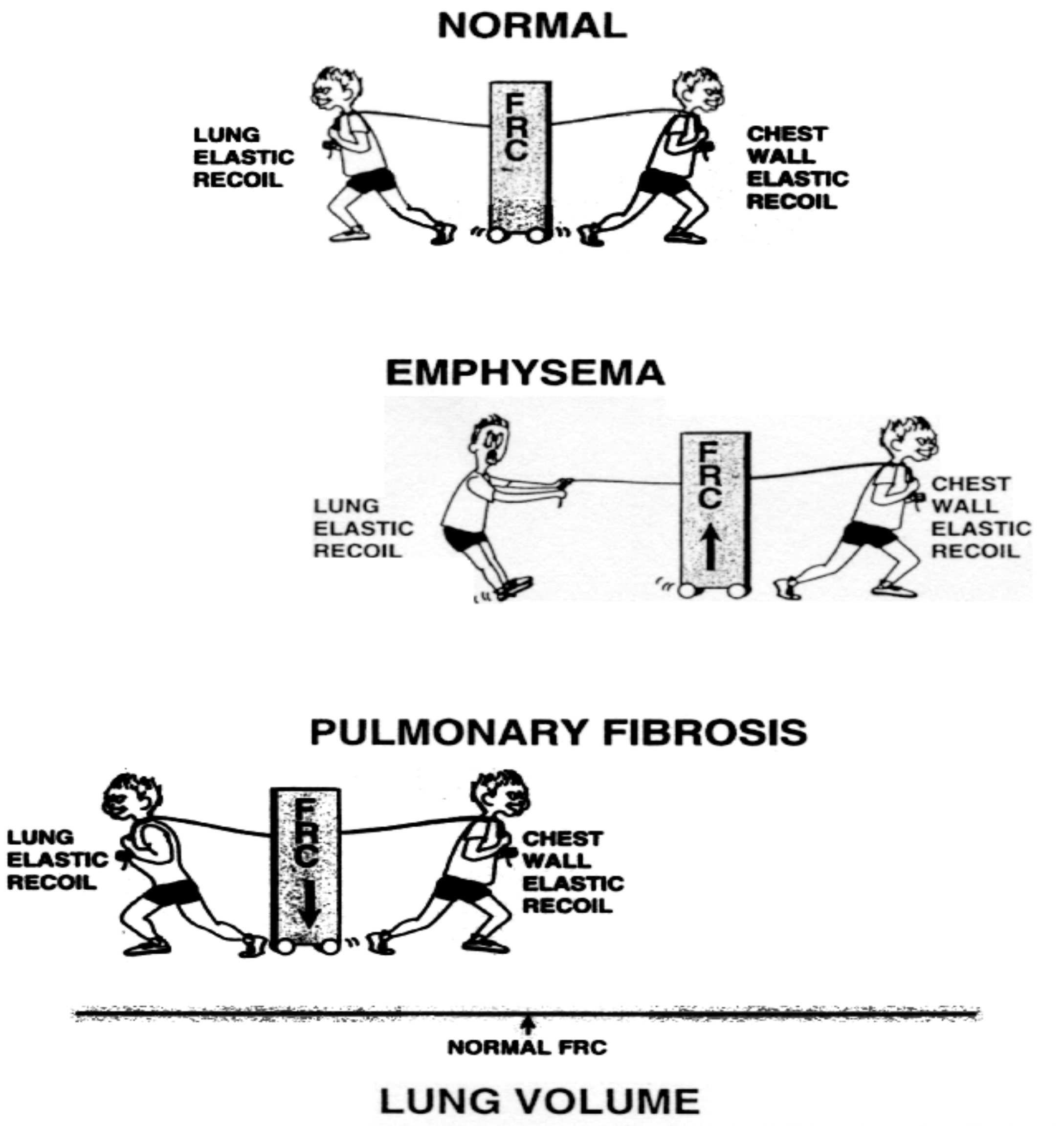


Static Compliance of the Lungs (C_L)

is obtained as the slope of the relaxation P-V curve of the lungs



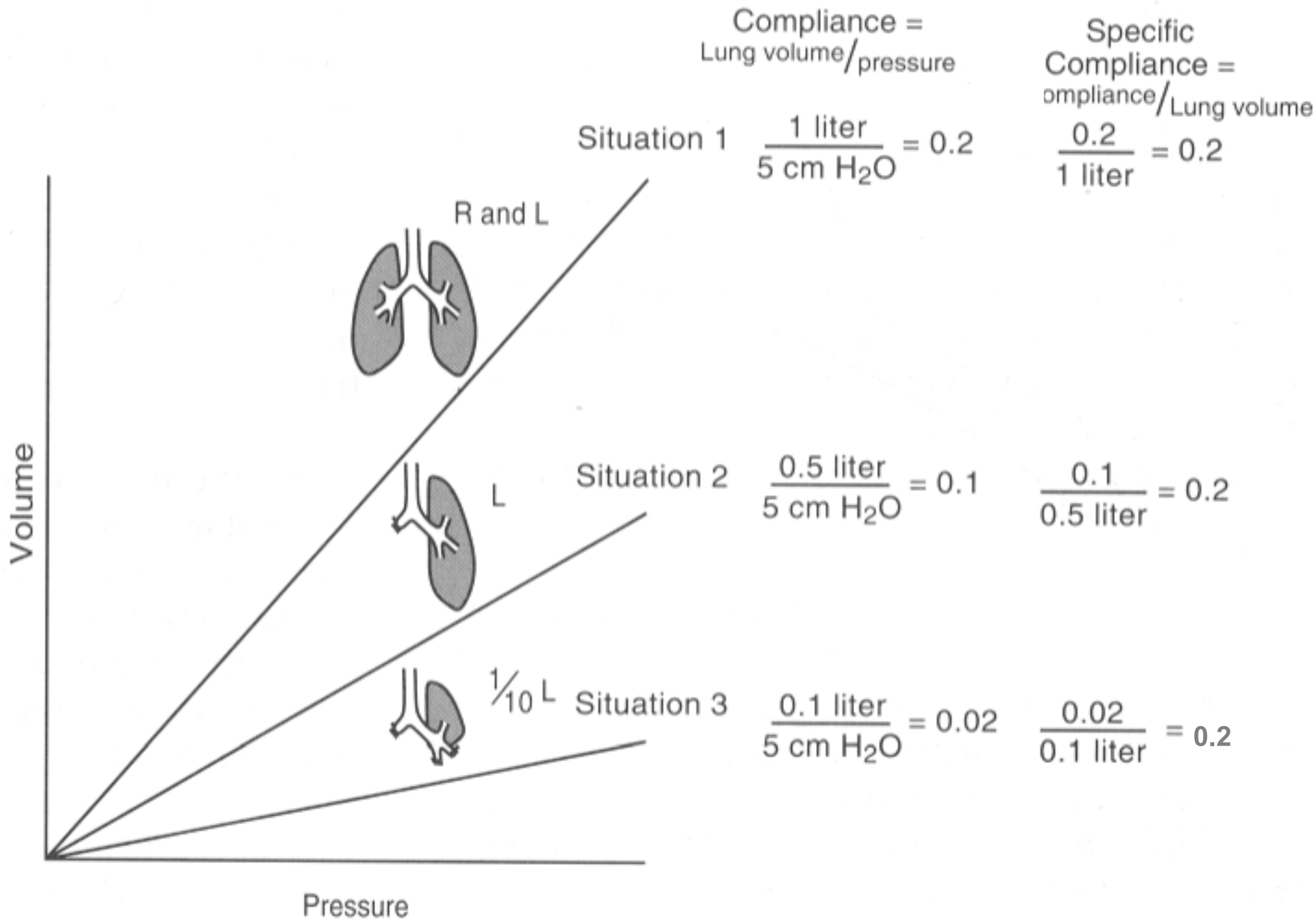
Changes in Lung Compliance affect FRC



“Static” versus “Specific”

Compliance of the Lungs

- Predict the static C_L of a patient with one lung resected.
- Clue: consider the method used to measure static compliance.



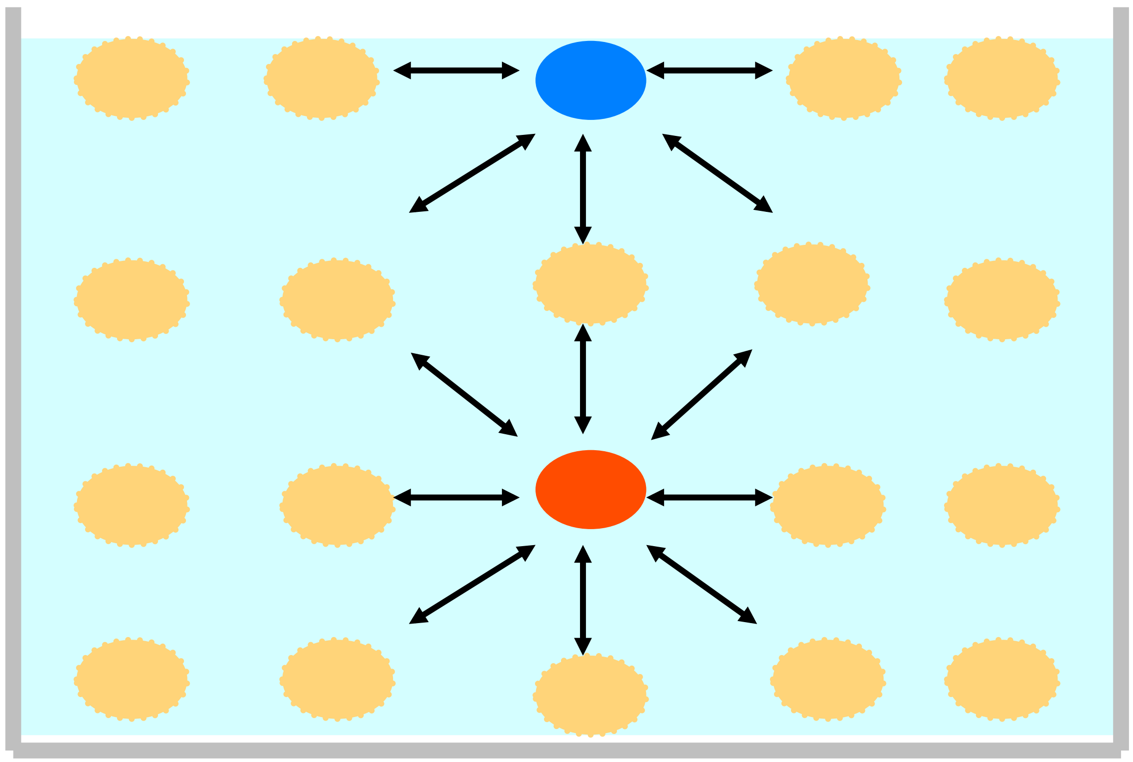
Compliance = Lung volume/pressure
Specific Compliance = ompliance/Lung volume
Situation 1
$\frac{1 \text{ liter}}{5 \text{ cm } H_2O} = 0.2$
$\frac{0.2}{1 \text{ liter}} = 0.2$
R and L
Situation 2
$\frac{0.5 \text{ liter}}{5 \text{ cm } H_2O} = 0.1$
$\frac{0.1}{0.5 \text{ liter}} = 0.2$
L
1/10 L
Situation 3
$\frac{0.1 \text{ liter}}{5 \text{ cm } H_2O} = 0.02$
$\frac{0.02}{0.1 \text{ liter}} = 0.2$
Volume
Pressure

“Static” Versus “Specific” Compliance of the Lungs

Which would give you insight into the intrinsic elasticity of the lung tissue independent of changes in lung volume?

Surface Tension

Water molecules at the surface of a liquid-gas interface are attracted strongly to the water molecules within the liquid mass. This cohesive force is called "surface tension".



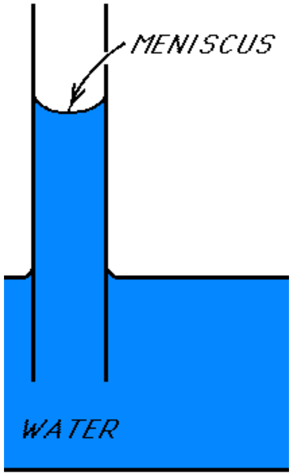
Surface tension makes it possible:

to float paper clips on water

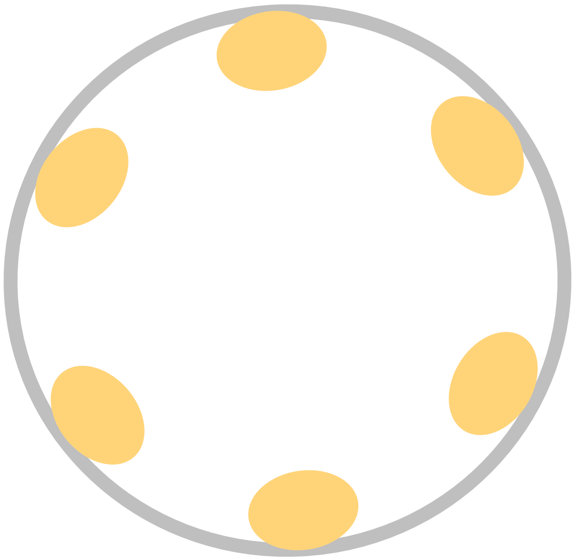
for insects to walk on water

maintain the shape of a droplet

reduces the meniscus curvature created by capillary action



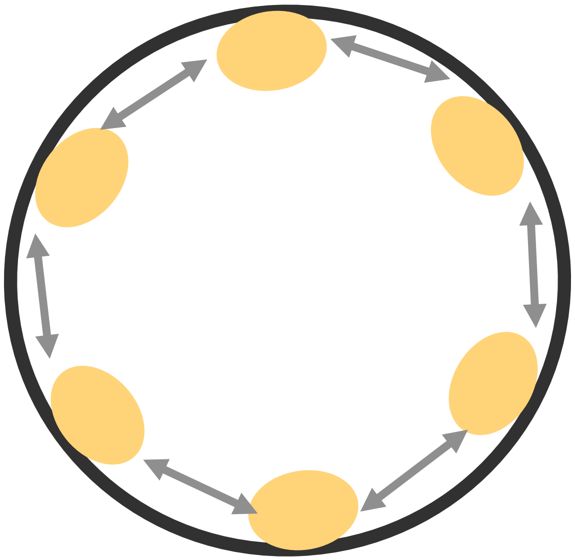
Alveolar Surface Tension



air entering the lungs is humidified + saturated with water vapour at body temperature.

water molecules cover the alveolar surface

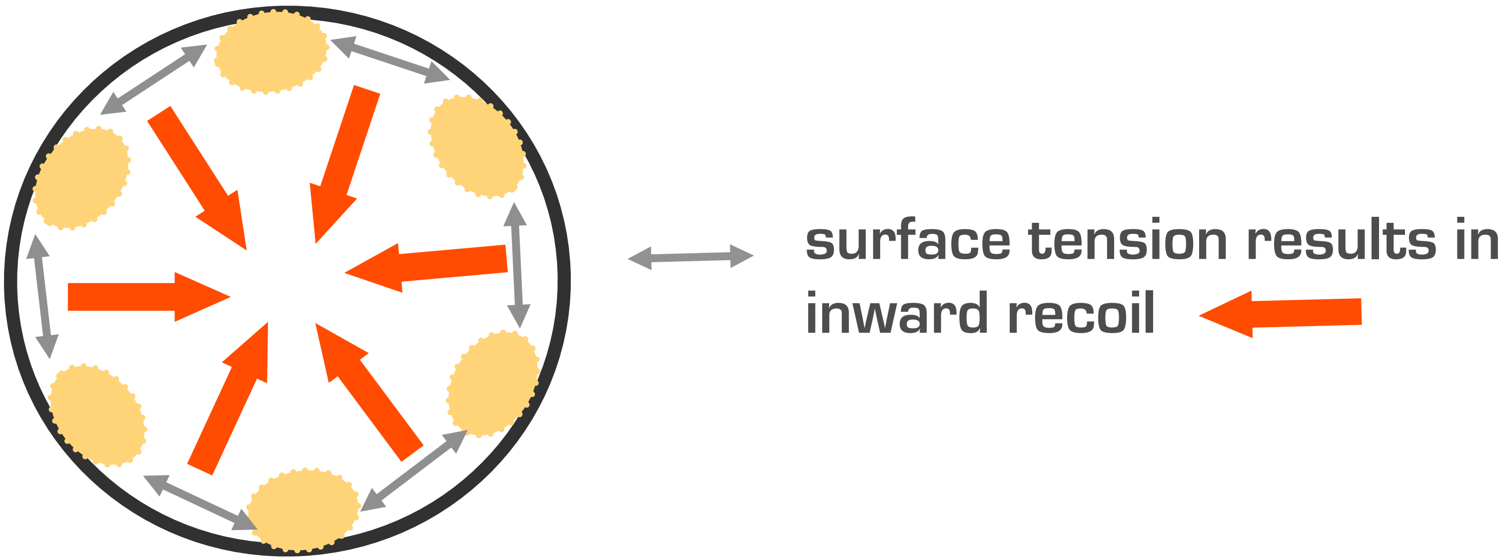
Alveolar Surface Tension

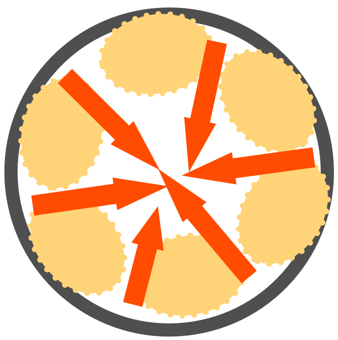


surface water molecules

create substantial

surface tension


surface tension results in
inward recoil



inward recoil collapses the alveolus

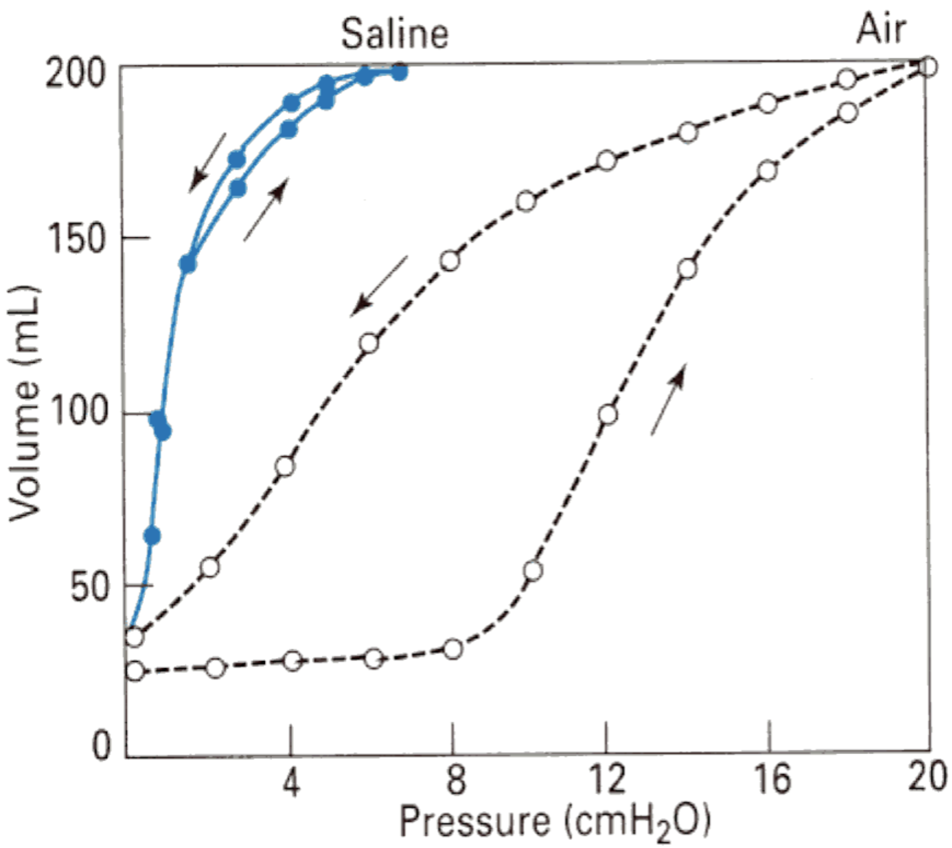
Premature & Unique Scientific Discovery in1929

Kurt von Neergaard
(1887-1947)

" The lung is unique among tissues in extraordinary ability to expand and retract. So far this has been regarded as due to the elasticity of the tissue itself particularly that of its elastic fibers ... so far one force has not been taken into account ...

*This force is **surface tension**".*

Pressure-Volume Curves for Excised Cat Lungs Inflated with Air or Saline (Brown, Clements et al. 1956)



Note two features:

1. more pressure required to inflate the air-filled lung
2. *hysteresis*

   Greek: shortcoming

- History dependence of physical systems
- The difference in the stress-strain relation in loading versus unloading
- A property of viscoelastic materials

Excised Cat Lung P-V Curve
Inflation with Air versus Saline

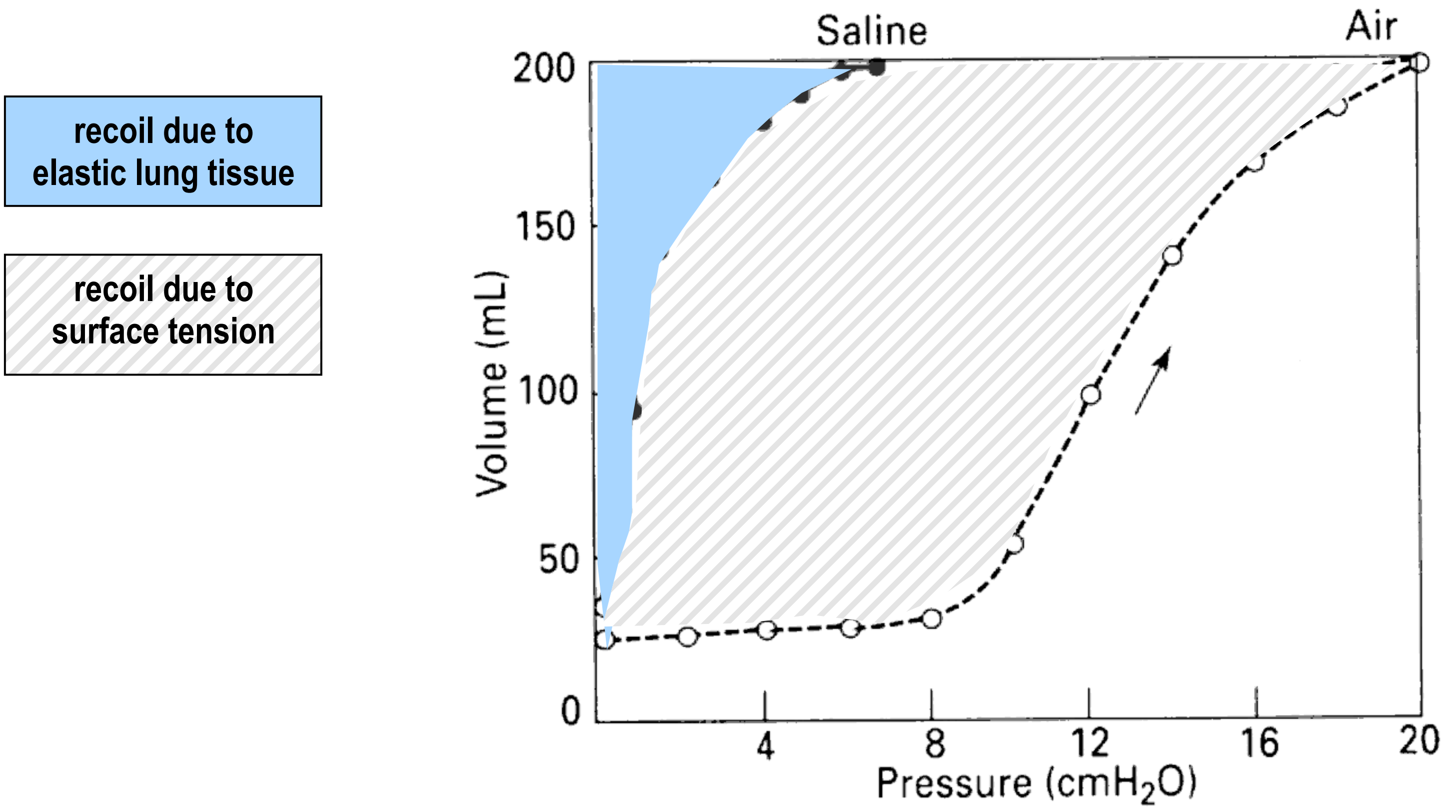
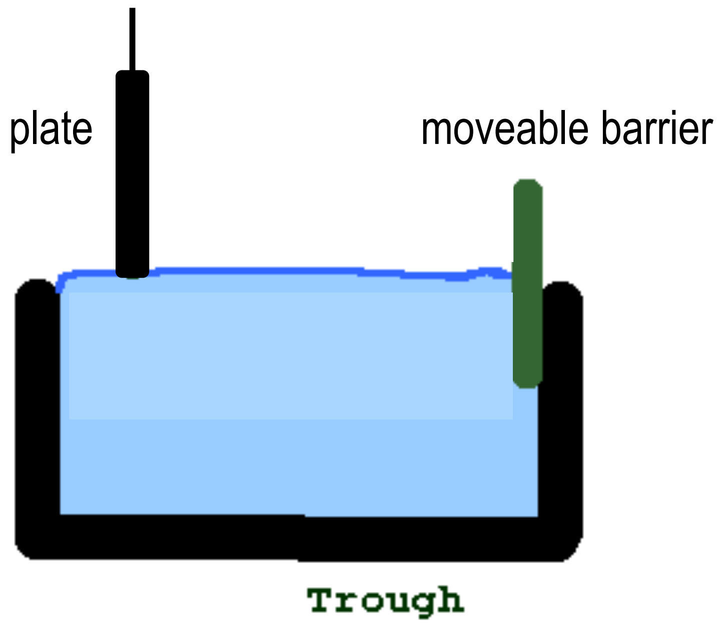
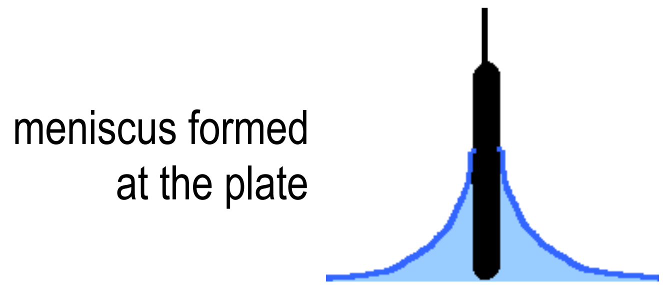


Figure 2–8. Pressure-volume curves for excised cat lungs inflated with air or saline.
(Reproduced with permission form Clements, 1965.)

What happened in the 25 years between 1930-1955?

Measuring Surface Tension, the classic method



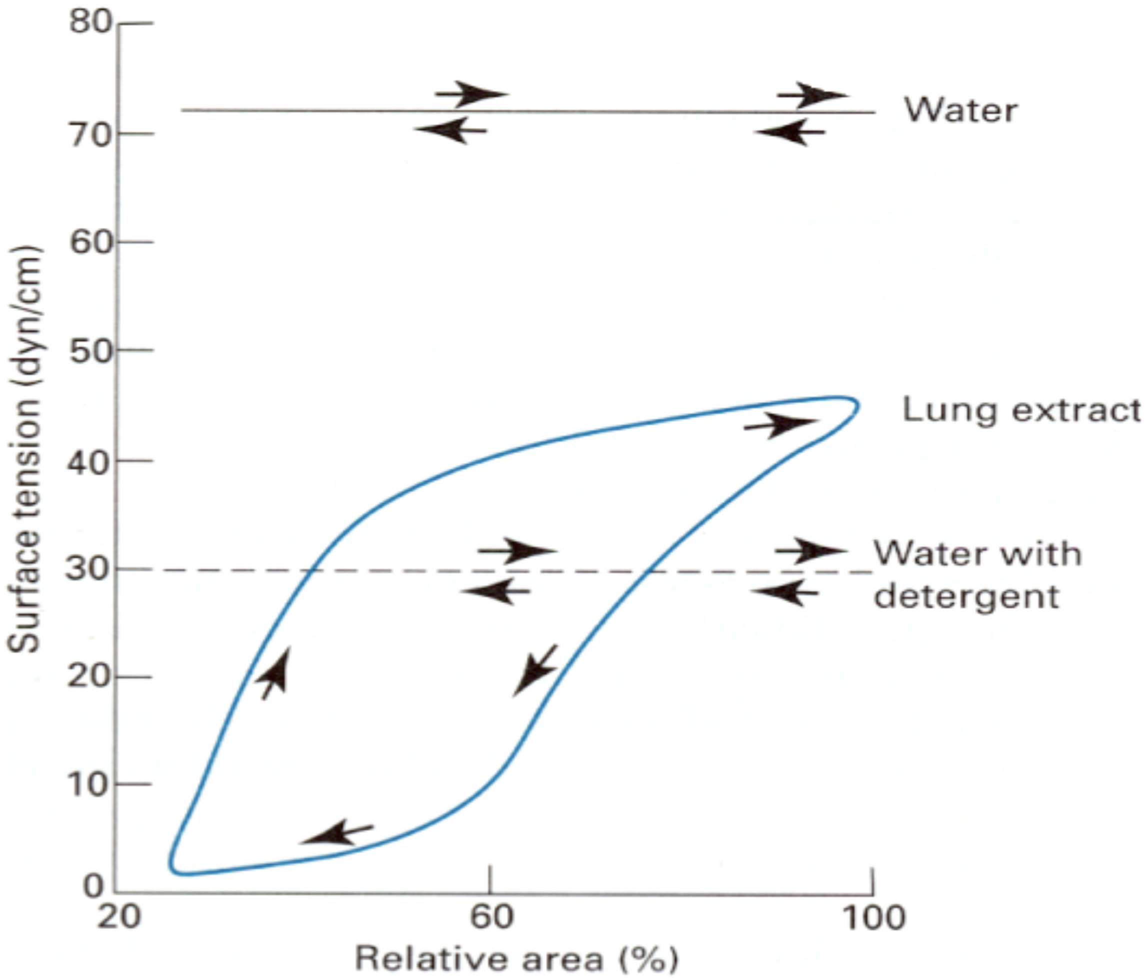


- a trough, a barrier and a plate
- the fluid forms a meniscus at the plate
- determine surface tension from: - the increased weight of the plate,
  - the height of the meniscus
  - or its downward force

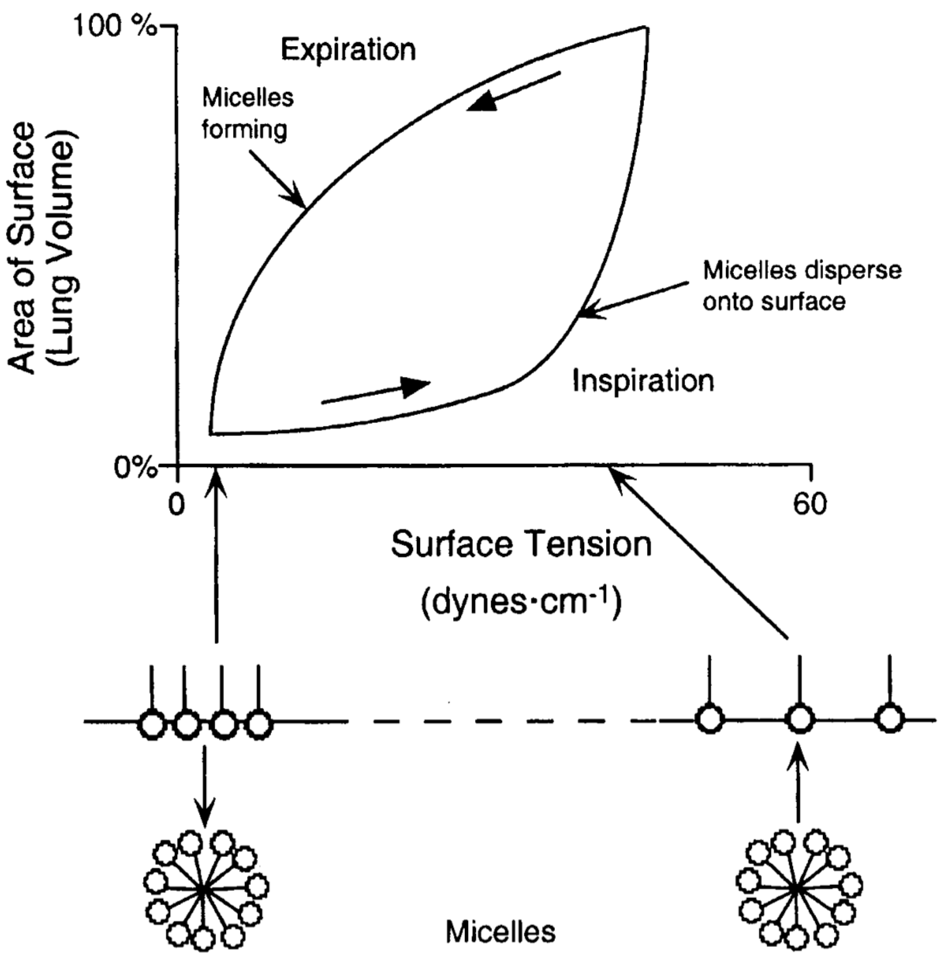
•Units are in terms of force across a line: dynes/cm or mN/m

-

Relationship between Surface Tension & Surface Area
(using the Langmuir-Wilhelmy Balance (Clements, 1957)



The Role of Micelle Formation in Hysteresis



Composition of Pulmonary Surfactant

90 % Lipids

mainly (80% phospholipids)

- 40% diphosphatidylcholine [DPPC]- key surface tension reducing agent
- 10% neutral lipids- mostly cholesterol

10% Proteins

- half of which are 4 unique proteins; surfactant protein A, B, C & D

- SPs are produced in type II alveolar cells and undergo post translational modification ending up in lamellar bodies (concentric rings of lipid & protein about 1 micron in diameter)

FAQ: Pulmonary Surfactant

- Appears late in gestation. Lamellar bodies are visible in the cytoplasm of type 2 pneumocytes as early as 20 weeks. Note the difference in appearance of lamellar bodies in the cytoplasm of type II cells *vs* adequacy of surfactant activity from lamellar body secretion of tubular myelin.
- Half life is short in animals: hours in adults, days in newborn. Humans?
- Stimulus to secretion : lung inflation, sigh
- Treatment of NRDS: : intratracheal exogenous pulmonary surfactant
  [porcine/semisynthetic/synthetic pulmonary surfactant]
  & prenatal corticosteroid
- First successful treatment of NRDS with pulmonary surfactant by Fujiwara et al. 1980

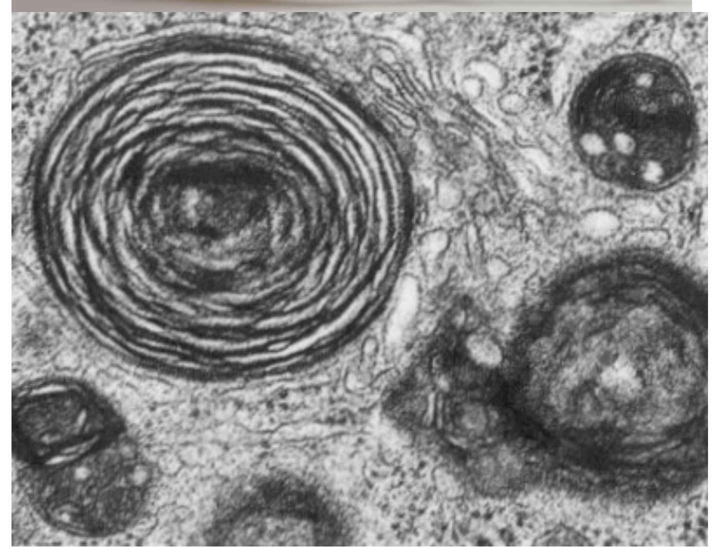
A CASE OF HIGH ALVEOLAR SURFACE TENSION

Neonatal Respiratory Distress Syndrome (NRDS)

Avery & Mead (1959) Surface properties & Hyaline Membrane Disease

Premature babies born with inadequate production of pulmonary surfactant have stiff lungs that are hard to inflate at birth

- life threatening condition
- ventilator dependent
- treated with semi-synthetic surfactant, intra-tracheal delivery
- mother is treated with corticosteroids during pregnancy



lamellar inclusion bodies

RESPIRATORY DISTRESS SYNDROMES

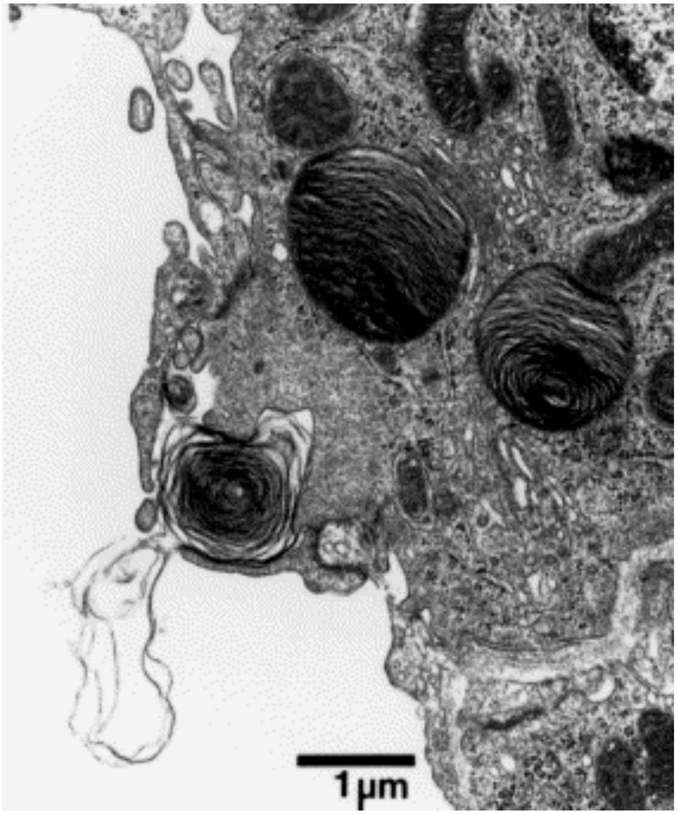
Most common cause of morbidity in preterm babies
Signs: apnea, cyanosis, grunting, inspiratory stridor, nasal flaring, poor feeding, tachypnea,

Other respiratory distress syndromes that affect surfactant include:

- Meconium aspiration syndrome (MAS)
- Pulmonary hemorrhage
- Acute Respiratory Distress syndrome
- Pulmonary alveolar proteinosis

Compare & contrast these 4 with respect to cause, signs & symptoms, pathology, affect on lung surfactant & lung function (personal research-group journal review)

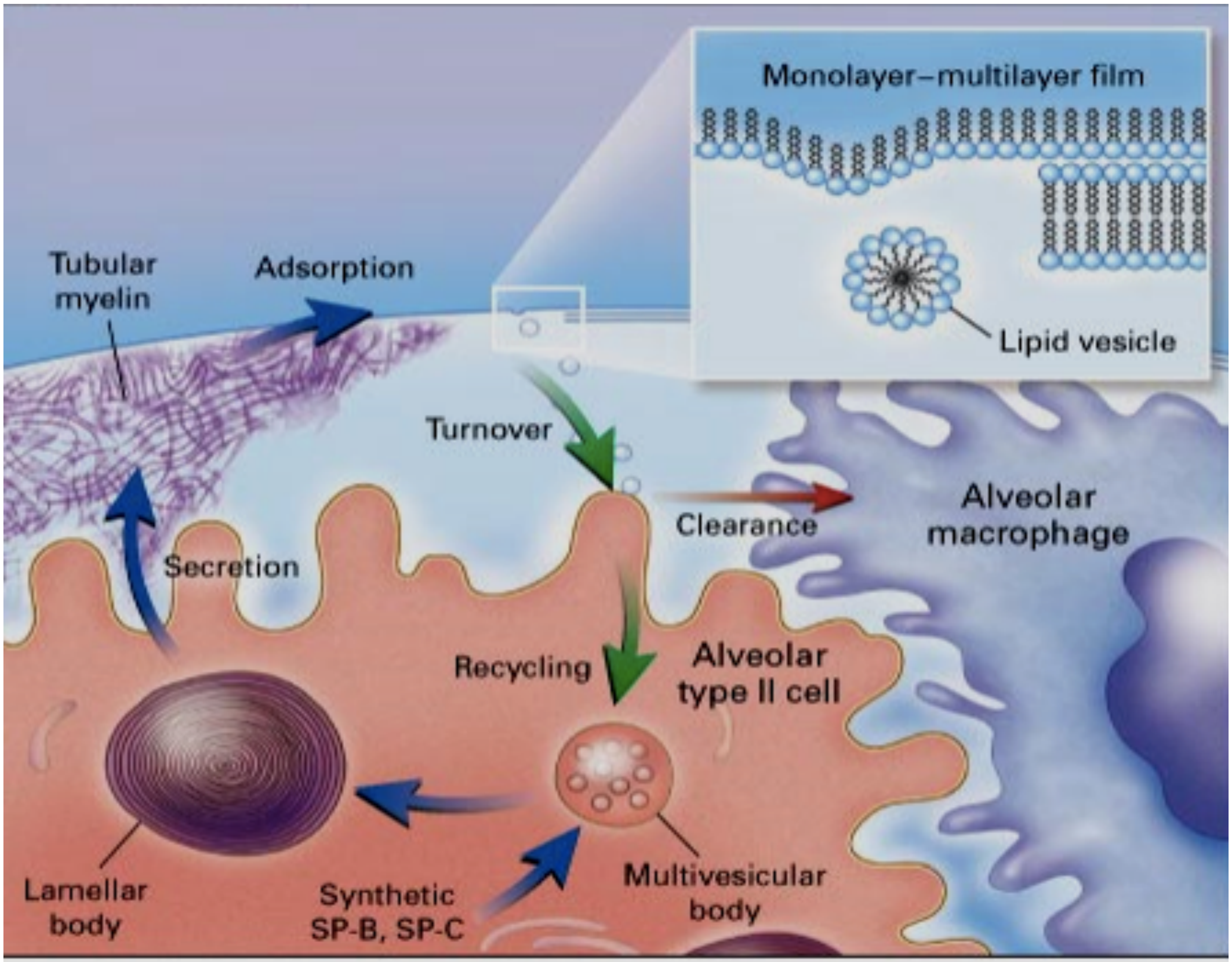
Surfactant is Produced, Stored & Secreted by Type II Alveolar Epithelial Cells



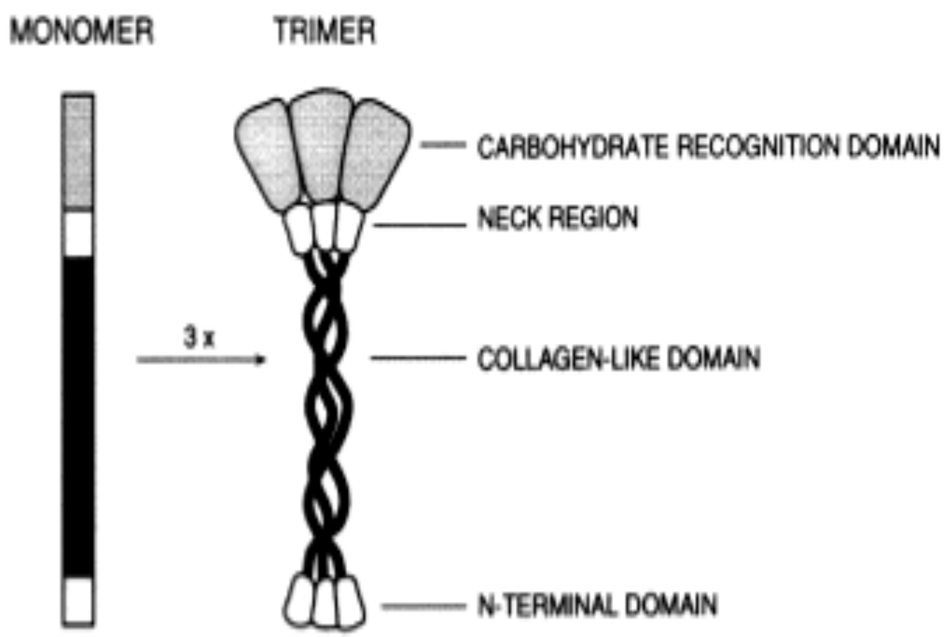
A lamellar body in the process of exocytosis from a type II cell (Rooney et al. (1994)

- production by 24-26 weeks gestation.
- surfactant phospholipids are assembled as bilayer membranes in the lamellar bodies.
- exocytosis of the lamellar body deposits tubular myelin surfactant on the alveolar surface
- SP-B & SP-C are essential for the transition to monolayer formation on the alveolar surface

Pulmonary Surfactant
synthesis, assembly, transport, secretion & recycling



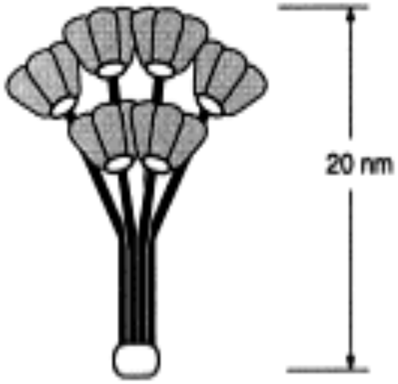
SP-A & SP-D - hydrophilic



CRD binds

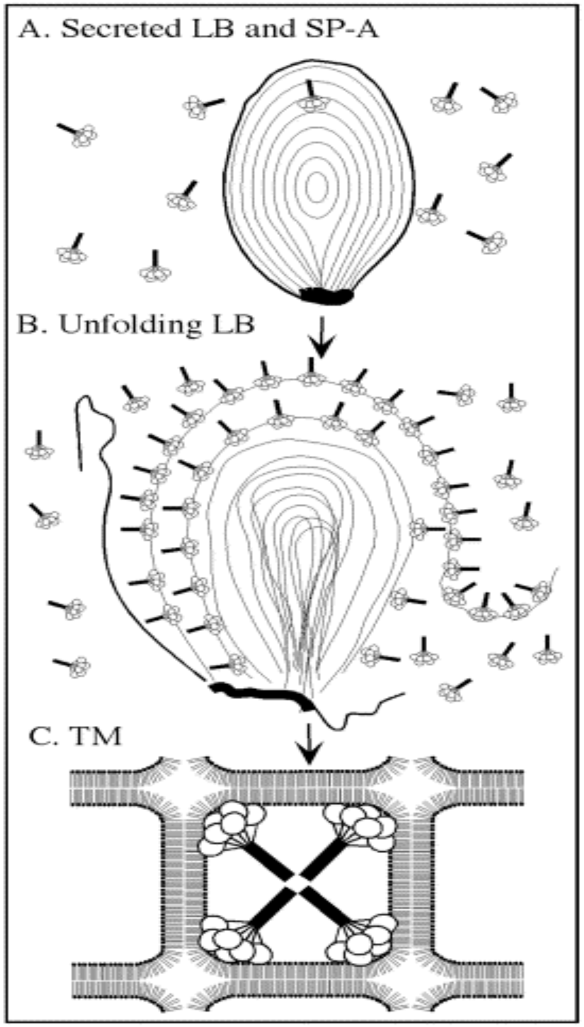
- Ca^{2+}
- carbohydrates
- phospholipids
- lipopolysaccharides
- surface of type II alveolar cells & macrophages
- microbes [viruses, bacteria, fungi]
- inhaled allergens [pollen grain, dust mites)

- oligomers of trimeric units
- members of collagenous carbohydrate binding proteins "collectins" that bind microbial pathogens
- also produced and secreted by larger airway sub-mucosal cells, Clara cells and by extrapulmonary tissue (CNS, GI, renal, reproductive, ocular systems & synovial fluid)-roles under intense study esp. in disease
- key function host defense innate immune response



SP-A

- first surfactant protein identified & most abundant
"bouquet" structure of six trimers
- MW=26-38 kD



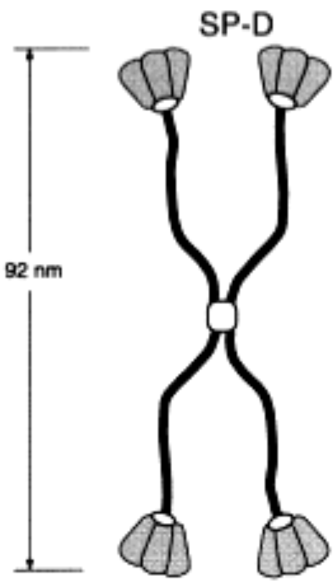
Functions

1. formation of tubular myelin
[lipid lattice with SP-A scaffolding]

2. binding to pathogens & neutralize them
(via multiple mechanisms: aggregation, apoptosis, phagocytosis, inhibition of growth, etc)

SP A knock-out mice lack tubular myelin formations. Mutations of SP-A genes suggest a role in lung fibrosis (misfolding protein in ER?)

SP-D



- largest surfactant protein, 43 kDa
- X-shaped dodecamer of 4 lollipop structures

Function- binding to pathogens & neutralize them (similar to SP-A role in the innate immune response)

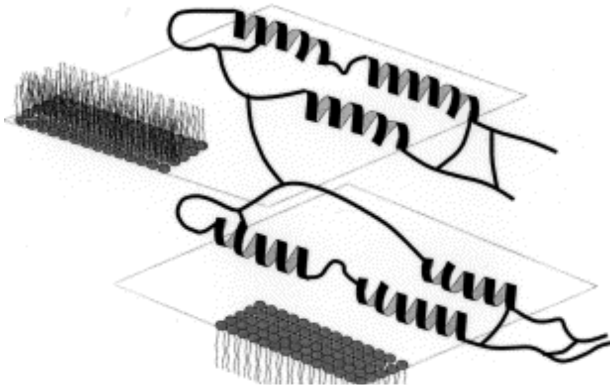
SP D knock-out mice

•have 3-4 times greater phospholipid than normal
•have larger pulmonary macrophages with foamy appearance
•develop emphysema

•current research focus: genetic mutations of SP-A & SP-D genes and transcription factors associated with severe lung disease in the newborns (review by Whitsett JA et al. 2015 Ann.Rev.Pathol)

• need for identification of their receptors

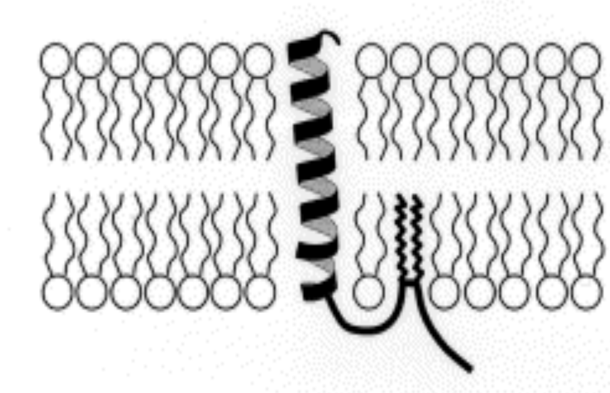
SP-B & SP-C (hydrophobic)



SP-B

- **α-helices** with disordered links, 17 kDa
- required for formation of tubular myelin
- necessary for lung function, humans with SP-B gene mutations die after birth as do SP B knock-out mice

SP-C



- **a single α-helix**, spans the length of a lipid bilayer
- smallest surfactant protein 4.2 kDa
- SP-C knock-out mice survive but develop interstitial pneumonitis & emphysema similar to patients with familial idiopathic fibrosis with SP-C gene mutations.
- severe cases are lethal & requires lung transplantation.

Potential Functions: enhance lipid insertion into the air/liquid interface (speed monolayer formation), enhance the stability and re-spreading of surface film.

P-V Curves for Excised Cat Lungs Inflated with Air or Saline

recoil due to elastic lung tissue

recoil due to surface tension

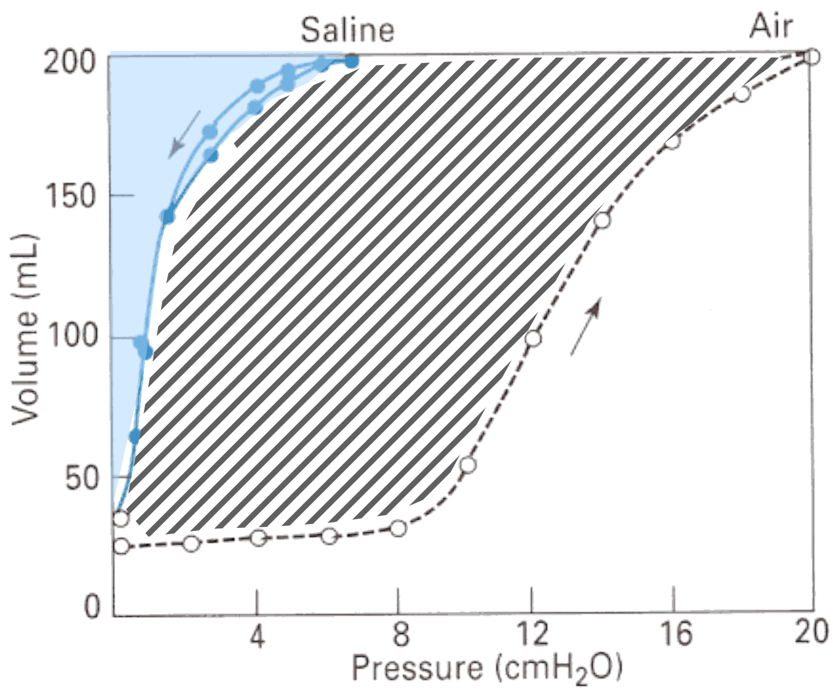


Figure 2–8. Pressure-volume curves for excised cat lungs inflated with air or saline. (Reproduced with permission form Clements, 1965.)

CONDITIONS WHERE CHEST WALL COMPLIANCE IS REDUCED

- **Scoliosis/Kyphoscoliosis-** abnormal lateral/ posterior curvature of the spine - deformity of unknown etiology

- **Ankylosing Sponylitis**- gradual immobility of vertebral joints & fixation of the ribs-unknown etiology

- **Obesity**

- **Neuromuscular Disorders** affecting the respiratory muscle & the nerves supplying them:

  Poliomyelitis

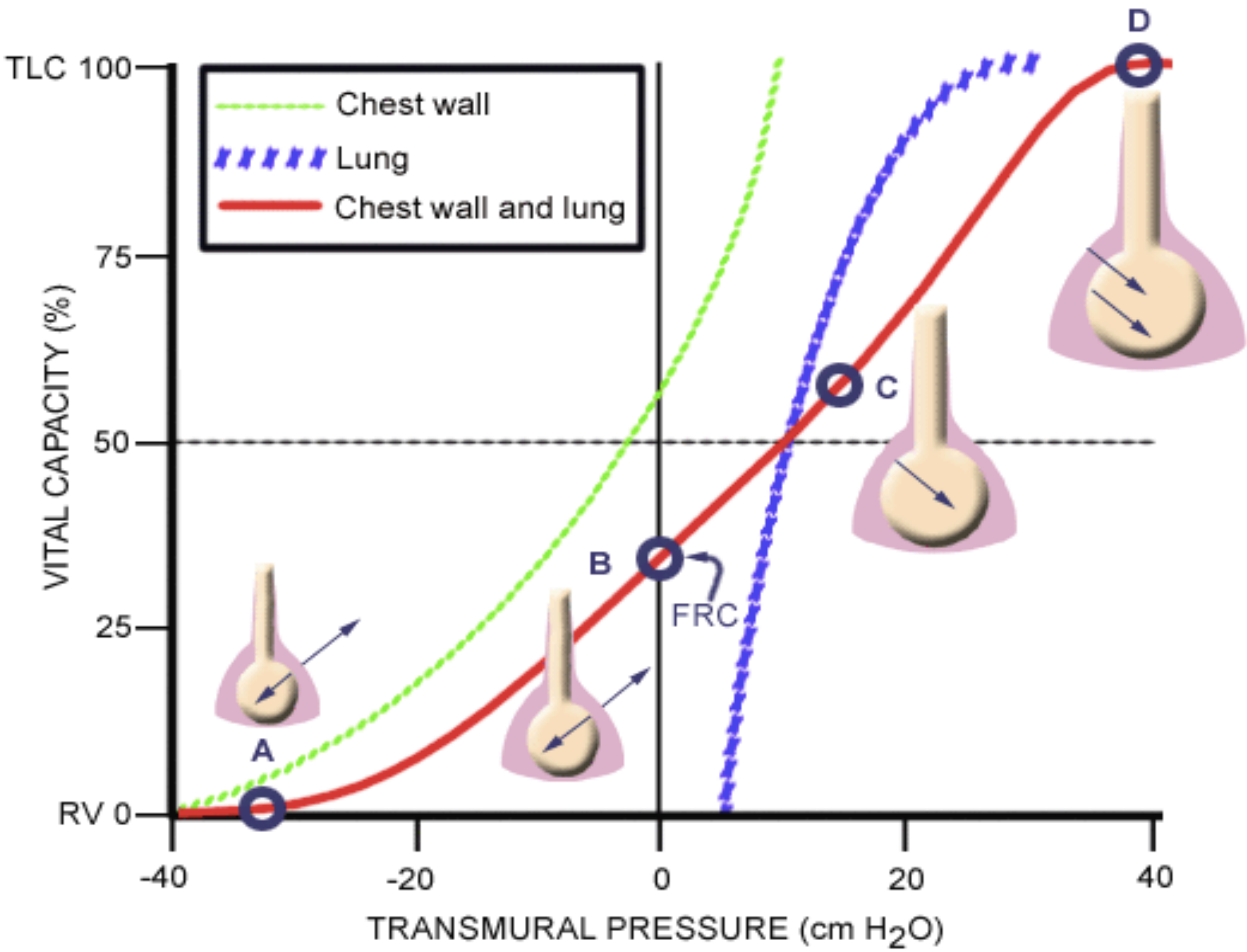
  Guillain-Barré Syndrome

  Amyotrophic Lateral Sclerosis

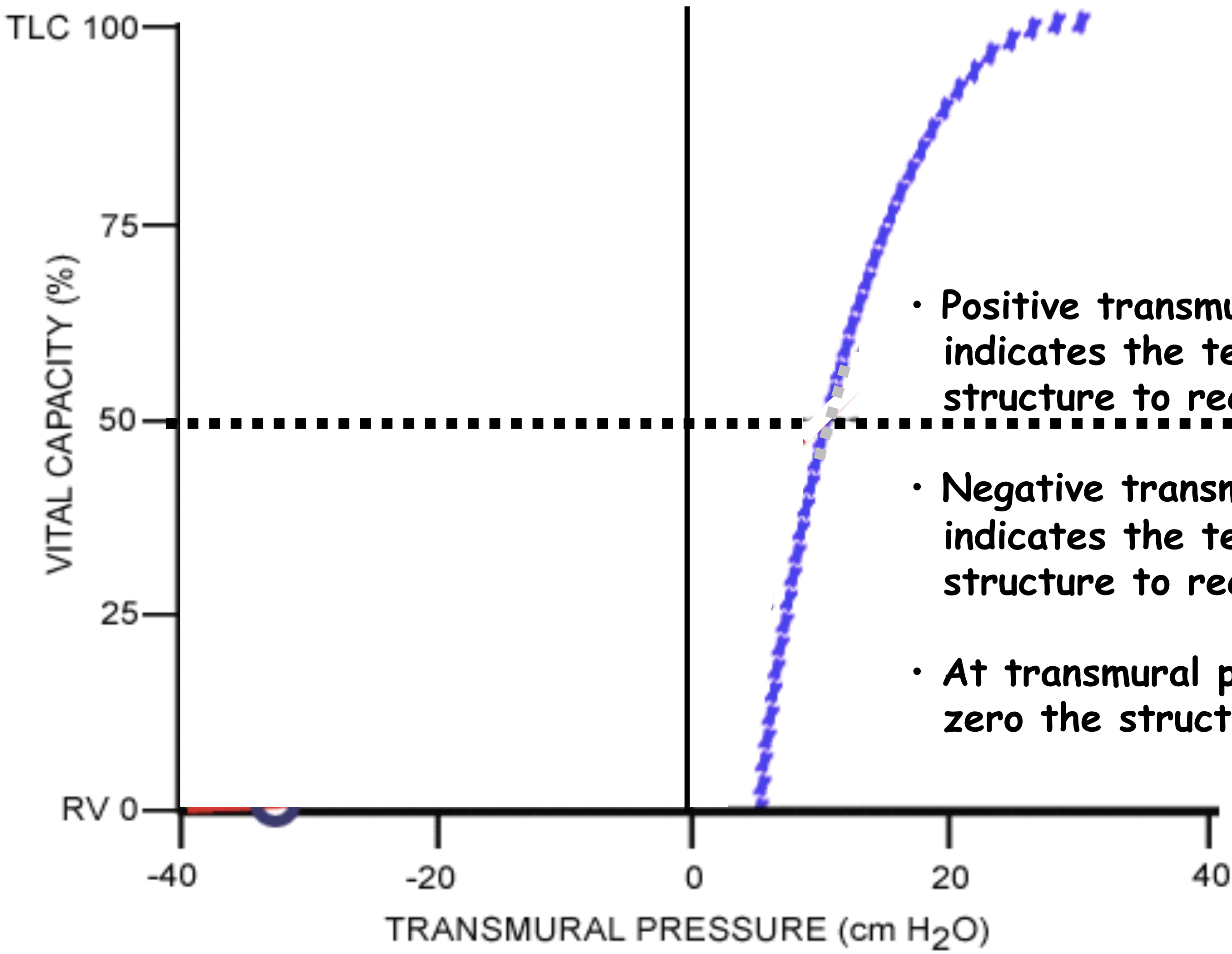
  Myasthenia Gravis

  Muscular Dystrophies

Relaxation Static Pressure-Volume Curves

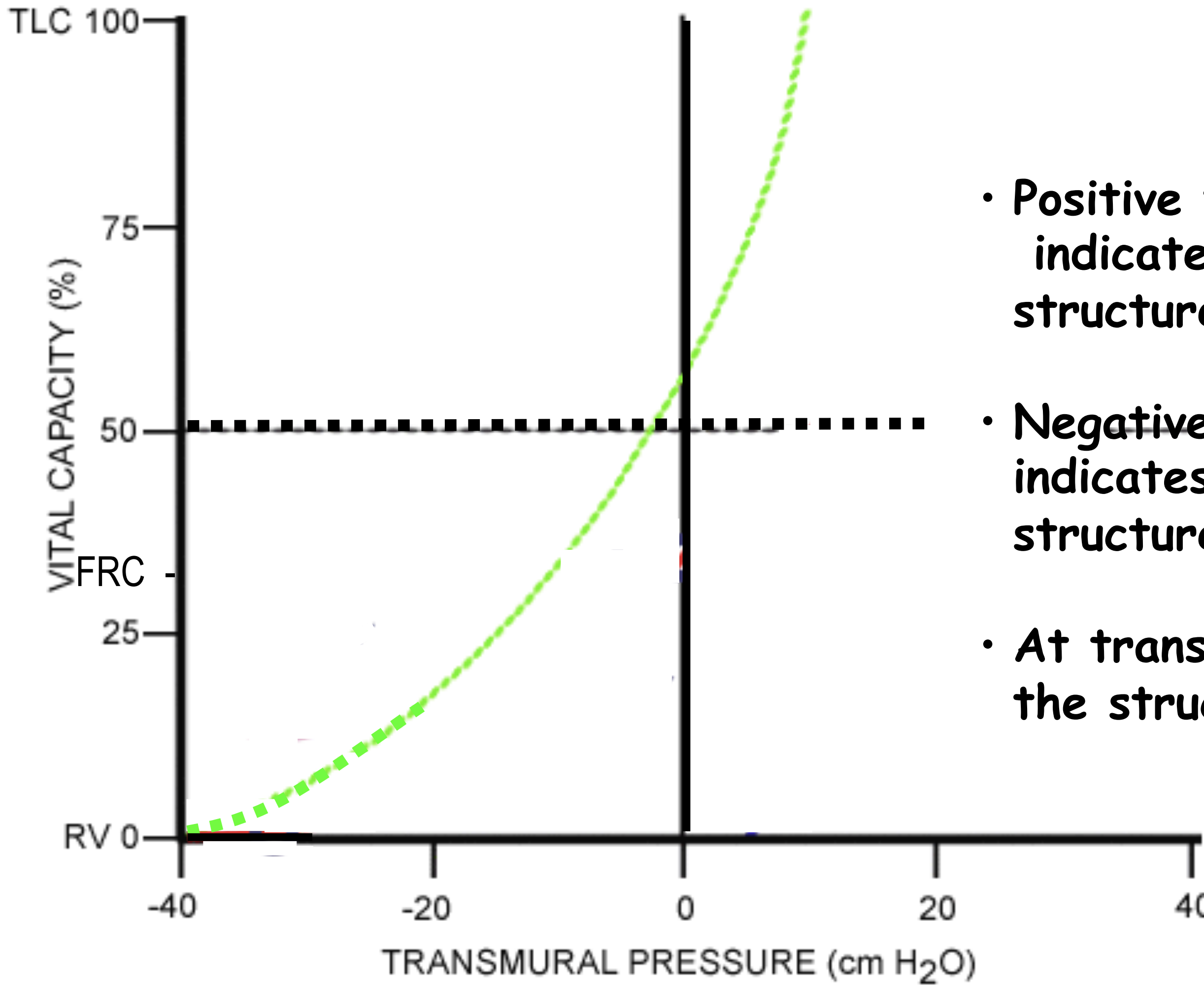


Relaxation Static Pressure-Volume Curve of the Lungs



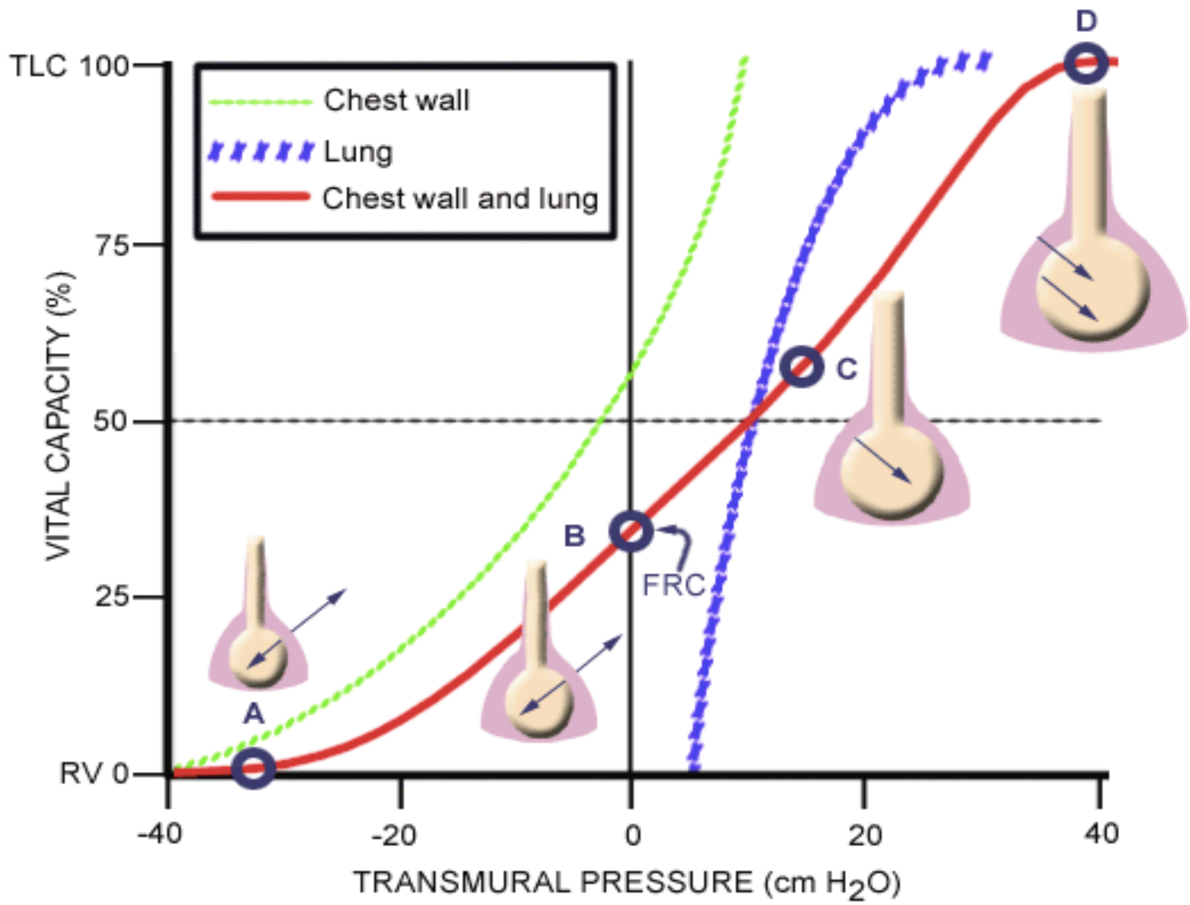
- Positive transmural pressure indicates the tendency of the structure to recoil inward.
- Negative transmural pressure indicates the tendency of the structure to recoil outward.
- At transmural pressure of zero the structure is at rest

Relaxation Static Pressure-Volume Curve of the Chest Wall



- Positive transmural pressure indicates the tendency of the structure to recoil inward.
- Negative transmural pressure indicates the tendency of the structure to recoil outward.
- At transmural pressure of zero the structure is at rest

Relaxation Static Pressure-Volume Curves



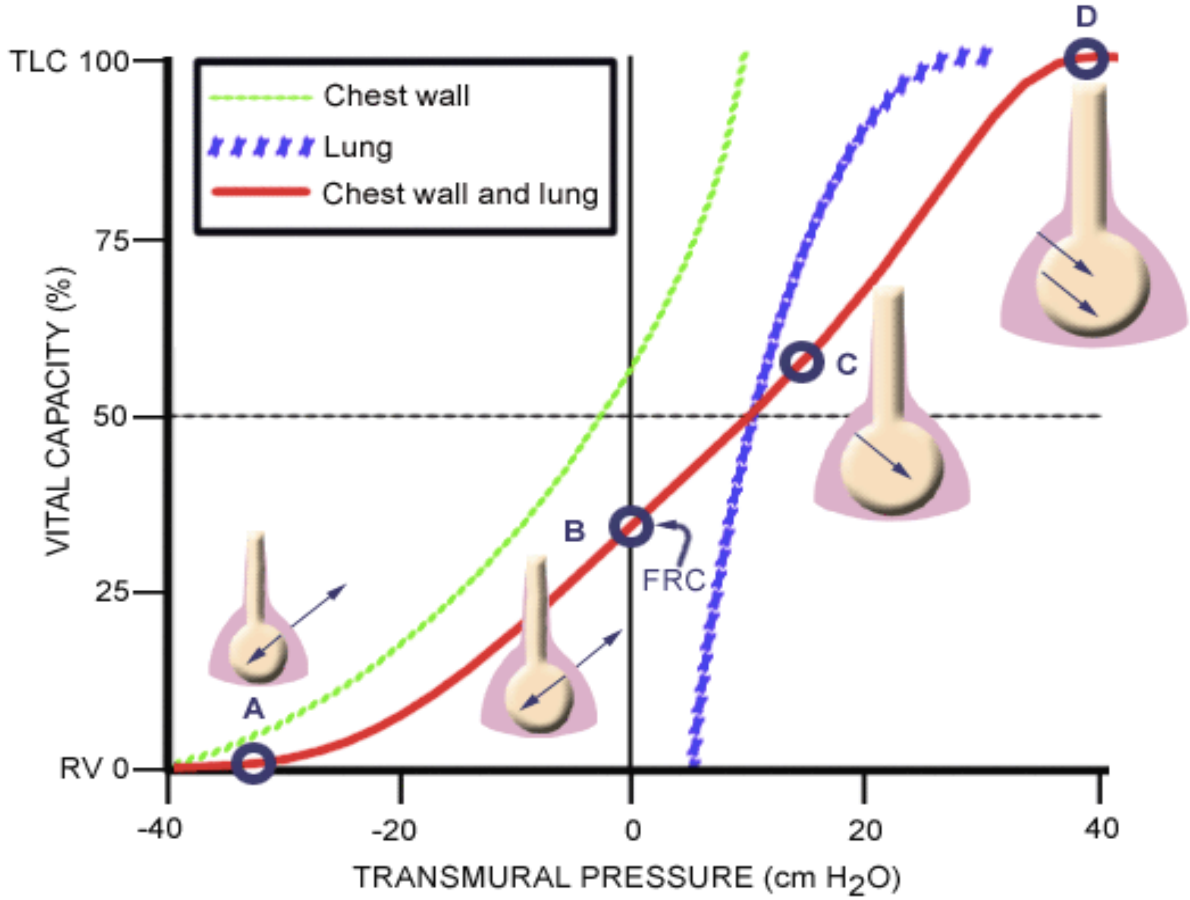
Point B: FRC is the volume at which the opposing recoil forces of the lungs & the chest wall balance. The inward recoil of the lungs (+5) is matched by the outward recoil of the chest wall (-5); the respiratory system is at rest (Prs=0)

Between B & 50 % VC (within the range of quiet tidal volume

Between Point C & D:

Between Point B & A:

Relaxation Static Pressure-Volume Curves



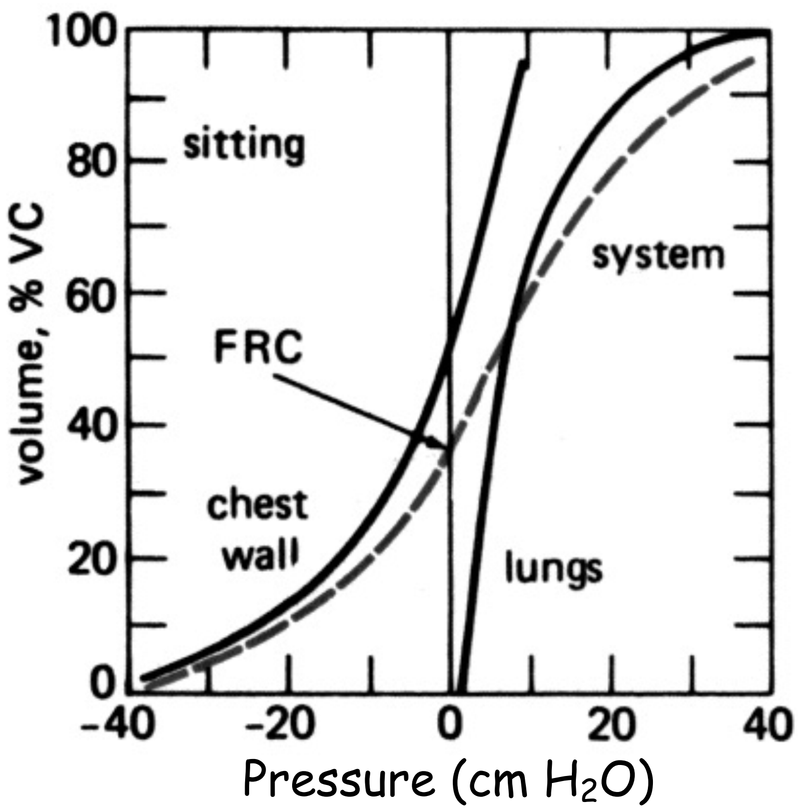
Point B: FRC is the volume at which the opposing recoil forces of the lungs & the chest wall balance. The inward recoil of the lungs (+5) is matched by the outward recoil of the chest wall (-5); the respiratory system is at rest (Prs=0)

Between B & 50 % VC (within the range of quiet tidal volume): The inward elastic recoil of the lungs is greater than outward recoil of the chest wall. Inspiration is active: muscles of inspiration contract to overcome the elastic recoil of the lungs. Expiration is passive, the result of inward lung recoil.

Between Point C & D: Both the lungs & chest wall recoil tendency is inward. Inspiratory muscles contract to overcome these two inward recoiling forces.

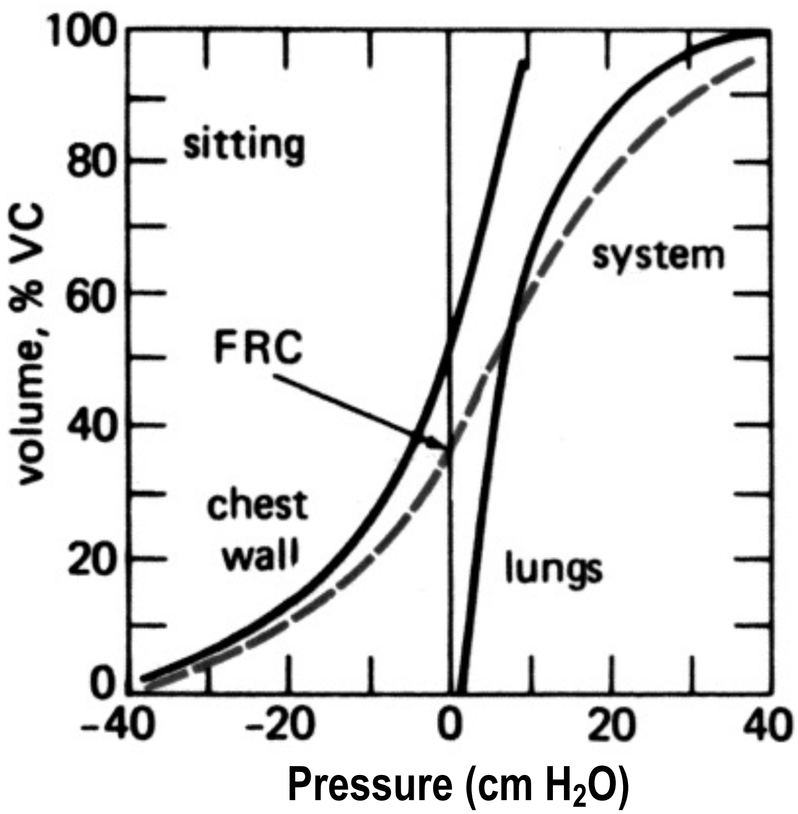
Between Point B & A: The outward recoil of the chest wall exceeds the inward recoil of the lungs. To deflate lungs to these volumes, expiratory muscles need to be recruited.

The Effect of Posture on the P-V Relationships

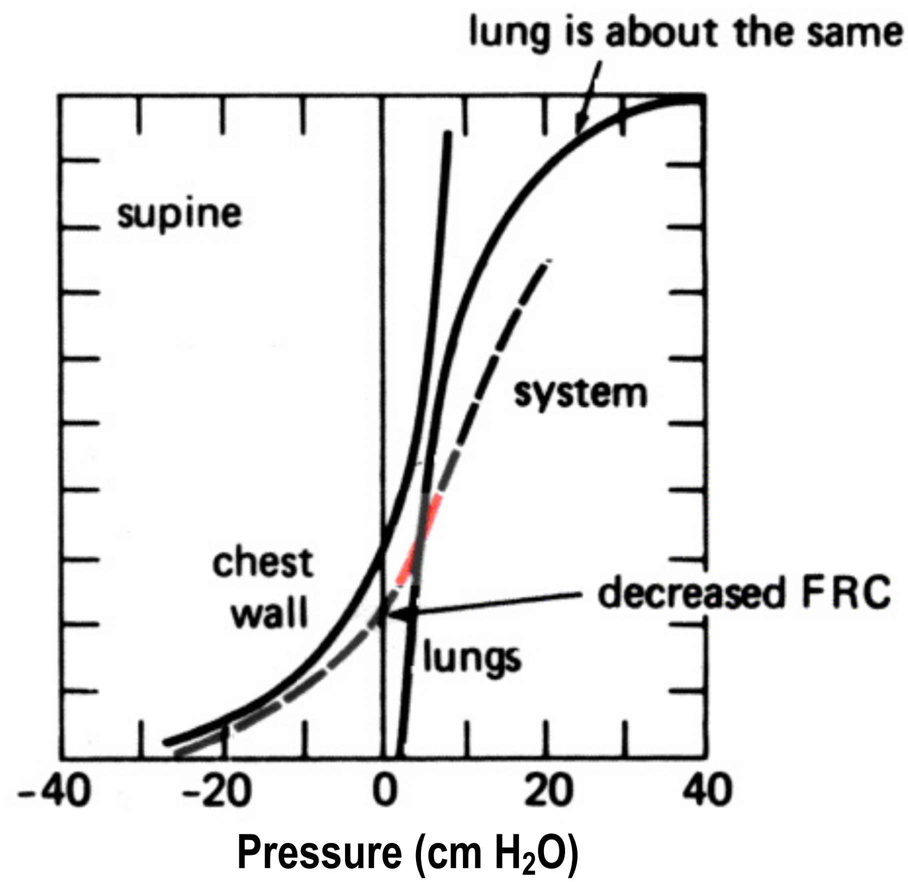


Sitting Position

The Effect of Posture on the P-V Relationships



Sitting



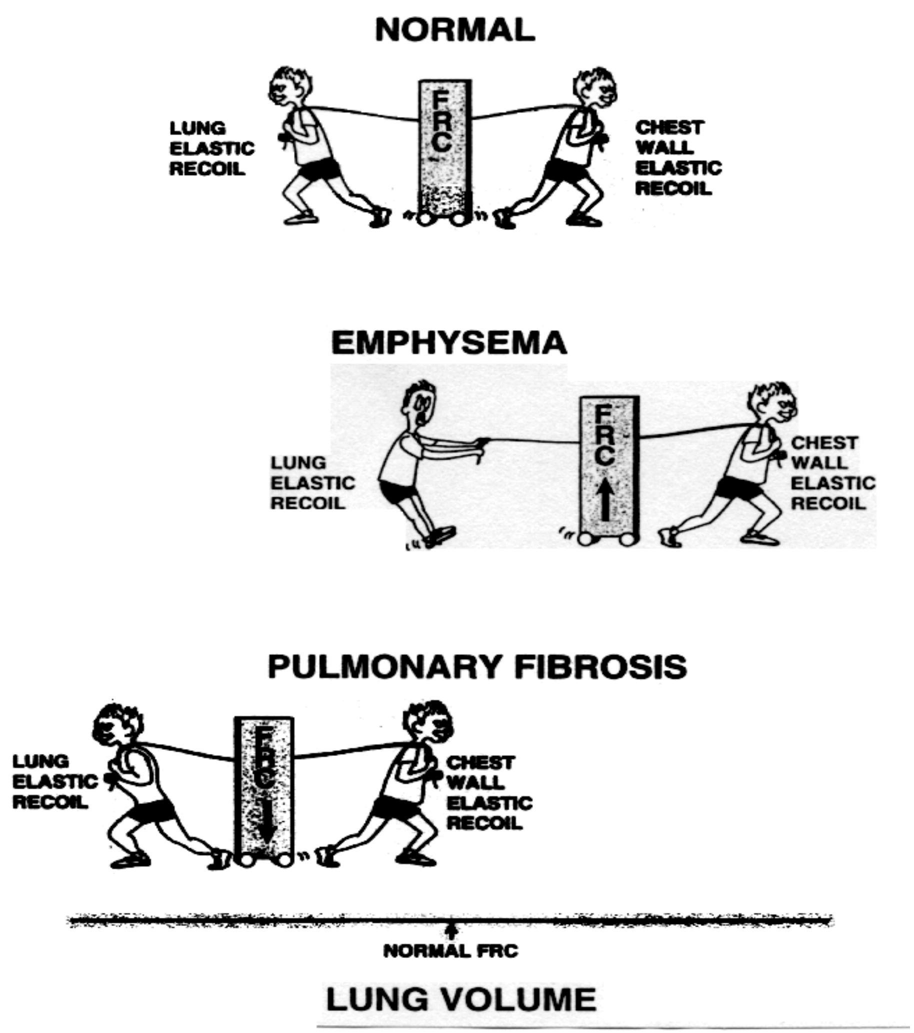
Supine

Predict the effect of __________ on FRC.

State the reasoning behind your prediction.

1. Obesity
2. Pregnancy
3. Bilateral paralysis of the diaphragm

Recall the Effect of Changes in Lung Compliance on FRC



SUMMARY

- Mechanical interactions between 2 elastic structures, the lungs & chest wall, determine lung volume.
- In order to inflate the lungs the inspiratory muscles must overcome 2 key factors: elastic recoil of the lungs & airways resistance.
- Elastic recoil of the lungs is inversely related to lung compliance.
- Lung compliance is determined by the P-V curve of the lungs. It is dependent on lung volume, tissue elasticity & alveolar surface tension.
- Surface tension is reduced by pulmonary surfactant.
- Pulmonary surfactant proteins aid in adsorption of surfactant to the air-liquid interface and function as components of the the innate immune activity at the alveolar surface.
- The compliance of the chest wall can be altered with changes in posture as well in disease states.
- Changes in the compliance of the lungs or the chest wall can alter FRC.