





11th Annual Dr. Ed Waits Respiratory Care Conference
June 21, 2023

CELLULAR RESPIRATION IN THE AEROBIC WORLD

AFTER A LONG BEGINNING ON AN ANAEROBIC PLANET

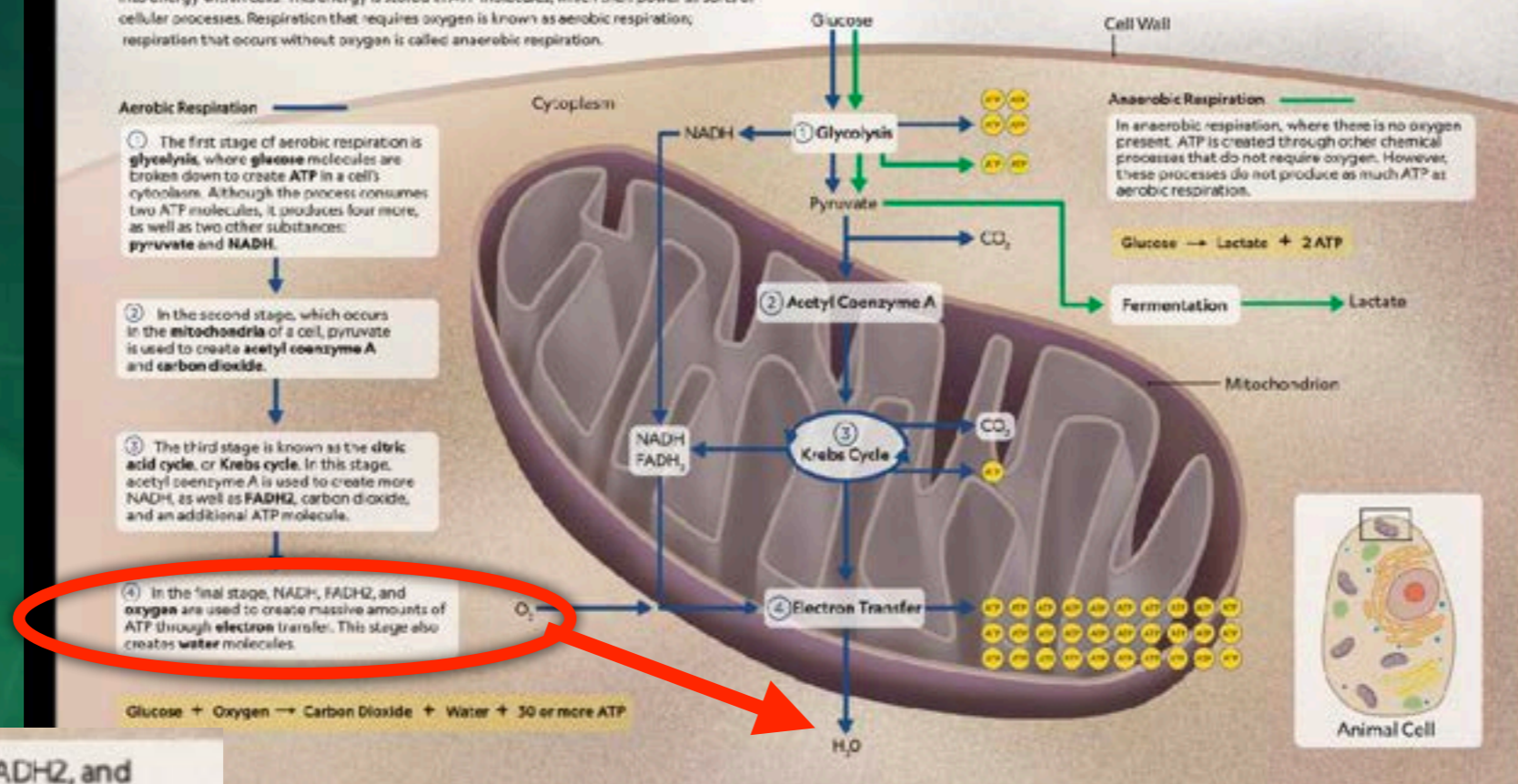
OXYGEN AND IRON

James R. Boogaerts, MD, PhD, FACC
UAB Division of Cardiovascular Disease



CELLULAR RESPIRATION

Cellular respiration is the process by which food, in the form of sugar (glucose), is transformed into energy within cells. This energy is stored in ATP molecules, which then power all sorts of cellular processes. Respiration that requires oxygen is known as aerobic respiration; respiration that occurs without oxygen is called anaerobic respiration.

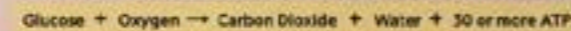
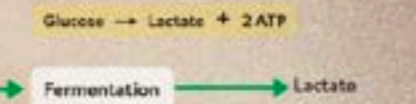


Aerobic Respiration

- 1 The first stage of aerobic respiration is **glycolysis**, where **glucose** molecules are broken down to create **ATP** in a cell's cytoplasm. Although the process consumes two ATP molecules, it produces four more, as well as two other substances: **pyruvate** and **NADH**.
- 2 In the second stage, which occurs in the **mitochondria** of a cell, pyruvate is used to create **acetyl coenzyme A** and **carbon dioxide**.
- 3 The third stage is known as the **tricarbalic acid cycle**, or **Krebs cycle**. In this stage, acetyl coenzyme A is used to create more **NADH**, as well as **FADH₂**, carbon dioxide, and an additional **ATP** molecule.
- 4 In the final stage, **NADH**, **FADH₂**, and **oxygen** are used to create massive amounts of **ATP** through **electron transfer**. This stage also creates **water** molecules.

Anaerobic Respiration

In anaerobic respiration, where there is no oxygen present, ATP is created through other chemical processes that do not require oxygen. However, these processes do not produce as much ATP as aerobic respiration.

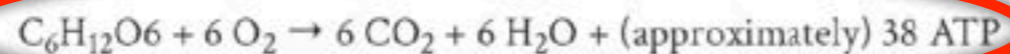


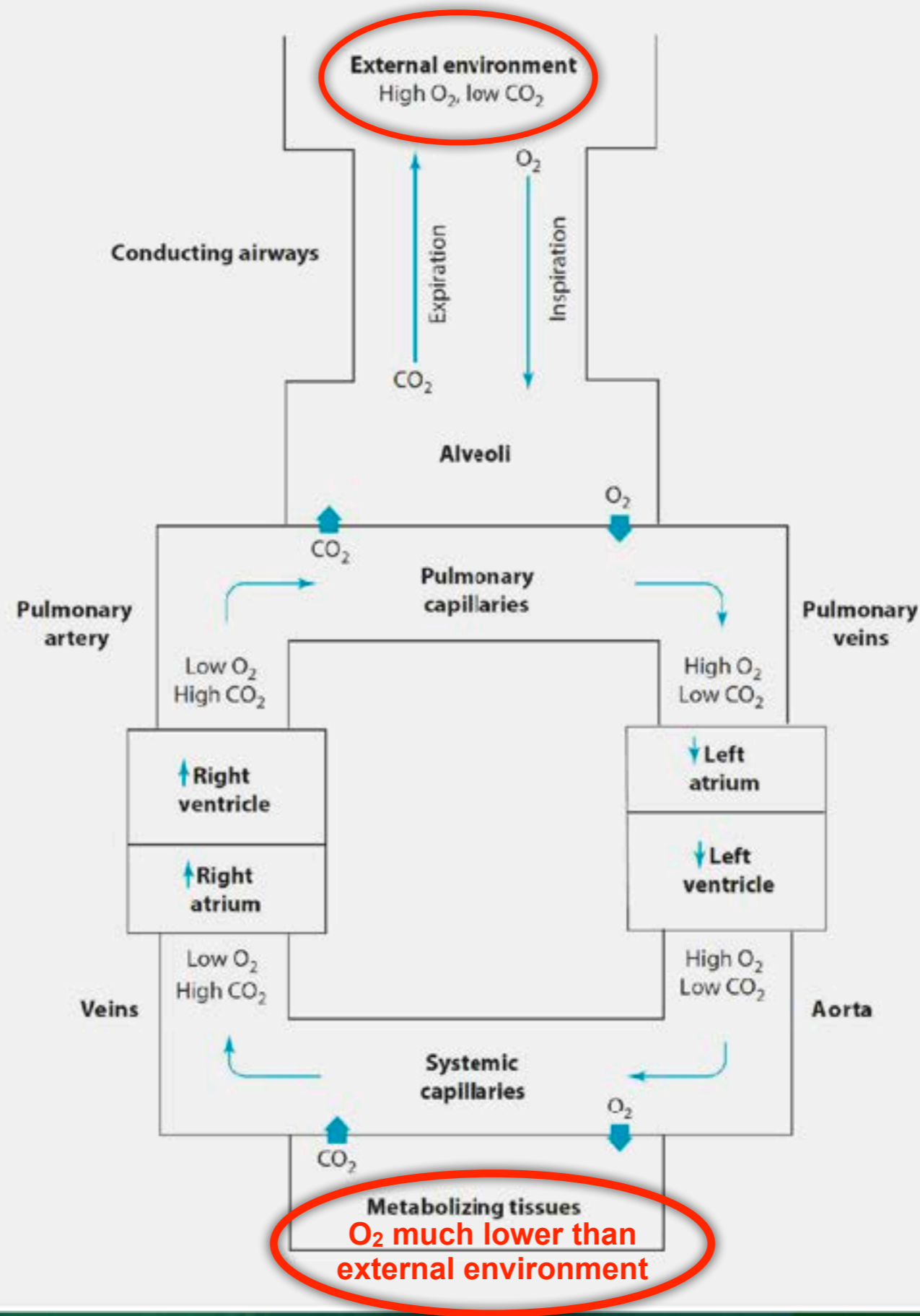
4 In the final stage, **NADH**, **FADH₂**, and **oxygen** are used to create massive amounts of **ATP** through **electron transfer**. This stage also creates **water** molecules.

SOURCE

AEROBIC RESPIRATION

Aerobic respiration requires oxygen. This is the reason why we breathe oxygen in from the air. This type of respiration efficiently releases a large amount of energy from glucose that can be stored as ATP. Aerobic respiration happens all the time in animals and plants, where most of the reactions occur in the mitochondria. Even some prokaryotes can perform aerobic respiration (although since prokaryotes don't contain mitochondria, the reactions are slightly different). The overall chemical formula for aerobic respiration can be written as:

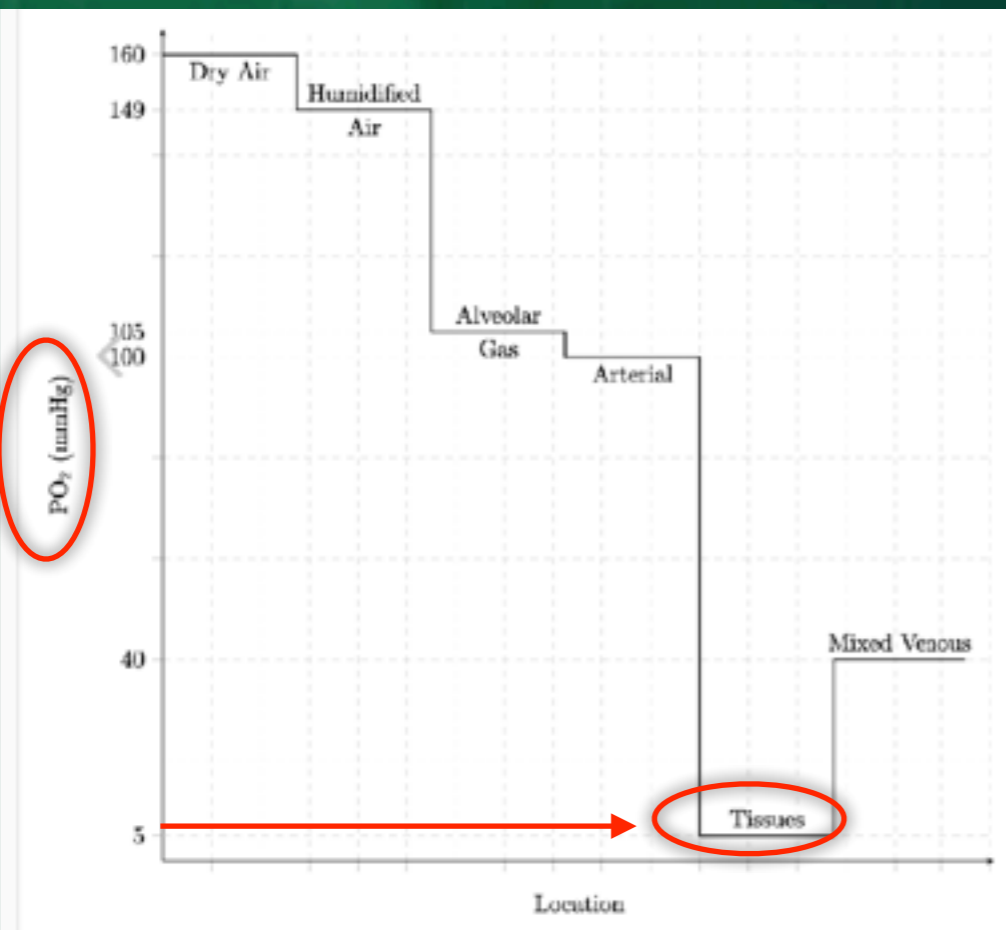




Oxygen Cascade

The oxygen cascade describes the transfer of oxygen from air to mitochondria.

- In each step of the cascade the P_{aO_2} falls. It demonstrates that oxygen delivery to tissues relies on the **passive transfer** of gas down **partial pressure gradients**.
- The steps of the cascade are:
 - Dry atmospheric gas
 - Humidified tracheal gas
 - Alveolar gas
 - Arterial blood
 - Mitochondria**
 - Venous blood



Atmospheric Gas

Atmospheric partial pressure of oxygen is a function of barometric pressure and the FiO_2 :

- $PO_2 = P_B \times FiO_2$, where:
 - P_B is 760mmHg
 - FiO_2 is 0.21
- Therefore, $PO_2 = 160\text{mmHg}$

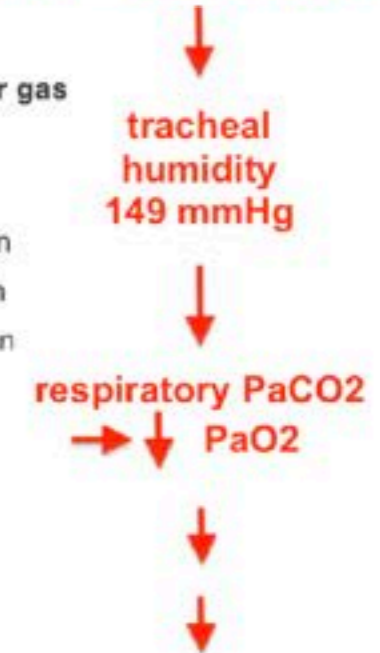
P_{iN_2} : 590 mmHg
 P_{iO_2} : 160 mmHg
 P_{iAr} : 7 mmHg
 P_{iCO_2} : 0.3 mmHg
 P_{iO_2} : 160 mmHg

Alveolar Gas

Ideal alveolar PO_2 is calculated using the alveolar gas equation:

$$P_{AO_2} = P_iO_2 - \frac{P_aCO_2}{R} + F, \text{ where:}$$

- P_{AO_2} is the alveolar partial pressure of oxygen
- P_iO_2 is the inspired partial pressure of oxygen
- P_aCO_2 is the arterial partial pressure of carbon dioxide
- R is the respiratory quotient, where $R = \frac{\text{Volume of } CO_2 \text{ produced}}{\text{Volume of } O_2 \text{ consumed}}$



Arterial Blood

- Normal arterial PO_2 is 100mmHg
 P_{aO_2} : 100 mmHg

Mitochondria

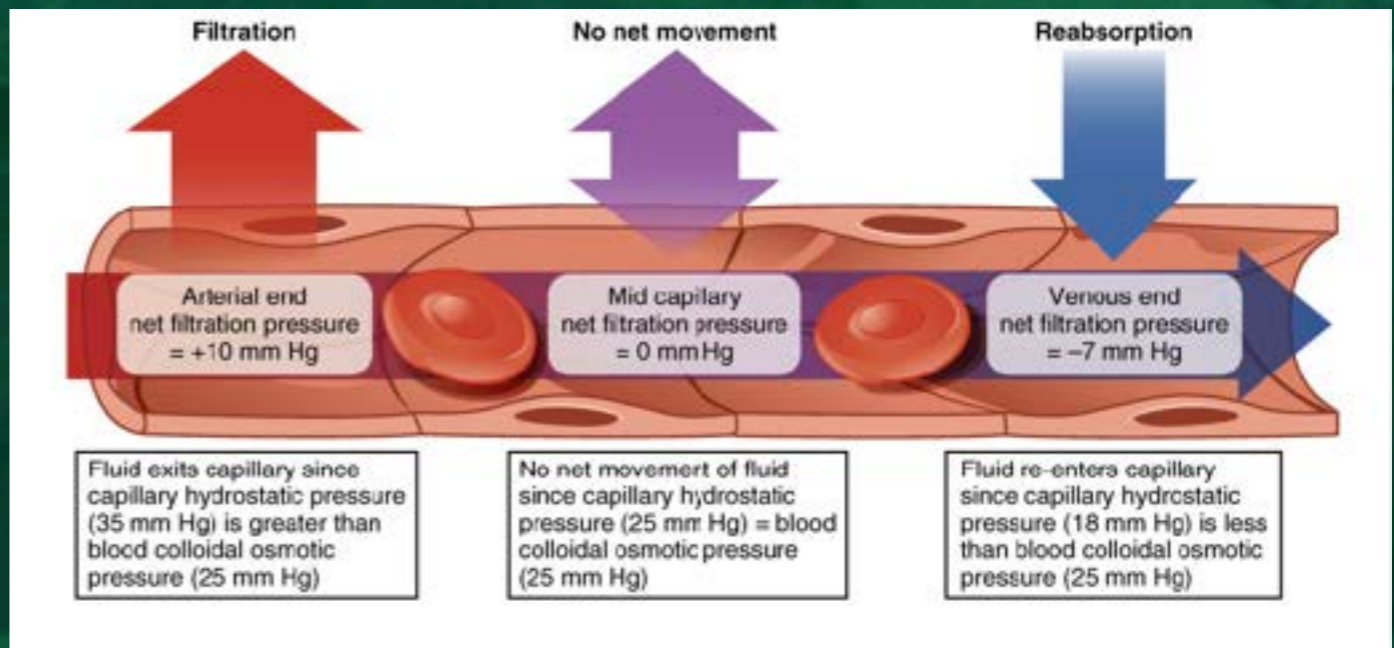
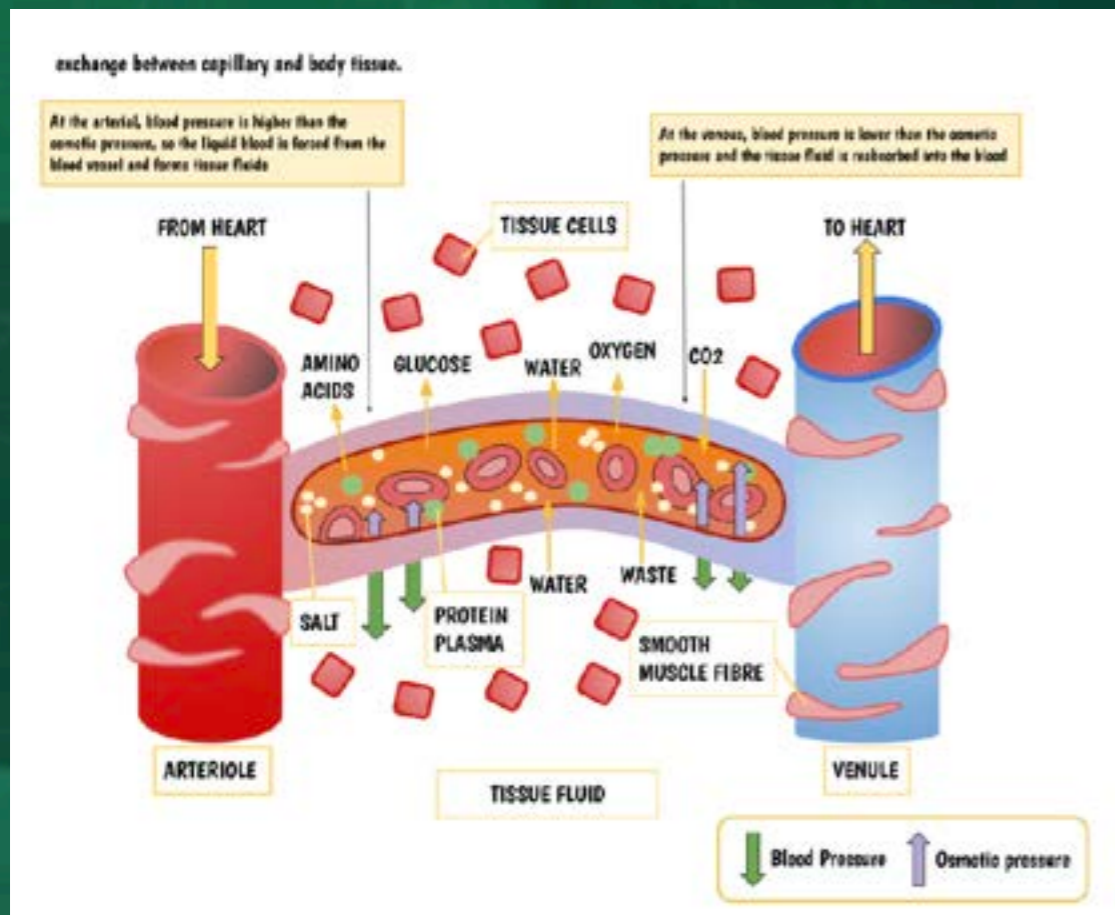
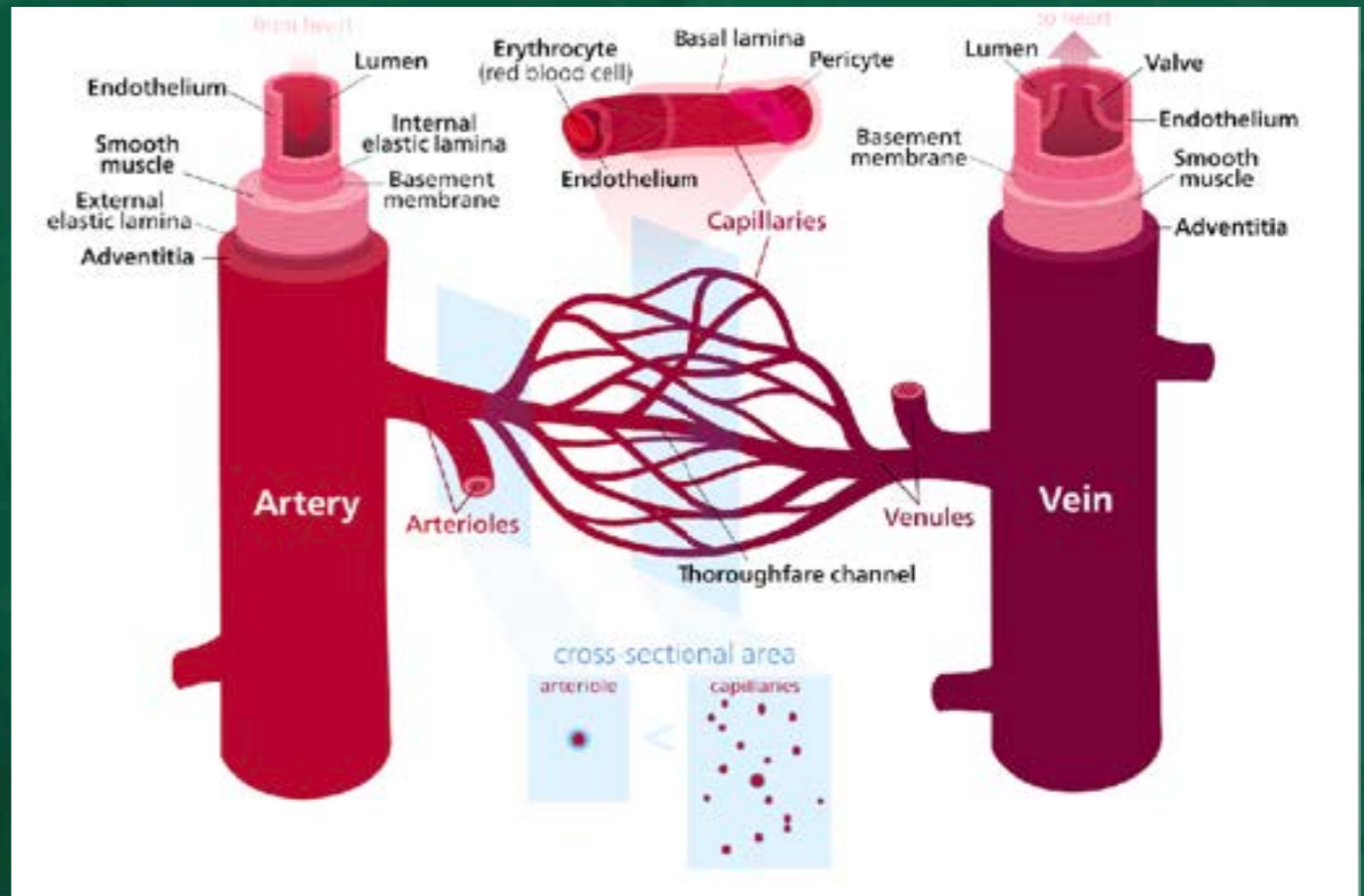
- PO_2 varies with metabolic activity, but typically quoted as 5mmHg
- The **Pasteur point** is the partial pressure of oxygen at which oxidative phosphorylation ceases, and is ~1mmHg

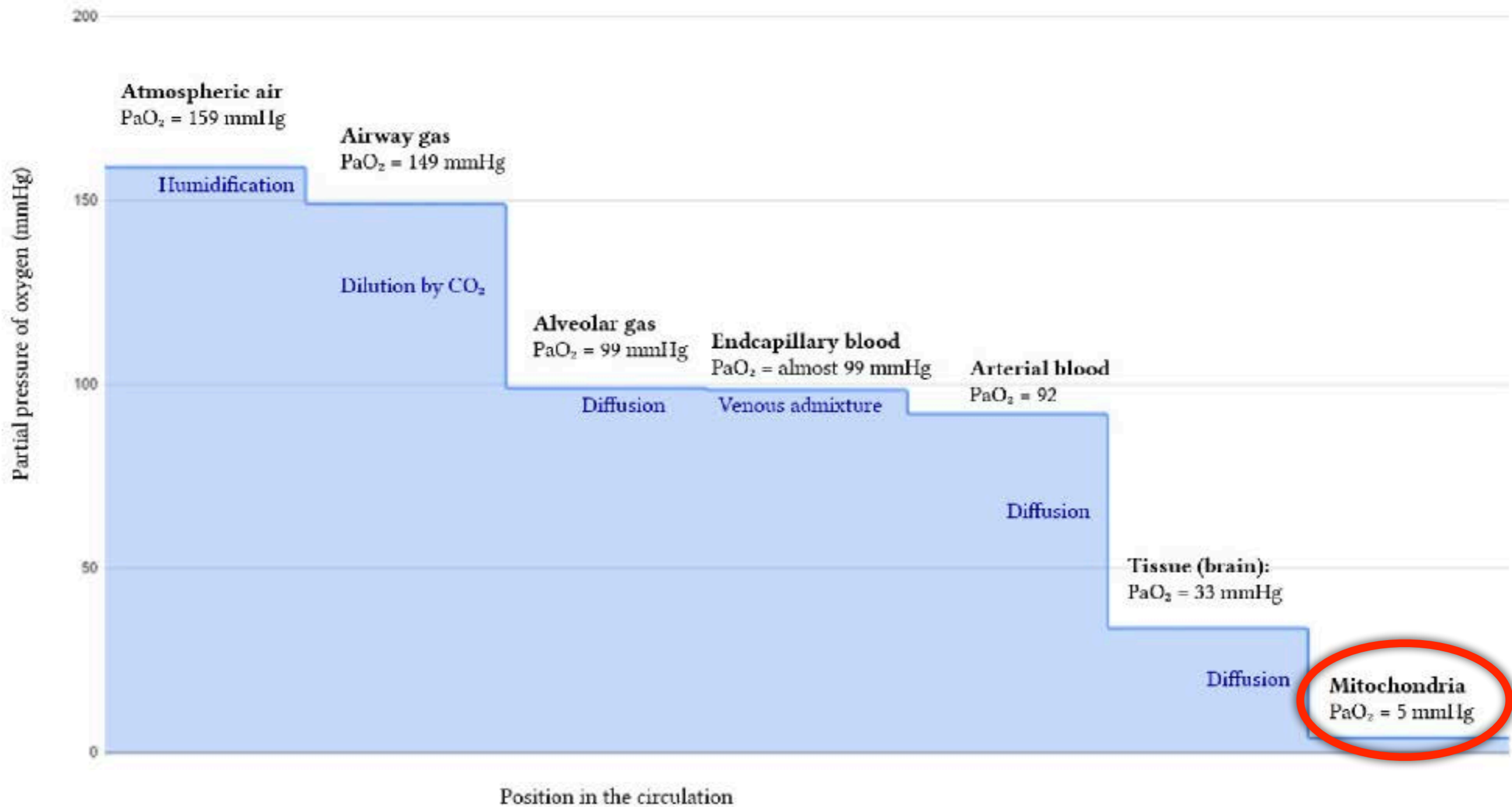
P_{aO_2} : 5 mmHg

Venous Blood

- PO_2 is greater than mitochondrial PO_2 . Mixed venous blood typically quoted as 40mmHg.
- Higher than mitochondria as not all arterial blood travels through capillary beds

P_{aO_2} : 40mmHg





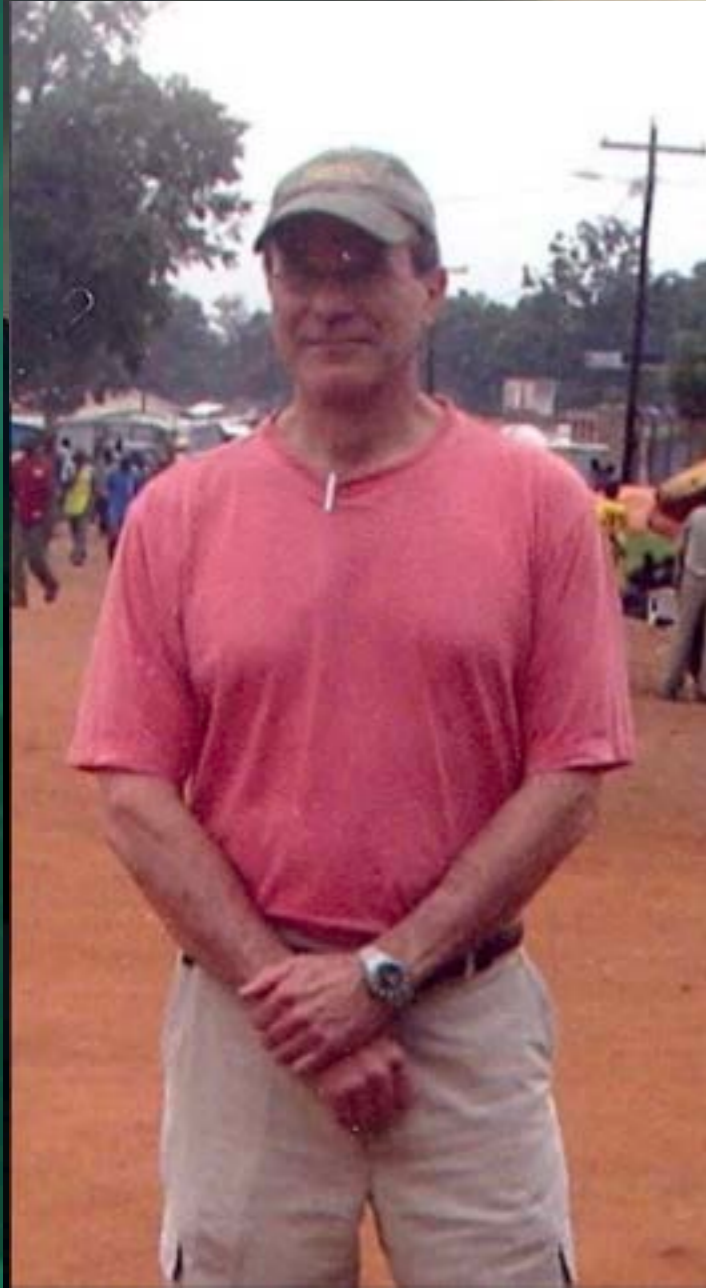
10th Annual Dr. Louis S. Pappas Educational Seminar
June 10, 2023

CELLULAR RESPIRATION IN THE AEROBIC WORLD

AFTER A LONG BEGINNING ON AN ANAEROBIC PLANET

OXYGEN AND IRON

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Dr. Pappas especially loved hiking and fishing in the Grand Tetons and Glacier National Park.





- ▶ Chapter 1 Function and Structure of the Respira...
- ▶ Chapter 2 Mechanics of Breathing
- ▶ Chapter 3 Alveolar Ventilation
- ▶ Chapter 4 Blood Flow to the Lung
- ▶ Chapter 5 Ventilation-Perfusion Relationships
- ▶ Chapter 6 Diffusion of Gases and Interpretation...
- ▶ Chapter 7 Transport of Oxygen and Carbon Dio...
- ▶ Chapter 8 Acid-Base Balance
- ▶ Chapter 9 Control of Breathing
- ▶ Chapter 10 Nonrespiratory Functions of the Lung
- ▶ Chapter 11 The Respiratory System Under Stress

Michael G. Levitzky, PhD
Emeritus Professor of Physiology
Louisiana State University Health Sciences Center
New Orleans, Louisiana

Pulmonary Physiology, Tenth Edition

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10th edition

Pulmonary Physiology

Michael G. Levitzky

McGraw Hill **LANGGE**

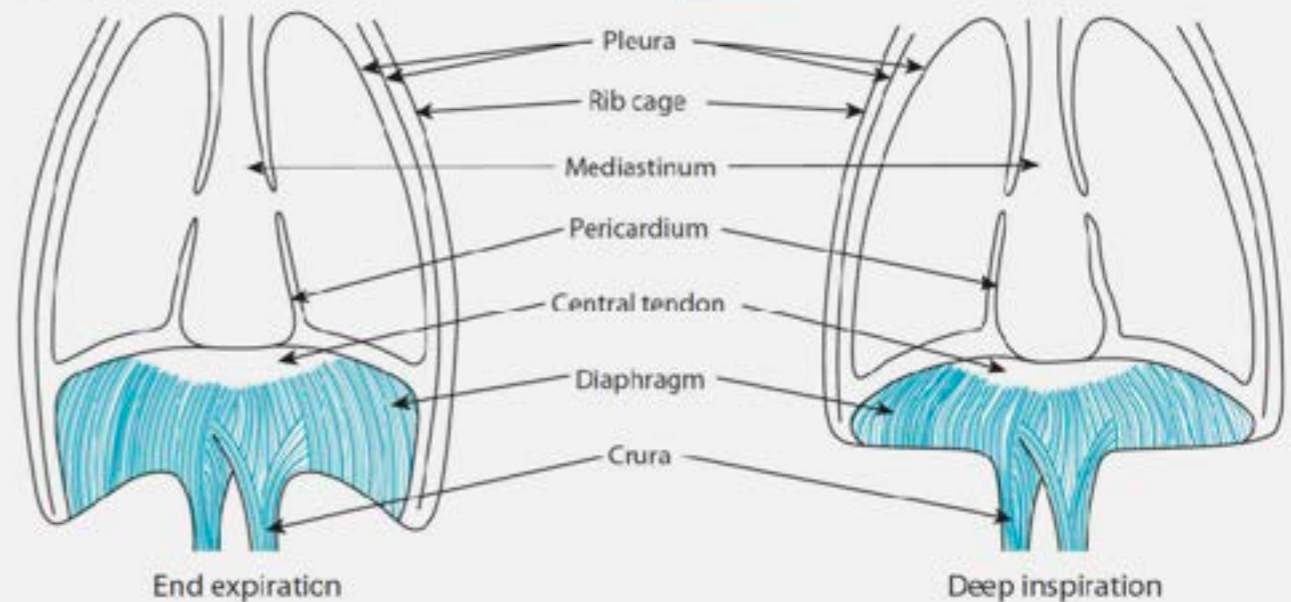


Figure 2-3. Illustration of the actions of diaphragmatic contraction in expanding the thoracic cavity.

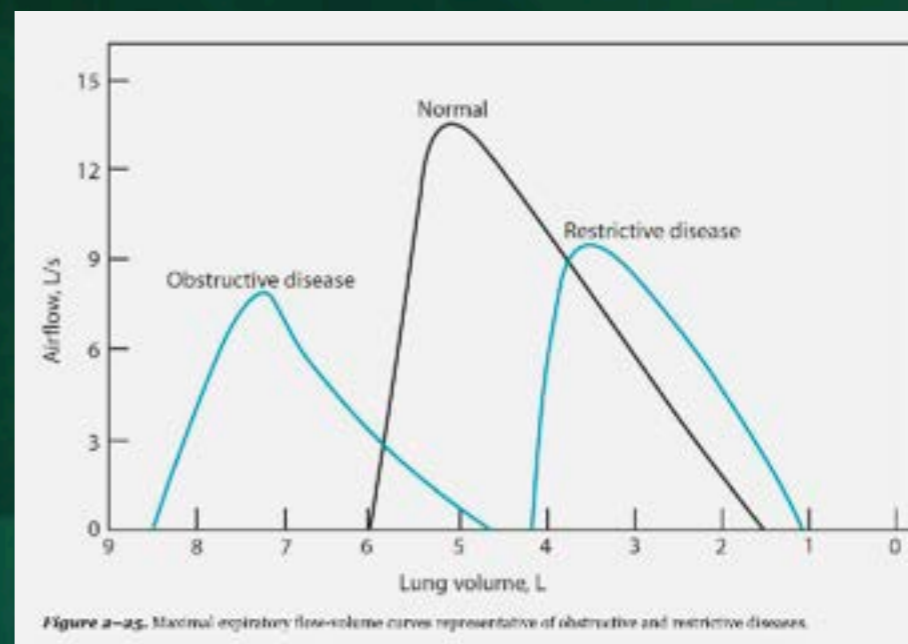
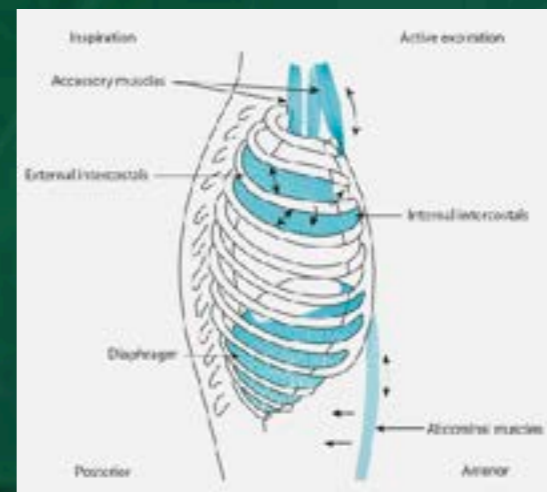


Figure 2-25. Maximal respiratory flow-volume curves representative of obstructive and restrictive diseases.

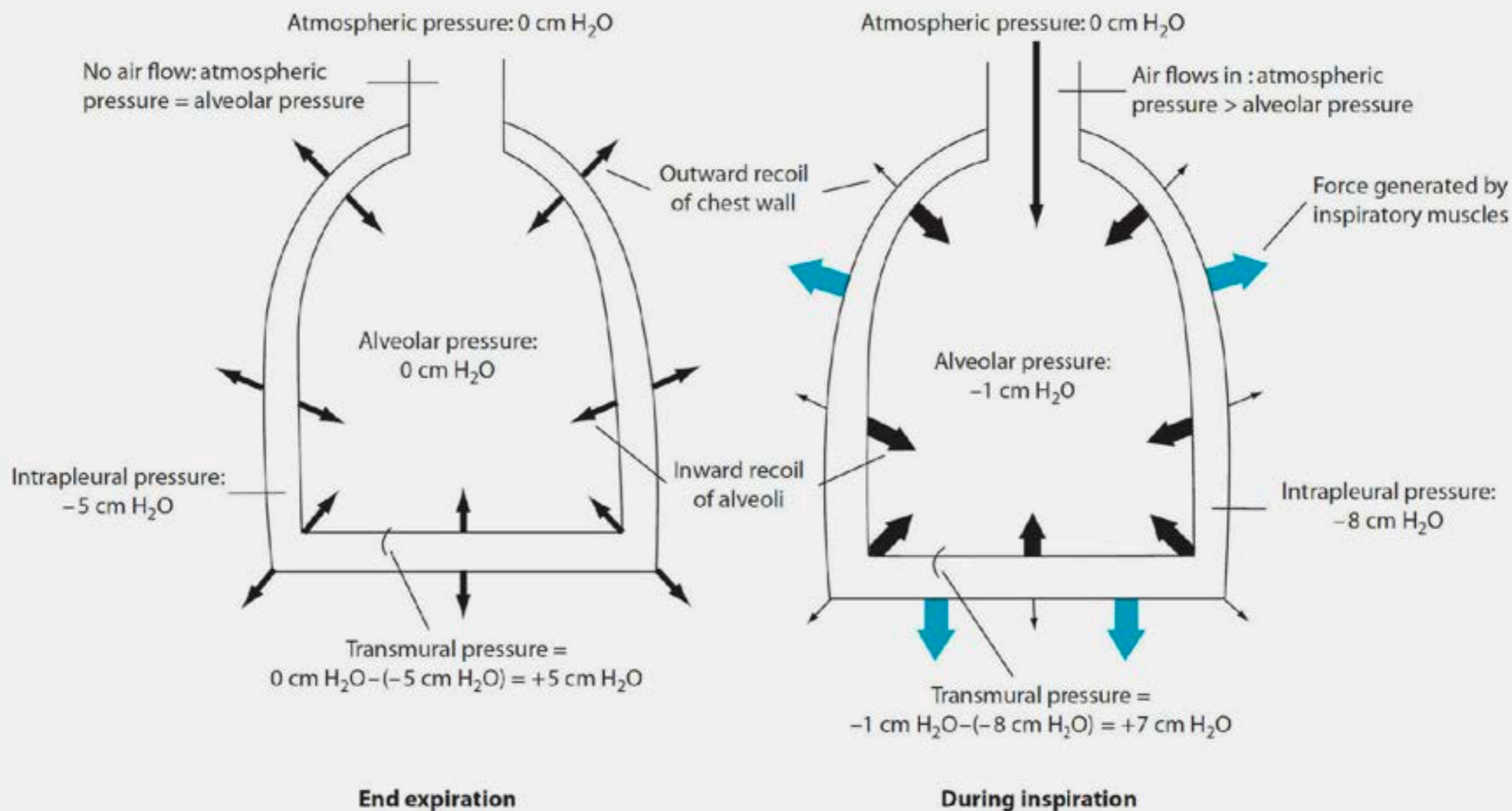


Figure 2-1. Representation of the interaction of the lung and chest wall. *Left:* At end expiration, the muscles of respiration are relaxed. The inward elastic recoil of the lung is balanced by the outward elastic recoil of the chest wall. Intrapleural pressure is -5 cm H₂O; alveolar pressure is 0. The transmural pressure difference across the alveolus is therefore 0 cm H₂O - (-5 cm H₂O), or 5 cm H₂O. Since alveolar pressure is equal to atmospheric pressure, no airflow occurs. *Right:* During inspiration, contraction of the muscles of inspiration causes intrapleural pressure to become more negative. The transmural

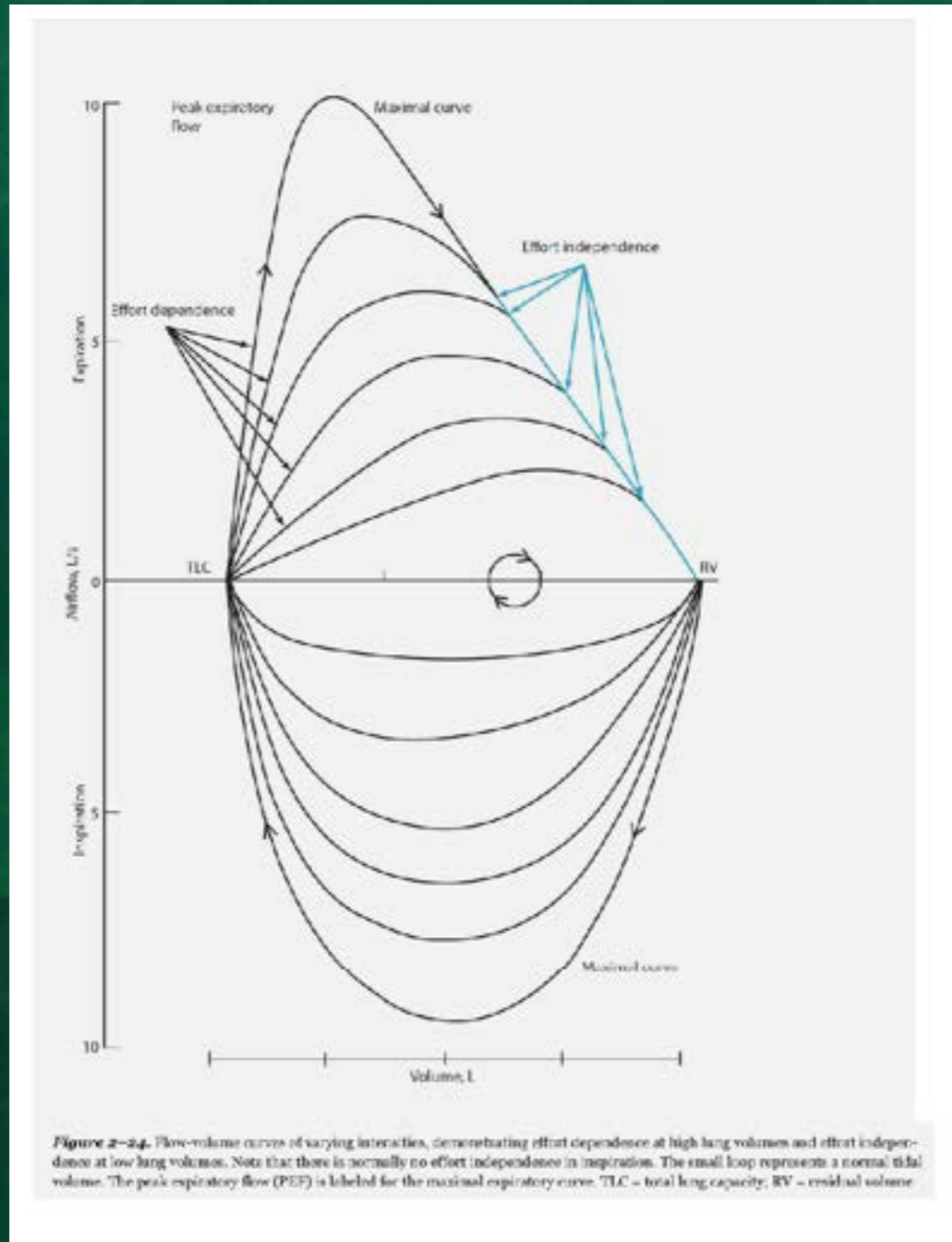
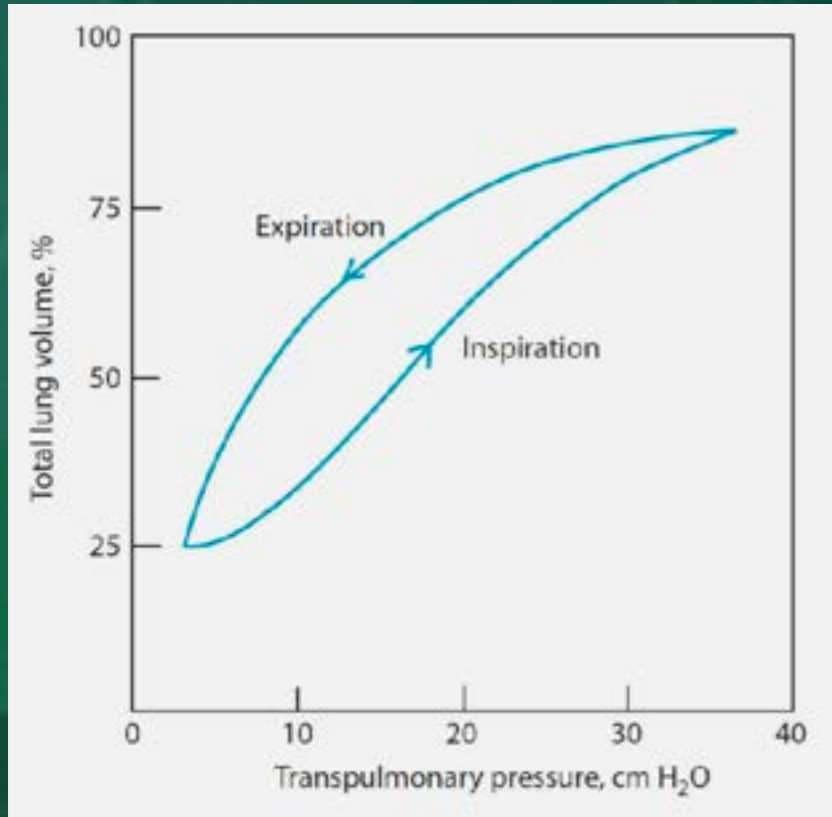
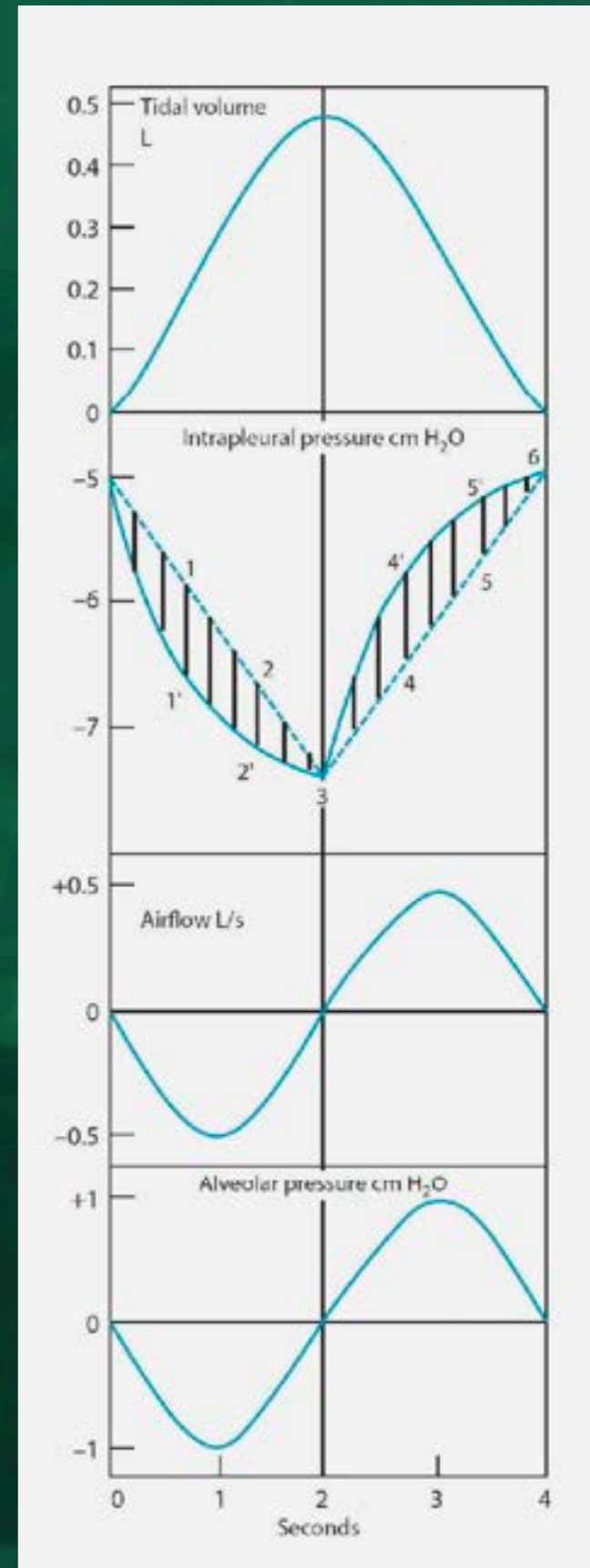


Figure 2-24. Flow-volume curves of varying intensities, demonstrating effort dependence at high lung volumes and effort independence at low lung volumes. Note that there is normally no effort independence in inspiration. The small loop represents a normal tidal volume. The peak expiratory flow (PEF) is labeled for the maximal expiratory curve. TLC = total lung capacity; RV = residual volume.



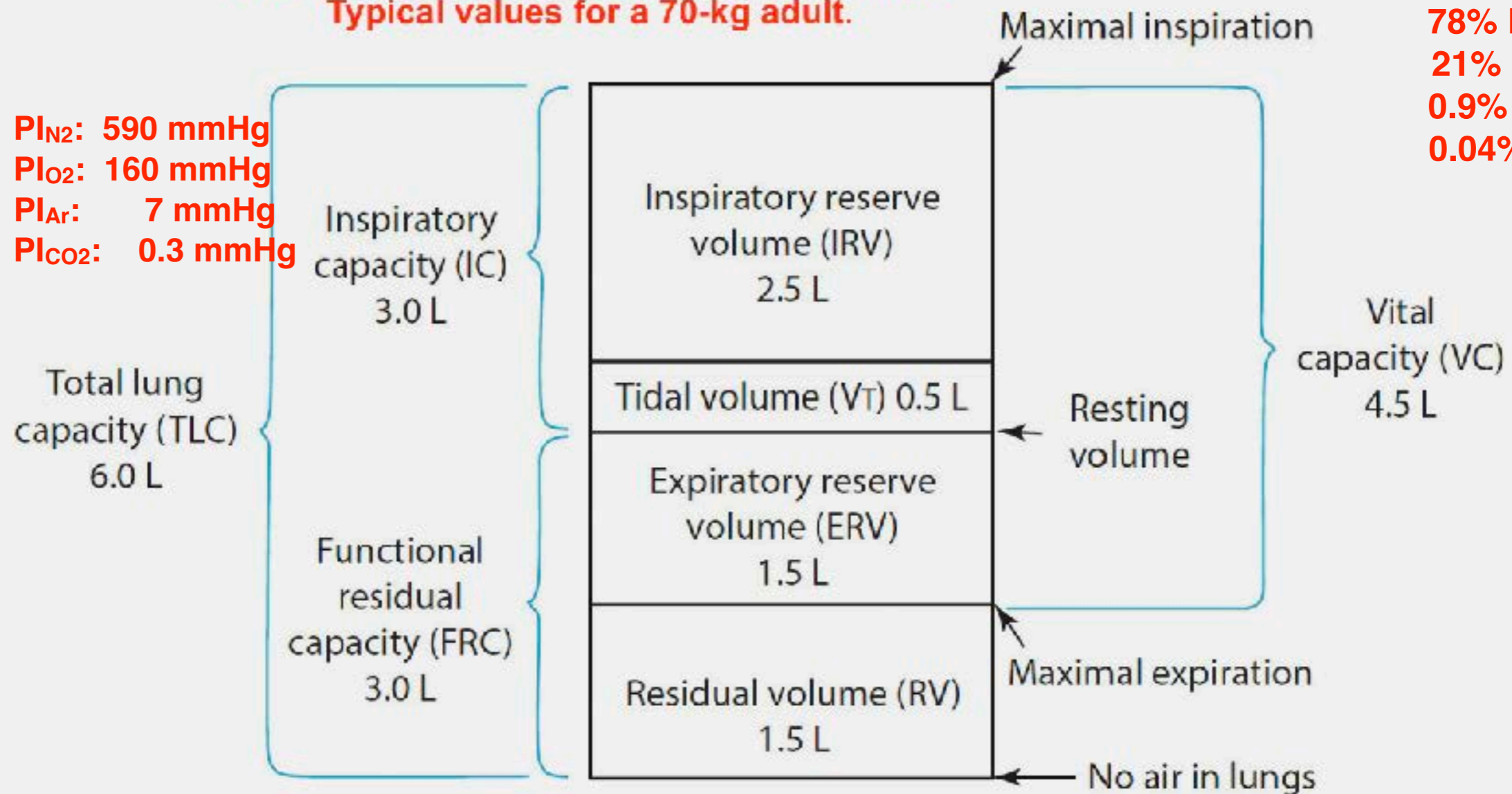
Pulmonary Physiology, Tenth Edition
 by Michael Levitzky | Aug 30, 2022

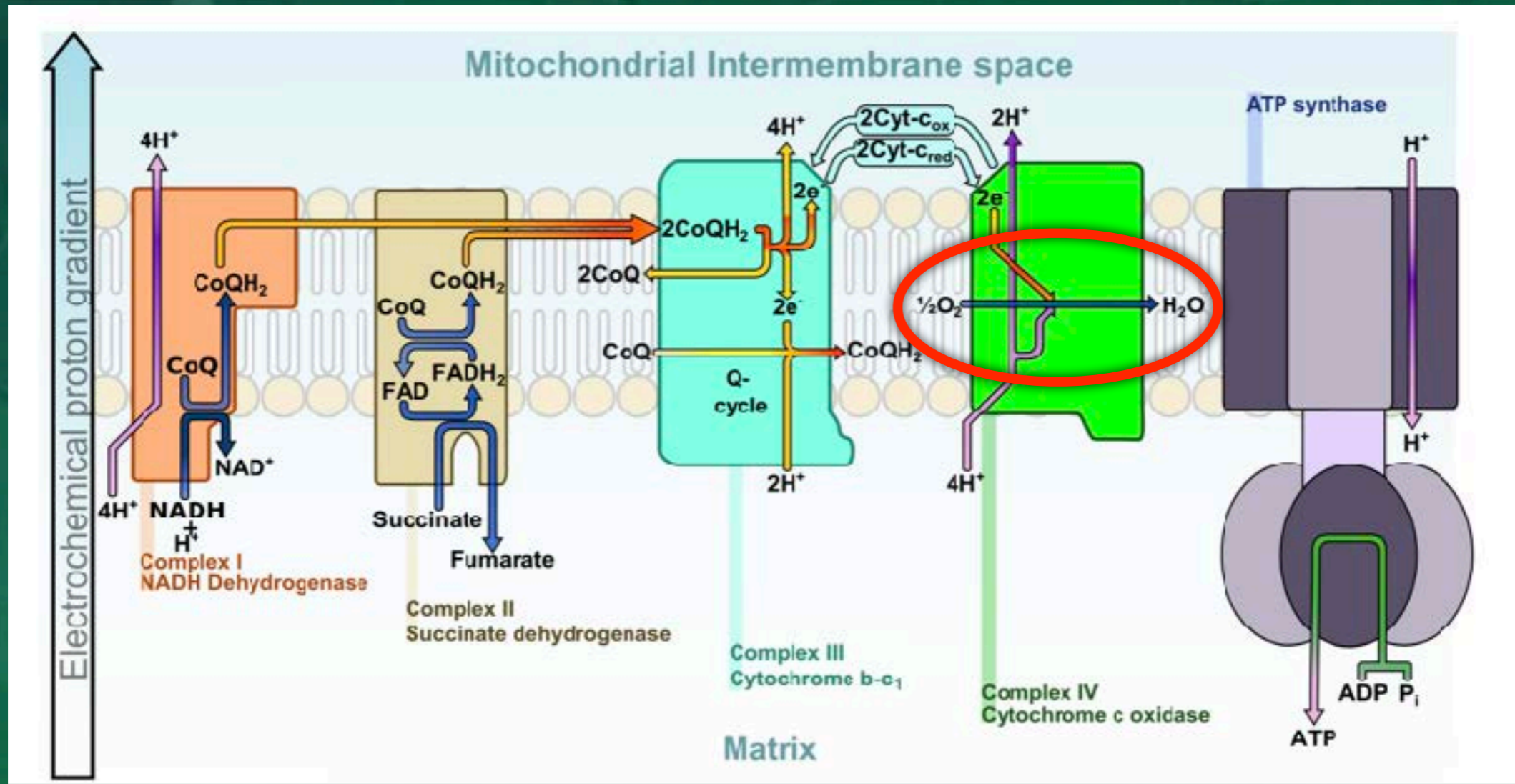
**The standard lung volumes and capacities.
Typical values for a 70-kg adult.**

Current atmosphere:

**78% N₂
21% O₂
0.9% Ar
0.04% CO₂**

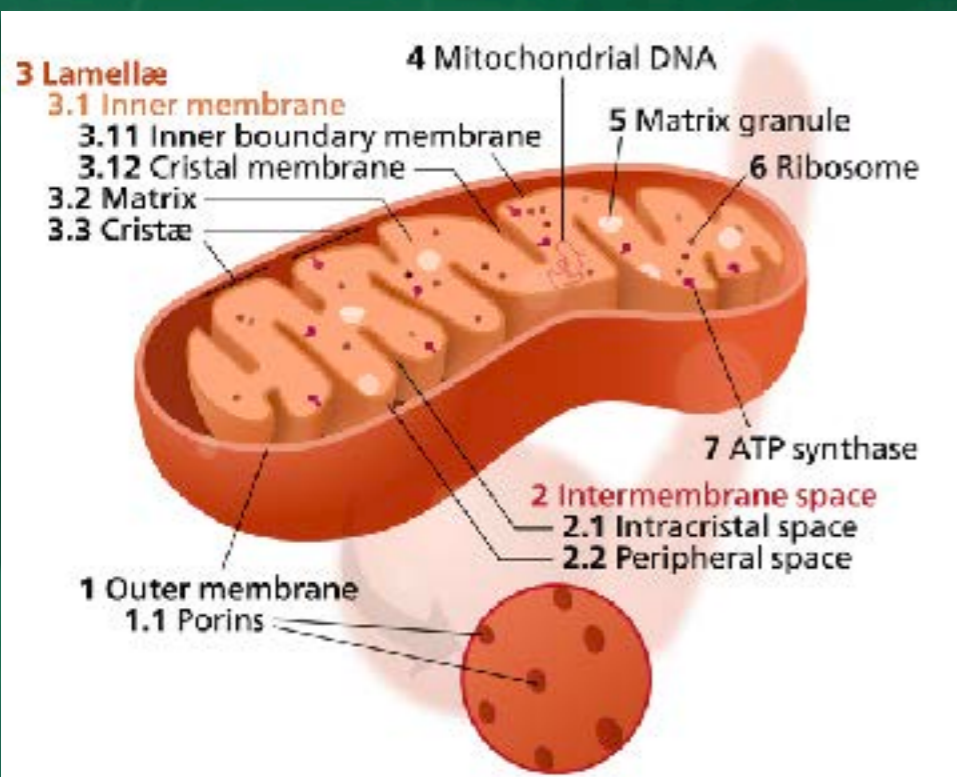
**P_IN₂: 590 mmHg
P_IO₂: 160 mmHg
P_IAr: 7 mmHg
P_ICO₂: 0.3 mmHg**





Oxygen is not only required for oxidative phosphorylation but also serves as the essential substrate for the formation of reactive oxygen species

Engulfment of aerobic proteobacteria by primordial anaerobic eukaryotes may have provided protection against the toxicity of increasing oxygen in the primordial atmosphere.



The Oxygen Cascade During Exercise in Health and Disease



Paolo B. Dominelli, PhD; Chad C. Wiggins, PhD; Tuhin K. Roy, PhD, MD; Timothy W. Secomb, PhD; Timothy B. Curry, PhD, MD; and Michael J. Joyner, MD

Abstract

The oxygen transport cascade describes the physiological steps that bring atmospheric oxygen into the body where it is delivered and consumed by metabolically active tissue. As such, the oxygen cascade is fundamental to our understanding of exercise in health and disease. Our narrative review will highlight each step of the oxygen transport cascade from inspiration of atmospheric oxygen down to mitochondrial consumption in both healthy active males and females along with clinical conditions. We will focus on how different steps interact along with principles of homeostasis, physiological redundancies, and adaptation. In particular, we highlight some of the parallels between elite athletes and clinical conditions in terms of the oxygen cascade.

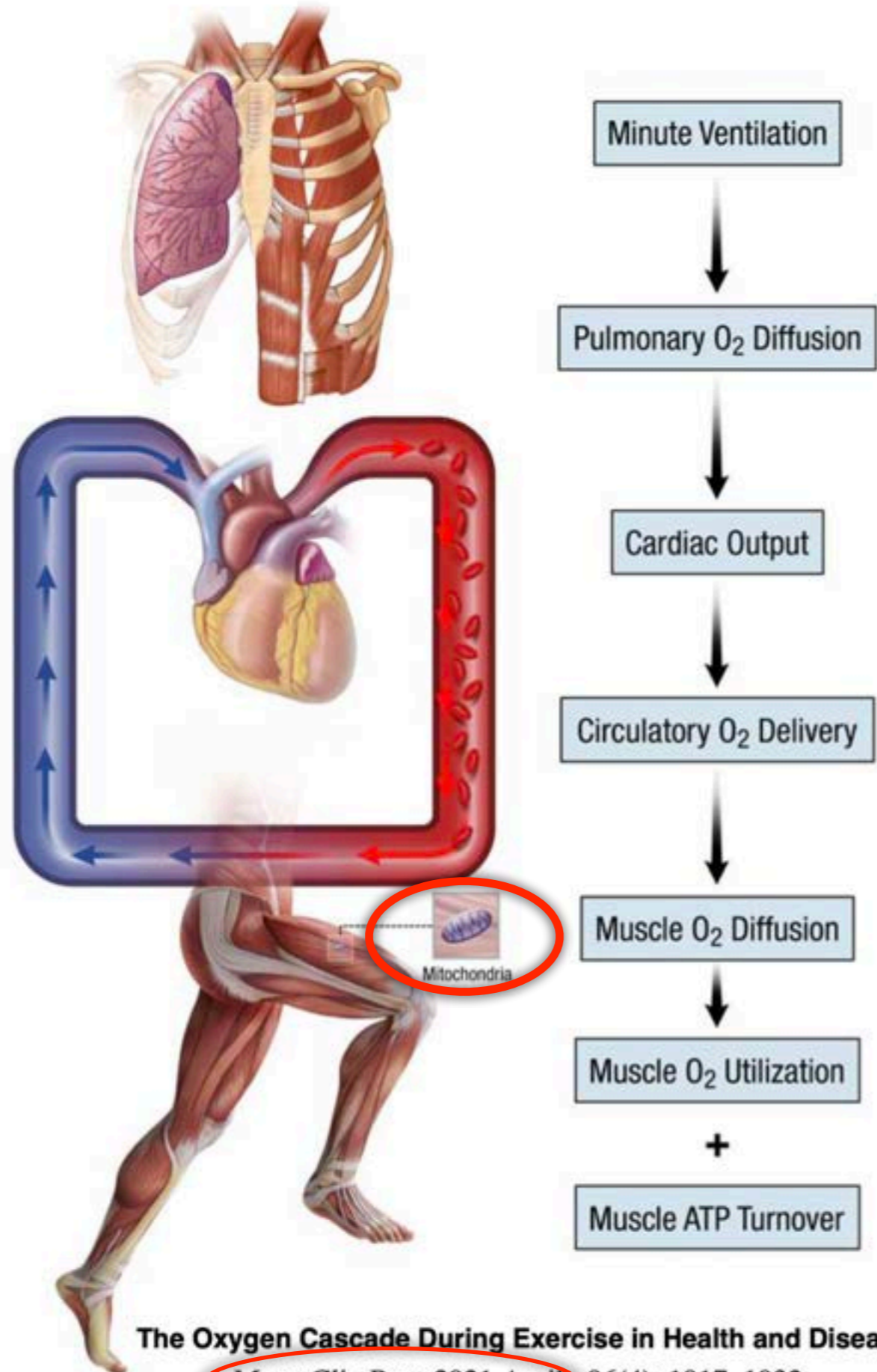
© 2020 Mayo Foundation for Medical Education and Research • Mayo Clin Proc. 2021;96(4):1017-1032

In the era of molecular biology it is easy to overlook the central role that the oxygen molecule plays in life. In complex organisms, where most cells are anatomically remote from atmospheric oxygen, a transport and gas exchange system is required to move oxygen from the air to the tissues and supports the continuous generation of adenosine triphosphate via oxidative metabolism. To defend whole body homeostasis, this system must be robust enough to sustain vast increases in oxidative metabolism during exercise, survive at high altitude, and — at the opposite end of the homeostatic spectrum — withstand substantial insults to key elements of the system associated with disease. In this review, we will follow the movement of oxygen from the air to the tissues and use examples ranging from elite athletes, rare patients, and comparative biology to show key principles of oxygen transport in humans. The impressive adaptive nature of the cardiopulmonary system will be emphasized and the redundant nature of physiological control mechanisms and related anatomical design features will be highlighted.

THE PROBLEM

The partial pressure of oxygen in air at sea level is ~150 mm Hg, but in the mitochondria of exercising skeletal muscle the partial pressure of oxygen can be ~100-fold lower without significant engagement of anaerobic energy metabolism. Thus, the question is, how does this happen and what systems are engaged as it occurs? In this context, it is also important to consider the range of oxygen consumption that can be seen in humans. In healthy young adults, resting metabolic rate is approximately $3.5 \text{ mL O}_2 \cdot \text{kg}^{-1}$ of body weight $\cdot \text{min}^{-1}$ and it can increase to more than $90 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in at least some of the most aerobically trained elite athletes.¹ At the opposite end of the O_2 uptake spectrum, even modest metabolic rates require physiological redundancies to be engaged in patients with diseases that hinder the ability to take up, transfer, and utilize oxygen. Notable examples include marked tachypnea or tachycardia even during very modest levels of exercise in patients with diseases, such as chronic obstructive pulmonary disease or congestive heart failure, along with a marked redistribution of blood flow away from inactive tissues to the active muscles.²

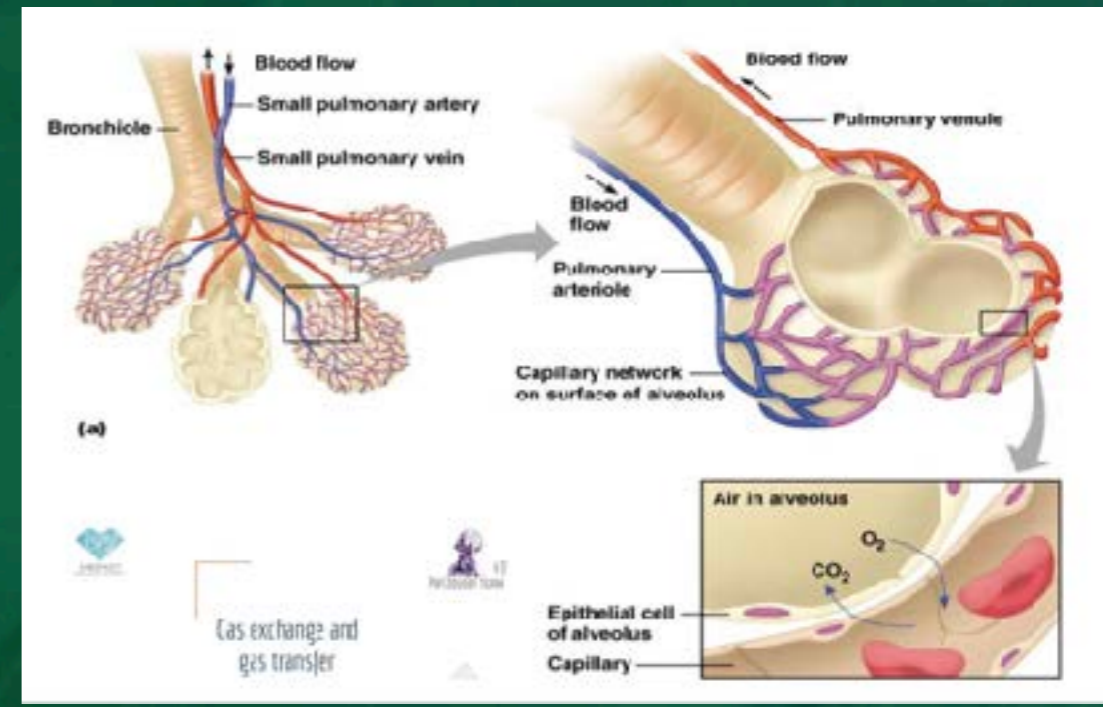
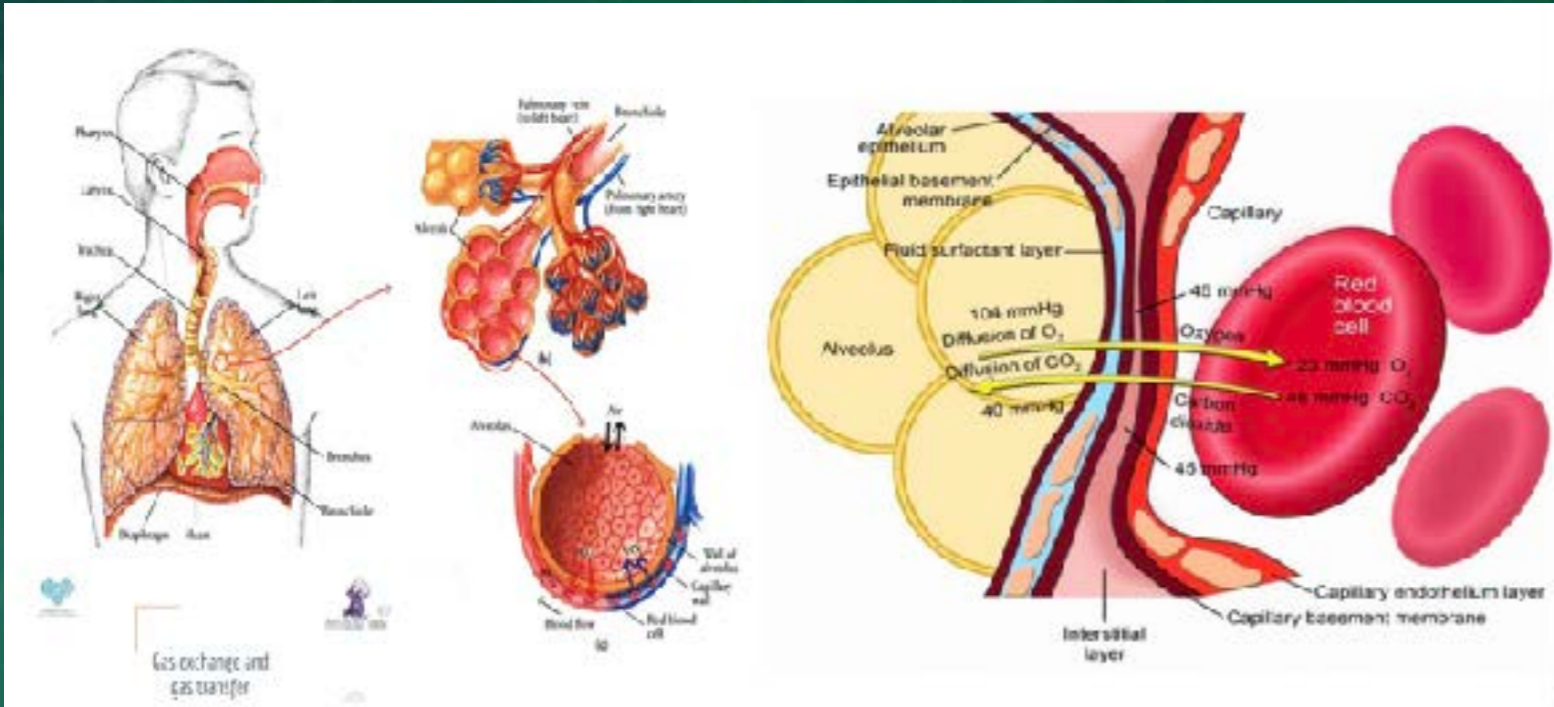
From the Department of Kinesiology, University of Waterloo, Ontario, Canada (PBD); Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN (CCW, TKR, TBC, MJJ); and the Departments of Physiology and Metabolism, University of Arizona, Tucson, (TWS).



The Oxygen Cascade During Exercise in Health and Disease

Mayo Clin Proc. 2021 April 96(4): 1017–1032.

- The partial pressure of oxygen in air at sea level is ~150 mmHg but in the mitochondria of exercising skeletal muscle the partial pressure of oxygen can be ~100-fold lower without significant engagement of anaerobic energy metabolism.



LAYERS OF THE RESPIRATORY MEMBRANE

Diffusion of oxygen from the alveolus into the red blood cell and diffusion of carbon dioxide in the opposite direction. Note the following different layers of the respiratory membrane:

1. A layer of fluid lining the alveolus
2. The alveolar epithelium
3. An epithelial basement membrane
4. Interstitial space
5. Capillary basement membrane
6. The capillary endothelial membrane

Partial pressure of gases

Lung

From pulmonary artery	Alveoli	To pulmonary vein
$PO_2 = 40$	$PO_2 = 105$	$PO_2 = 100$
$PCO_2 = 46$	$PCO_2 = 40$	$PCO_2 = 40$

Tissue

Systemic veins	Body cells	Systemic arteries
$PO_2 = 40$	$PO_2 = 100$	$PO_2 = 100$
$PCO_2 = 46$	$PCO_2 = 40$	$PCO_2 = 40$

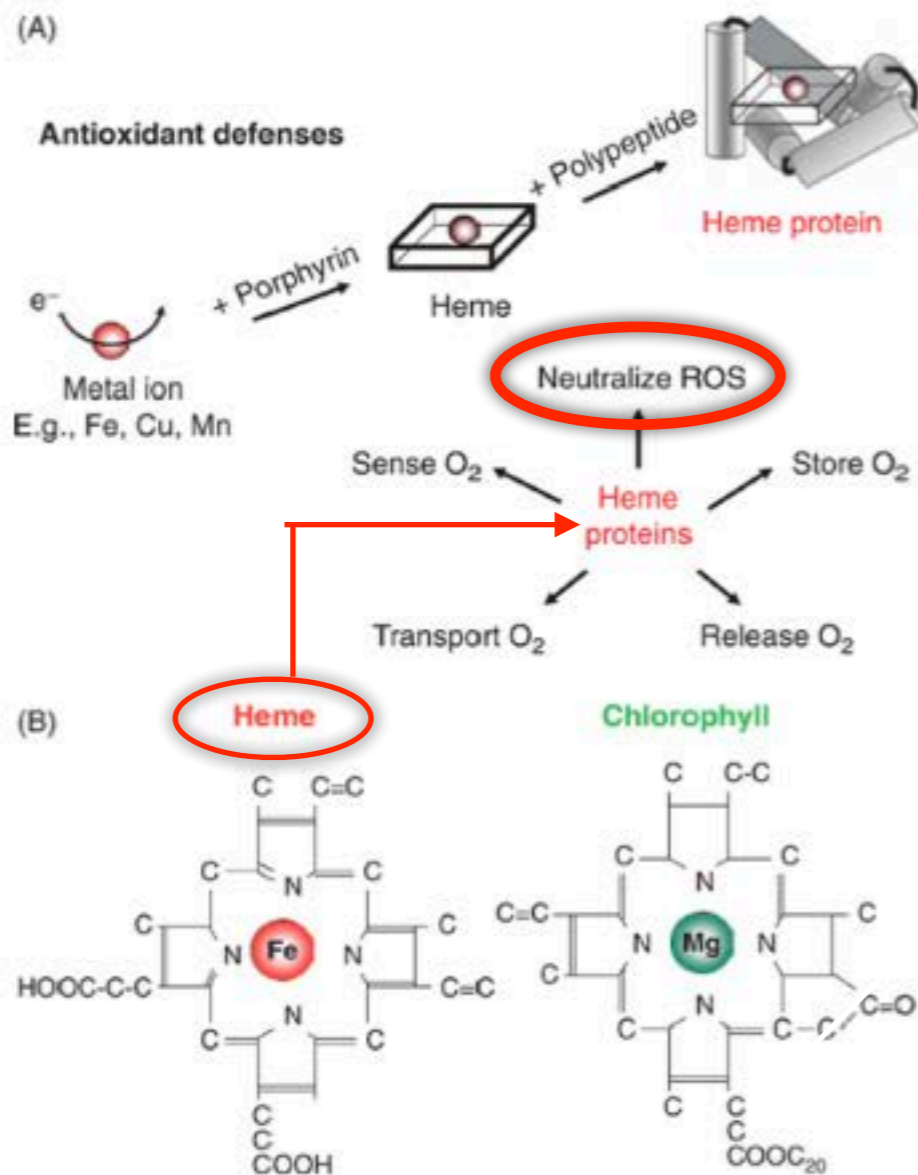


Figure 2.

(A) Transitional metals ions functioned as signaling and antioxidant molecules in the earliest organisms. A molecular cage, for example, porphyrin ring, trapped these metal ions, for example, forming a heme molecule. Adding various polypeptides modulated the action of heme, resulting in heme proteins. By exaptation heme proteins participated in the neutralization of reactive O₂ species as well as the sensing, storage, transport, and release of O₂. (B) Structure of heme (containing iron) is remarkably similar to that of chlorophyll (containing magnesium).

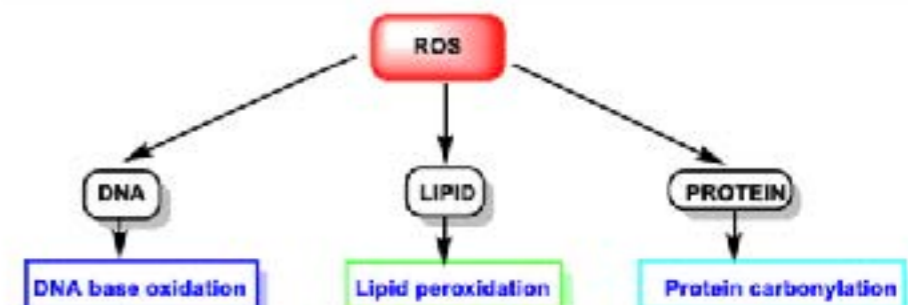
Reactive oxygen species (ROS)

are highly reactive chemicals formed from diatomic oxygen (O₂).

Examples of ROS:

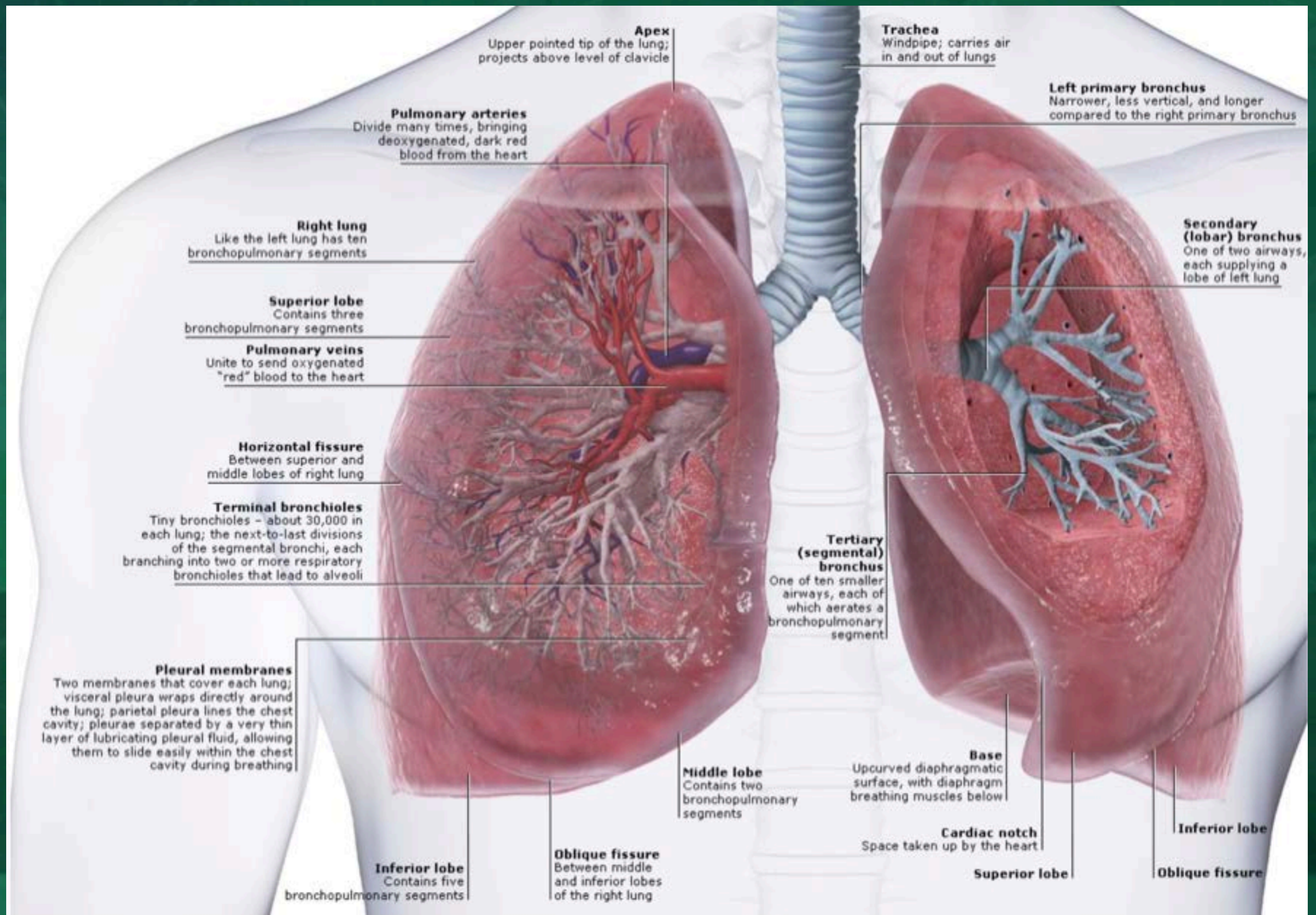
peroxides, superoxide, hydroxyl radical, singlet oxygen, and alpha-oxygen.

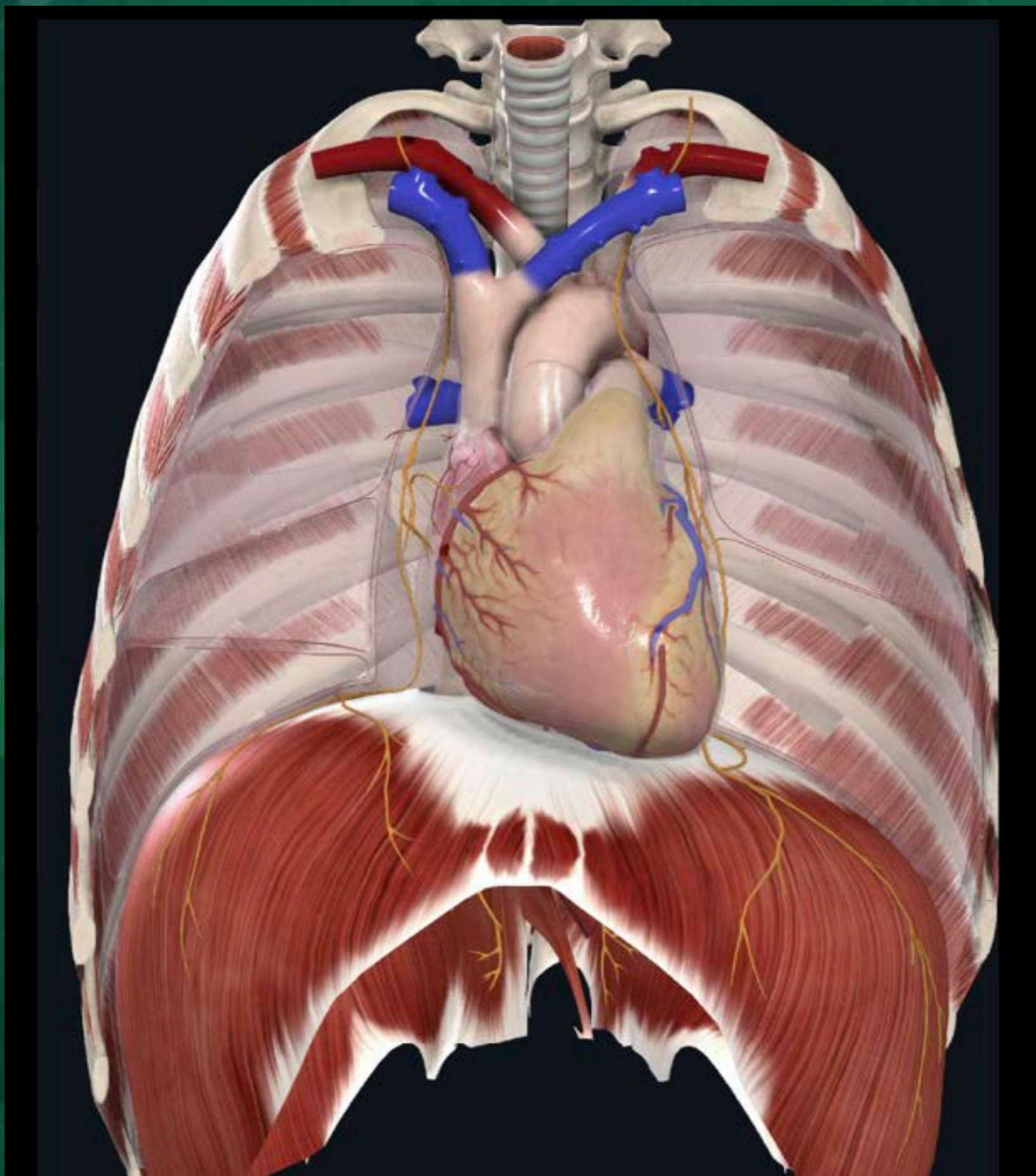
ROS action on DNA, lipids and proteins lead to DNA base oxidation, lipid peroxidation and protein carbonylation, respectively. * Unpaired electron.



What will be covered:

- 1) How *elemental* Iron (Fe) and Oxygen (O) got their start
- 2) How *molecular* O₂ in oceans and atmosphere rose long after life began ... how Fe²⁺ delayed that rise
- 3) Why Iron (Fe) is central to cellular metabolism
- 4) Why aerobic (O₂) cellular respiration became dominant in a previously anaerobic world





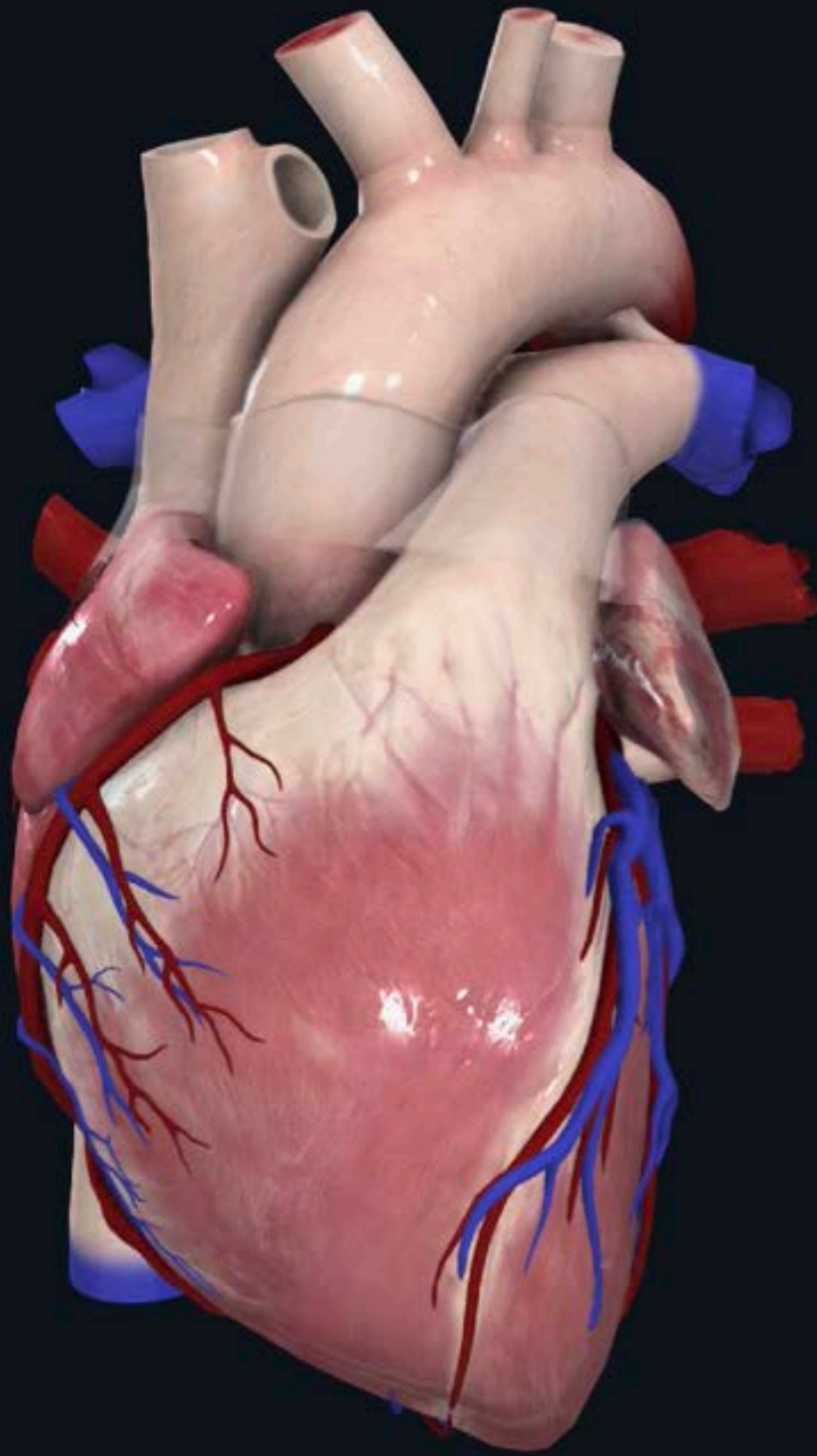
What you see depends on your perspective.



near

far

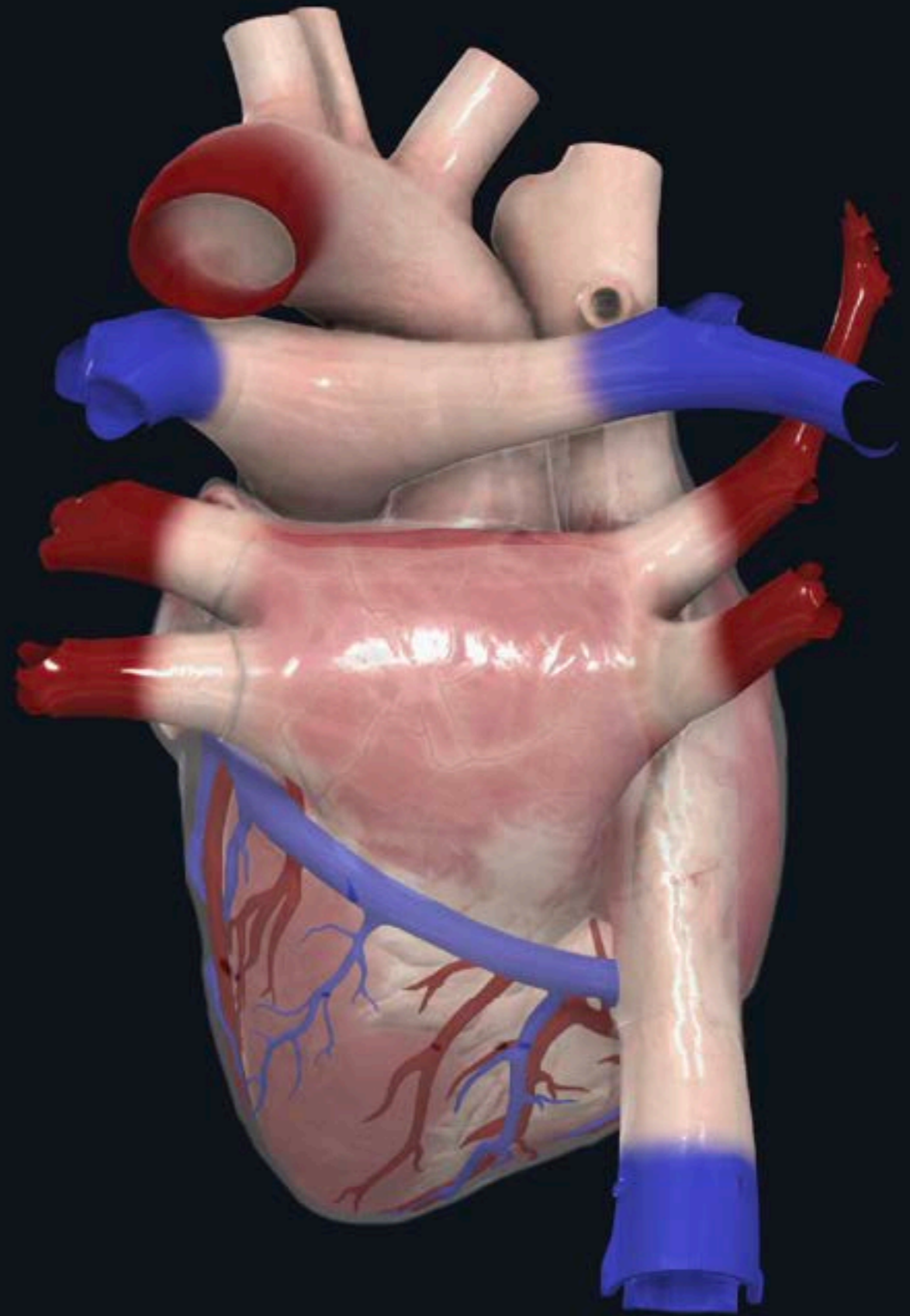
Tidal Locking - You've only ever seen half of the Moon in the sky. Earth's Moon rotates, but it takes precisely as long for the Moon to spin on its axis as it does to complete its monthly orbit around Earth. As a result, the Moon never turns its back to us. In fact, all the solar system's large moons are tidally locked with their planets.



front

Complete **Anatomy** 2023

3D4MEDICAL



back

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

We shall not cease from exploration

And the end of all our exploring

Will be to arrive where we started

And know the place for the first time.

T.S. Eliot --- "Little Gidding" ... *Four Quartets*

Right there in front of you

... that's where it always is ...

with just a little knowing,

looking becomes seeing,

opening doors into

extraordinary worlds



"From the abundance, accessibility and richness of this iron ore, its proximity to the coal field and to the navigation of the Tombigbee River, I can hardly doubt that, like the coal itself, [Birmingham] is destined, at no distant day, to be a source of great mineral wealth to Alabama." - 1846

Sir Charles Lyell

Principles of Geology - 1830

PRINCIPLES OF GEOLOGY

OR THE
MODERN CHANGES OF THE EARTH
AND ITS INHABITANTS

CONSIDERED AS ILLUSTRATIVE OF GEOLOGY

By SIR CHARLES LYELL, BART., M.A., F.R.S.

"Verū acie ut per cerasa sive" - Bacon
"The stony rocks are not perennial, but the daughters of Time" - Linnæus, Spet. Nat. ed. 2, Stockholm, 1748, p. 209
"Avald all the revolutions of the globe the scenery of Nature has been molten, and her laws are the only things that have resisted the general movement. The rivers and the rocks, the seas and the continents, have been changed in all their parts; but the laws which direct those changes, and the sides to which they are subject, have remained essentially the same" - Playfair, Illustrations of the Huttonian Theory, 1785

ELEVENTH AND ENTIRELY REVISED EDITION

In Two Volumes—Vol. I.

Illustrated with Maps, Plates, and Woodcuts

LONDON
JOHN MURRAY, ALBEMARLE STREET
1872

Within 30 years, Birmingham would spring from the earth at the spot where coal, limestone and iron ore—which gives Red Mountain its color and name -- naturally existed within 20 miles of one another. Birmingham became known as the Magic City because it burst forth from the mountain as if by magic, with 3,086 residents according to the 1880 census.

Verba volant, scripta manent.

Spoken words fly away, written words remain.

Location of relevant webpages on imageessays.com:

	<u>index page</u>
respiration	4
water	4
ATP	4
adenosine	4
oxygen	3
iron	3
membrane	3
hemoglobin	3
rbc	3
breath	1
mitochondria	1
stromatolite	1
archaea	1
proton	1

imageessays

respiration

images: ***** Cellular Respiration In the Aerobic World ... After a Long Beginning on an Anaerobic Planet ... OXYGEN and IRON ***** - pdf slideshow

essay: ***** Respiration and Ventilation *****

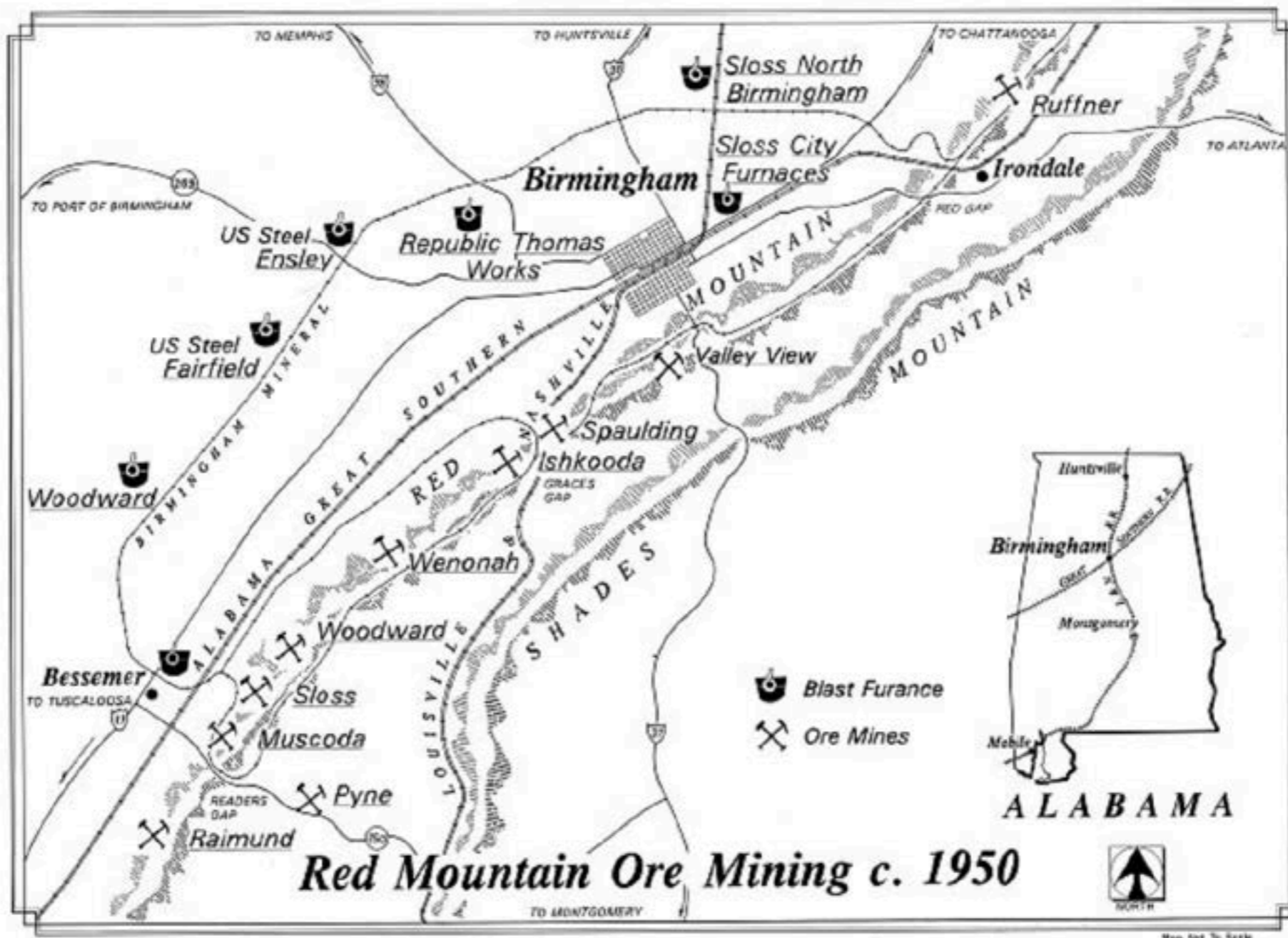
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RED MOUNTAIN MINING OPERATIONS

Jefferson County, Alabama

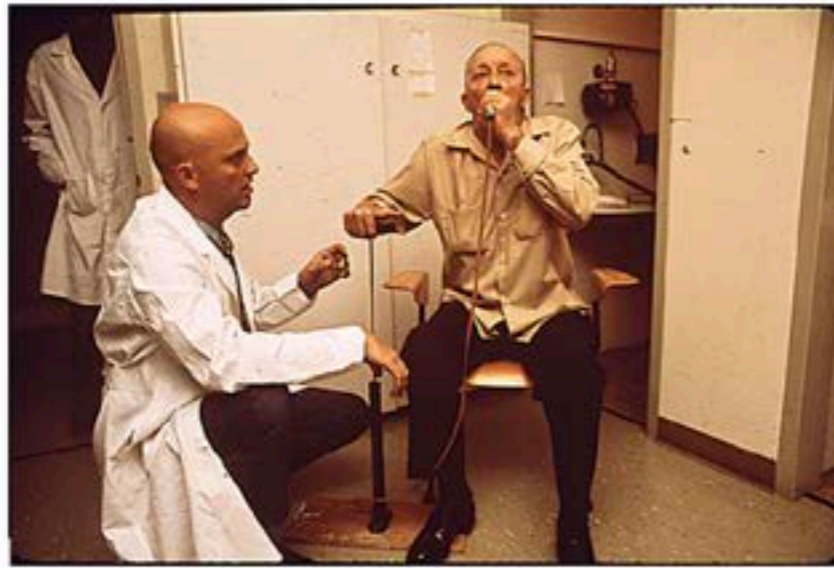


Birmingham: A Powerful History Forged from Iron



The Ensley Works operated between 1888 and 1976 and became part of U.S. Steel in 1907.
For years, it was the largest steel producer in the Southeast.

atlantafed.org



Ben Vaughn Branscomb (1924 – 2016) was a pioneering pulmonologist and distinguished professor emeritus at **UAB**.

He attended the Asheville School and Duke and, due to the need for medical practitioners in World War II, was admitted to medical school there at age 17. After graduating he served briefly on a destroyer during the war. Later, during his internship at the University of Chicago, Branscomb contracted tuberculosis from a patient. He was admitted to the Adirondack Cottage Sanitarium at Saranac Lake, New York.

While there he decided on his specialty and used a full-time job in the sanitarium's research laboratory to begin his training as a pulmonary physiologist. In 1950 he was recalled to military duty in the Korean War before he completed his residency there. He convinced military officials to post him as a researcher for the United States Public Health Service Commissioned Corps, where he pioneered the study of pulmonary function at the National Heart

Once discharged, he was recruited to the **Medical College of Alabama** by **Tinsley Harrison**. Soon after his arrival, Branscomb began setting up pulmonary laboratories at area hospitals equipped to administer the "flow-volume loop" test for breathing capacity that he developed. He became a pioneer of research into emphysema and personally tested 200 members of the 88th United States Congress in July 1963 using a mobile diagnostic unit of his own design. His own research established quantitative links between lung disease and smoking and air pollution.

Branscomb provided critical support to the **Greater Birmingham Alliance to Stop Air Pollution (GASP)** and was the only medical specialist appointed to the Alabama Air Pollution Control Commission in 1971.



Birmingham - 1966

Downtown Birmingham December 1966 – photo courtesy of Jefferson County Department of Health

"Smoke City." In the 1960s, that is what truckers used to call Birmingham when they reached the outskirts of Alabama's largest city – the self proclaimed "Pittsburgh of the South."

Before the [Clean Air Act](#) was passed in 1970, soot and smog engulfed Birmingham.

GASP



Birmingham - 1956

Downtown Street in Birmingham December 1956 – Photo courtesy of the Jefferson County Department of Health

Synthesis of the Elements in Stars*

E. MARGARET BURBIDGE, G. R. BURBIDGE, WILLIAM A. FOWLER, AND F. HOYLE

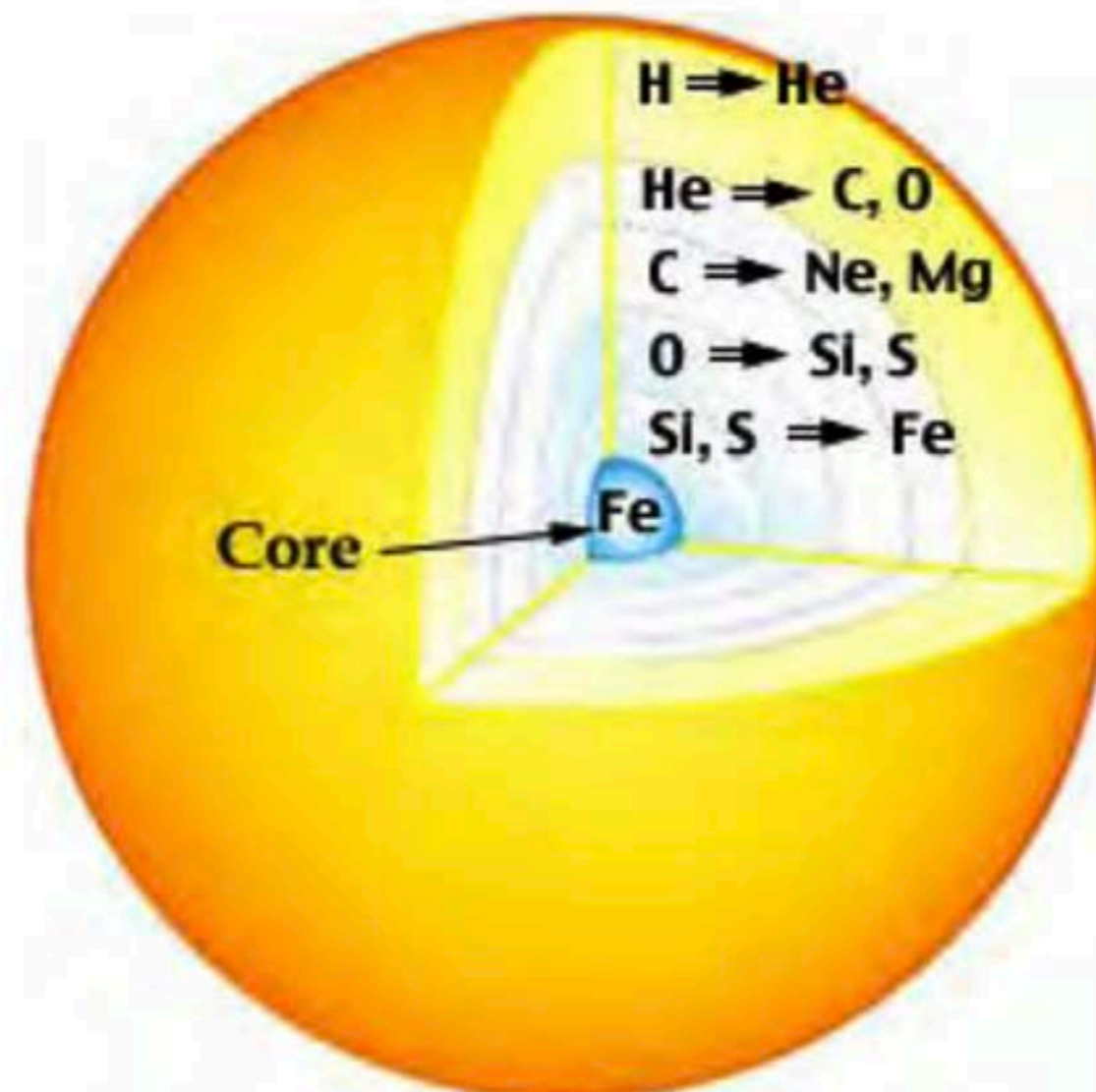
*Kellogg Radiation Laboratory, California Institute of Technology, and
Mount Wilson and Palomar Observatories, Carnegie Institution of Washington,
California Institute of Technology, Pasadena, California*

“It is the stars, The stars above us, govern our conditions”;
(*King Lear*, Act IV, Scene 3)

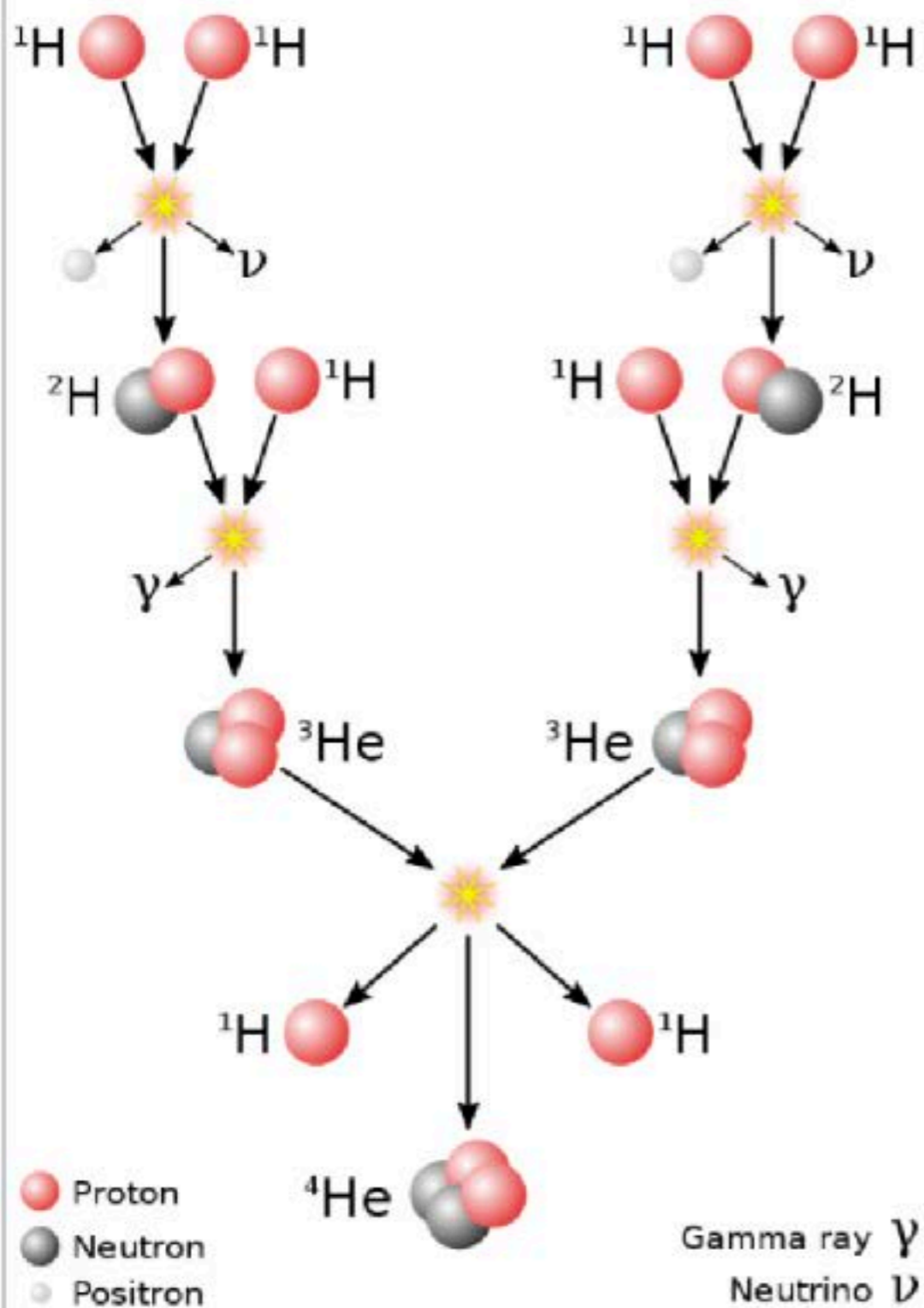
but perhaps

“The fault, dear Brutus, is not in our stars, But in ourselves,”
(*Julius Caesar*, Act I, Scene 2)

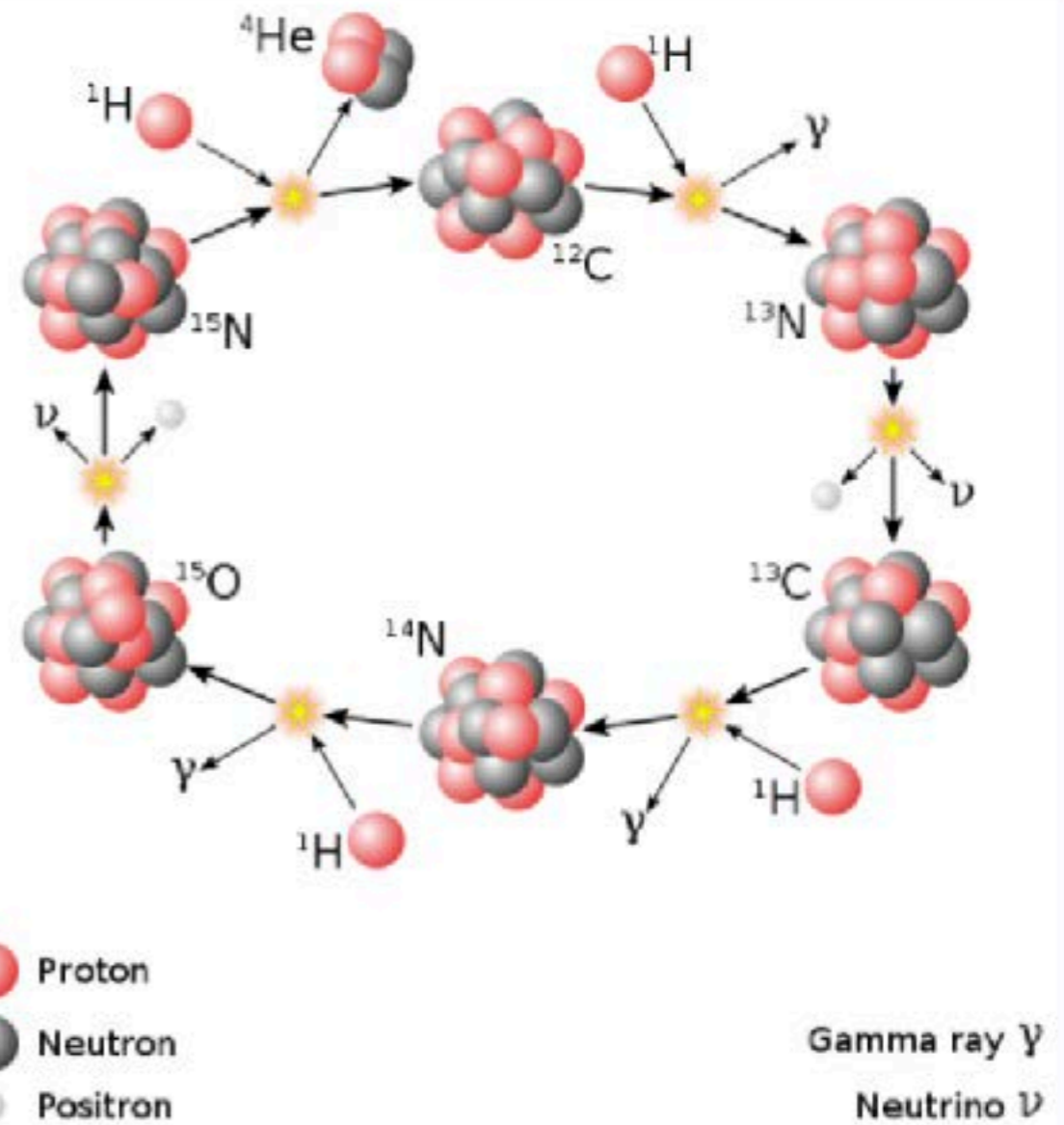
Oxygen and Iron
are elements
formed by nuclear fusion
in the core of stars



Nuclear fusion of Hydrogen atoms in the core of stars results in formation of a number of elements, including **Oxygen** and **Iron**.



Proton-proton chain reaction



CNO-I cycle

The helium nucleus is released at the top-left step.

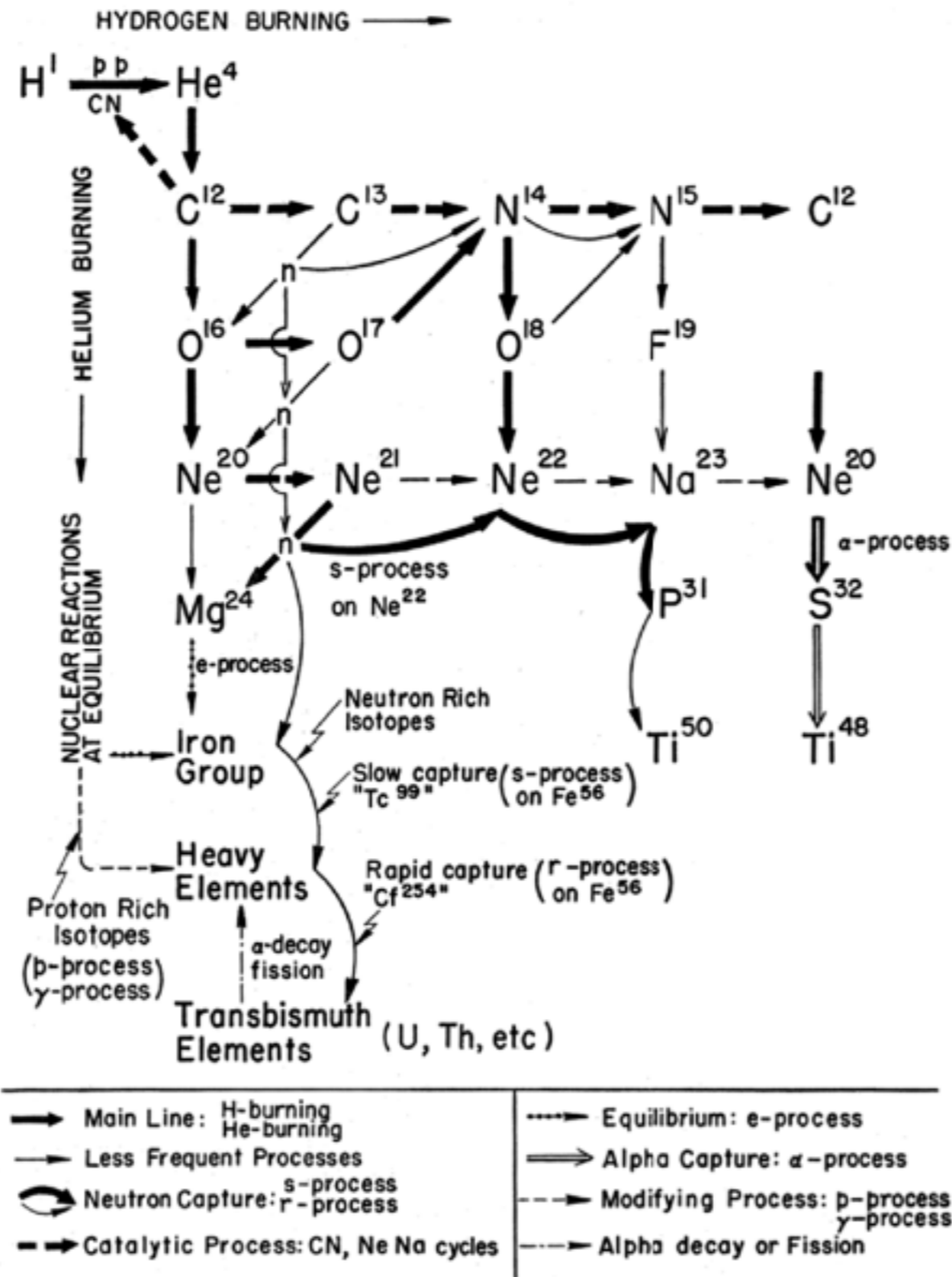


FIG. 1.2. A schematic diagram of the nuclear processes by which the synthesis of the elements in stars takes place. Elements synthesized by interactions with protons (hydrogen burning) are listed horizontally. Elements synthesized by interactions with alpha particles (helium burning) and by still more complicated processes are listed vertically. The details of the production of all of the known stable isotopes of carbon, nitrogen, oxygen, fluorine, neon, and sodium are shown completely. Neutron capture

Iron Deficiency

Iron deficiency was an absolute state in the early universe. Large, first-generation stars consume hydrogen and produce helium in their 10 million degree plasma fusion furnace cores. Helium nuclei accumulate, concentrate, fuse, and raise core temperature to 100 million degrees. Further fusion forms beryllium and then carbon. Helium-carbon collisions produce **oxygen**, then neon, magnesium, and silicon.

At this point, though, a crisis develops. Although the concentric shells of **oxygen**, carbon, helium, and hydrogen continue to produce enormous quantities of fusion-derived energy, the accumulating silicon core approaches a thermodynamic dead end. At 4 billion degrees, silicon fusion forges a new element, **iron**, into existence. The nuclear stability of the rapidly forming **iron** atoms is greater than that of any other, even more massive, as yet unformed elements that might result from further fusion.

Therefore, **iron** in the stellar core cannot serve as fuel for exothermic nuclear fusion and provide the immense energy output necessary to heat the core and counterbalance the persistent struggle toward gravitational collapse.

Supernova

As the **iron** core cools and compresses, the temperature increases. However, iron nuclei are so stable that no further fusion can occur. Instead, **iron** nuclei succumb to high-energy gamma radiation and photodissociate into helium, triggering a catastrophic collapse under the gravitational pressures of the outer layers. Incredible densities are generated, causing electrons to penetrate protons, forming neutrons and neutrinos. The rebounding shock wave of this collapse accelerates neutrons and neutrinos outward, while the bulk of the core becomes sealed off forever as a new black hole is formed.

The outer layers of the star explode outward at speeds approaching 0.1 c, forming a **supernova**. Neutrons riding the shock wave overtake the exploding layers of silicon, oxygen, carbon, and lighter elemental nuclei. Collision with these elements results in neutron capture and the progressive formation of all the heavier elements.

1 H																	2 He
3 Li	4 Be											5 B	6 C	7 N	8 O	9 F	10 Ne
11 Na	12 Mg											13 Al	14 Si	15 P	16 S	17 Cl	18 Ar
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba	57-70 * Lu	71 Hf	72 Ta	73 W	74 Re	75 Os	76 Ir	77 Pt	78 Au	79 Hg	80 Tl	81 Pb	82 Bi	83 Po	84 At	85 Rn
87 Fr	88 Ra	89-102 * Lr	103 Rf	104 Db	105 Sg	106 Bh	107 Hs	108 Mt	109 Uun	110 Uuu	111 Uub	112 Uuq	113 Uuq				
* Lanthanide series		57 La	58 Ce	59 Pr	60 Nd	61 Pm	62 Sm	63 Eu	64 Gd	65 Tb	66 Dy	67 Ho	68 Er	69 Tm	70 Yb		
* Actinide series		89 Ac	90 Th	91 Pa	92 U	93 Np	94 Pu	95 Am	96 Cm	97 Bk	98 Cf	99 Es	100 Fm	101 Md	102 No		

hydrogen 1 H 1.0079																	helium 2 He 4.0026						
lithium 3 Li 6.941	beryllium 4 Be 9.0122																	boron 5 B 10.811	carbon 6 C 12.011	nitrogen 7 N 14.007	oxygen 8 O 15.999	fluorine 9 F 18.998	neon 10 Ne 20.180
sodium 11 Na 22.990	magnesium 12 Mg 24.305																	aluminum 13 Al 26.982	silicon 14 Si 28.086	phosphorus 15 P 30.974	sulfur 16 S 32.065	chlorine 17 Cl 35.453	argon 18 Ar 39.948
potassium 19 K 39.098	calcium 20 Ca 40.078	scandium 21 Sc 44.956	titanium 22 Ti 47.867	vanadium 23 V 50.942	chromium 24 Cr 51.996	manganese 25 Mn 54.938	iron 26 Fe 55.845	cobalt 27 Co 58.933	nickel 28 Ni 58.693	copper 29 Cu 63.546	zinc 30 Zn 65.39	gallium 31 Ga 69.723	germanium 32 Ge 72.61	arsenic 33 As 74.922	selenium 34 Se 78.96	bromine 35 Br 79.904	krypton 36 Kr 83.80						
rubidium 37 Rb 85.468	strontium 38 Sr 87.62	yttrium 39 Y 88.906	zirconium 40 Zr 91.224	niobium 41 Nb 92.906	molybdenum 42 Mo 95.94	technetium 43 Tc [98]	ruthenium 44 Ru 101.07	rhodium 45 Rh 102.91	paladium 46 Pd 106.42	silver 47 Ag 107.87	cadmium 48 Cd 112.41	indium 49 In 114.82	tin 50 Sn 118.71	antimony 51 Sb 121.76	tellurium 52 Te 127.60	iodine 53 I 126.90	xenon 54 Xe 131.29						
cesium 55 Cs 132.91	barium 56 Ba 137.33	57-70 *	lutetium 71 Lu 174.97	hafnium 72 Hf 178.49	tantalum 73 Ta 180.95	tungsten 74 W 183.84	rhenium 75 Re 186.21	osmium 76 Os 190.23	iridium 77 Ir 192.22	platinum 78 Pt 195.08	gold 79 Au 196.97	mercury 80 Hg 200.59	thallium 81 Tl 204.38	lead 82 Pb 207.2	bismuth 83 Bi 208.98	polonium 84 Po [209]	astatine 85 At [210]	radon 86 Rn [222]					
francium 87 Fr [223]	radium 88 Ra [226]	89-102 * *	lawrencium 103 Lr [260]	rutherfordium 104 Rf [261]	dubnium 105 Db [262]	seaborgium 106 Sg [263]	bohrium 107 Bh [264]	hassium 108 Hs [265]	meitnerium 109 Mt [266]	unnilium 110 Uun [271]	ununium 111 Uuu [272]	unbibium 112 Uub [273]	unseptadium 114 Uuq [286]										

* Lanthanide series

lanthanum 57 La 138.91	cerium 58 Ce 140.12	praseodymium 59 Pr 140.91	neodymium 60 Nd 144.24	promethium 61 Pm [145]	samarium 62 Sm 150.36	europium 63 Eu 151.96	gadolinium 64 Gd 157.25	terbium 65 Tb 158.93	dysprosium 66 Dy 162.50	holmium 67 Ho 164.93	erbium 68 Er 167.26	thulium 69 Tm 168.93	ytterbium 70 Yb 173.04
actinium 89 Ac [227]	thorium 90 Th 232.04	protactinium 91 Pa 231.04	uranium 92 U 238.03	neptunium 93 Np [237]	plutonium 94 Pu [244]	americium 95 Am [243]	curium 96 Cm [247]	berkelium 97 Bk [247]	californium 98 Cf [251]	einsteinium 99 Es [252]	fermium 100 Fm [257]	mendelevium 101 Md [258]	nobelium 102 No [259]

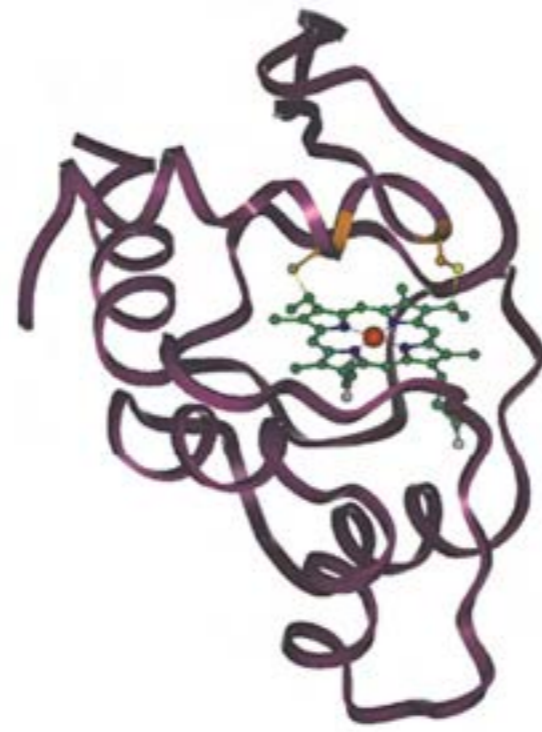
** Actinide series

Iron and Oxygen are the most abundant elements on earth: 35% and 30%, respectively.

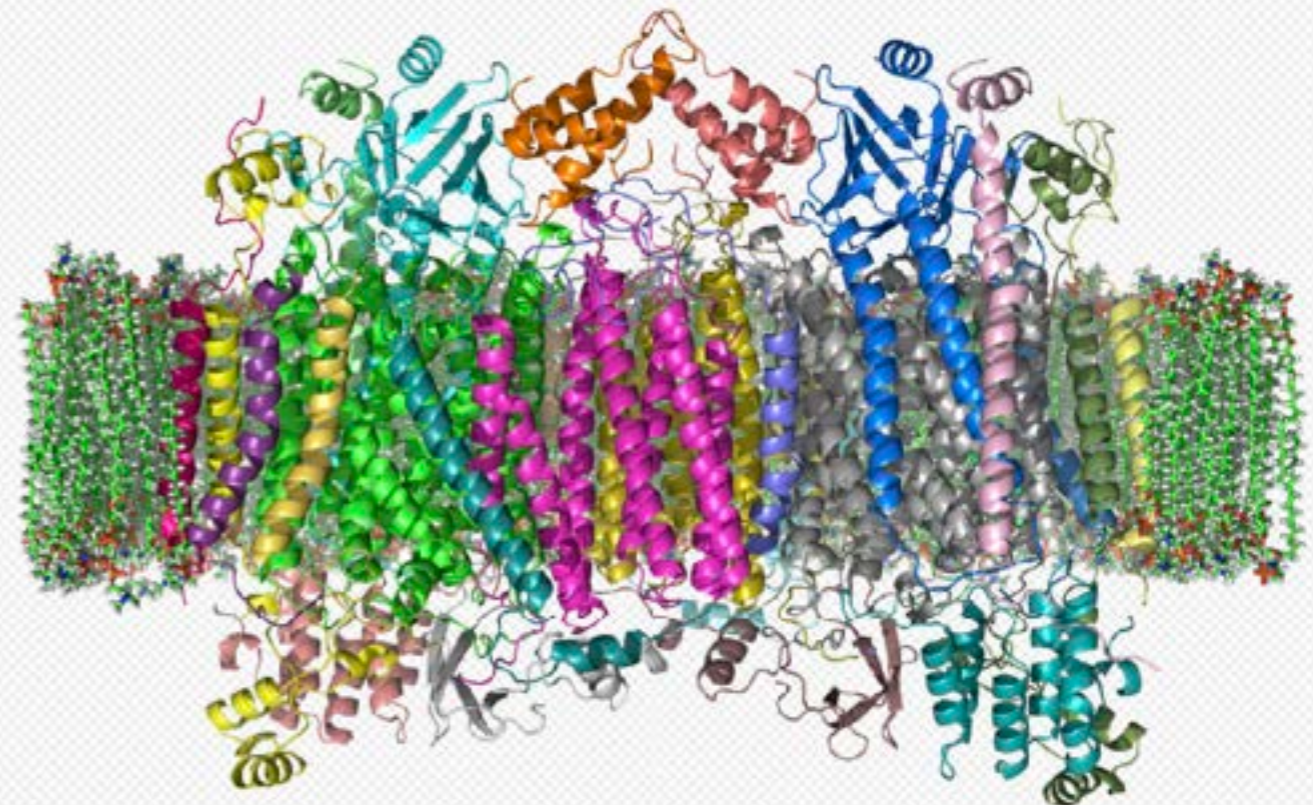
Most of the **iron** is concentrated in the planet's core, while the crust contains 6% by mass.



heme



cytochrome



cytochrome c oxidase in membrane

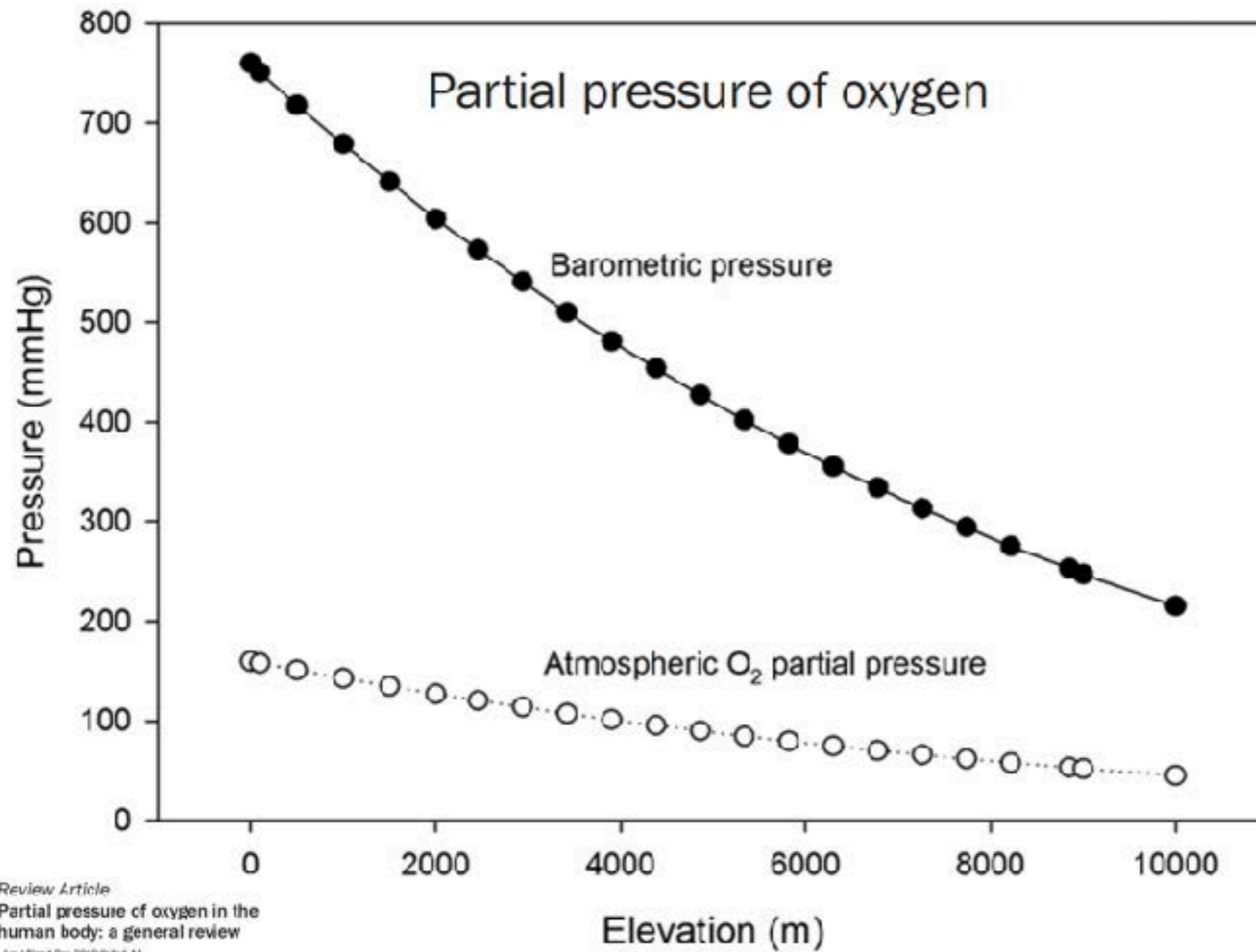
Regarding the composition of the atmosphere:

- 1) Earth's atmosphere is not the same in every location on the planet.

(3rd dimension: altitude)

- 2) Earth's atmosphere has not been the same throughout the history of the planet.

(4th dimension: time)

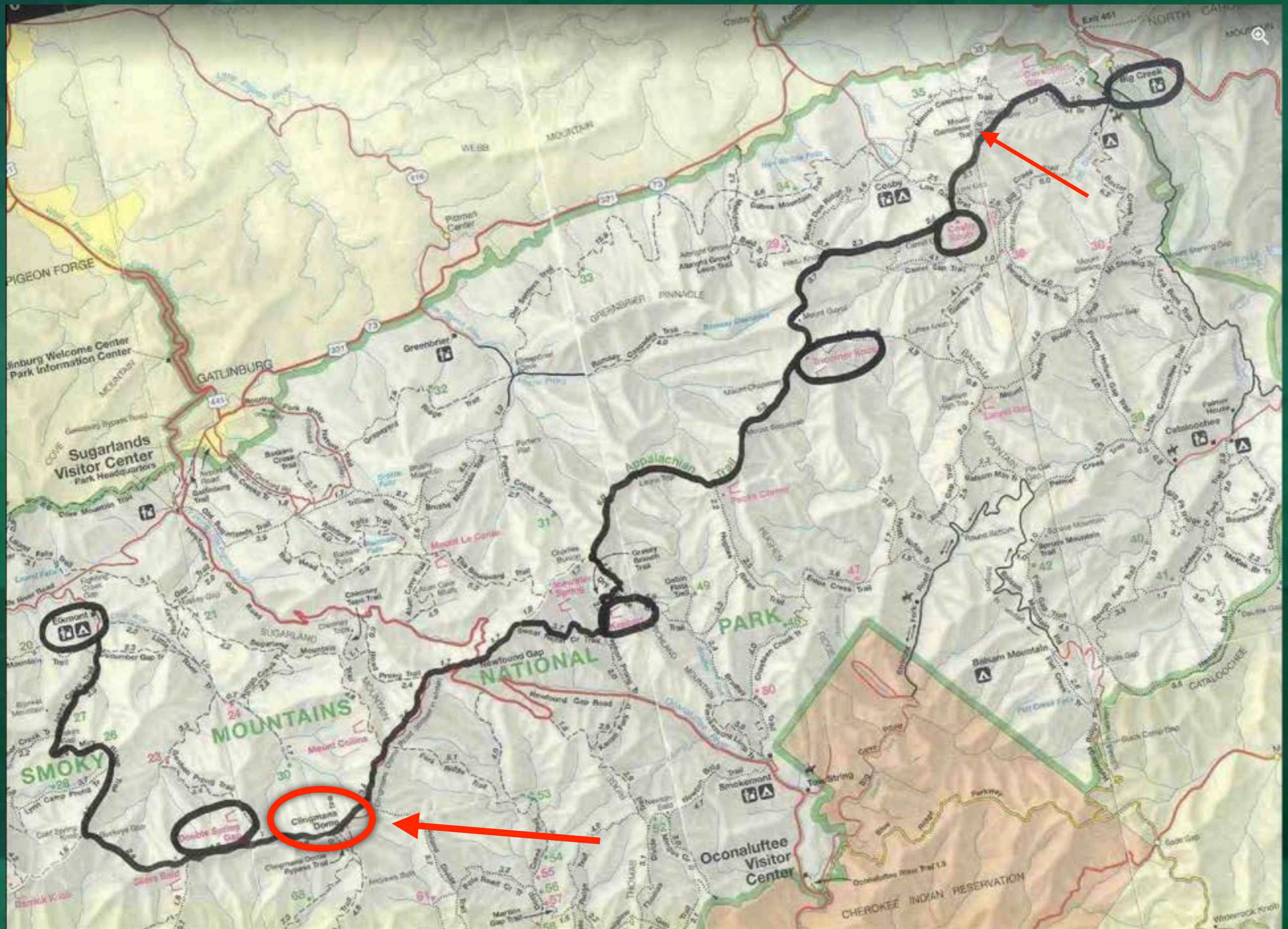


Review Article
Partial pressure of oxygen in the
human body: a general review
Am J Blood Res 2019;9(1):1-04

1) Earth's atmosphere is not the same
in every location on the planet.

(*3rd dimension: altitude*)

LOCATION	ELEVATION (ft.)	ATMOSPHERIC PRESSURE $P_B=760(e^{-a/7924})$ (mmHg.)	OXYGEN PRESSURE (= 21% atmospheric pressure) (mmHg.)
▶ Gulf Shores	0	▶ 760	160
▶ Birmingham	650	740	155
Cades Cove	1800	710	150
Spence Field	4900	635	133
Newfound Gap	5050	630	132
▶ Clingman's Dome	6643	▶ 595	125
Thunderhead	5500	620	130
Jackson Hole	6447	600	126
Yellowstone Lake	7730	570	120
Grant Village	7810	570	120
Old Faithful	7400	580	122
Jackson Lake	6772	590	124
Colter Bay Village	6840	590	124
Jenny Lake	6783	590	124
Inspiration Point	7200	585	123
Fork of Cascade Canyon	7800	560	118
Lake Solitude	9035	540	113
▶ Paintbrush Divide	10700	▶ 520	109
Holly Lake	9410	530	111
Hurricane Pass	10400	520	109
Alaska Basin	8900	540	113
Death Canyon Trailhead	6800	590	124
Death Canyon Shelf	9500	530	111
Fox Creek Pass	9560	530	111
Lupine Meadows trailhead	6700	590	124
Surprise Lake	9700	525	110
▶ Mt. Everest	29035	▶ 225	47



**Mt. Cammerer
4,928 ft.**





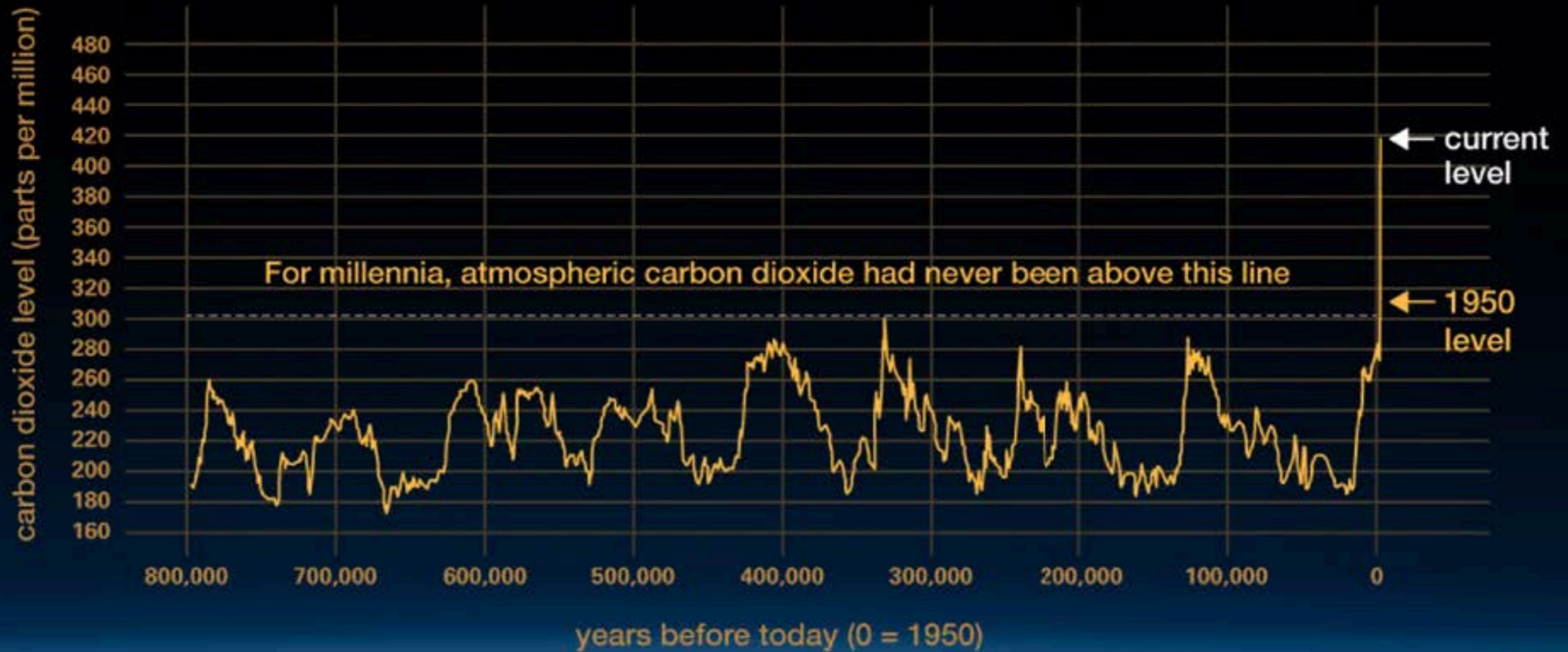
78% N₂**21% O₂****0.9% Ar****0.04% CO₂**

HIGH ALTITUDE PHYSIOLOGY

The adaptability of human physiological processes to significant variations in environmental conditions is remarkable. The ability of the respiratory system to modify its function in response to altitude is an example. As seen in the last issue of this guide, there is a decreasing partial pressure of oxygen (O₂) as one ascends. Carbon dioxide (CO₂), the other major gas of importance in cellular respiration, also diminishes in pressure, but its content is negligible (0.04%) in the present earth atmosphere.

Interestingly, CO₂, not O₂, is the gas that normally regulates minute-to-minute ventilation (breathing). As the level of CO₂ increases in the blood, the acidity of the blood increases slightly (pH decreases); specialized neurons in the brainstem sense this and cause an increased ventilatory drive (heavier breathing). This is the usual control system of breathing. In the normal circumstance, if the lungs/ventilatory system is maintaining adequately low CO₂ levels, the O₂ levels will be just fine.

However:



climate.nasa.gov

HIGH ALTITUDE PHYSIOLOGY

Acute Mountain Sickness (AMS)

As discussed in the second issue of this guide, it is the adaptive transfer of ventilatory control from the predominant central (brainstem) CO₂/pH receptors to the peripheral (aortic/carotid body) O₂ chemoreceptors that characterizes acclimatization to increased altitude. This adjustment takes a variable amount of time and individuals vary in their ability to acclimatize. Interestingly, an individual's level of physical conditioning / fitness does not predict readiness of acclimatization or tendency to develop AMS.

As it turns out, the altitudes that we will be experiencing in Yellowstone and the Grand Tetons are just at the borderline where AMS might be considered likely. It would be different if we were planning ascent of Grand Teton peak (13770 ft.), at which altitude, AMS symptoms of some degree might be expected in >25% of people.

So, what is AMS, what causes it, what are the symptoms, how can its likelihood be diminished? Hypoxemia (relatively low O₂ levels in the blood) is the abnormality that results in the changes that cause AMS symptoms. As mentioned, there is a period of acclimatization to altitude during which hypoxemia (low O₂ in the blood) is not sufficient to drive the ventilatory rate upward to correct the problem, since the CO₂/pH regulation dominates control of ventilation.

Grand Teton summit: 13,770 feet

Atmospheric pressure: 448 mmHg

PI_{O_2} : 94 mmHg





... near Mt. Whitney summit



August 2018 Mt. Whitney trek

Mt. Whitney summit: 14,505 ft.



oldest and youngest sons on Mt. Whitney summit



Atmospheric pressure: 440 mmHg

PO_2 : 93 mmHg



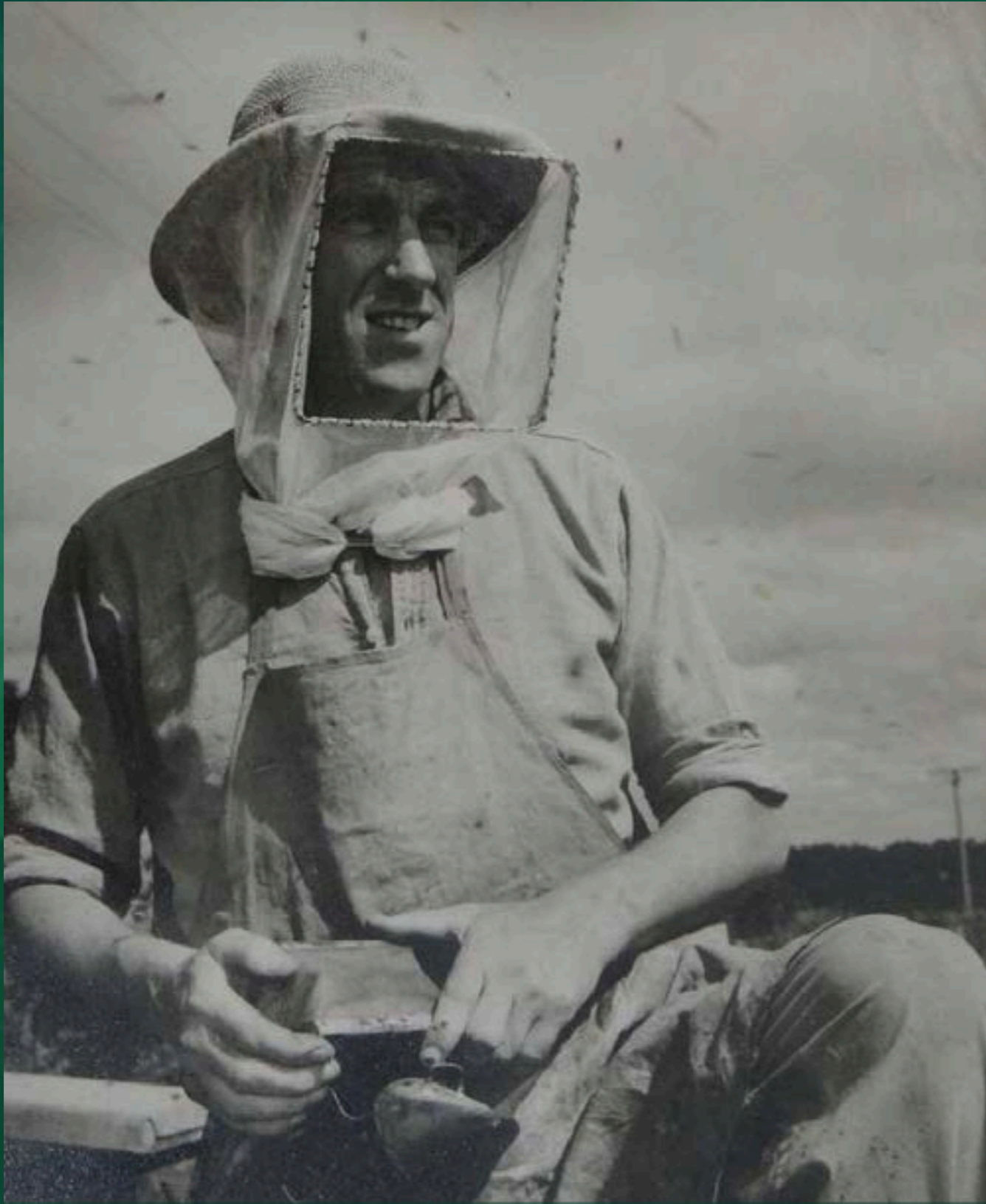
Apiopolis apiary



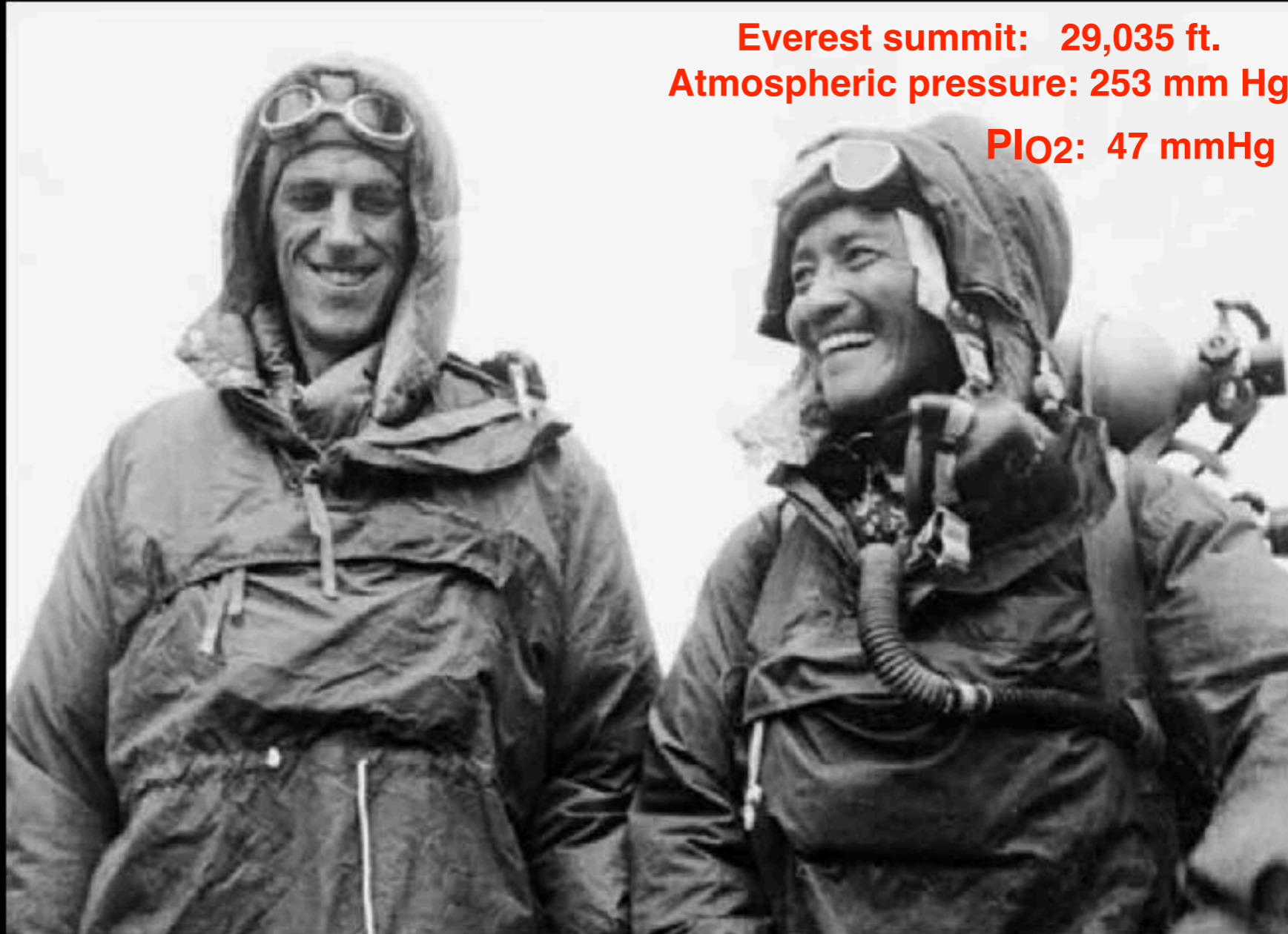
in Aldridge Gardens



See: [imagessays.com/#/apiopolis](https://www.imagessays.com/#/apiopolis)

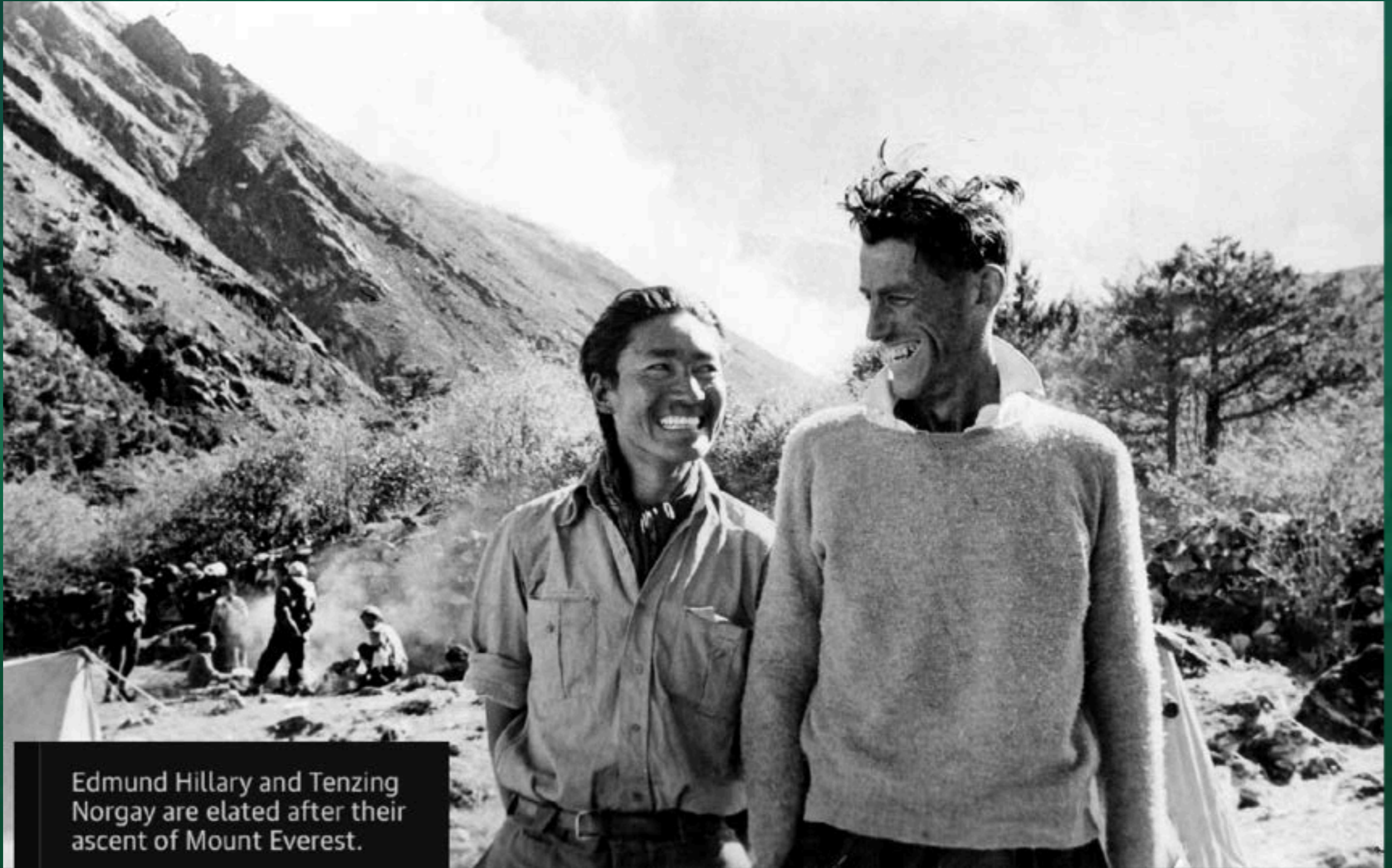


**New Zealand beekeeper
Edmund Hillary**



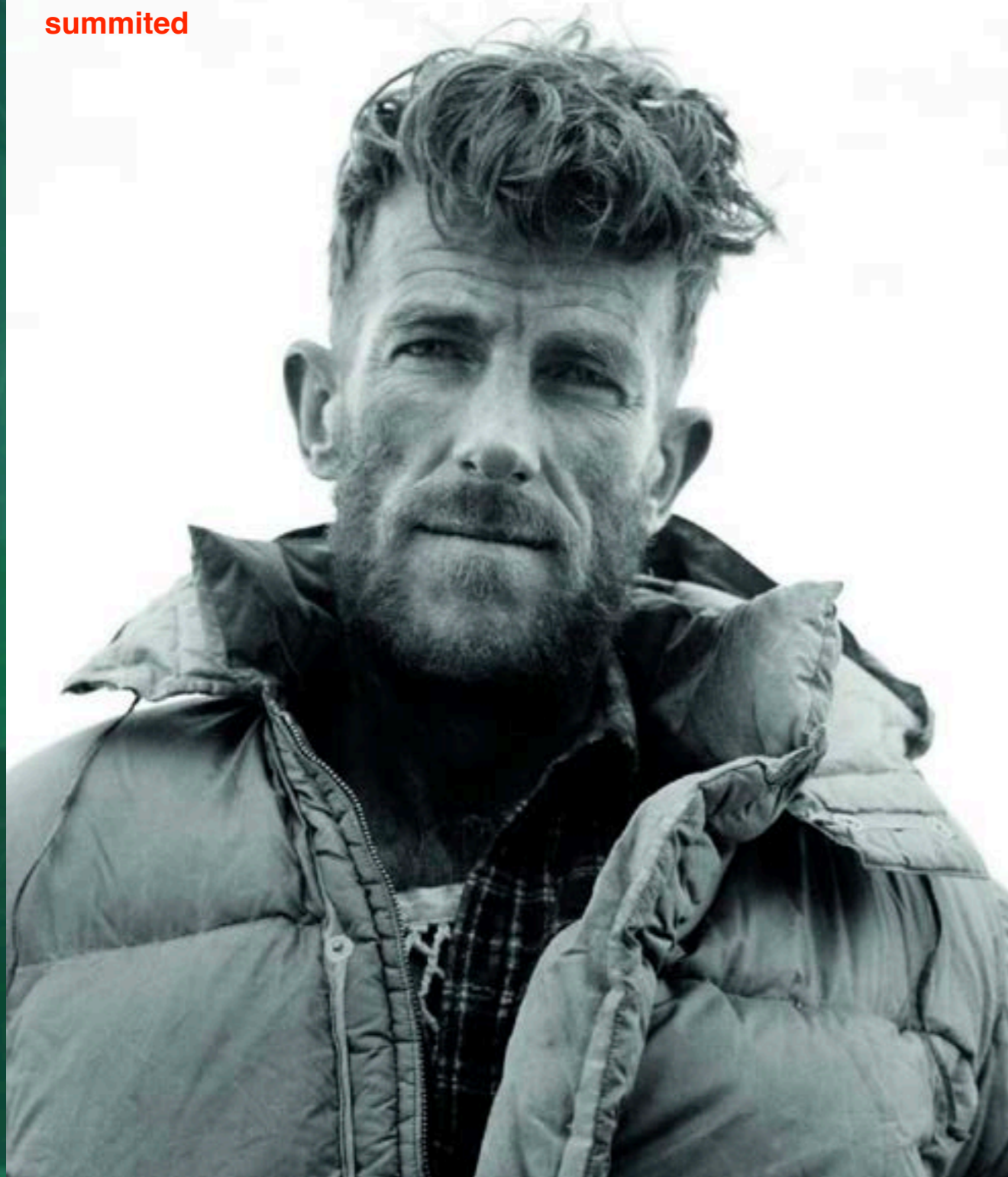
Everest summit: 29,035 ft.
Atmospheric pressure: 253 mm Hg
 P_{IO_2} : 47 mmHg

On May 29, 1953, mountaineers Edmund Hillary and Tenzing Norgay set foot atop Mount Everest, the world's highest mountain. They were the first ever to reach its 29,029-foot peak.



Edmund Hillary and Tenzing Norgay are elated after their ascent of Mount Everest.

May 29, 1953
Mt. Everest
summitted



June 2, 1953
Queen Elizabeth II
crowned



On June 2, 1953, Princess Elizabeth was crowned as Queen Elizabeth II.

source

June 6, 1953
Sir Edmund Hillary
knighted



On June 6, 1953, Edmund Hillary was appointed Knight Commander of the Order of the British Empire

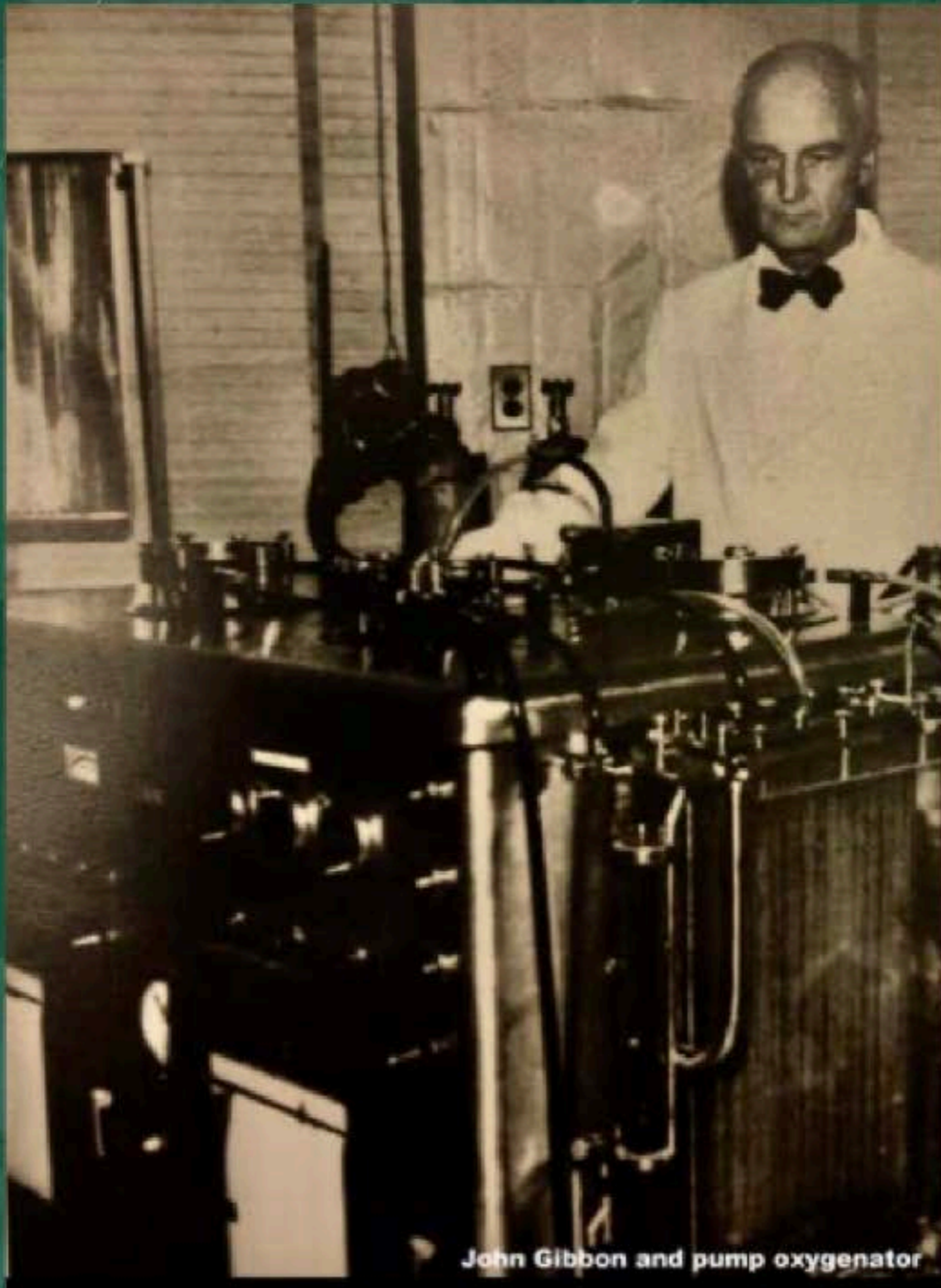
Sir John Hunt (L), leader of the British Everest expedition, and Sir Edmund Hillary (R) arrive at Lancaster House for reception, being given in their honor. Earlier they had been received by Queen Elizabeth who knighted the two men.

... also in 1953:

o **1953. John Gibbon**

- the first successful cardiac surgery (ASD repair) using a pump-oxygenator

**Jefferson Medical College
Philadelphia**



John Gibbon and pump oxygenator

UAB THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM

Knowledge that will change your world

... two years later:



John Kirklin

o **1955. John Kirklin**

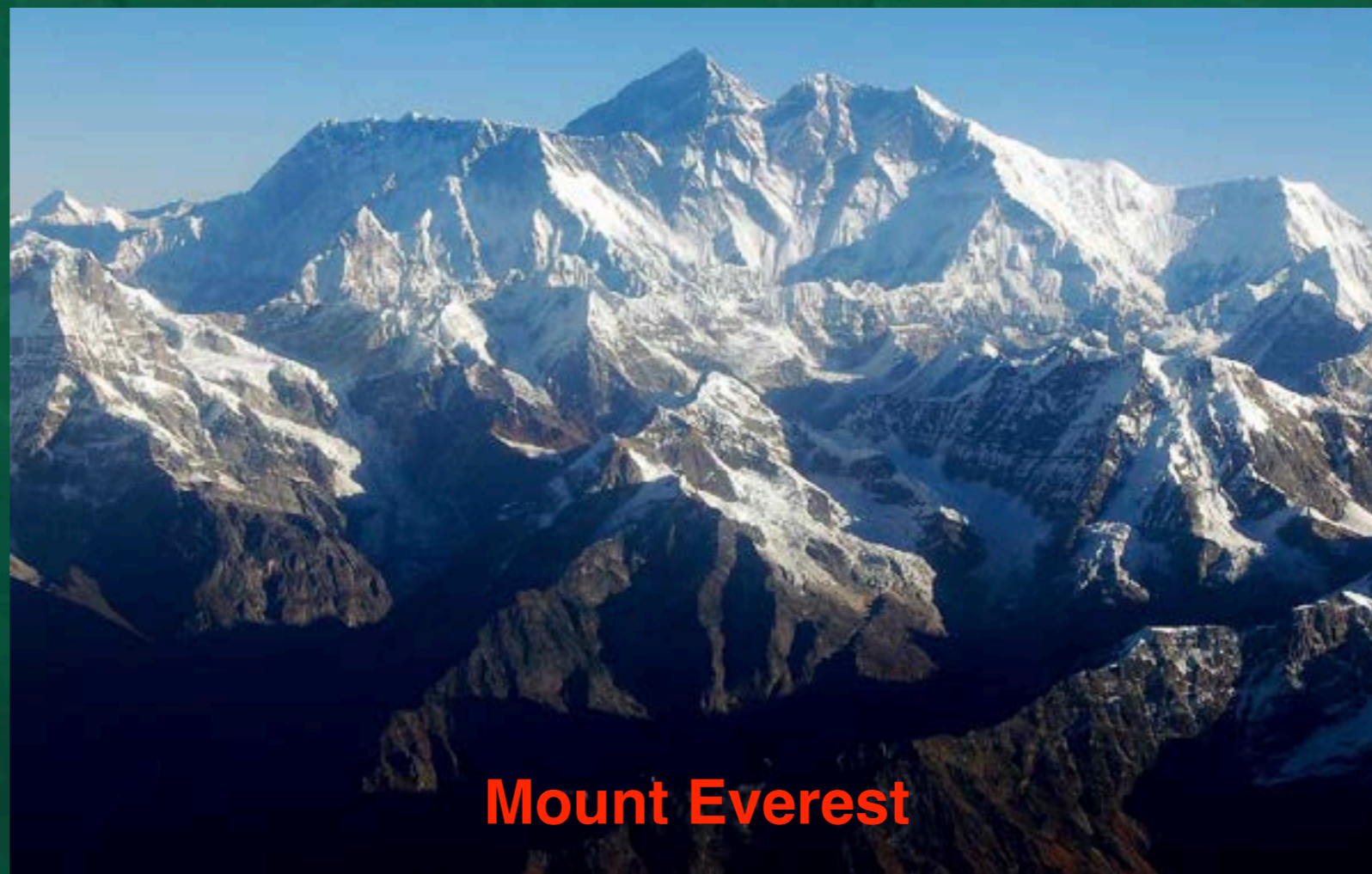
- the second successful cardiac surgery (VSD repair) using a pump-oxygenator ('Mayo-Gibbon bypass machine')

For a brief period of time (1955–1956), there were only 2 hospitals in the world where open heart surgery was being done on a daily basis: Lillehei at the University of Minnesota and, 60 miles away, John Kirklin at the Mayo Clinic. Surgeons came in droves from all over the world to see these 2 men at work.

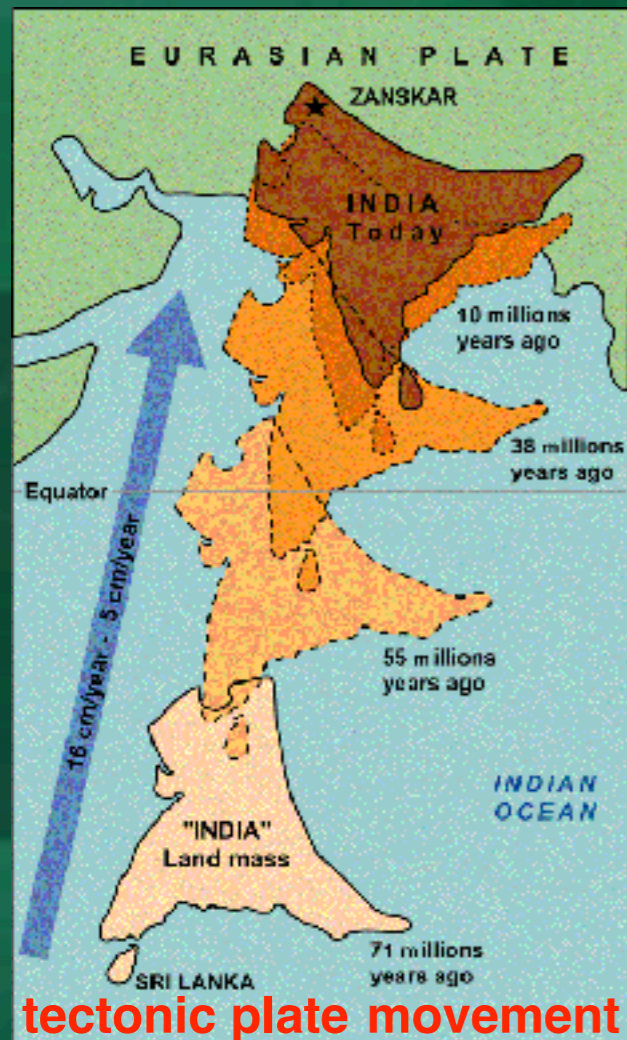
In 1966, Dr Kirklin became surgeon-in-chief and chairman of the Department of Surgery at UAB.



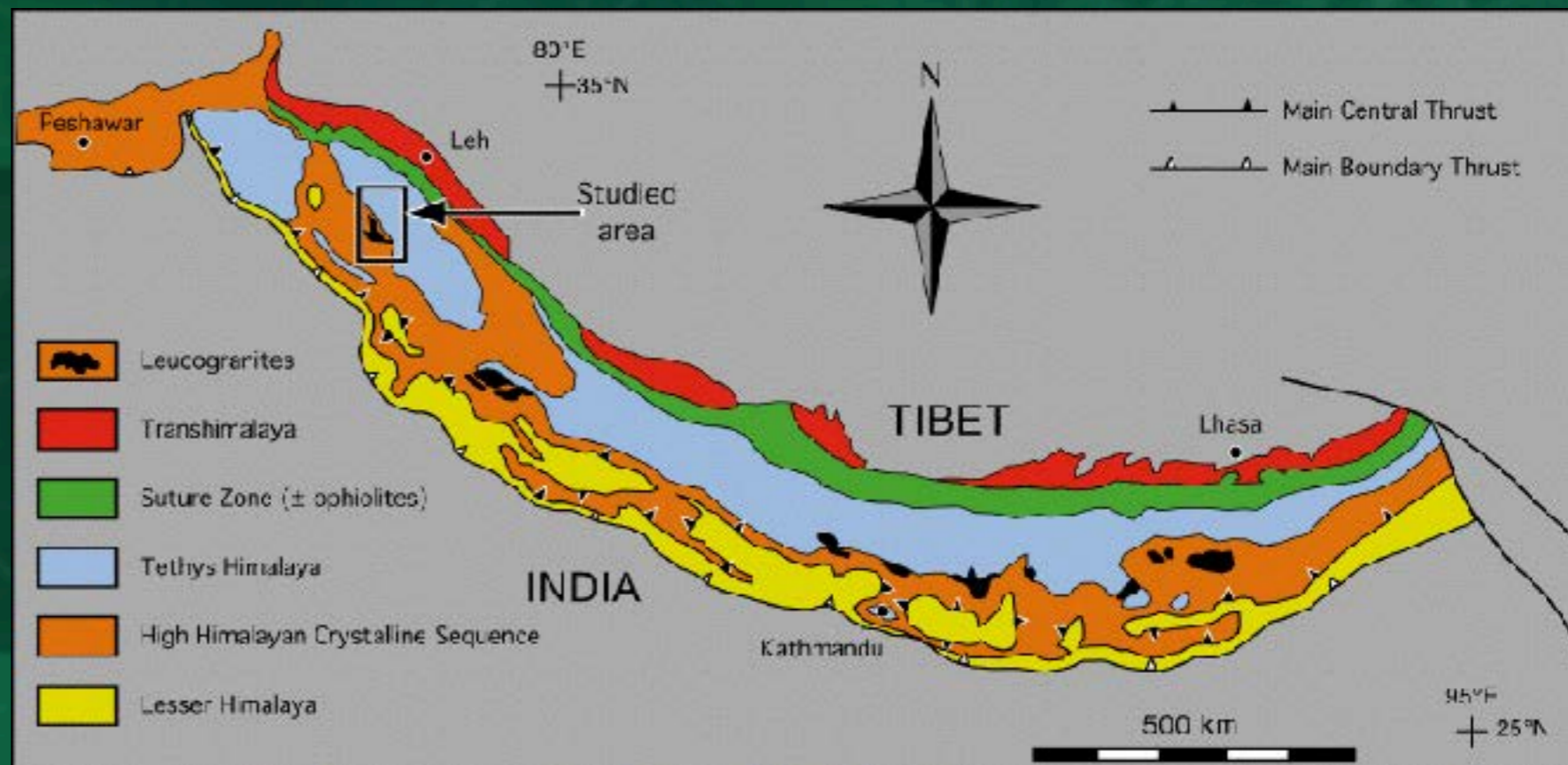
Earth in the Cretaceous

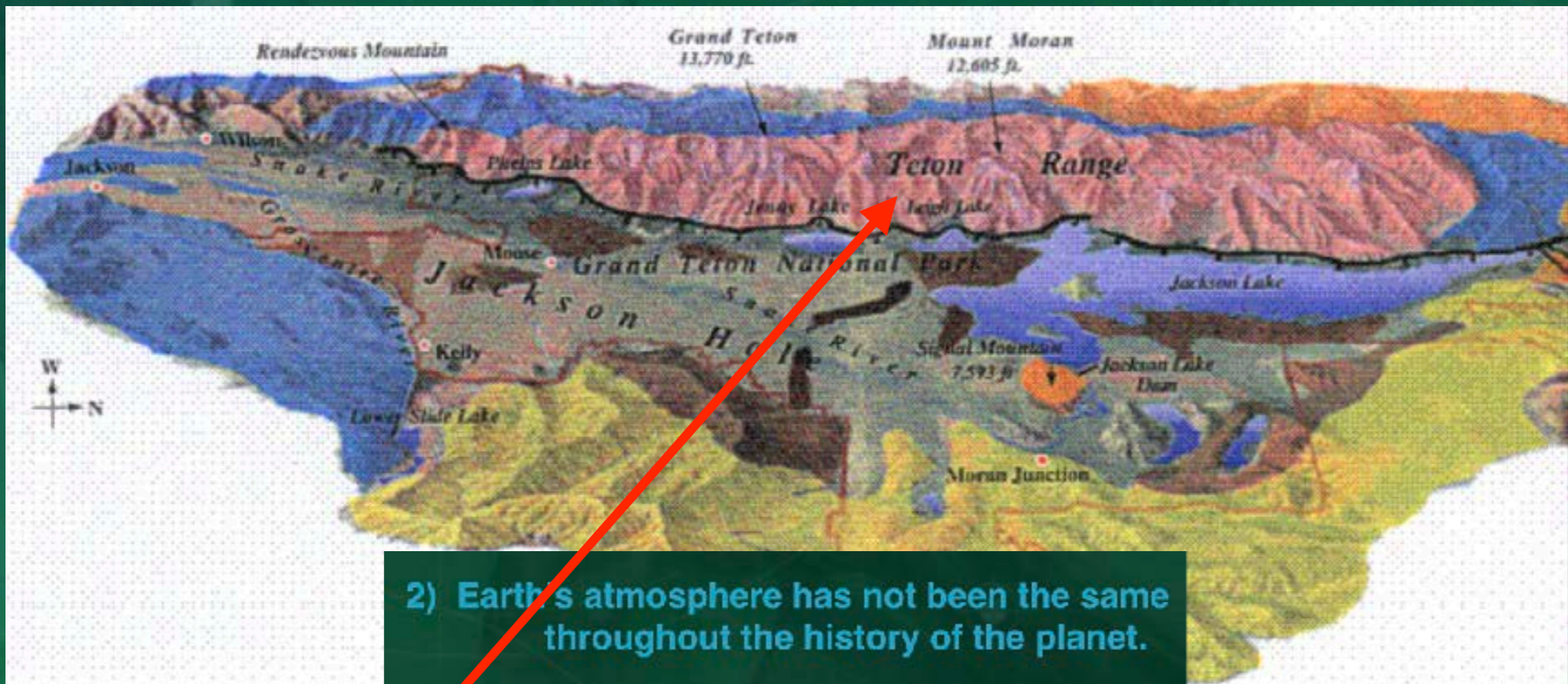


Mount Everest



tectonic plate movement





2) Earth's atmosphere has not been the same throughout the history of the planet.
 (4th dimension: time)

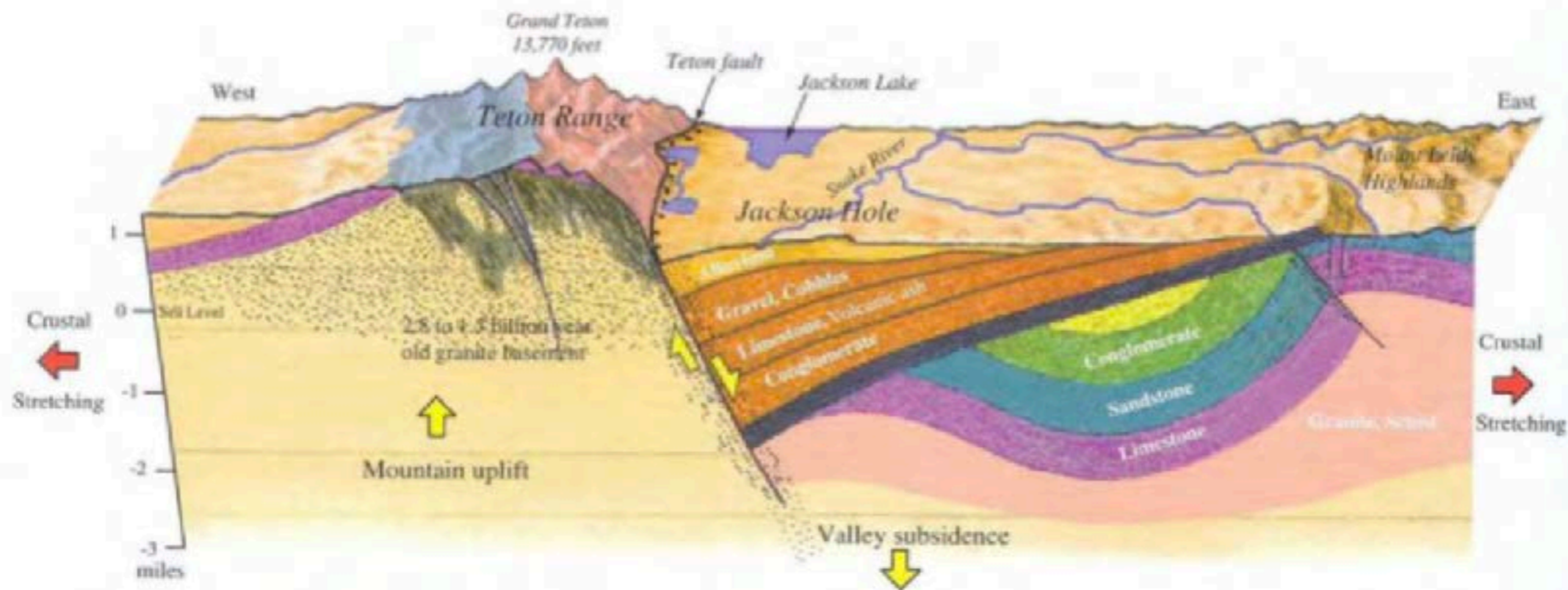
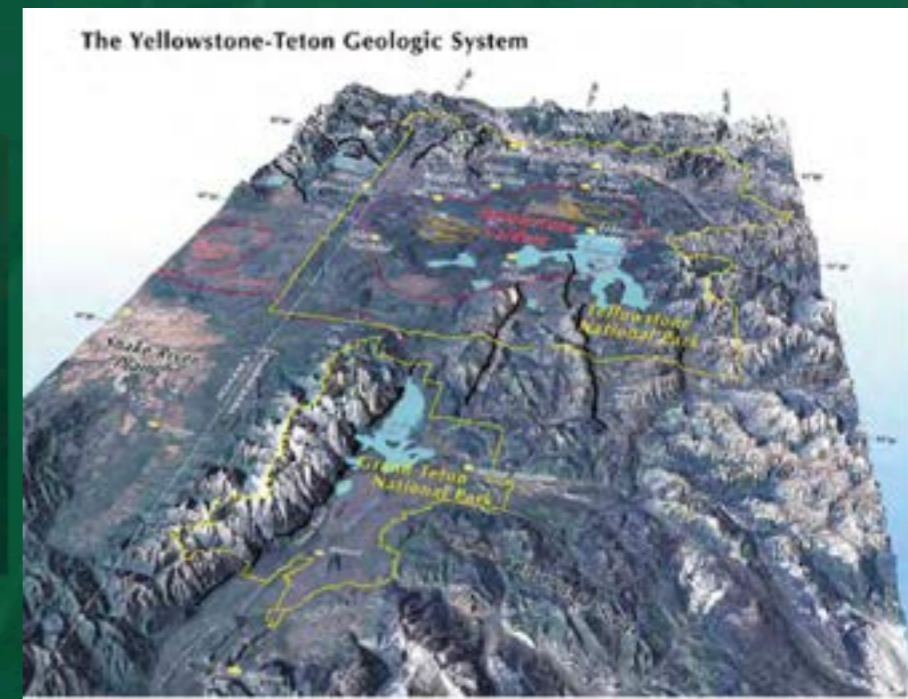
Legend

	2.8 and 1.5 billion year old crystalline basement: granitic and metamorphic rocks.
	540 to 245 million year old rocks primarily deposited in a deep ocean: limestone, sandstone, shale and dolomite.
	245 to 66 million year old rocks deposited mainly in a shallow ocean: siltstone, limestone, sandstone, gypsum, conglomerates, coal beds and shale.
	60 million to 3 million year old volcanic conglomerates, tuff, clay stone, sandstone deposited in shallow lakes accompanied by local volcanism.
	2 million year old rhyolite and welded tuff deposited during Yellowstone's first giant, caldera-forming volcanic eruption.
	150,000 to 14,000 year old glacial outwash and till deposited by glaciers.
	1.6 million year old to present, landslide and stream deposits, gravel, sand and alluvium.

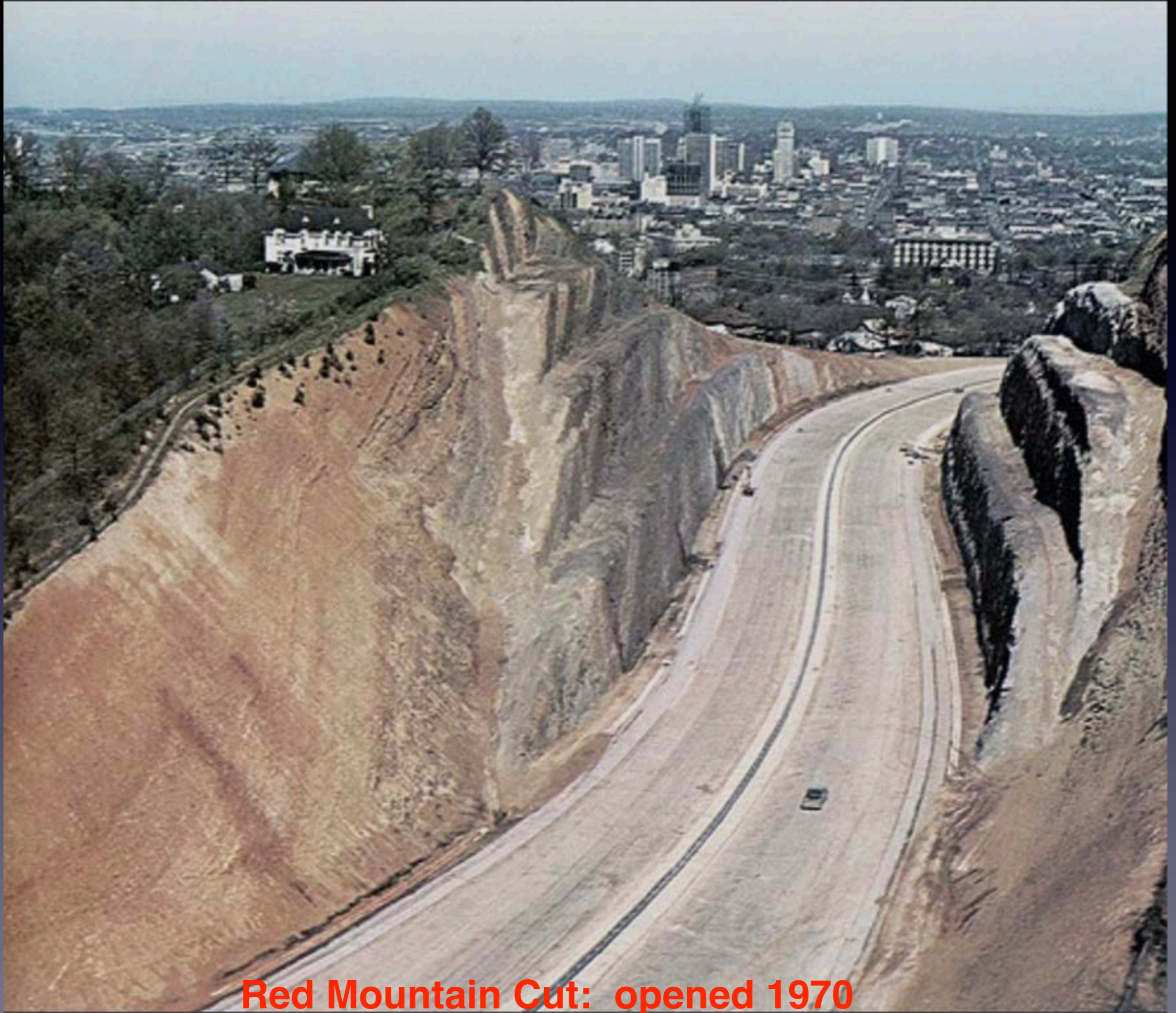


2) Earth's atmosphere has not been the same throughout the history of the planet.

(4th dimension: time)



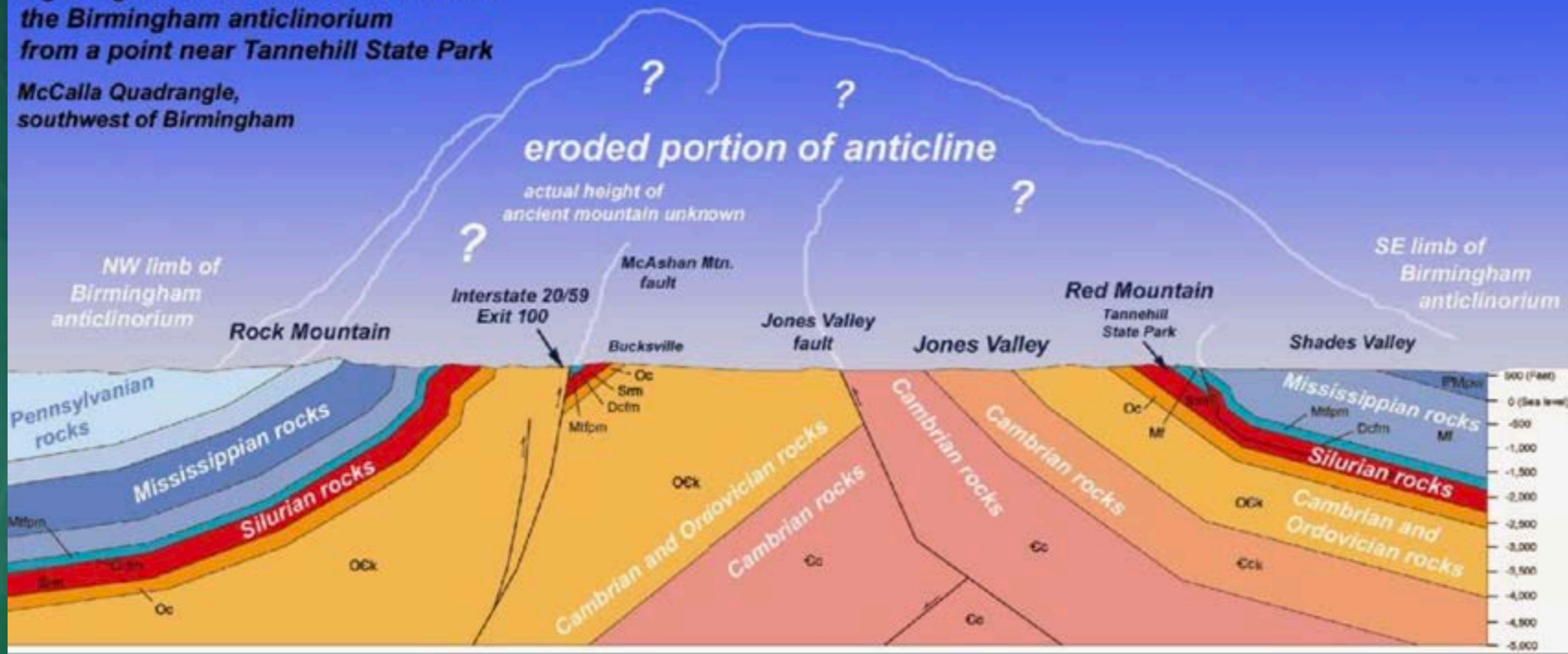
5.3 ~ Cross section showing the fault-caused westward tilt of rocks on the west side of the Teton Range and beneath Jackson Hole. Total movement on the Teton fault and from earlier mountain-building is about 6 miles, which is the elevation difference between rock layers high in the mountains and their projected location beneath Jackson Hole.



Red Mountain Cut: opened 1970

a geological cross section view inside the Birmingham anticlinorium from a point near Tannehill State Park

McCalla Quadrangle, southwest of Birmingham



Digging and grading took 7 years, from 1962 to 1969, and the cut was opened to traffic in 1970. The removal of 2 million cubic yards of the ridge of Red Mountain exposed over 190 million years of geologic strata dating to over 500 million years ago.

The Ordovician, Silurian, Devonian and Mississippian geologic periods are visible in the cut. Special features include caves, volcanic ash layers, the Red Mountain fault line, prehistoric reefs and beaches, fossils, and fossil tracks.

Significantly, the cut reveals the cross-section of the red ore seam that spurred Birmingham's development and a layer containing fossils of a unique Silurian trilobite species.

ROADSIDE GEOLOGY OF ALABAMA



Roadside Geology of Alabama

Paperback – April 15, 2023

by Mark Steltenpohl (Author), Laura Steltenpohl (Author),
Chelsea Feeney (Illustrator)



Mark Steltenpohl is an emeritus professor at Auburn University with more than 40 years of experience as a field geologist. **Laura Steltenpohl** taught science for 20 years at Auburn High School, mostly Chemistry, Physics, and Earth Science.

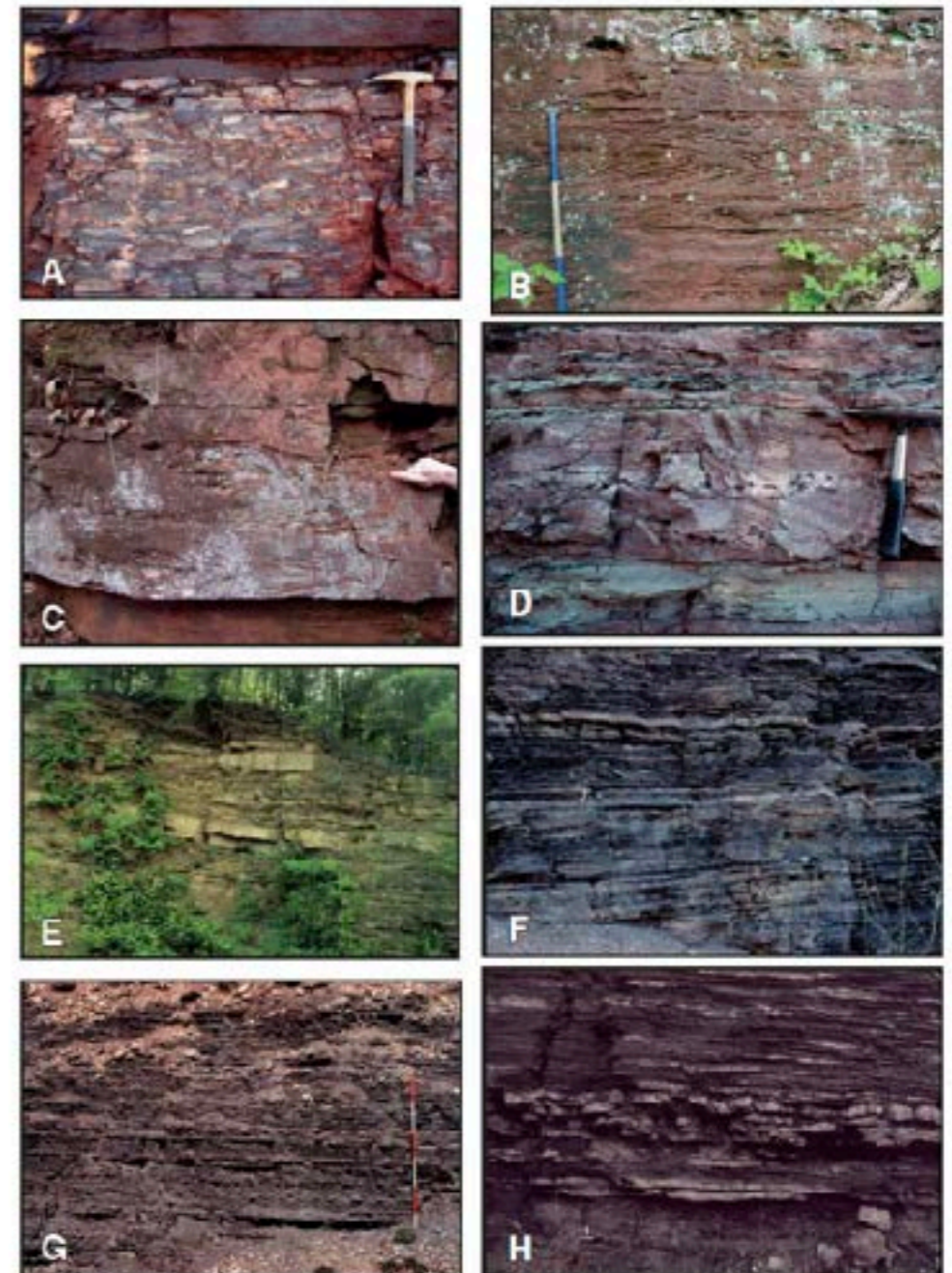


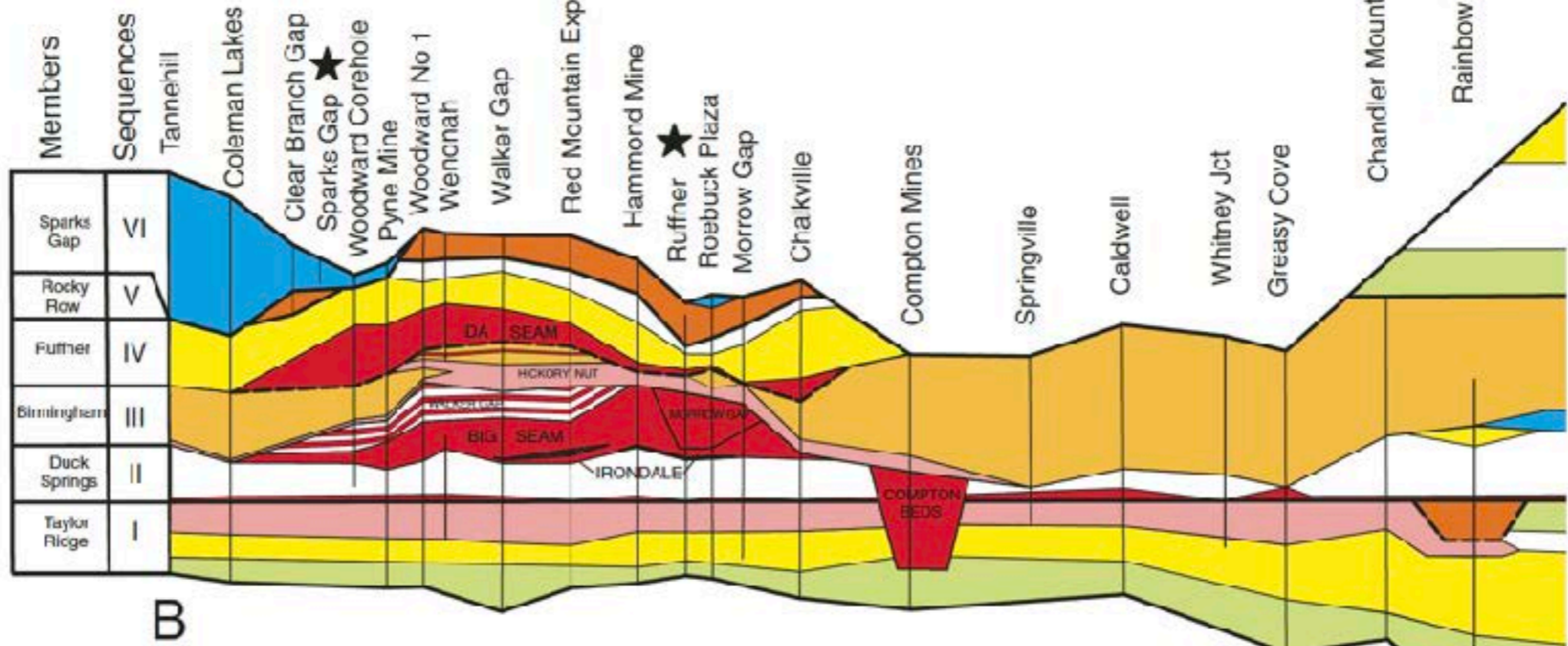
Figure 6. Major lithofacies in Red Mountain Formation. Inch staff scaled in feet, hammer ~1 foot. (A) Facies 1 Conglomeratic ravinement lag from the Kidney bed between the Big and Brodick seams at the type section. Intracasts include fibritic and unfoliated ironstone and limestone. (B) Facies 1. Cross-bedded ironstone from tidal inlet facies, Merren Gap beds at Ruffner Mines, Alabama. (C) Facies 1. Ripple-bed (bar-ringstone) cross-beds from Merren Gap tidal channel, Ruffner Mines, AL. (D) Facies 1. Cross-bedded tidal-delta sandstone interbedded with estuarine shale, Walter Gap beds, type section. (E) Facies 3. Hummocky cross-bedded sandstone facies, Taylor Ridge Member, Estelle, Georgia. (F) Facies 5. Thin, fine-grained graded sandstones (storm beds) interbedded with shale, Taylor Ridge Member, Ringgold, GA. (G) Facies 5. Shale with thin siltstone storm beds, base of Taylor Ridge Member, Ringgold, GA. (H) Facies 6. Interbedded limestone-shale facies; base of Birmingham Member, Duck Springs, AL.

Stratigraphy and depositional environments in the Silurian Red Mountain Formation of the southern Appalachian basin

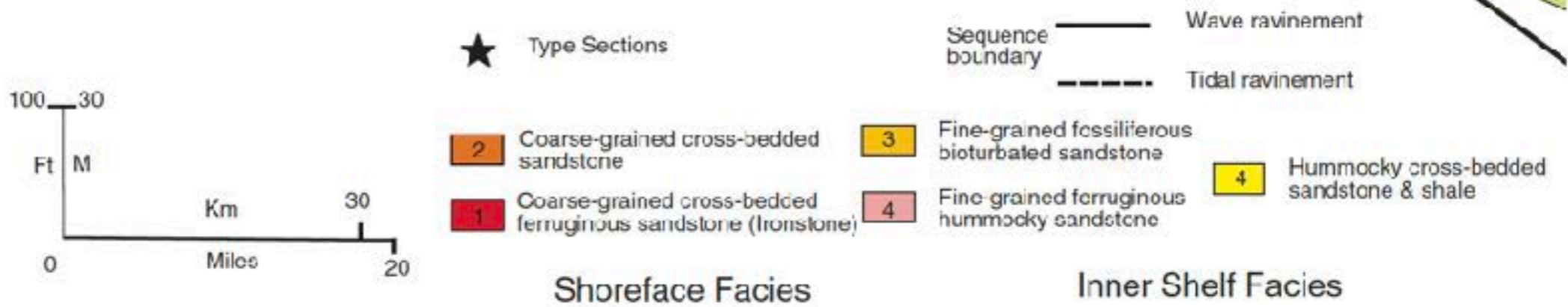
The Geological Society of America - Field Guide 39 - 2015

Timothy M. Chowns* - Department of Geosciences, University of West Georgia
Andrew K. Rindsberg* - Department of Biological & Environmental Sciences, University of West Alabama

Southwest



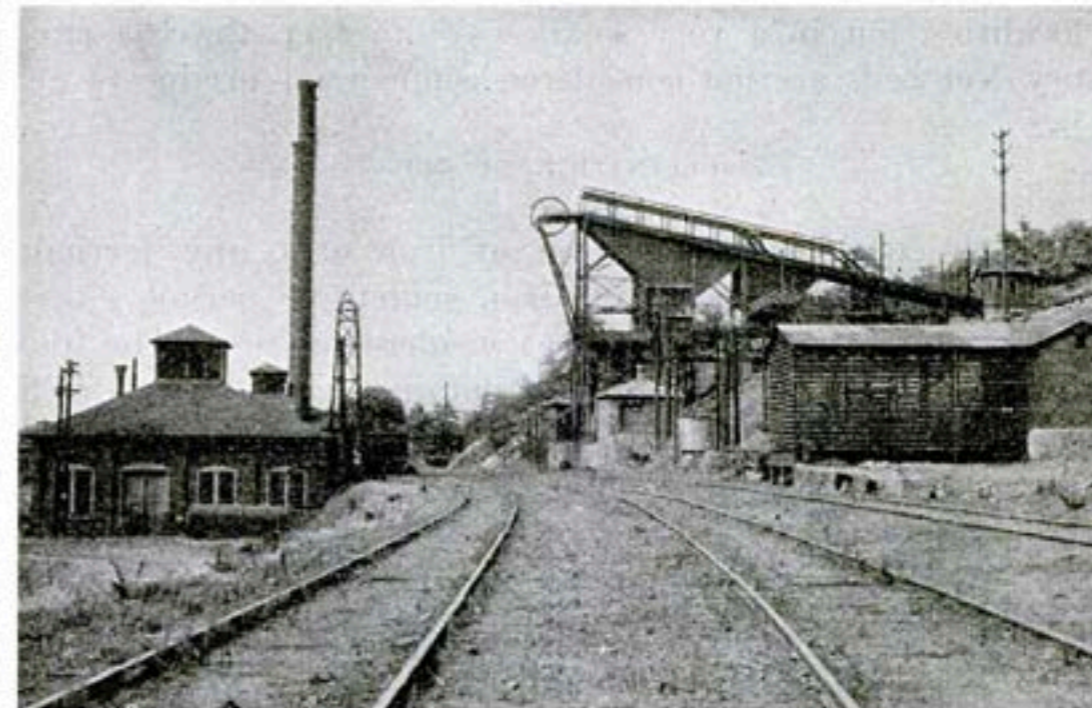
Birmingham Platform



There are both Red Iron Ore (Hematite) and Brown Iron Ore (Limonite) deposits in the vicinity of Birmingham. These deposits are the southeastern continuation of the Silurian Clinton Iron Formation which extends from New York State along the Appalachian Mountains. Red Mountain on the east side of the city was the location for most of the iron mines. Many antebellum charcoal furnaces utilized the Brown Limonite Ore; however, after the Civil War, the mainstay of the iron and steel industry was the Red Mountain Hematite Ore. The hematite ore beds were in the Red Mountain Formation with a dip of about 16° . The greatest production came from the "Big Seam." This seam was 15-22 feet thick and divided into parts by a small bed of slate. Smaller amounts of production came from the thinner Ida and Irondale Seams located above and below the Big Seam respectively.



Entrance to a Red Mountain Underground Iron Mine, ca 1908.. (Library of Congress)



Ore tipple and railroad loading facilities at a Red Mountain Iron Ore Mine, ca 1923. (USBM)

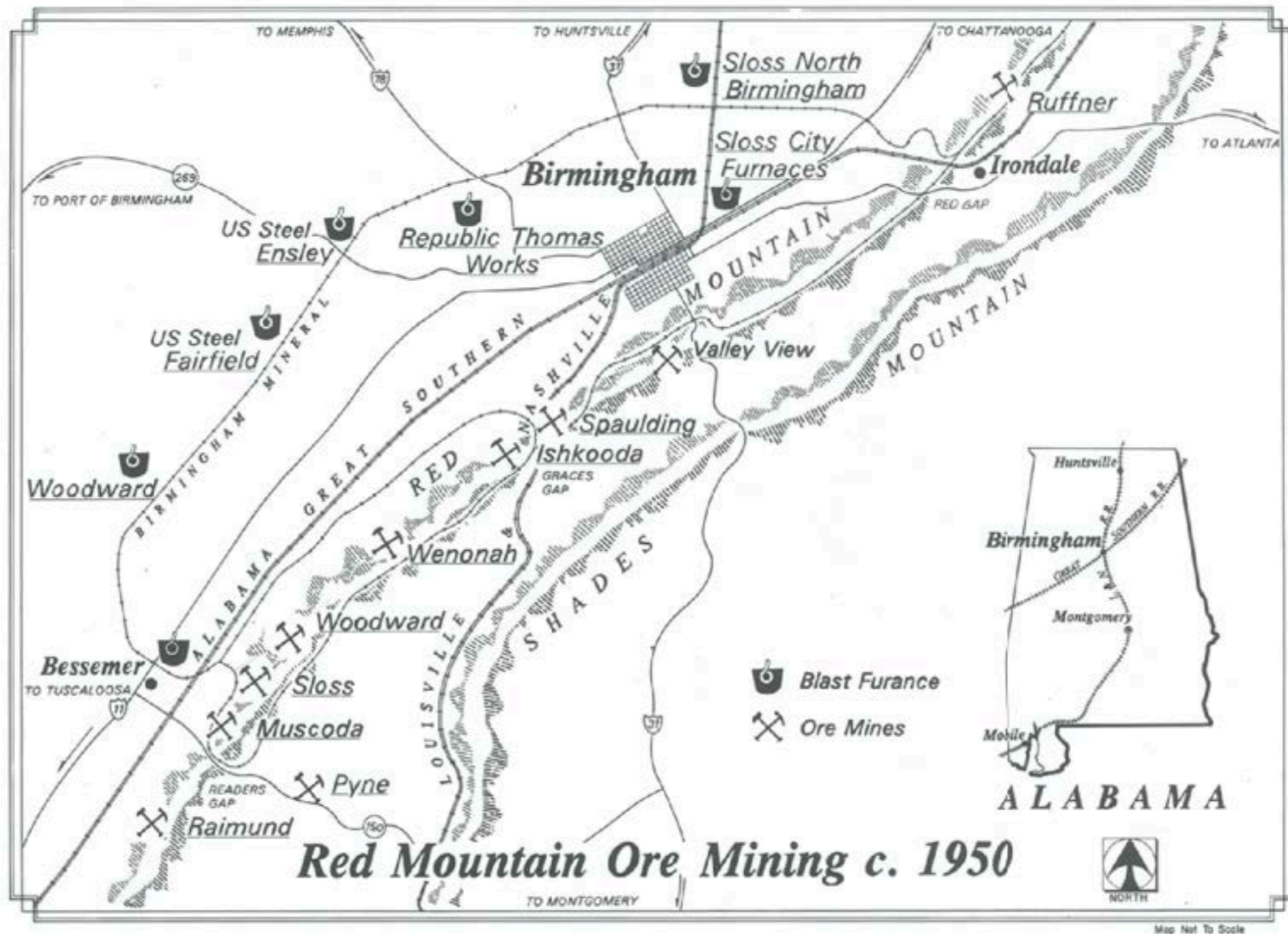


Figure 16. Location of major mines along Red Mountain. (From Morris and White, 1997.)



1970



2022

See: **Red Mountain Cut Project pics**



ROCK FACE
STABILIZATION & NETTING
AS NEEDED

TRAIL IS BUILT
ON-GRADE

EDUCATIONAL SIGNAGE
HIGHLIGHTING GEOLOGY

FACE OF CUT CLEARED
OF VEGETATION &
LOOSE ROCK

GMC

2025



DOWNTOWN
BIRMINGHAM


MINE ENTRANCE
GATEWAY

RED MOUNTAIN CUT
TRAIL

20TH AVE. S.

ON-STREET TRAIL TO
21ST AVE S.
&
ON-STREET PARALLEL
PARKING

21ST STREET SOUTH
BECOMES ONE-WAY

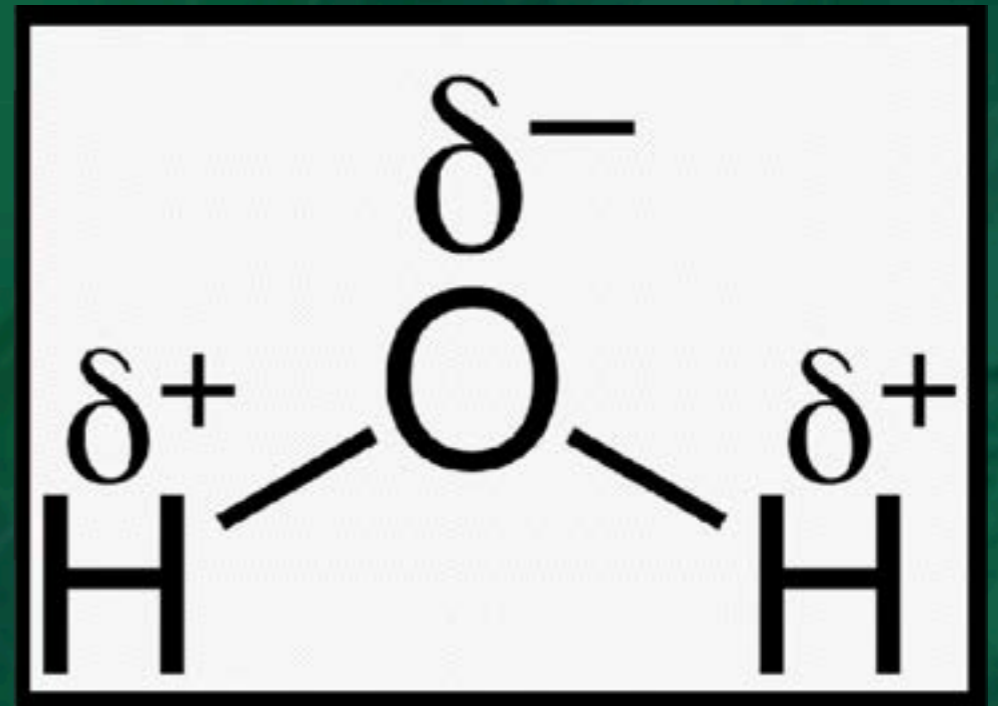
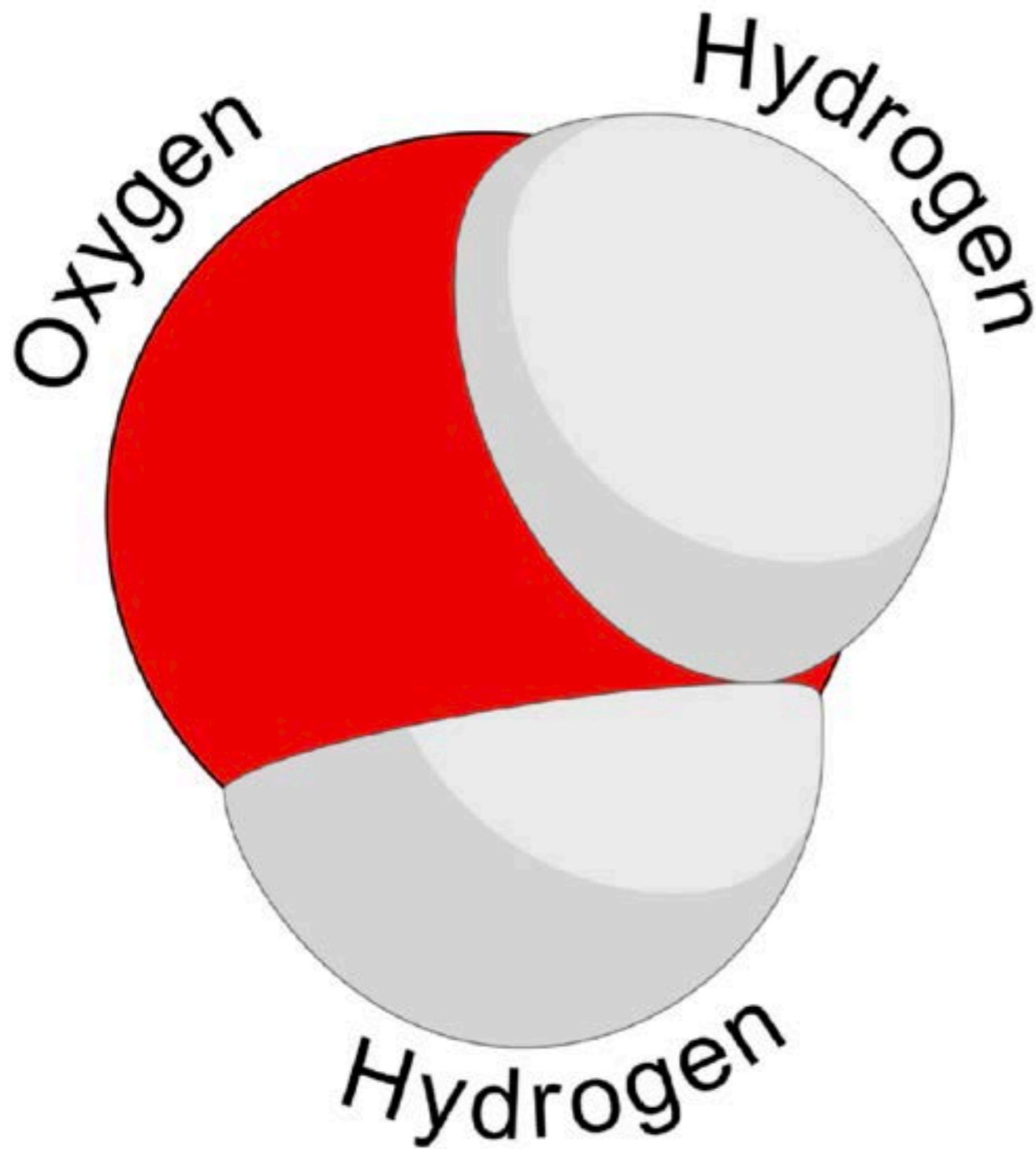
An architectural rendering of a pedestrian and bicycle trail. The trail is a wide, light-colored path that ascends a hillside. It is bordered on both sides by a guardrail system consisting of vertical posts and stainless steel netting. To the left of the trail, a multi-lane highway with several cars is visible. The hillside to the right is covered in green grass and trees. In the foreground, the backs of several people are visible as they walk along the path. The sky is bright with scattered clouds.

**TRAIL CLIMBS FROM 21ST SOUTH TO
1ST BENCH OF THE RED MOUNTAIN CUT**

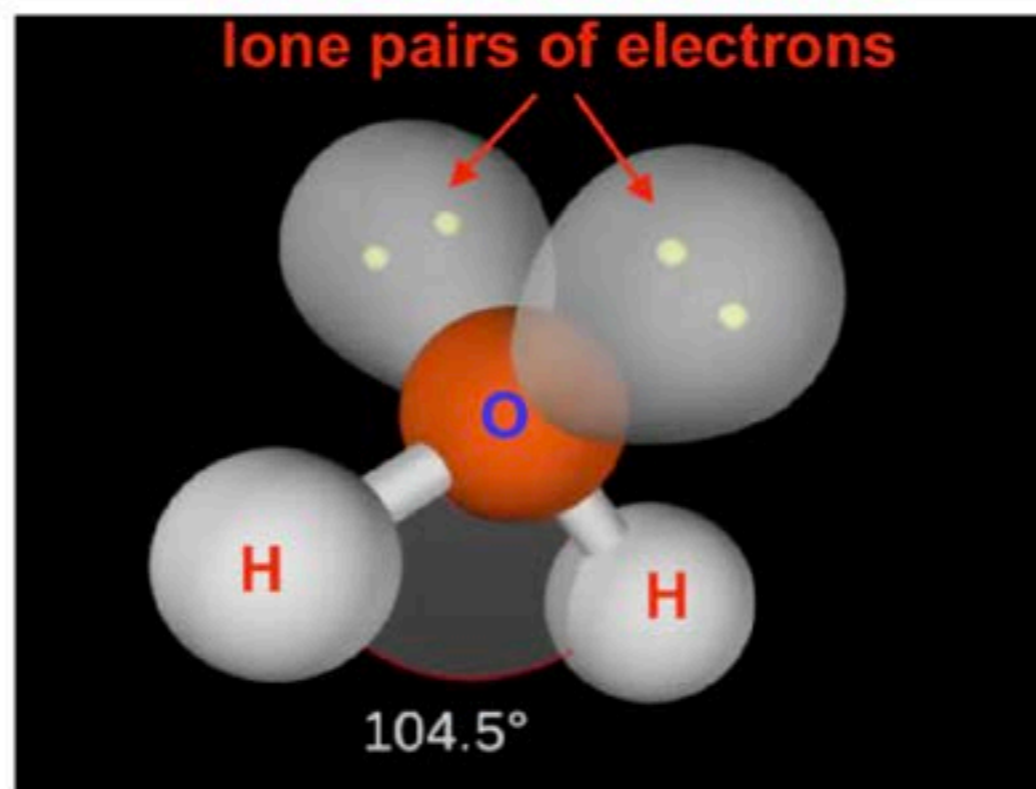
**GUARDRAIL HEIGHT: 54 INCHES,
STAINLESS STEEL NETTING**

**14 FT WIDE PATH,
LESS THAN 5° SLOPE**

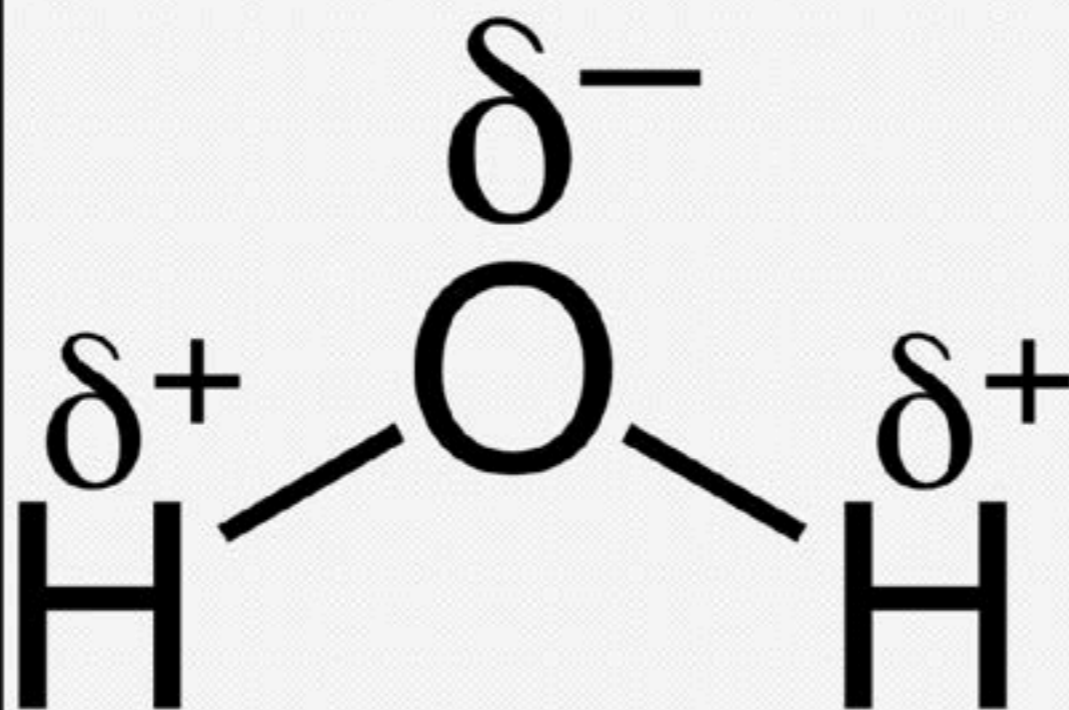
GMC

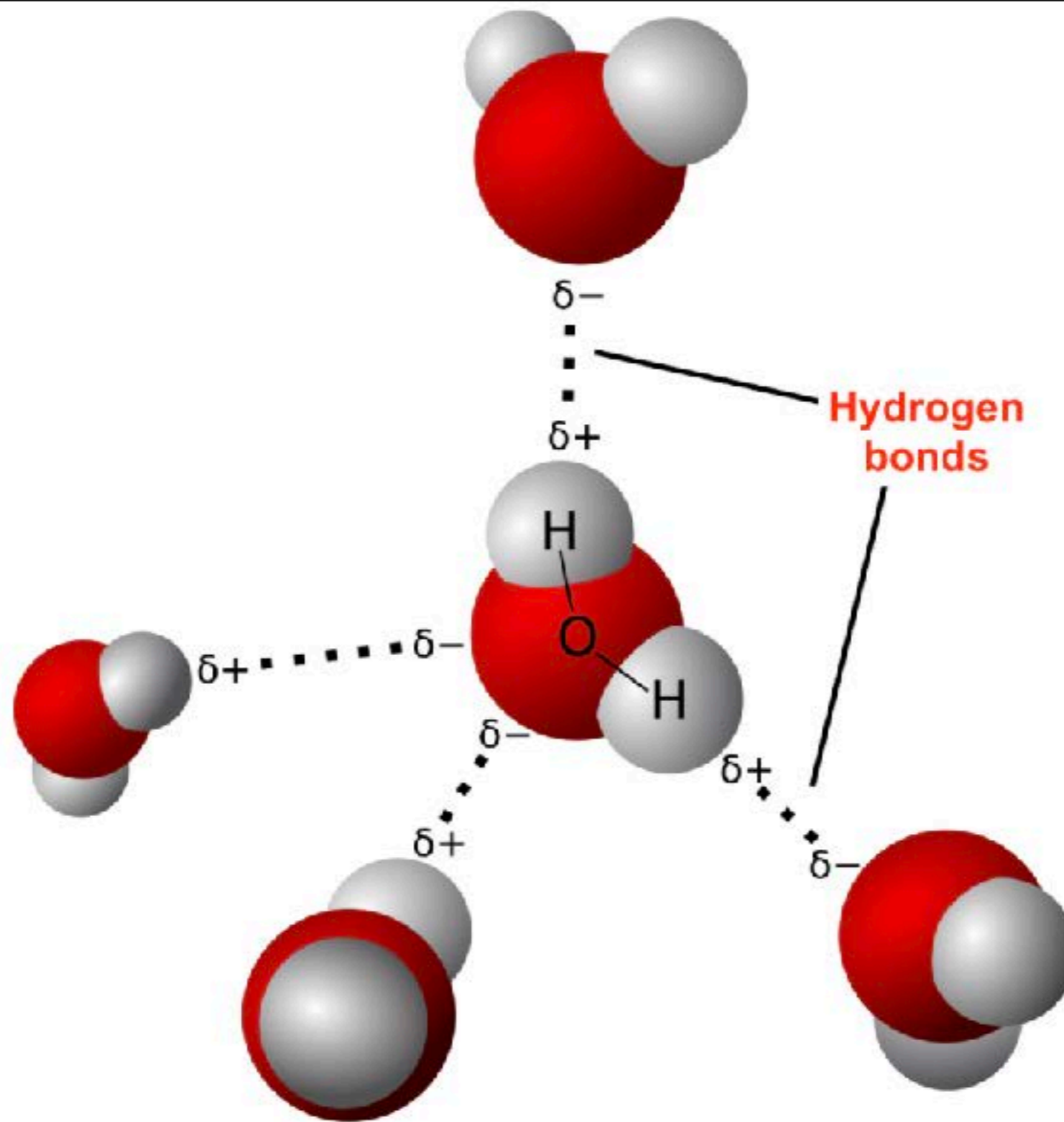


The angular structure of the H₂O molecule results in its electrical polarity, which is necessary for the function of membranes, which are the essential boundaries of living cells.



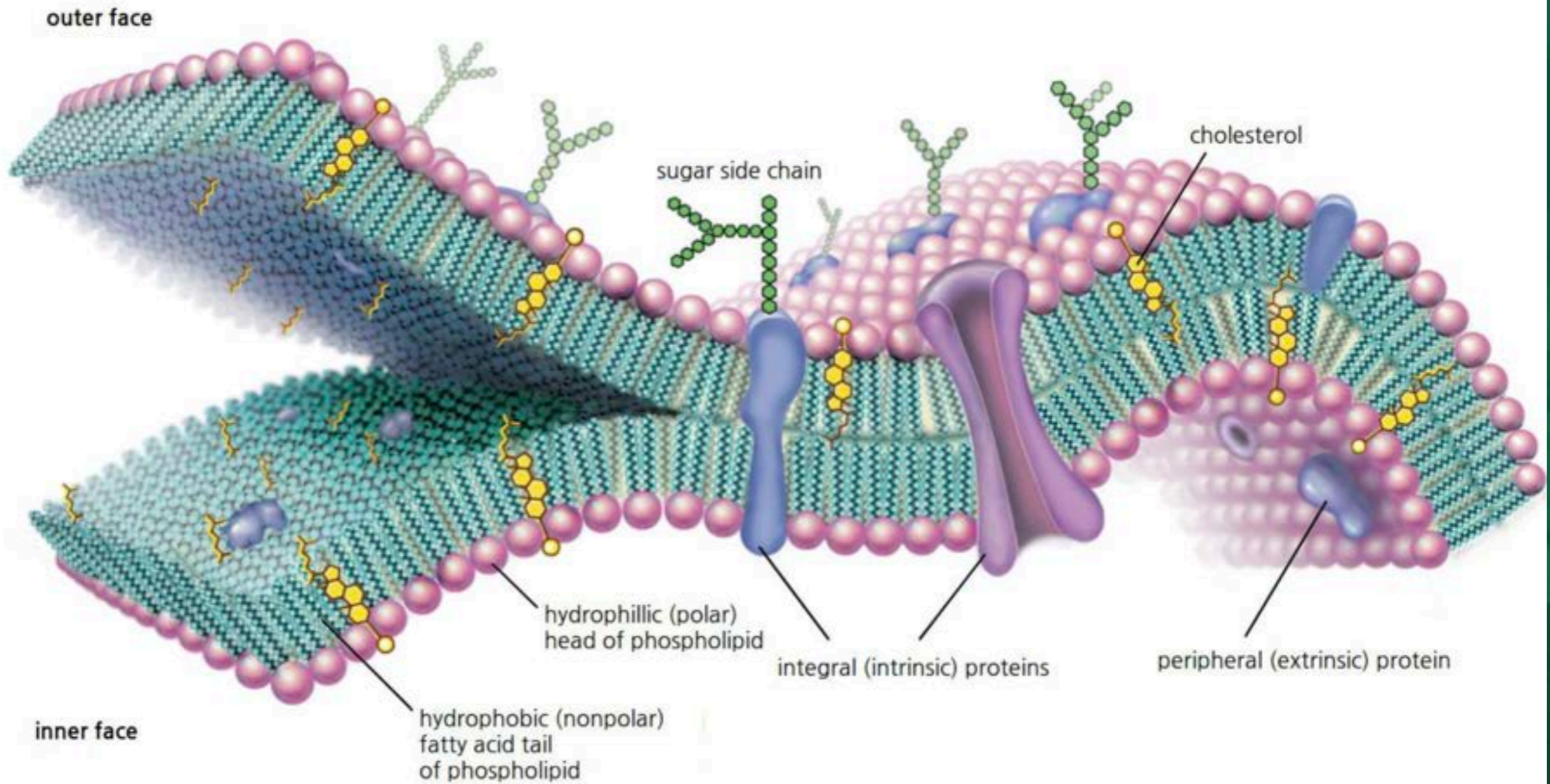
There are six electrons in the outer orbital of an oxygen atom. In a water molecule, two of these electrons bond with the lone electron of each hydrogen atom to form two "bond pairs". The remaining four oxygen electrons pair up to form two "lone pairs". (It is energetically favorable for electrons with opposite spins to form pairs.)





The weak hydrogen bonds formed between water molecules are responsible for many of the unique properties of liquid water.

The bipolar lipid membrane always forms the boundary of every cell, separating the aqueous internal living system from the aqueous external nonliving environment.

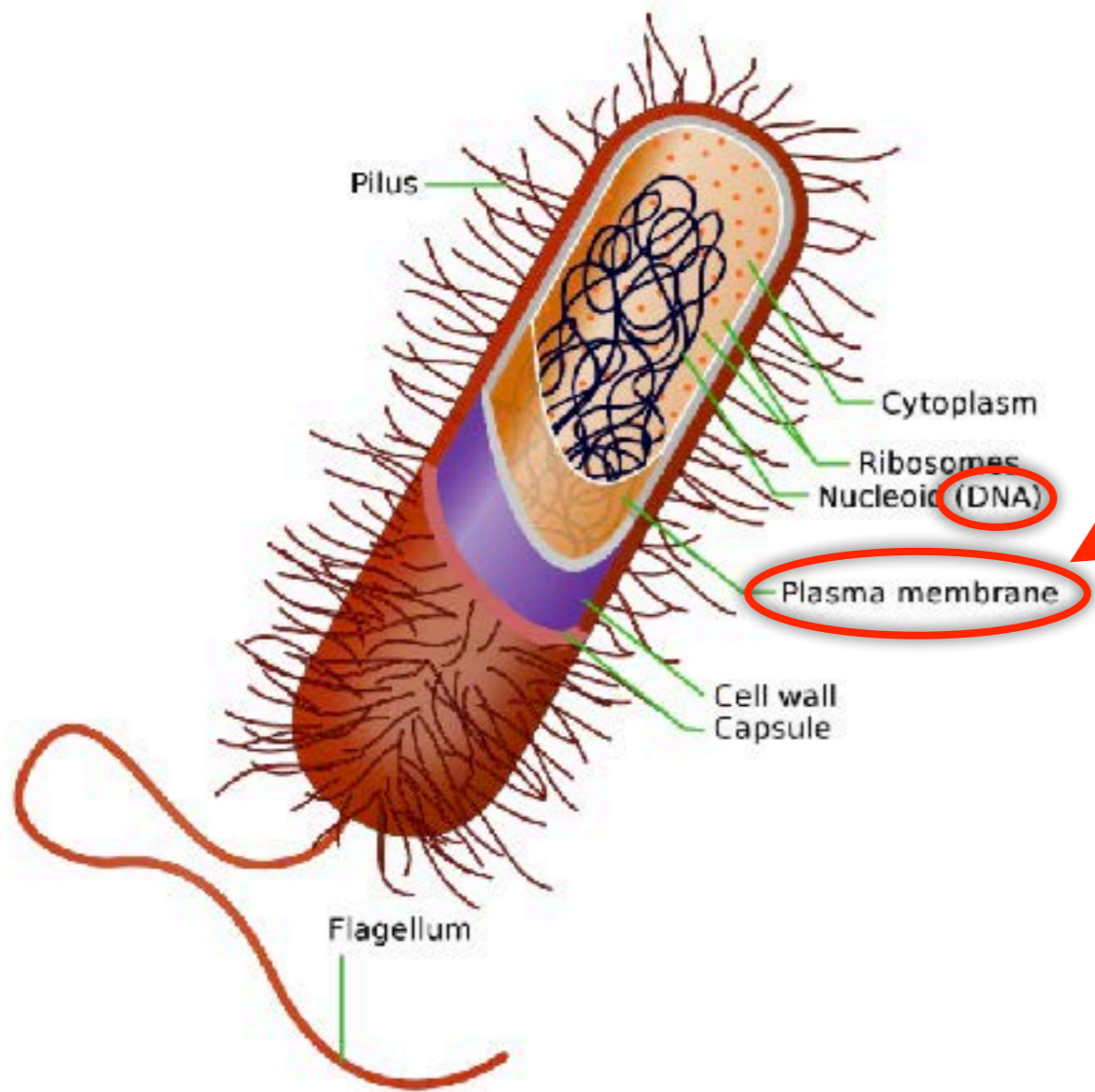


Rudolph Virchow is best remembered today for his succinct proclamation (1858) of one of biology's universal laws:

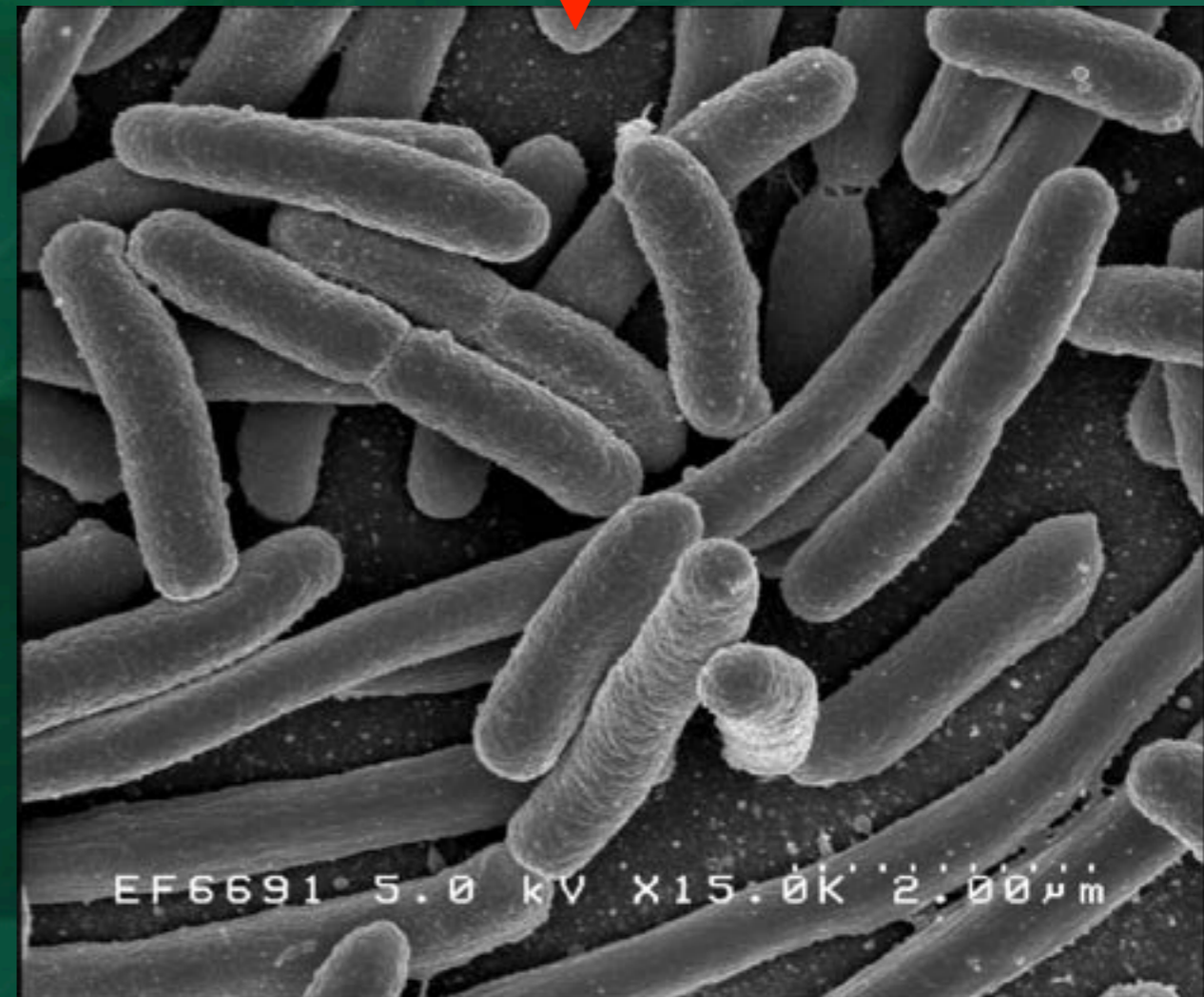
Omnis cellula e cellula.

Every cell comes from a preexistent cell.

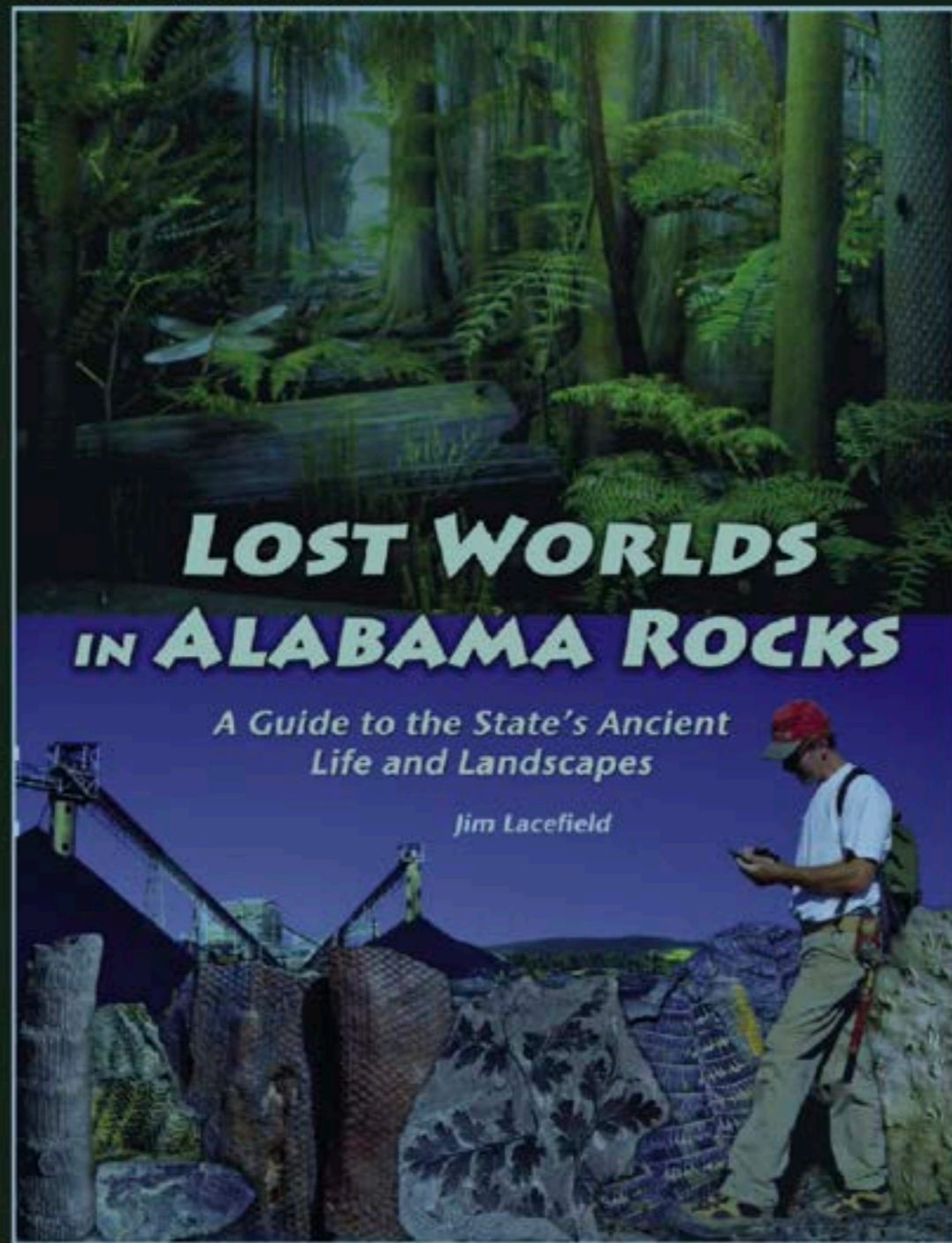
Omnis cellula e cellula



Every cell is contained by a bilayer lipid membrane, which separates the aqueous living system inside from the aqueous environment outside.



Revised and Expanded Second Edition



The Alabama Museum of Natural History

c. 2013

A Timetable of Alabama Geologic History

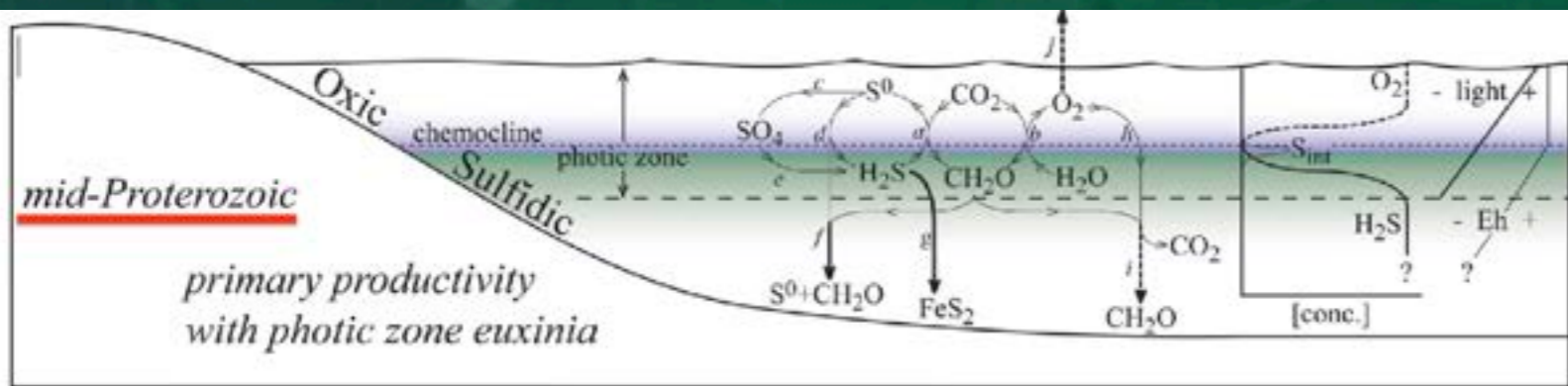
Time Period	When Began (in millions of years)	Significant Events in Alabama's Geologic History	
Cenozoic Era	Quaternary 10,000 years 2.6	Holocene our present epoch of Earth history Pleistocene the "Ice Age"; Alabama ecosystems unlike today—northern tree species, megafauna	
	Tertiary Period	Pliocene 5	Alabama landscape undergoes slight uplift, deep erosion of uplands
		Miocene 23	Earth's climate becomes unstable; fossil pollen studies show deciduous trees start to dominate Alabama forests
	Epochs	Oligocene 34	Alabama climate warm and wet, forests still contain many tropical tree species; lignite coal forms in Gulf coastal marshes
		Eocene 56	Alabama climate warm and wet, forests still contain many tropical tree species; lignite coal forms in Gulf coastal marshes
Mesozoic Era	Cretaceous 146	sea levels very high, warm oceans cover most of Alabama; "Selma chalk" forms offshore; dinosaurs roam tropical jungles	
	Jurassic 200	opening of the Gulf of Mexico; Alabama climate still hot and dry; rich oil deposits form along edge of young, expanding Gulf	
	Triassic 251	supercontinent of Pangaea begins to rift apart; Alabama moves north of the equator; state's climate and landscape desert-like	
Paleozoic Era	Permian 299	probable peak of Appalachian Mtn. formation, Alabama locked within dry interior of Pangaea, no rocks from this time known from the state	
	Carboniferous	Pennsylvanian 318	"Coal Age" forests; Pangaea forms
		Mississippian 359	widespread limestones deposited
	Devonian 416	sometimes called the "age of fishes", but land plants and animals also diversify and move farther from the water's edge	
	Silurian 444	Birmingham's Red Mountain iron ores form; terrestrial (land) environments first invaded by plants and animals	
	Ordovician 488	tropical seas cover most of the state; Alabama rocks show mountain-building, volcanic activity was nearby to the east	
	Cambrian Period 542 million years ago	Alabama on passive margin of ancient North American continent Laurentia; earliest fossils appear in Alabama rocks	
"Precambrian"	"Precambrian" (represents about 87% of the Earth's history)	first multicellular organisms appear in the fossil record Grenville mountain-building episode; deep crust beneath Alabama added	
	Proterozoic Eon 2.5 billion	first "free" oxygen accumulates in the Earth's atmosphere	
	Archaean Eon 3.8 billion 4 billion	earliest fossilized bacteria appear in the geologic record age of Earth's oldest known rocks	

Life and the Land Through Time

Life and the Land Through Time

Timeline of life and land in Alabama:

- 4 billion years ago:** Earliest fossilized bacteria appear in the geologic record.
- 3.8 billion years ago:** Earliest fossilized bacteria appear in the geologic record.
- 2.5 billion years ago:** First "free" oxygen accumulates in the Earth's atmosphere.
- 1.8 billion years ago:** First eukaryotic cells (have nucleus) appear.
- 1.5 billion years ago:** Banded iron formations.
- 1.2 billion years ago:** Cyanobacteria ("blue-green algae") live photosynthetically without oxygen through photosynthesis.
- 1.0 billion years ago:** First eukaryotic cells (have nucleus) appear.
- 800 million years ago:** First eukaryotic cells (have nucleus) appear.
- 600 million years ago:** First eukaryotic cells (have nucleus) appear.
- 542 million years ago:** Cambrian explosion; first multicellular organisms appear in the fossil record.
- 488 million years ago:** Ordovician period; tropical seas cover most of the state.
- 444 million years ago:** Silurian period; Birmingham's Red Mountain iron ores form.
- 416 million years ago:** Devonian period; sometimes called the "age of fishes".
- 359 million years ago:** Mississippian period; widespread limestones deposited.
- 318 million years ago:** Pennsylvanian period; "Coal Age" forests.
- 299 million years ago:** Permian period; probable peak of Appalachian Mtn. formation.
- 251 million years ago:** Triassic period; supercontinent of Pangaea begins to rift apart.
- 200 million years ago:** Jurassic period; opening of the Gulf of Mexico.
- 146 million years ago:** Cretaceous period; sea levels very high, warm oceans cover most of Alabama.
- 56 million years ago:** Eocene epoch; Alabama climate warm and wet.
- 34 million years ago:** Oligocene epoch; Alabama climate warm and wet.
- 23 million years ago:** Miocene epoch; Earth's climate becomes unstable.
- 5 million years ago:** Pliocene epoch; Alabama landscape undergoes slight uplift.
- 2.6 million years ago:** Pleistocene epoch; the "Ice Age"; Alabama ecosystems unlike today.
- 10,000 years ago:** Holocene epoch; our present epoch of Earth history.



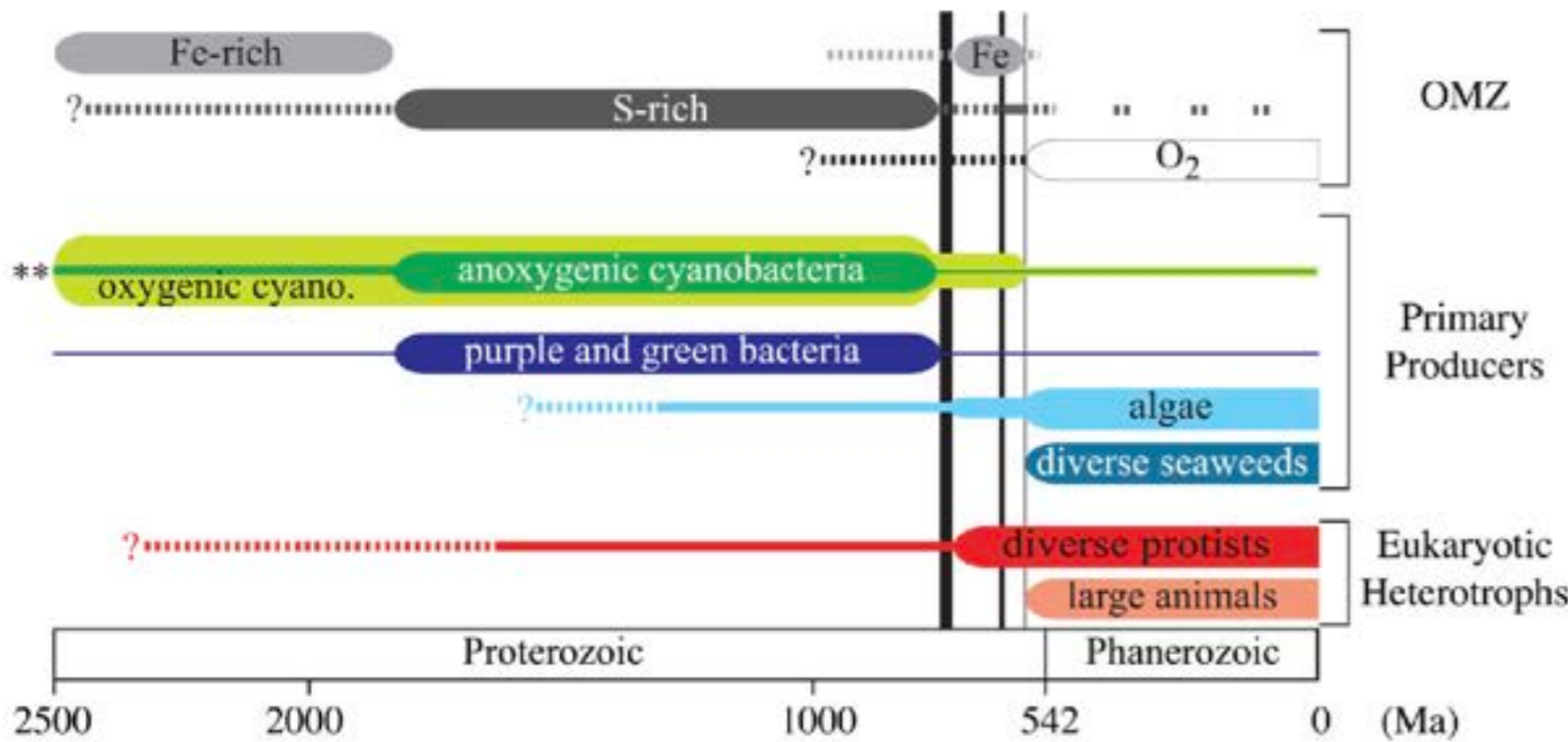
Anoxygenic photosynthesis modulated Proterozoic oxygen and sustained Earth's middle age

D. T. Johnston^{1,2,3,4}, F. Wolfe-Simon^{1,2,3,4}, A. Pearson^{1,2,3,4}, and A. H. Knoll^{1,2,3,4}

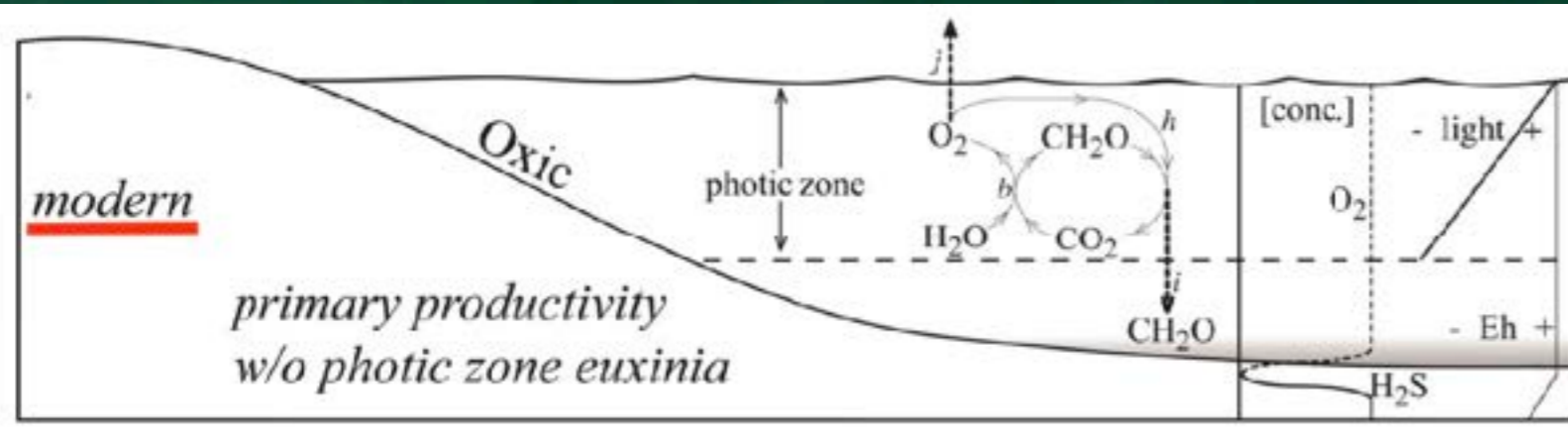
¹Department of Earth and Planetary Sciences, Harvard University, 20 Oxford Street, Cambridge, MA, 02138; and ²Department of Organismic and Evolutionary Biology, Harvard University, 76 Oxford Street, Cambridge, MA, 02138

Contributed by A. H. Knoll, August 14, 2009 (sent for review January 6, 2009)

PNAS - 2009



Molecular oxygen (O₂) began to accumulate in the atmosphere and surface ocean ca. 2,400 million years ago (Ma), but the persistent oxygenation of water masses throughout the oceans developed much later, perhaps beginning as recently as 580–550 Ma. For much of the intervening interval, moderately oxidic surface waters lay above an oxygen minimum zone (OMZ) that tended toward euxinia (anoxic and sulfidic). Here we illustrate how contributions to primary production by anoxygenic photoautotrophs (including physiologically versatile cyanobacteria) influenced biogeochemical cycling during Earth's middle age, helping to perpetuate our planet's intermediate redox state by tempering O₂ production. Specifically, the ability to generate organic matter (OM) using sulfide as an electron donor enabled a positive biogeochemical feedback that sustained euxinia in the OMZ. On a geologic time scale, pyrite precipitation and burial governed a second feedback that moderated sulfide availability and water column oxygenation. Thus, we argue that the proportional contribution of anoxygenic photosynthesis to overall primary production would have influenced oceanic redox and the Proterozoic O₂ budget. Later Neoproterozoic collapse of widespread euxinia and a concomitant return to ferruginous (anoxic and Fe²⁺ rich) subsurface waters set in motion Earth's transition from its prokaryote-dominated middle age, removing a physiological barrier to eukaryotic diversification (sulfide) and establishing, for the first time in Earth's history, complete dominance of oxygenic photosynthesis in the oceans. This paved the way for the further oxygenation of the oceans and atmosphere and, ultimately, the evolution of complex multicellular organisms.



Evolution of Air Breathing: Oxygen Homeostasis and the Transitions from Water to Land and Sky

Connie C. W. Hsia¹, Anke Schmitz², Markus Lambertz², Steven F. Perry², and John N. Maina³

¹Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, Texas

²Institut für Zoologie, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Germany

³Department of Zoology, University of Johannesburg, Johannesburg, South Africa

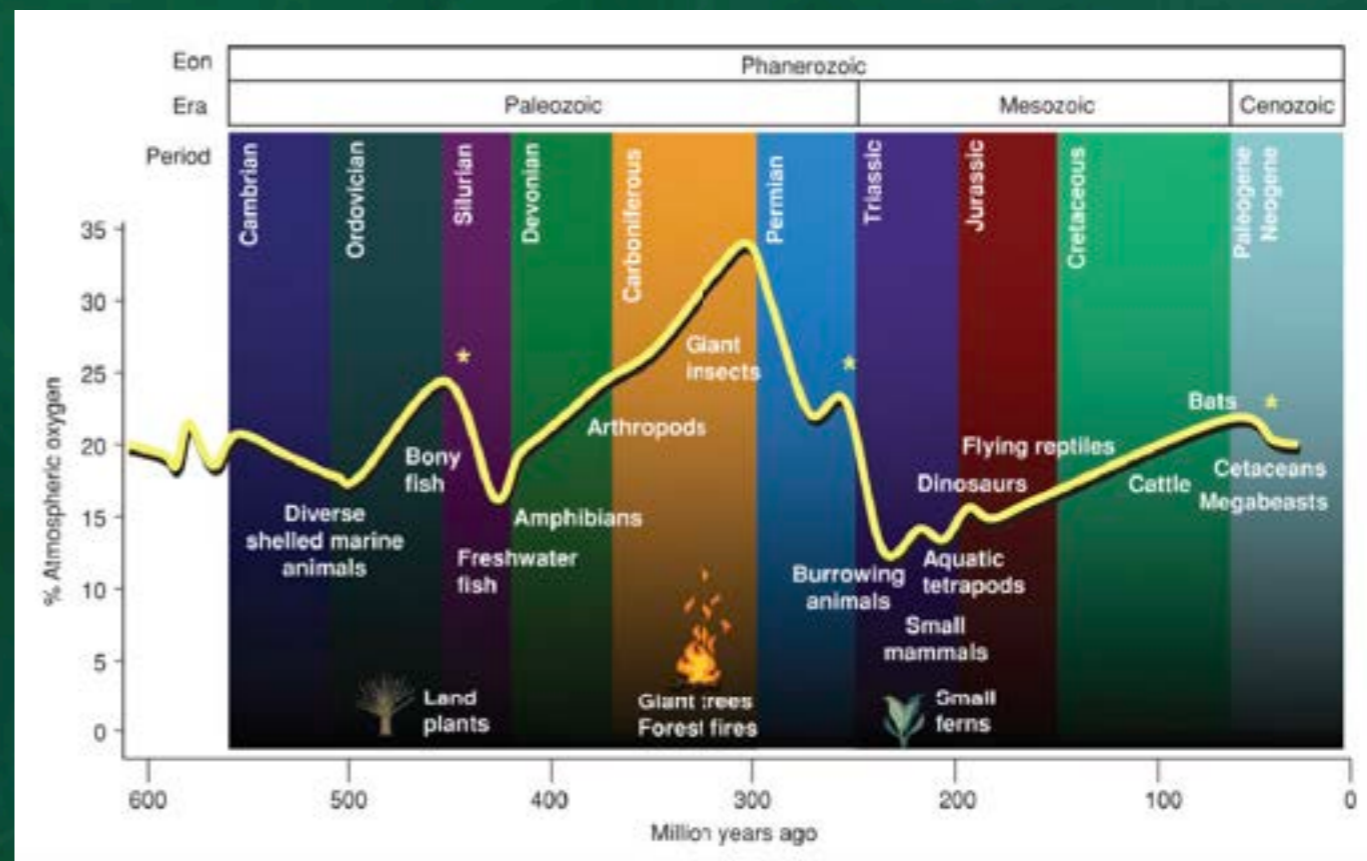
Abstract

Life originated in anoxia, but many organisms came to depend upon oxygen for survival, independently evolving diverse respiratory systems for acquiring oxygen from the environment. Ambient oxygen tension (PO_2) fluctuated through the ages in correlation with biodiversity and body size, enabling organisms to migrate from water to land and air and sometimes in the opposite direction. Habitat expansion compels the use of different gas exchangers, for example, skin, gills, tracheae, lungs, and their intermediate stages, that may coexist within the same species; coexistence may be temporally disjunct (e.g., larval gills vs. adult lungs) or simultaneous (e.g., skin, gills, and lungs in some salamanders). Disparate systems exhibit similar directions of adaptation: toward larger diffusion interfaces, thinner barriers, finer dynamic regulation, and reduced cost of breathing. Efficient respiratory gas exchange, coupled to downstream convective and diffusive resistances, comprise the “oxygen cascade” — step-down of PO_2 that balances supply against toxicity. Here, we review the origin of oxygen homeostasis, a primal selection factor for all respiratory systems, which in turn function as gatekeepers of the cascade. Within an organism's lifespan, the respiratory apparatus adapts in various ways to upregulate oxygen uptake in hypoxia and restrict uptake in hyperoxia. In an evolutionary context, certain species also become adapted to environmental conditions or habitual organismic demands. We, therefore, survey the comparative anatomy and physiology of respiratory systems from invertebrates to vertebrates, water to air breathers, and terrestrial to aerial inhabitants. Through the evolutionary directions and variety of gas exchangers, their shared features and individual compromises may be appreciated.

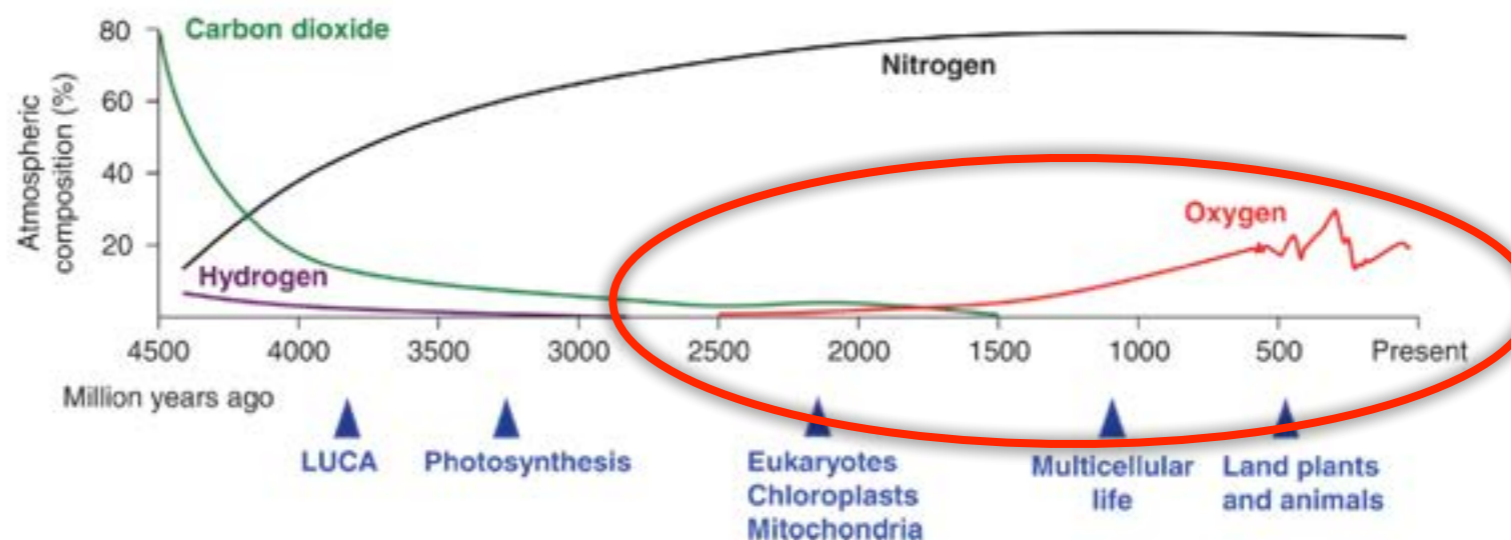
Connie Hsia, M.D.

Professor

Department of Internal Medicine
Division of Pulmonary and Critical Care Medicine
UT Southwestern Medical Center

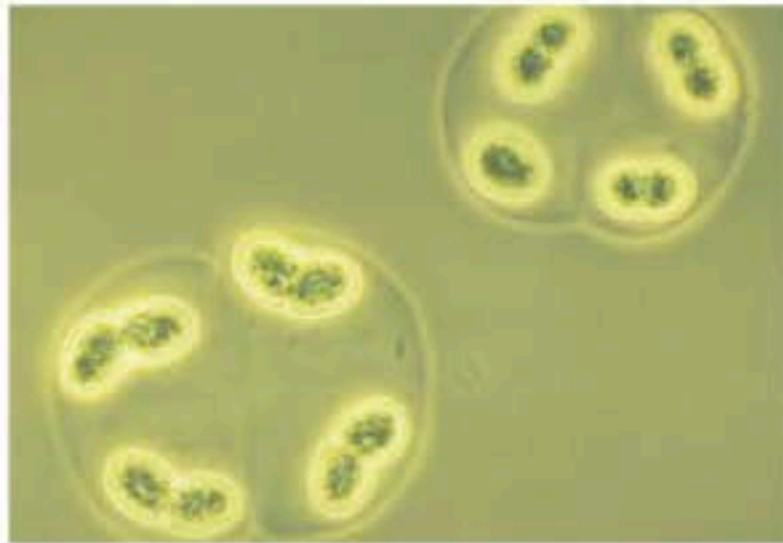


Hsia et al.



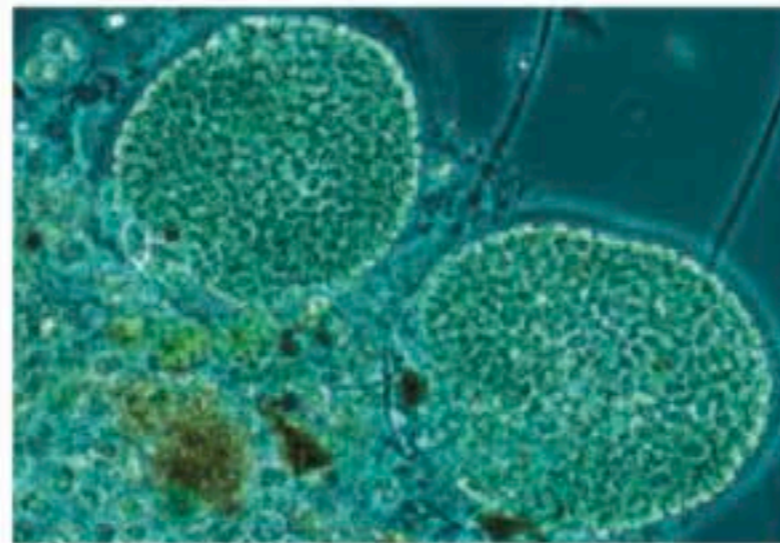
STROMATOLITES: Interaction of Microbes with Sediments





Susan Blam and Norman Pace

(a)



Daniel H. Buckley

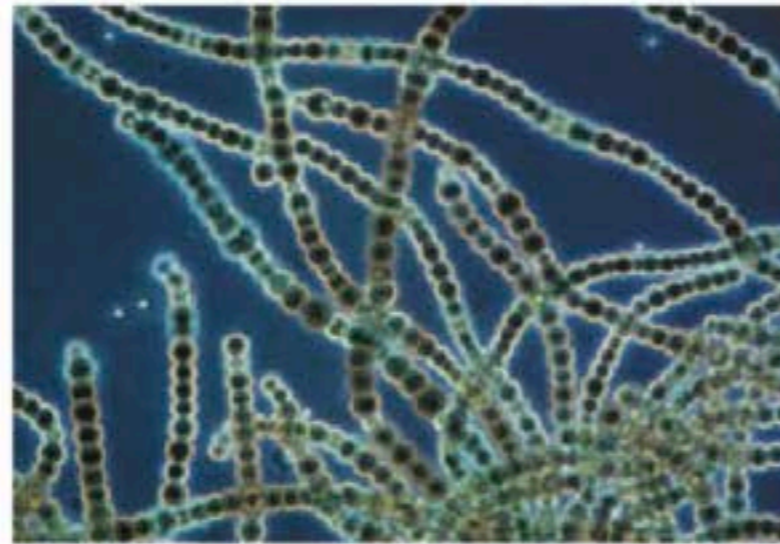
(b)



Daniel H. Buckley

(c)

Figure 15.2 The five major morphological types of *Cyanobacteria*. (a) Unicellular, *Gloeotheca*; a single cell measures 5–6 μm in diameter; (b) colonial, *Pleurocapsa*; these structures are $>50 \mu\text{m}$ in diameter and contain hundreds of cells; (c) filamentous, *Lyngbya*; a single cell measures about 10 μm wide; (d) filamentous heterocystous, *Nodularia*; a single cell measures about 10 μm wide; (e) filamentous branching, *Fischerella*; a cell is about 10 μm wide. See how morphological diversity relates to phylogenetic diversity in Figure 15.3.



Daniel H. Buckley

(d)



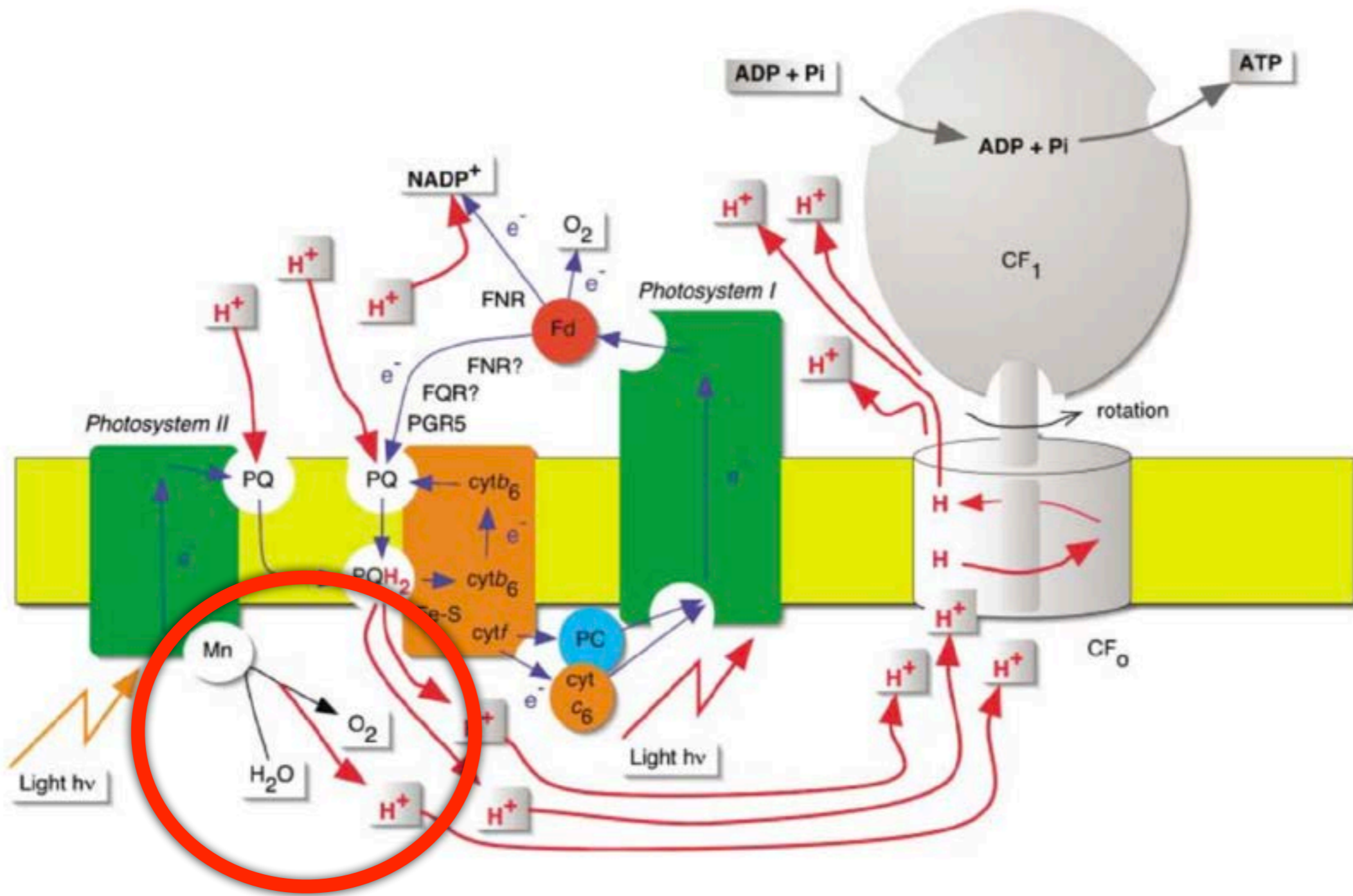
Daniel H. Buckley

(e)

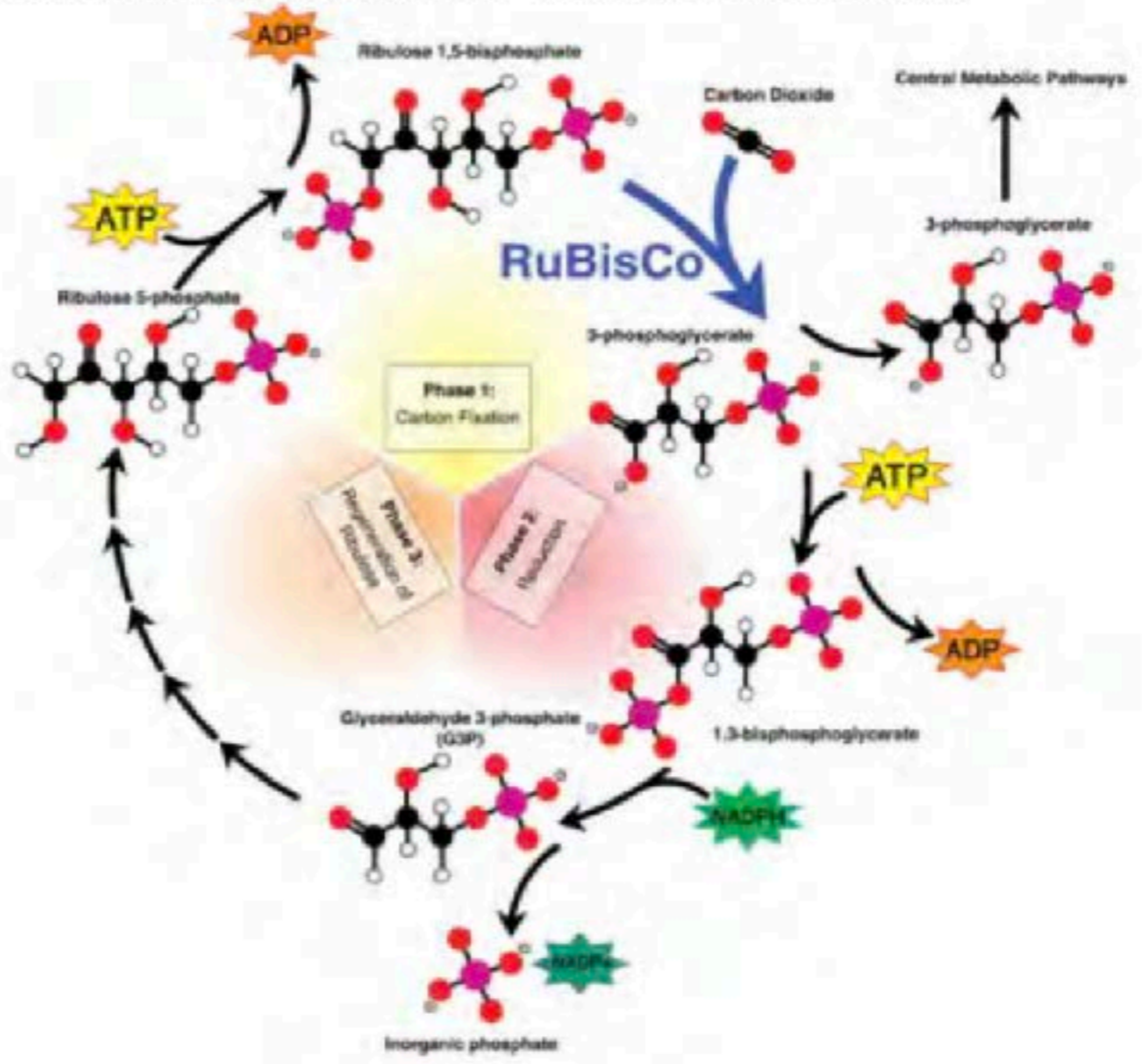
Cyanobacteria are photosynthetic organisms responsible for ~25% of the organic carbon fixation on earth.

A key step in carbon fixation is catalyzed by ribulose biphosphate carboxylase/ oxygenase

RuBisCO - the most abundant enzyme on the planet



With **ATP** available to drive the reactions, here is what occurs next:



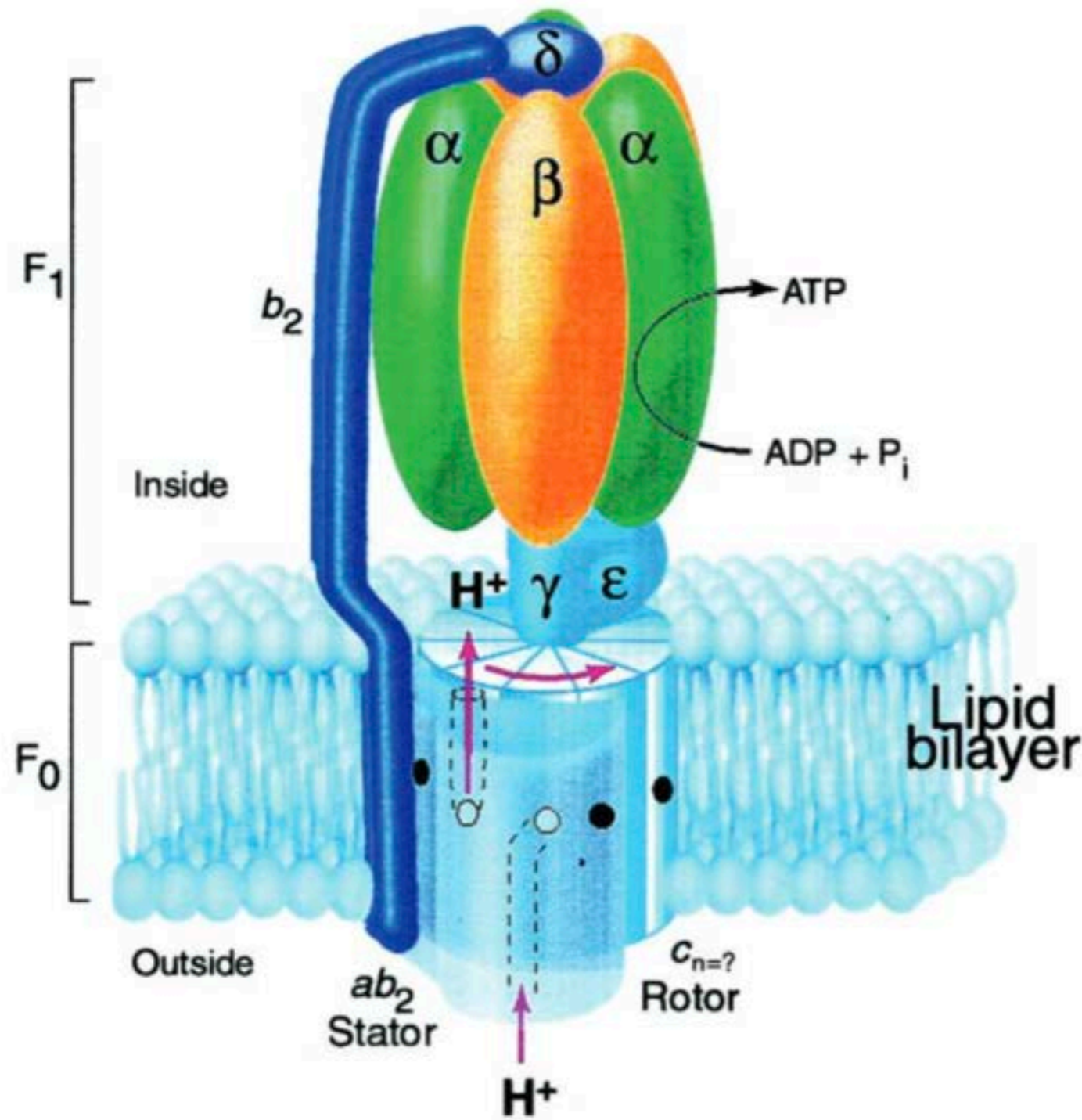


FIG. 7. The components of ATP synthase, a rotary motor. Protons enter the 10 proton channels in the membrane-bound F₀ component, where they bind to Asp⁶¹, and are subsequently released to the opposite side of the membrane via an outlet channel after F₀ rotation (arrow). The γε-subunits are attached to the F₀ ring and also rotate relative to the F₁ component, which catalyzes ATP synthesis (or breakdown if the reaction is driven backwards), which is thus driven by the proton-motive force. [From Jiang et al. (495), copyright 2001 National Academy of Sciences, USA.]



mitochondrial membrane proton pump: making ATP

- 2 min. Harvard video

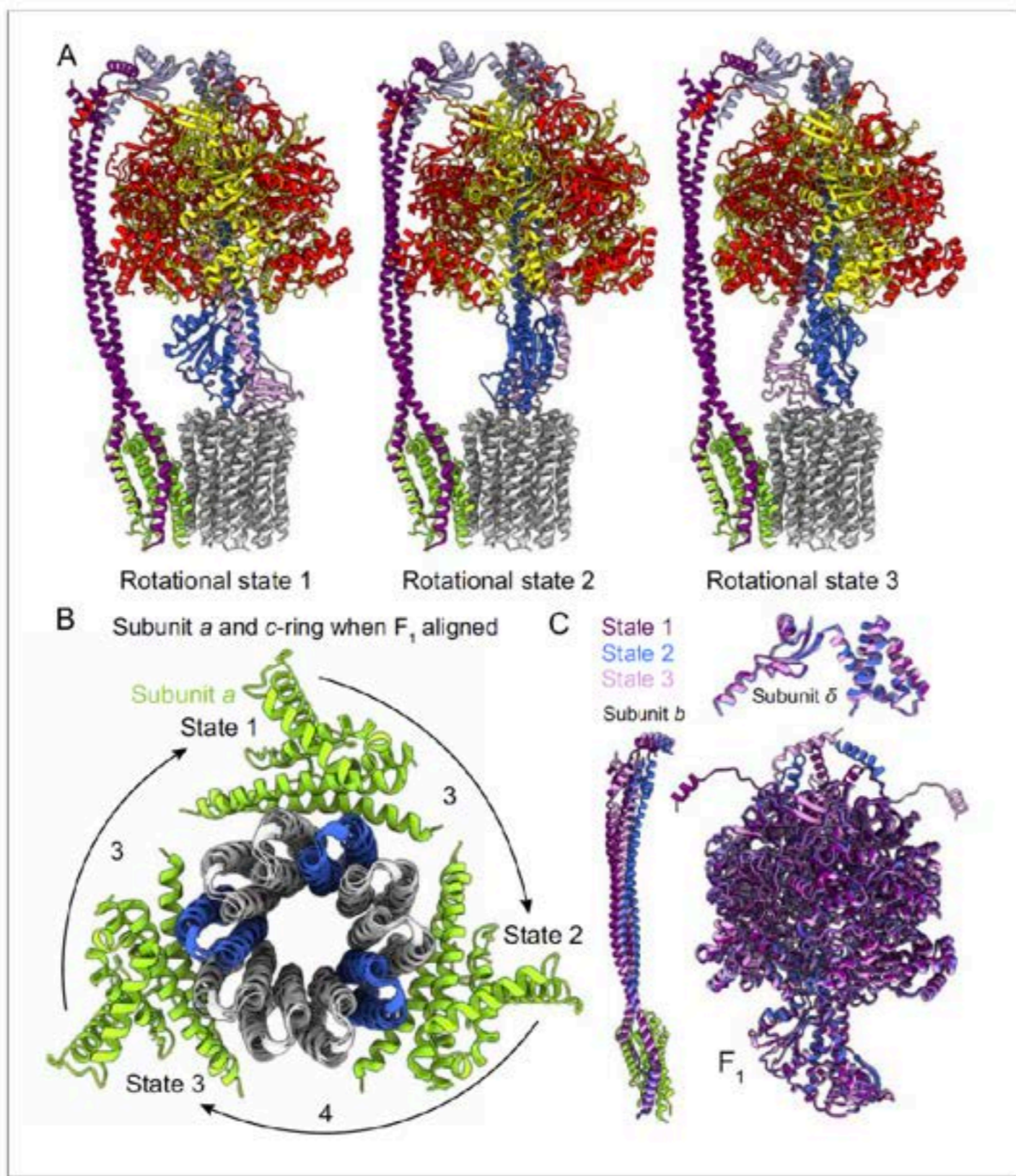
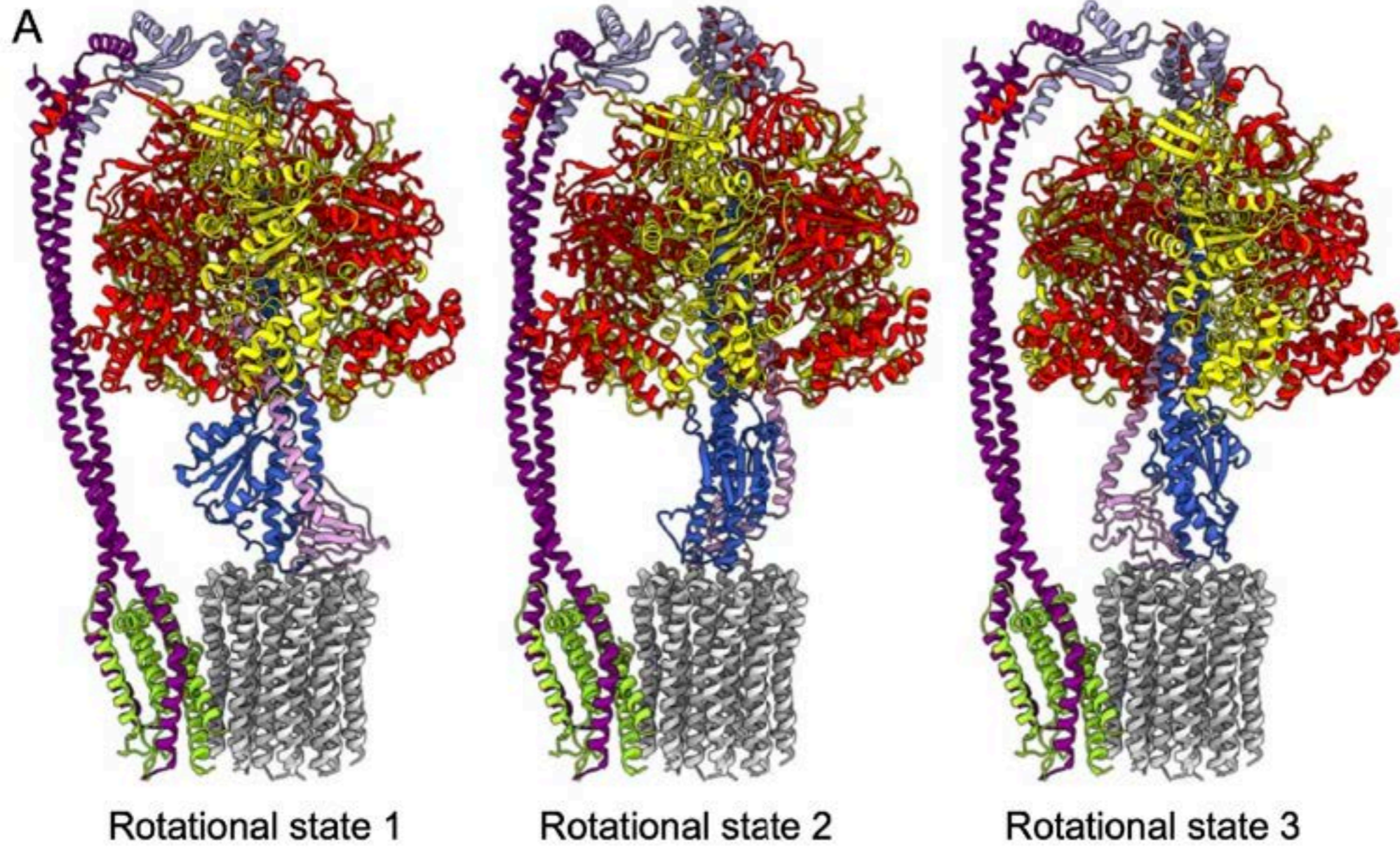


Figure 2. Rotational states of ATP synthase. (A) Atomic models of the three rotational states of *Bacillus* PS3 ATP synthase with subunits coloured the same as in Figure 1. (B) Top view of the *c*-ring and subunit *a* of the three rotational states from the cytoplasm when the F_1 regions of the three states are aligned. Rotation steps of the complex between states are -3, 4, and 3 *c*-subunits. (C) Comparison of the atomic models of subunits *b*, δ , and other F_1 region subunits in the different rotational states. The *b* subunits appear to be the most flexible part of the enzyme.
 DOI: <https://doi.org/10.7554/eLife.43128.008>



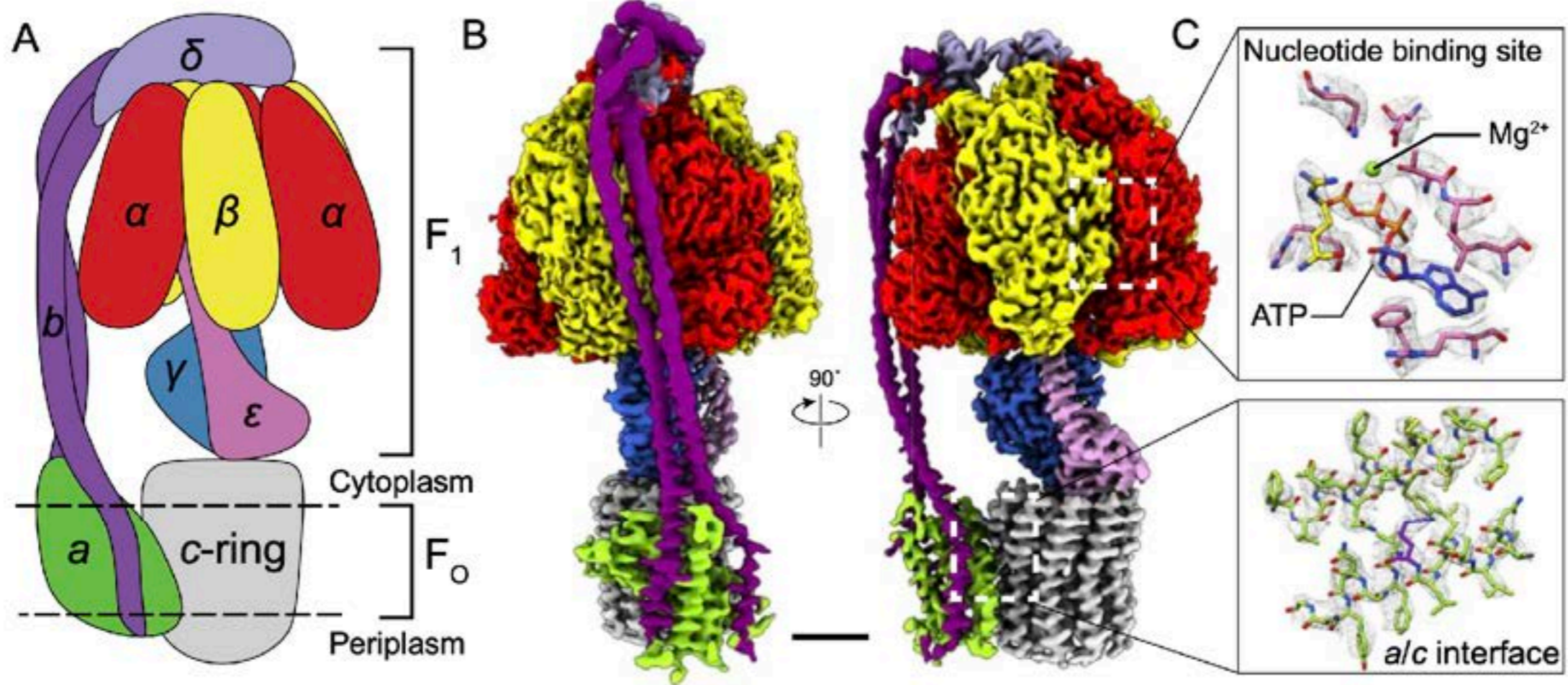


Figure 1. Overall structure of *Bacillus* PS3 ATP synthase. (A) Cartoon of ATP synthase. (B) Cryo-EM map of ATP synthase with subunits coloured the same as the cartoon. (C) Example map density that allowed construction of an atomic model. Scale bar, 30 Å.

DOI: <https://doi.org/10.7554/eLife.43128.002>

Banded Iron Formation

Part of Hall of Planet Earth

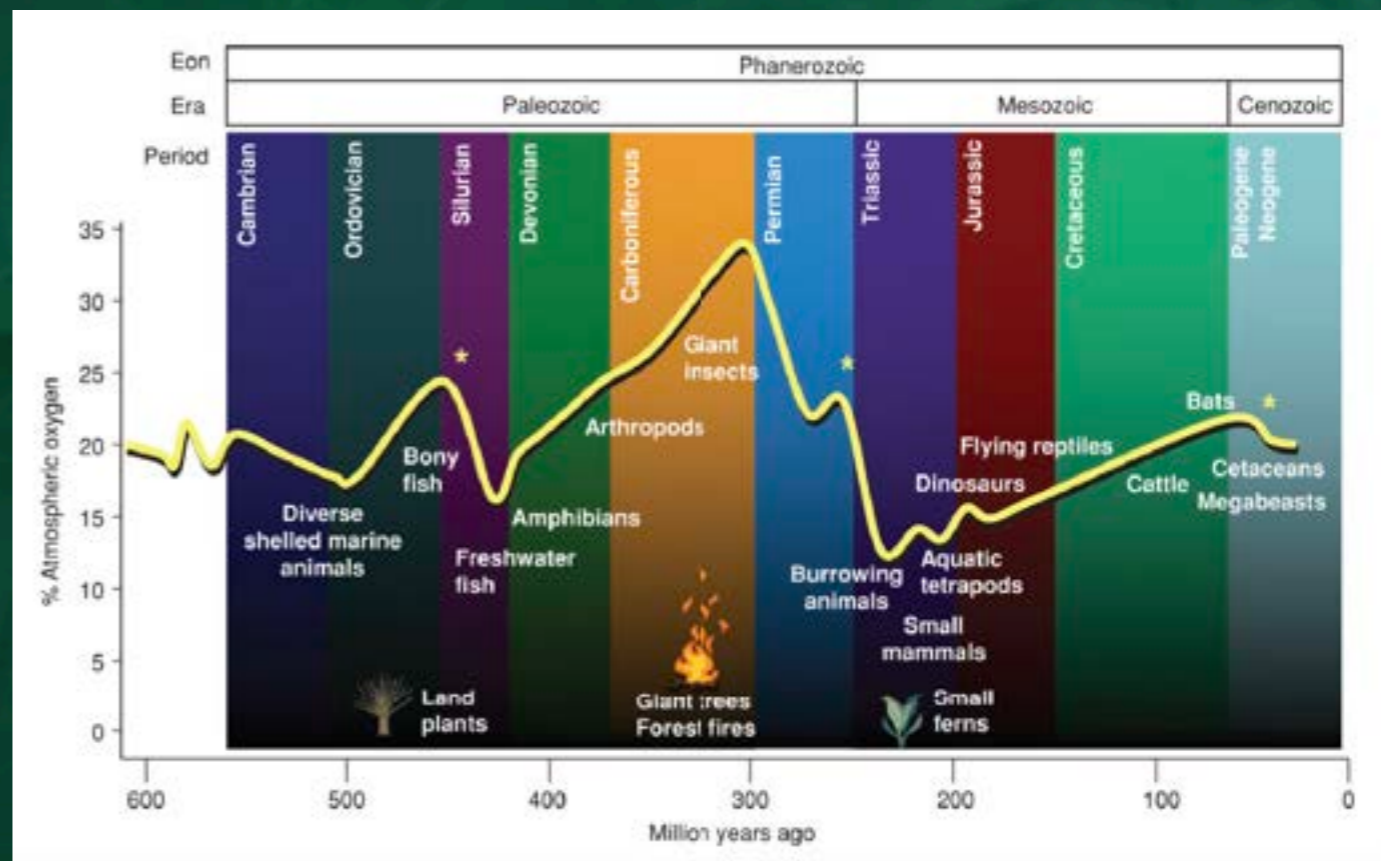
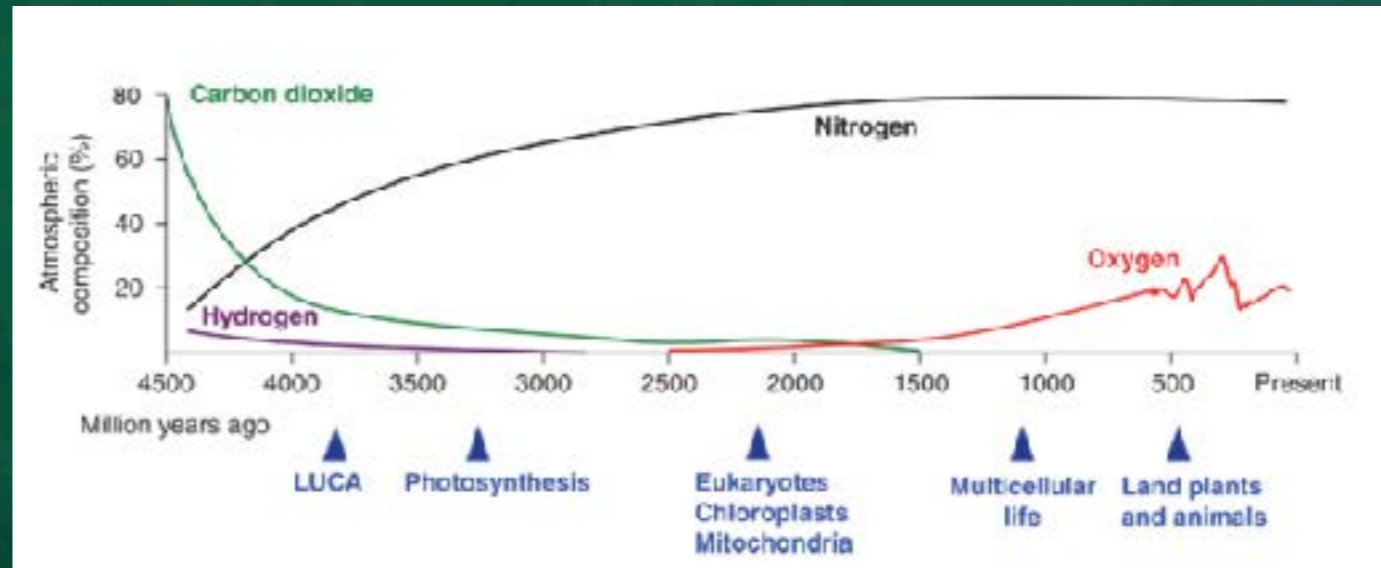


A nearly 3-billion-year-old banded iron formation from Canada shows that the atmosphere and ocean once had no oxygen.

Photosynthetic organisms were making oxygen, but it reacted with the iron dissolved in seawater to form iron oxide minerals on the ocean floor, creating banded iron formations.

The dark layers in this boulder are mainly composed of magnetite (Fe_3O_4) while the red layers are chalcedony, a form of silica (SiO_2) that is colored red by tiny iron oxide particles. Some geologists suggest that the layers formed annually with the changing seasons.

This rock records a time from the Earth's distant past, when evolving life profoundly influenced the planet's evolution. The oxygen that is now in the Earth's atmosphere was not there at the beginning. Early life began to generate oxygen by converting the Sun's energy into food. That caused the iron that was dissolved in the oceans to precipitate out as iron oxide minerals. This rock, with its layers of red jasper and iron magnetite, was formed billions of years ago as part of that process. It is a reminder that life made our atmosphere breathable.





Banded Iron Formation (BIF)

Early Proterozoic probably from near Marquette in the Upper Peninsula of Michigan; red quartz layers and black layers of specular hematite and magnetite. The layering is thought to be produced biannually in shallow seas. In general, banded iron formations of the oxide-carbonate-silicate-sulphide type occur in Archean greenstone belts and reached their peak development in the early Proterozoic basins about 2000-1800 Ma ago. Mid-late Proterozoic and Phanerozoic basins do not contain BIF of this type. In contrast, iron formations containing chamosite-goethite-siderite are unknown in the Precambrian but are found in Phanerozoic basins. The occurrence of the Precambrian BIF's is thought to be related to anoxic conditions of the early atmosphere. As oxygen content of the atmosphere and ocean waters increased, the solubility of iron decreased. With these changes in solubility, transport of iron in the entire weathering cycle would have decreased. Iron would remain in soils and not be found in solution in ocean waters after the atmosphere became oxygen-rich.





Evidence of Archean life: Stromatolites and microfossils

J. William Schopf^{a,*}, Anatoliy B. Kudryavtsev^b,
Andrew D. Czaja^c, Abhishek B. Tripathi^c

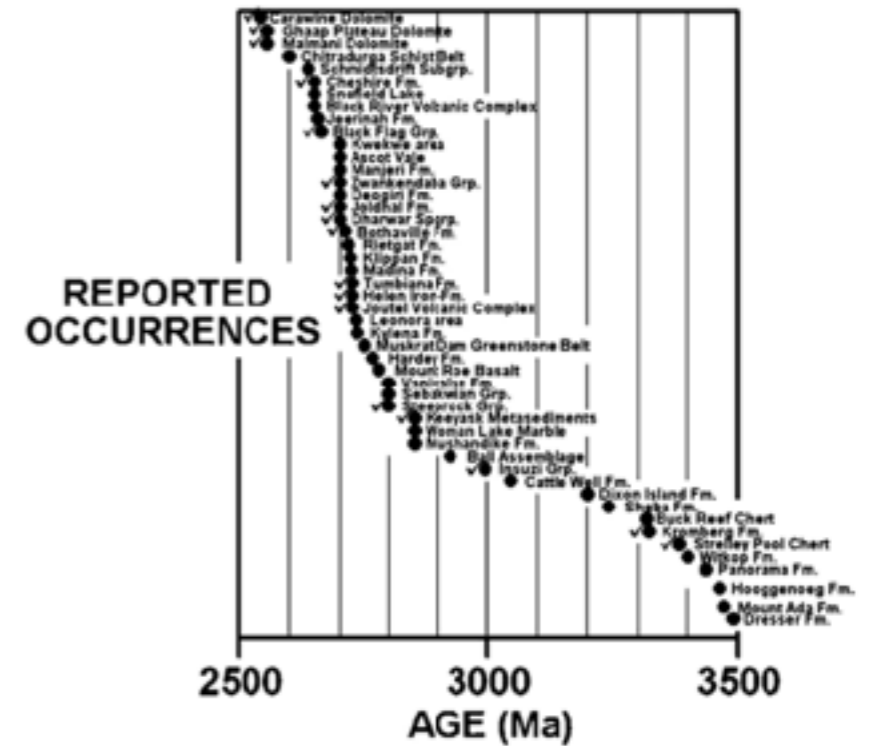
^a Department of Earth and Space Sciences, Center for the Study of Evolution and the Origin of Life (Institute of Geophysics and Planetary Physics), Molecular Biology Institute, and NASA Astrobiology Institute, University of California, Los Angeles, CA 90095, USA

^b Center for the Study of Evolution and the Origin of Life (Institute of Geophysics and Planetary Physics, and NASA Astrobiology Institute), University of California, Los Angeles, CA 90095, USA

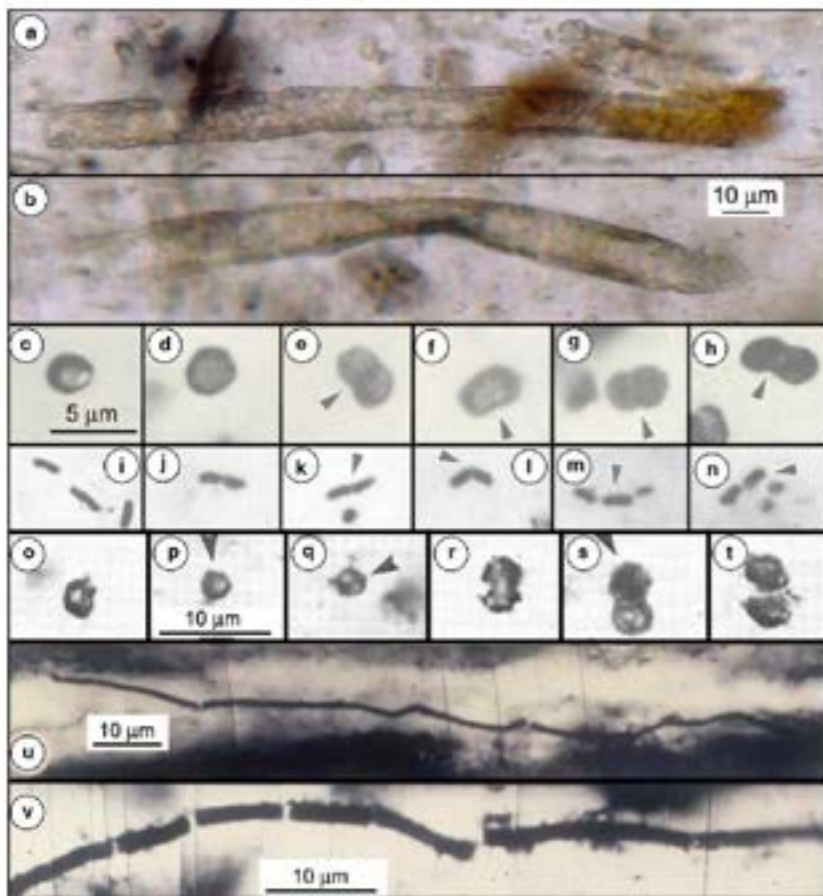
^c Department of Earth and Space Sciences, Center for the Study of Evolution and the Origin of Life (Institute of Geophysics and Planetary Physics), University of California, Los Angeles, CA 90095, USA

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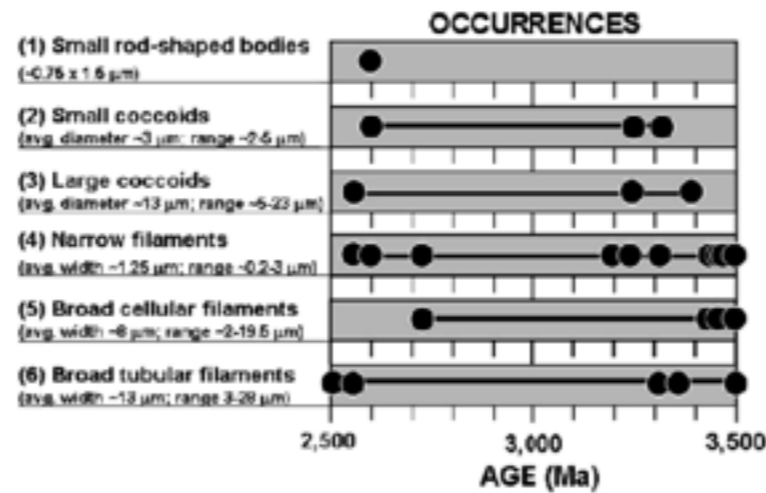
ARCHEAN STROMATOLITES



J.W. Schopf et al. / Precambrian Research 158 (2007) 141–155



J.W. Schopf et al. / Precambrian Research 158 (2007) 141–155



J.W. Schopf et al. / Precambrian Research 158 (2007) 141–155

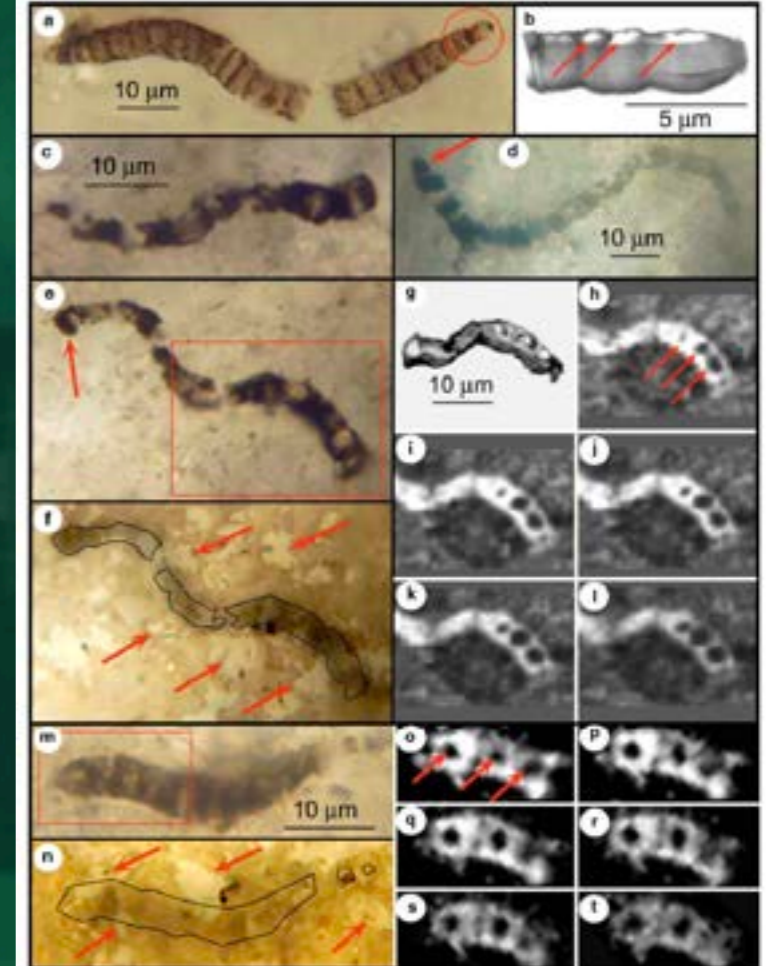


Fig. 3. Representative Archean microfossils in petrographic thin sections: (a) and (b) broad prokaryotic (oscillatorian cyanobacteria-like) tubules (*Cylindrocapsa ennescoensis*) from the ~2516 Ma Ghaubas Formation of South Africa (Klein et al., 1987; Buick, 2000); scale bar is 10 μm. (c) Solitary or paired (dorsed by arrows) microbial coccolidal anicella, and (d) solitary or paired (dorsed by arrows) bacilliform tuboid anicella from the ~2900 Ma Monte Cristo Formation of South Africa (Langer, 1986; Buick, 2001); scale for parts (c) and (d) shows a 5 μm.

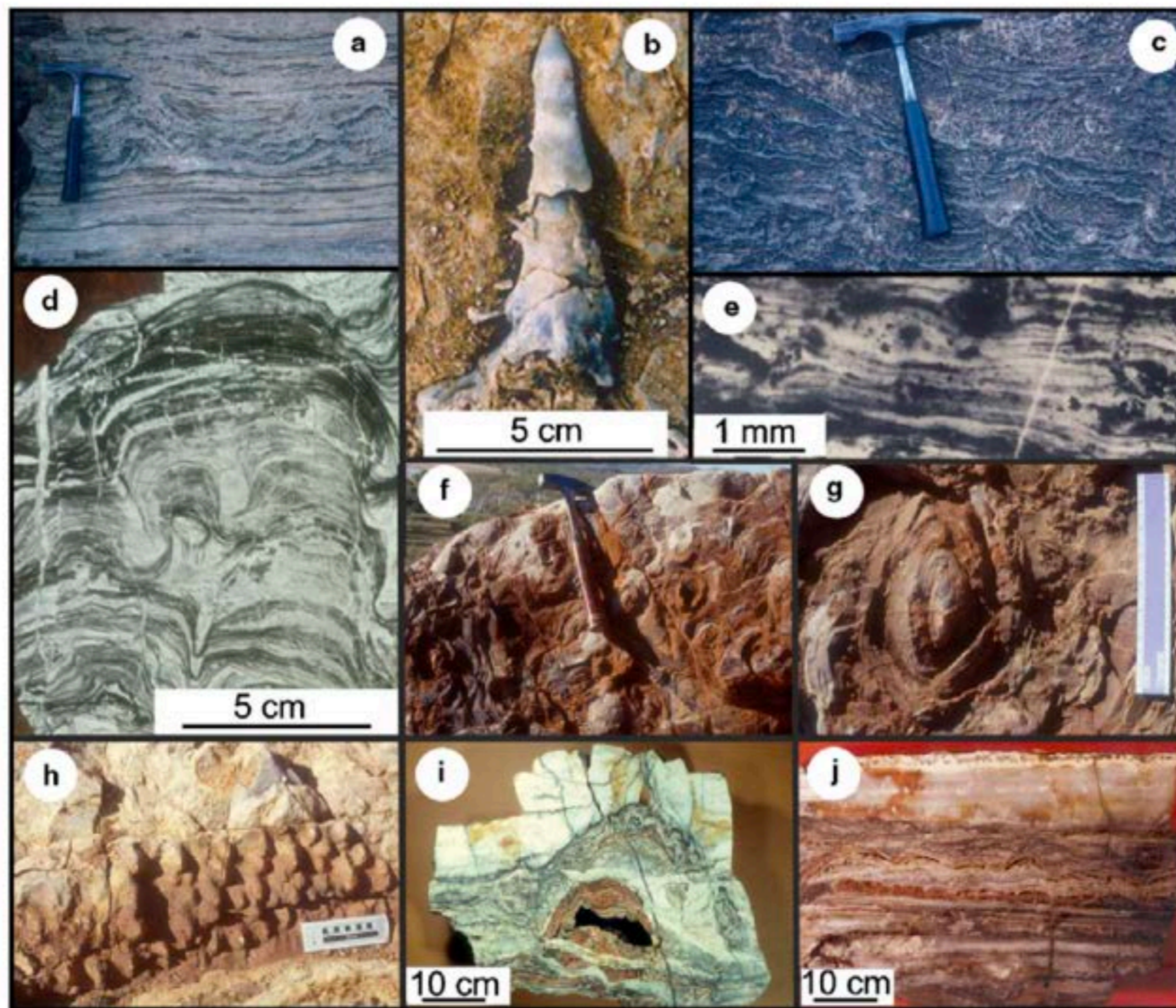


Fig. 2. Representative Archean stromatolites: (a–c) Stratiform and conical stromatolites from the ~2985 Ma Insuzi Group, South Africa (Beukes and Lowe, 1989); photo in (b) courtesy of N.J. Beukes. (d) Laterally linked, low relief stratiform to domical stromatolitic mats from the ~3245 Ma Fig Tree Group of South Africa (Byerly et al., 1986); photo courtesy of D.R. Lowe. (e) Stratiform microbial mats from the ~3320 Ma Kromberg Formation of South Africa (Walsh and Lowe, 1985). (f–h) Conical stromatolites from the ~3388 Ma Strelley Pool Chert of Western Australia (Hofmann et al., 1999; see also Allwood et al. 2007 of *Precambrian Research*, p. 198); scale in (g) = 20 cm; scale in (h) = 10 cm. (i) Domical and (j) stratiform stromatolites from the 3496 Ma Dresser Formation, Western Australia (Walter et al., 1980; Buick et al., 1981).



Chemostratigraphy of Paleoproterozoic carbonate successions of the Wyoming Craton: tectonic forcing of biogeochemical change?

A. Bekker^{a,*}, J.A. Karhu^b, K.A. Eriksson^a, A.J. Kaufman^c

^a Department of Geological Sciences, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA

^b Department of Geology, University of Helsinki, P.O. Box 64, FIN-00014 Helsinki, Finland

^c Department of Geology, University of Maryland at College Park, College Park, MD 20742, USA

Accepted 11 October 2002

Abstract

The Archean Wyoming Craton is flanked on the south and east by belts of Paleoproterozoic supracrustal successions whose correlation is complicated by lack of geochronologic constraints and continuous outcrop. However, carbonate units in these successions may be correlated by integrating carbon isotope stratigraphy with lithostratigraphy. The ~10 km thick Paleoproterozoic Snowy Pass Supergroup in the Medicine Bow Mountains was deposited on the present-day southern flank of the Wyoming Craton; it contains three discrete levels of glacial diamictite correlative with those in the Huronian Supergroup, on the southern margin of the Superior Craton. The Nash Fork Formation of the upper Snowy Pass Supergroup is significantly younger than the uppermost diamictite and was deposited after the end of the Paleoproterozoic glacial epoch. Carbonates at the base of the Nash Fork Formation record remarkable ¹³C-enrichment, up to +28‰ (V-PDB), whereas those from overlying members of the lower Nash Fork Formation have ^δ¹³C values between -6 and +8‰. Carbonates from the upper Nash Fork Formation above the carbonaceous shale have carbon isotope values ranging between 0 and +2.5‰. The transition from high carbon isotope values to these near 0‰ in the Nash Fork Formation is similar to that at the end of the ca. 2.2–2.1 Ga carbon isotope excursion in Fennoscandia. This chemostratigraphic trend and deposition of BIFs, Mn-rich lithologies, carbonaceous shales and phosphonates at the end of the global ca. 2.2–2.1 Ga carbon isotope excursion are likely related to ocean overturn associated with the final breakup of the Kenorland supercontinent. Correlative carbonates from the Slaughterhouse Formation in the Sierra Madre, WY, and from the Whalen Group in the Rawhide Creek area in the Hartville Uplift, WY, have highly positive carbon isotope values. In contrast, carbonates from other exposures of the Whalen Group in the Hartville Uplift and all carbonate units in the Black Hills, SD, have carbon isotope values close to 0‰. Combined with existing geochronologic and stratigraphic constraints, these data suggest that the Slaughterhouse Formation and the succession exposed in the Rawhide Creek area of the Hartville Uplift are correlative with the lower and middle Nash Fork Formation and were deposited during the ca. 2.2–2.1 Ga carbon isotope excursion. The Estes and Roberts Draw formations in the Black Hills and carbonates from other exposures in the Hartville Uplift postdate the ca. 2.2–2.1 Ga

* Corresponding author. Present address: Department of Earth and Planetary Sciences, Harvard University, 20 Oxford Street, Cambridge, MA 02138, USA. Fax: +1 617 495 2835.

E-mail address: abekker@fas.harvard.edu (A. Bekker).

Paleozoic Era	Permian	299	probable peak of Appalachian Mtn formation, Alabama locked within dry interior of Pangaea, no rocks from this time known from the state	
	Carboniferous	Pennsylvanian	318	"Coal Age" forests; Pangaea forms
		Mississippian	359	widespread limestones deposited
	Devonian	416	sometimes called the "age of fishes", but land plants and animals also diversify and move further from the water's edge	
	Silurian	444	Birmingham's Red Mountain iron ores form; terrestrial (land) environments first invaded by plants and animals	
	Ordovician	488	tropical seas cover most of the state; Alabama rocks show mountain-building, volcanic activity was nearby to the east	
"Precambrian"	Cambrian Period	542 million years ago	Alabama on passive margin of ancient North American continent Laurentia; earliest fossils appear in Alabama rocks	
	"Precambrian" (represents about 87% of the Earth's history)		Greenville mountain-building episode; deep crust beneath Alabama added	
	Proterozoic Eon	2.5 billion	first "free" oxygen accumulates in the Earth's atmosphere	
	Archaean Eon	3.8 billion	earliest fossilized bacteria appear in the geologic record	
		4 billion	age of Earth's oldest known rocks	

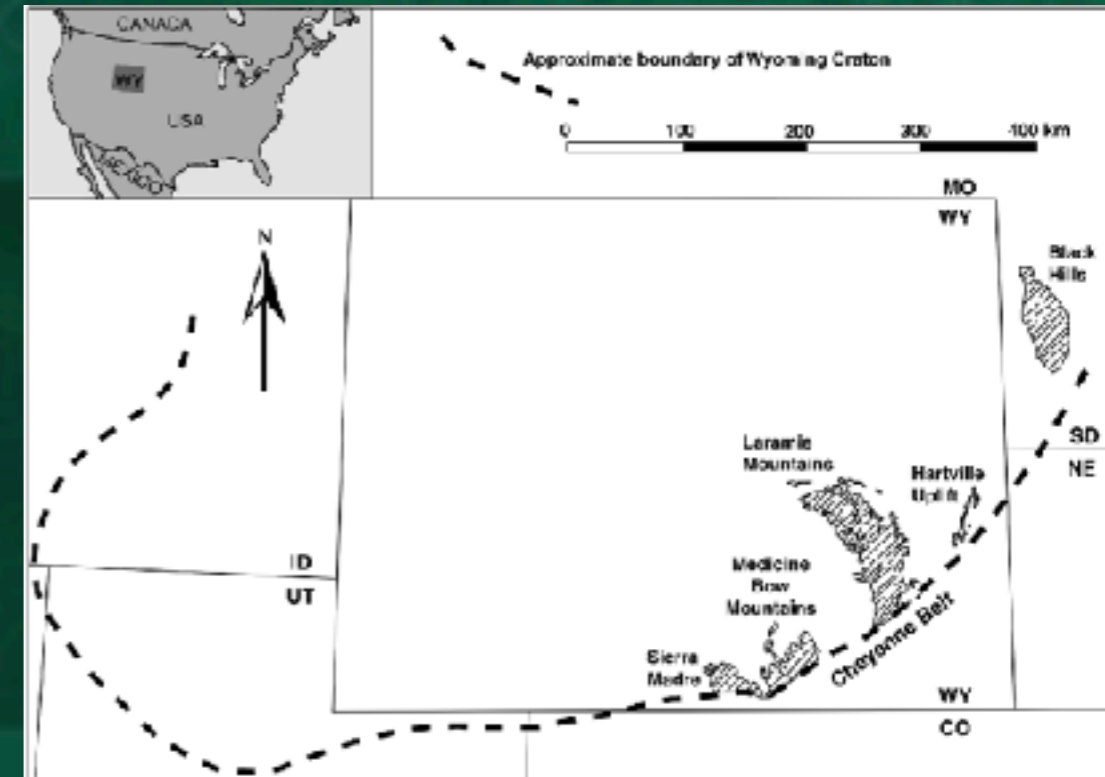


Fig. 1. Location of Paleoproterozoic sedimentary successions on the southeastern margin of the Wyoming Craton.





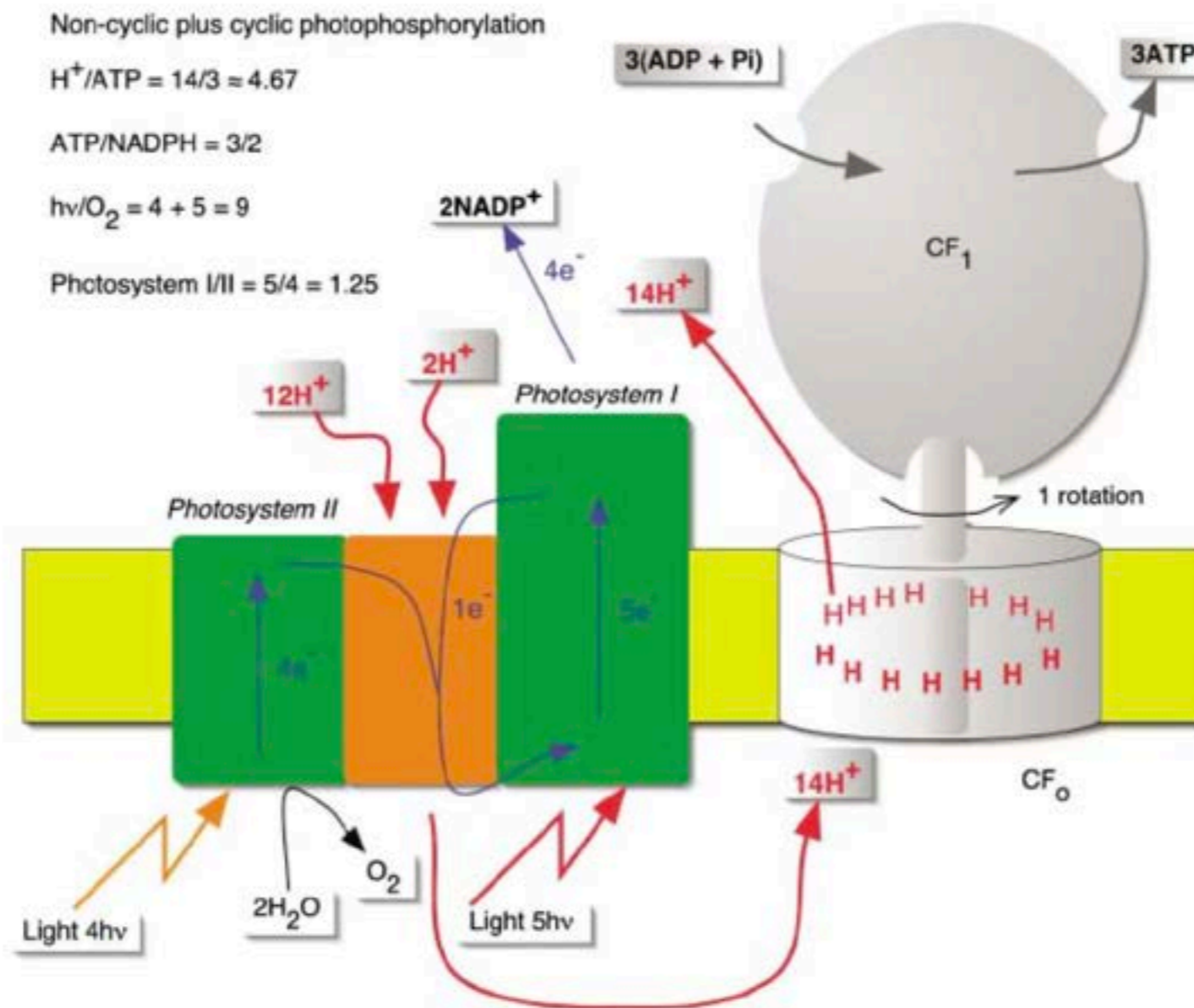
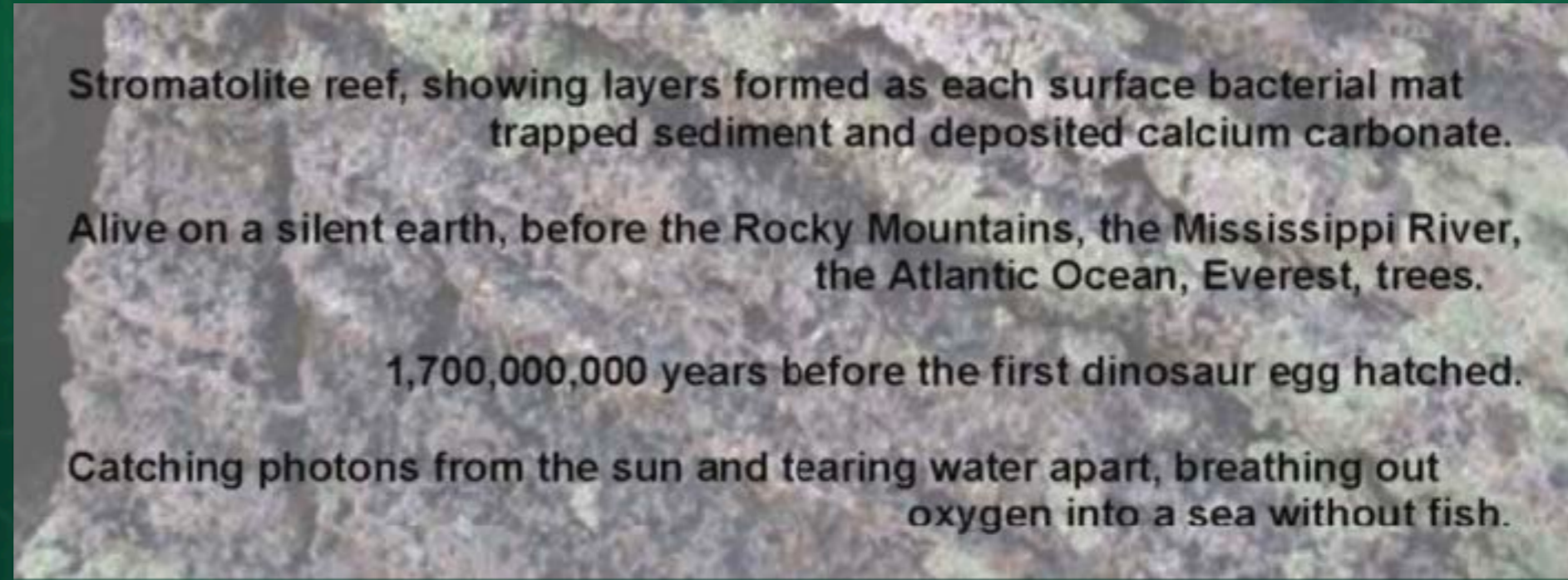
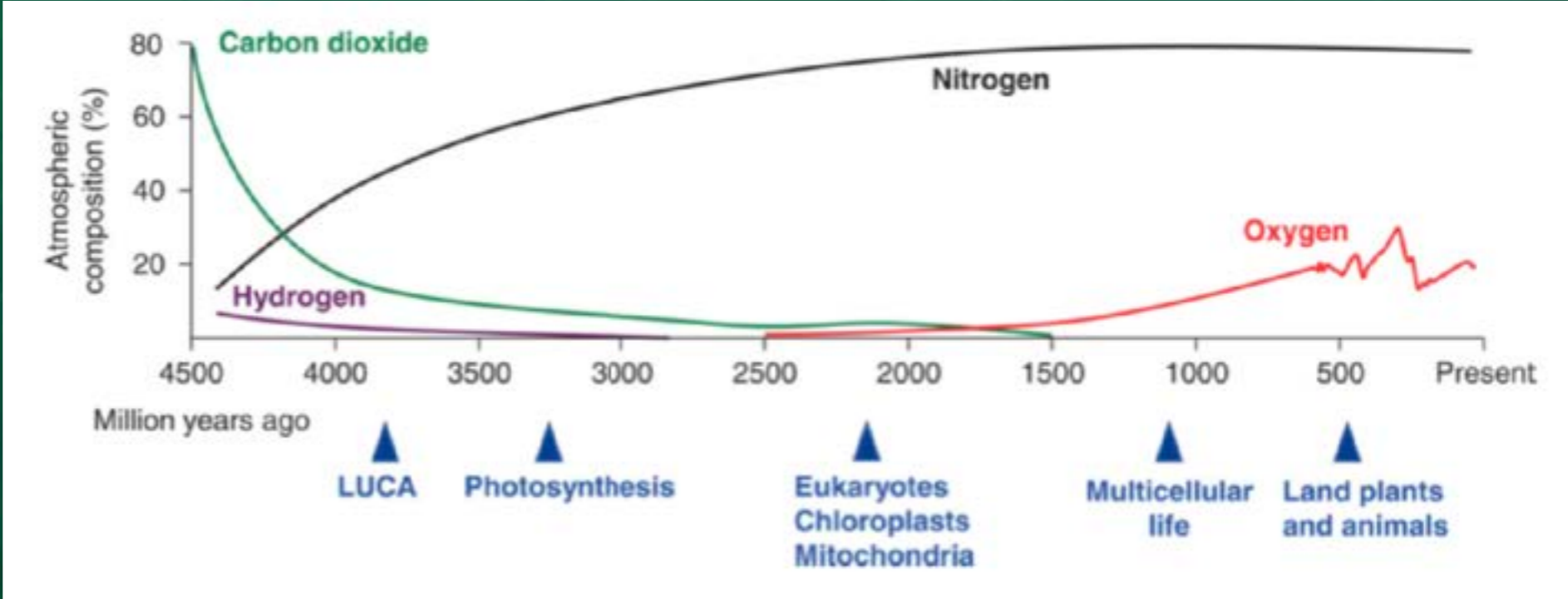
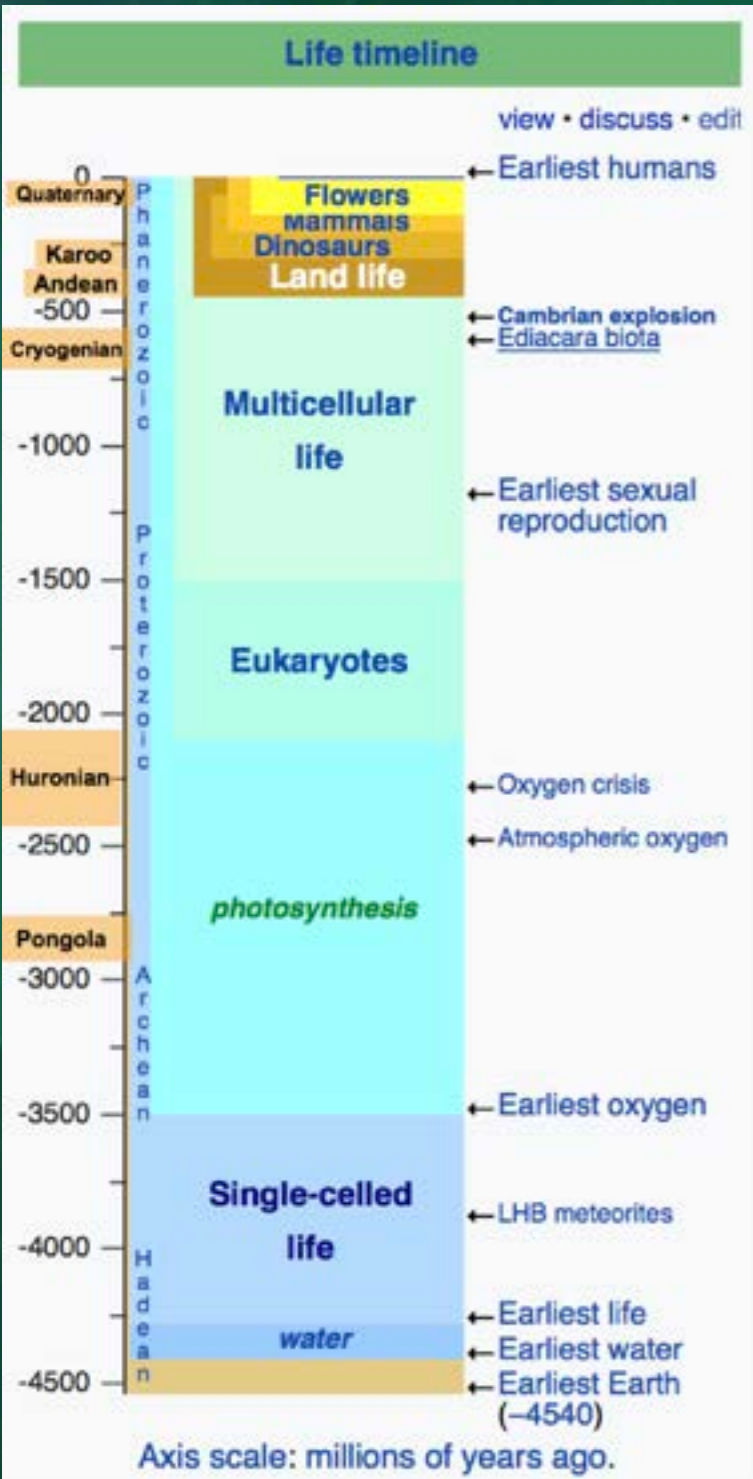


Figure 2. Coupling Quanta, Electrons, Protons, and ATP

Combined cyclic and noncyclic photophosphorylation, assuming $H^+/3ATP = 14$. Stoichiometries are depicted for four electrons transferred from H_2O to $NADP^+$ (cf. Figure 1). This gives one O_2 molecule and two NADPH molecules. Three ATP molecules will be made, provided photosystem I recycles one electron in order to contribute two protons to the proton motive force.



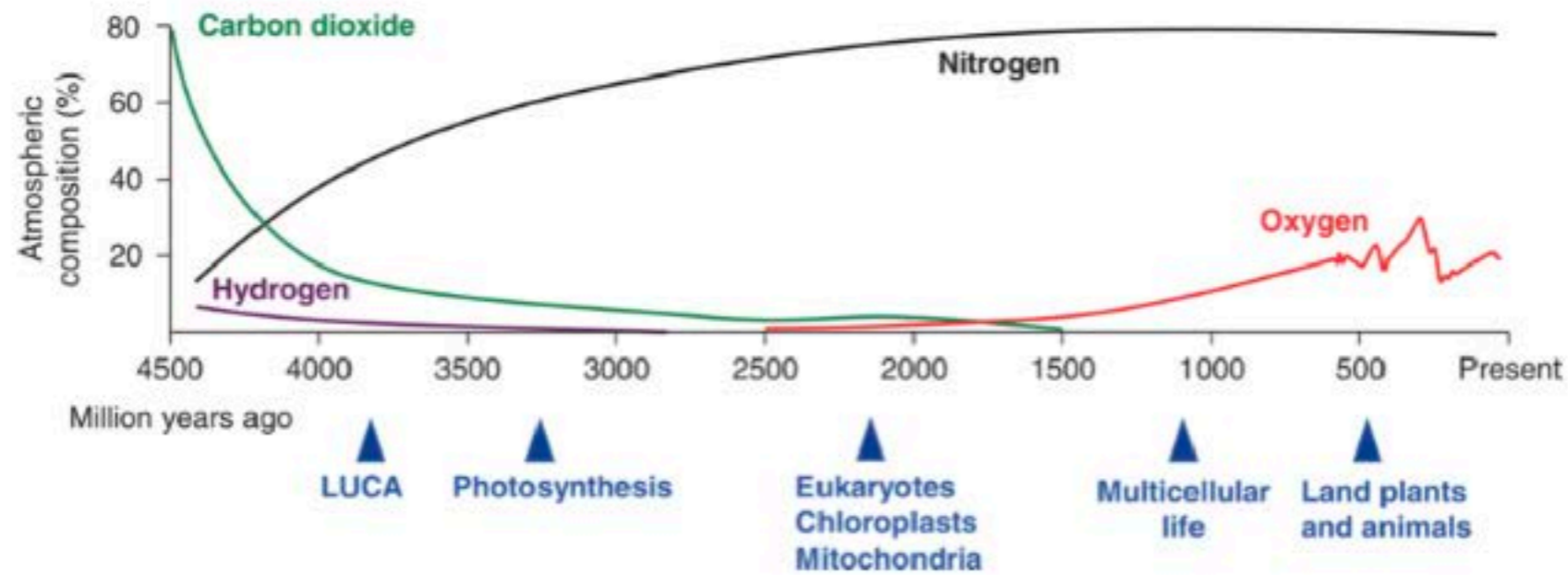
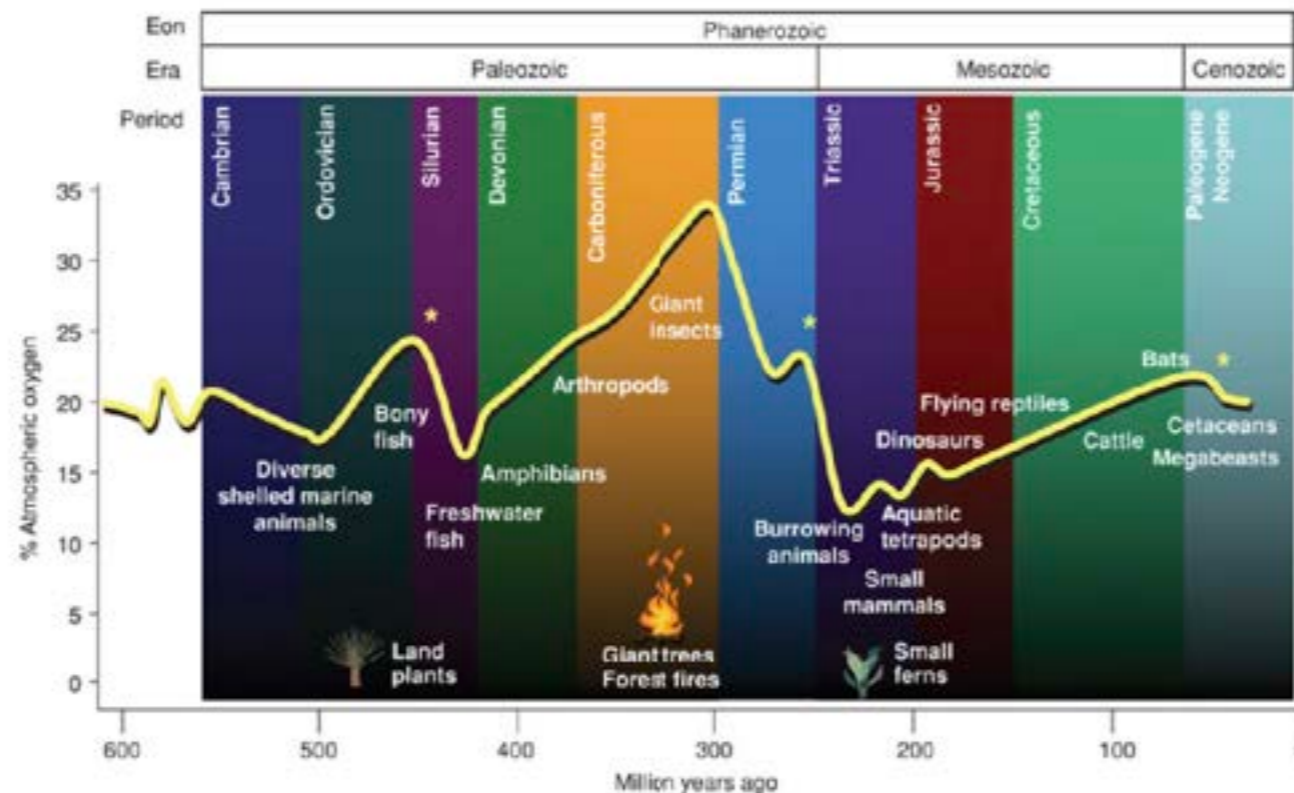


Figure 4.

A general model of early evolution and atmospheric O₂ concentration. Last Universal Common Ancestor (LUCA) was anaerobic and unicellular, but possessed heme proteins and their equivalents for antioxidation and reactive O₂ species-mediated cell signaling and possibly ATP production. Photosynthesis by cyanobacteria led to O₂ accumulation, which was initially stored in rocks and sediments but later enriched the atmosphere. Eukaryotic plant and animal cells evolved that can more efficiently produce and utilize O₂, leading to multicellular organisms of increasing complexity. Around 500 Ma, atmospheric O₂ level reached the contemporary range, coinciding with an explosive appearance of terrestrial plants and animals.



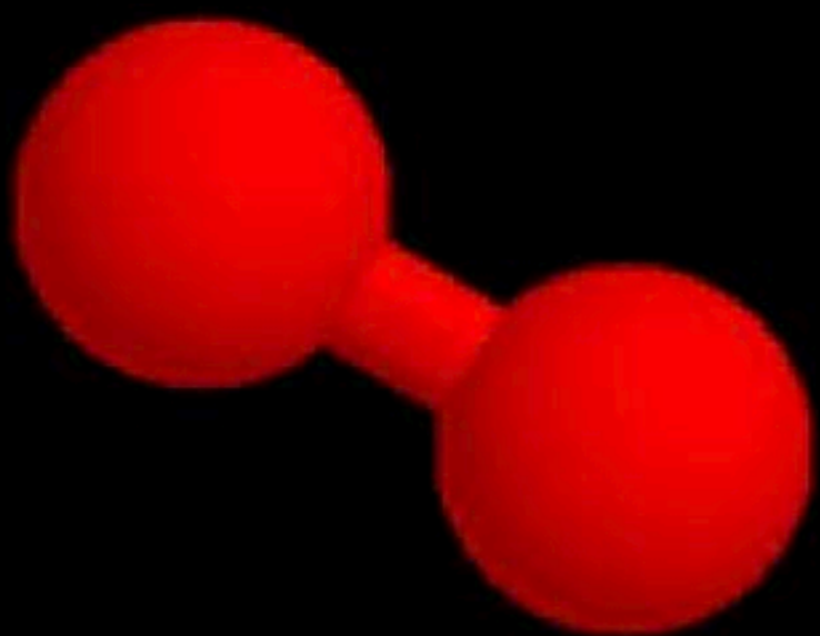
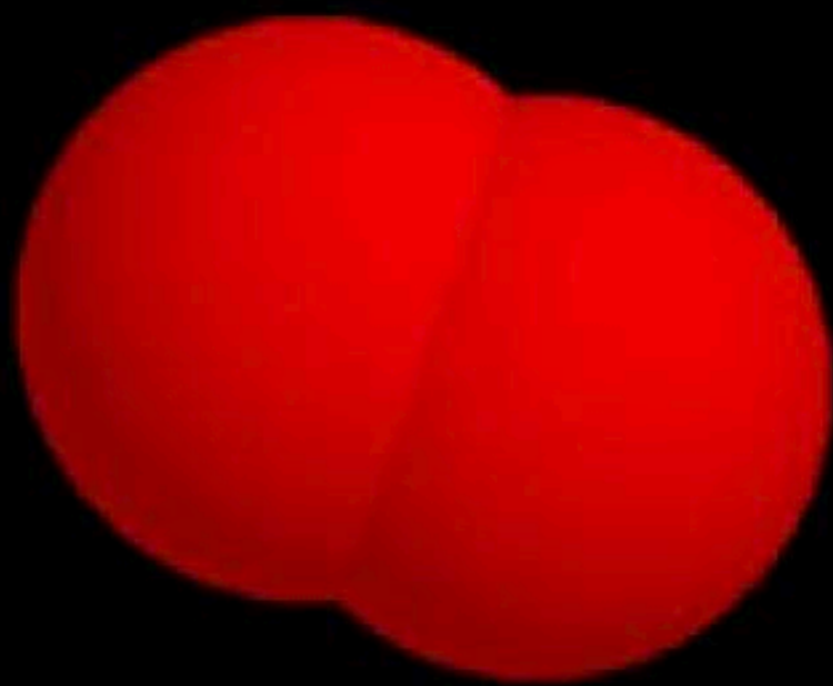
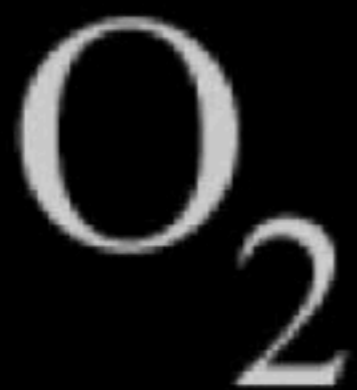








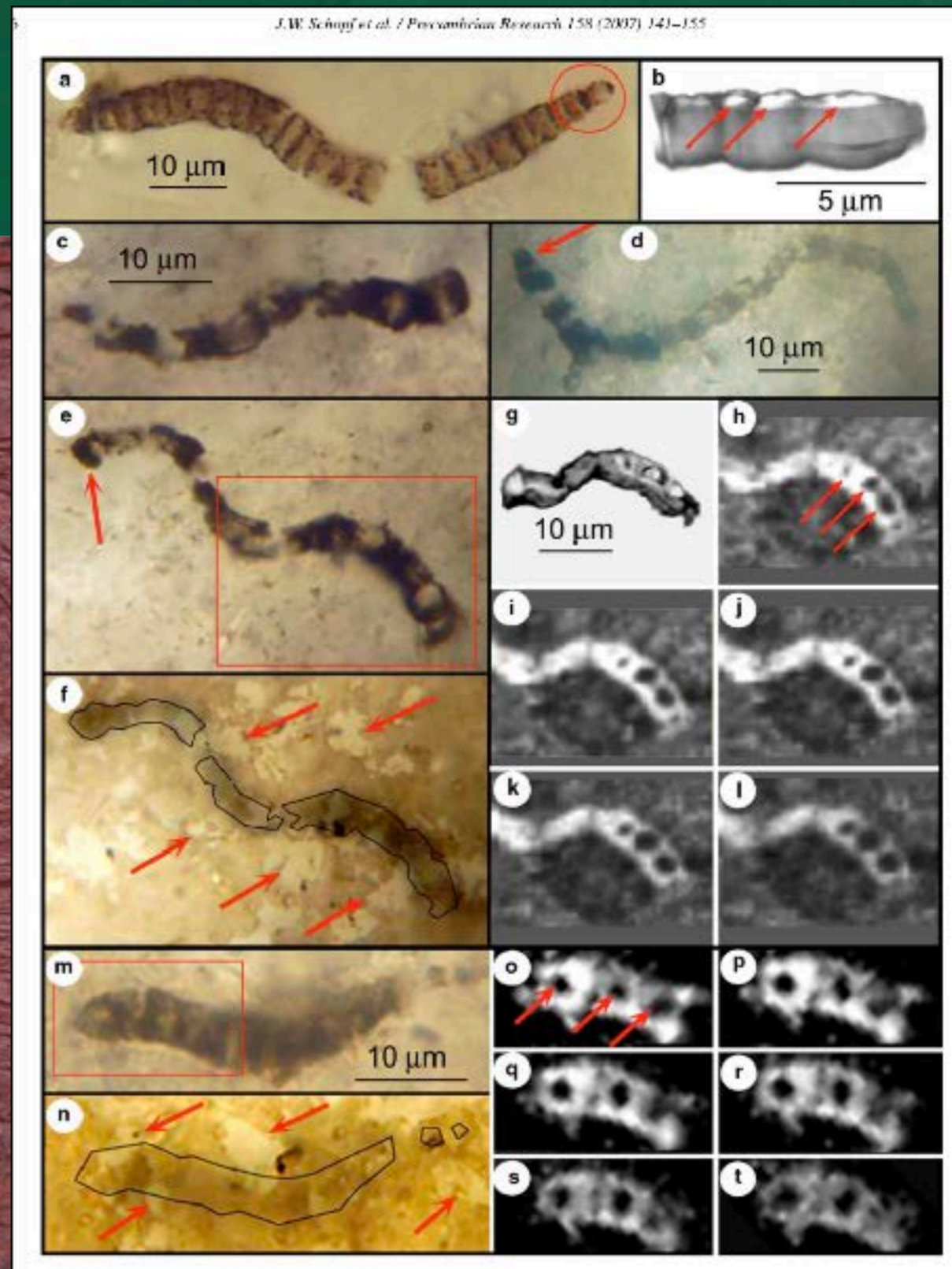






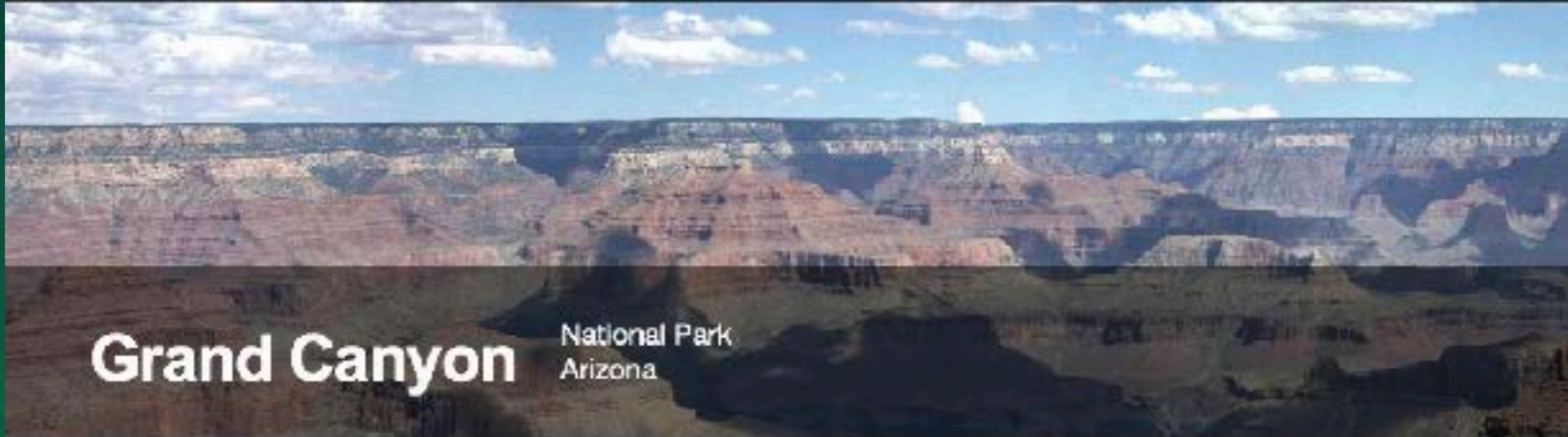


stromatolite fossil
along S. Kaibab Trail
- Grand Canyon -





National Park Service



Grand Canyon

National Park
Arizona

Marine Fossils

With marine environments creating many of the sedimentary rock layers in the canyon over the past 525 million years, marine fossils are quite common. Species changed over time, but similar fossils can be found in most of the marine-based rocks at Grand Canyon.



Stromatolites fossil.

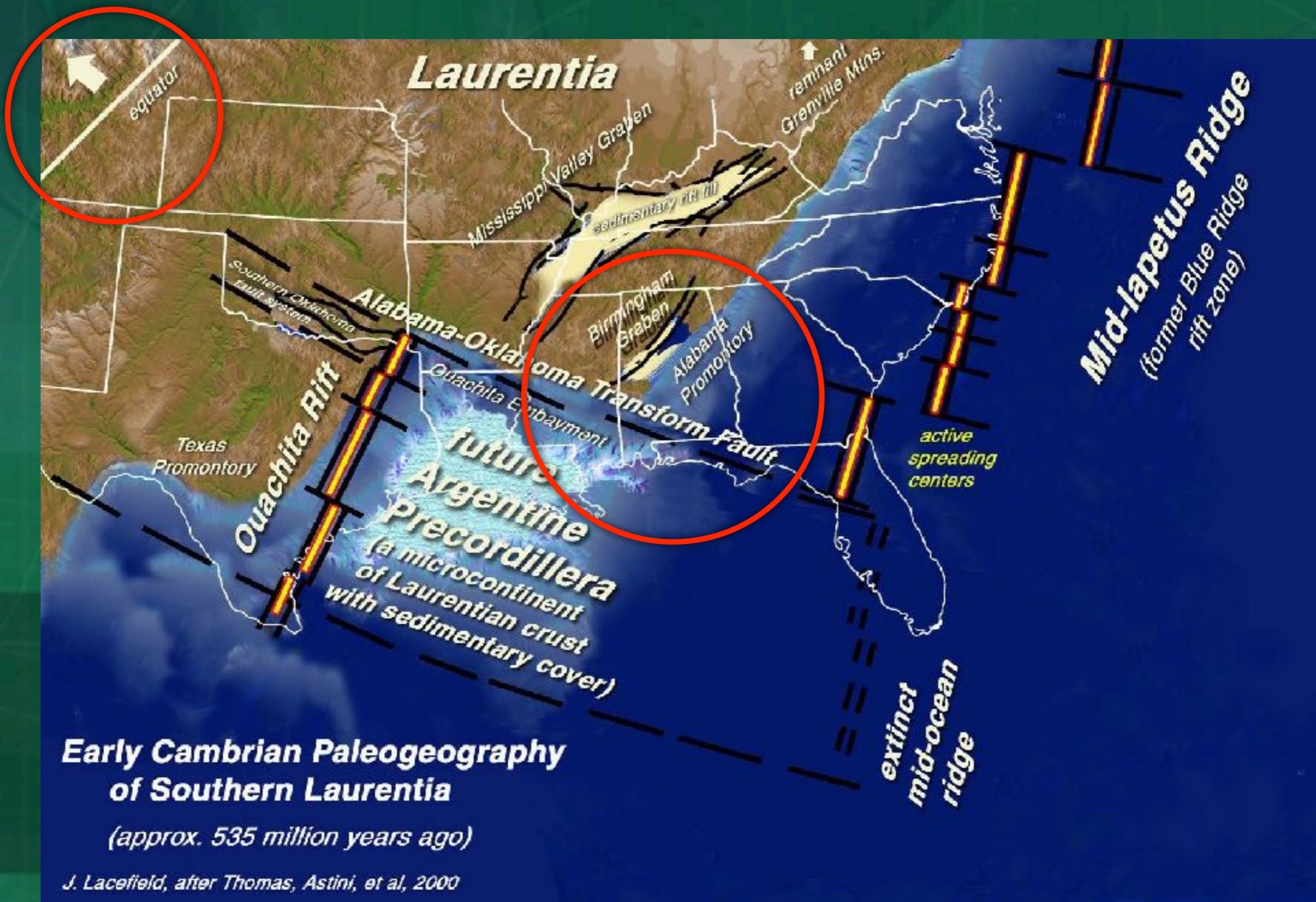
Stromatolites

The oldest fossils at Grand Canyon are 1,200 million to 740 million years old. Stromatolites are the limestone structures formed by photosynthesizing bacteria called cyanobacteria. They created layers of alternating slimy bacteria and sediment in very shallow water, dominating shallow seas until predators, such as trilobites, came into the picture. Today stromatolites only live in a few shallow ocean areas with high salinity. The salinity deters predation and allows the stromatolites to survive.











geologic evidence suggests that what was then the southern part of Alabama and several adjoining states may have rifted away from the rest of North America during the supposedly calm early part of the Cambrian Period and drifted across the expanding ocean basin, eventually to become part of what is now Argentina.

During the latter half of the Cambrian, sea levels continued to rise and cover much of the North American continent, depositing marine rocks over a wide area that today is exposed as dry land. This sea level rise, or **transgression**, was not a smooth event, and included many episodes of **regression**, or falls in sea level, occurring within the general pattern of rise. The flatness of the Cambrian landscape allowed shallow ocean waters to move easily back and forth across a large part of the continent.

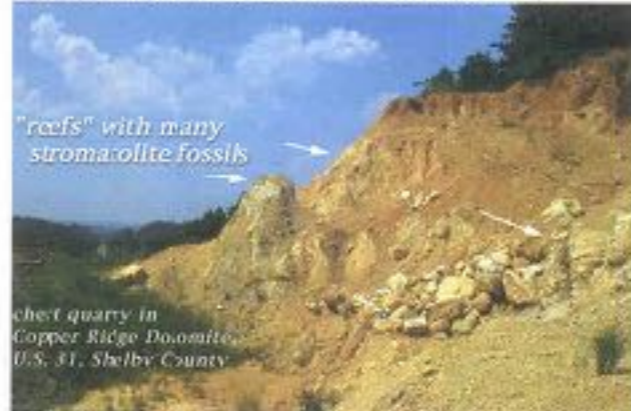
The oldest of the Cambrian-aged rocks in Alabama is a set of sandstones and shales geologists call the **Chilhowee Group** that were deposited at or near the ocean's edge as the sea began its initial transgressive rise. Above these clastic rocks is a series of limestones and dolostones that were deposited on the shallow marine shelf. The oldest of these carbonate rocks is called the **Shady Dolomite**. Above the Shady are found the **Rome** (Early Cambrian) and **Conasauga** (Middle Cambrian) **Formations** and lower **Knox Group**, that includes the Copper Ridge Dolomite. Several of these carbonate-based rocks have been replaced by silica to form chert. A few contain thick bands of evaporation minerals, suggesting that this shallow sea had restricted circulation and even dried up in places under the hot, tropical sun.

Rocks from the Cambrian Period crop out over a fairly limited area of the state, mostly in the Valley and Ridge Province. These outcrops are places where the folds of the Appalachians have moved

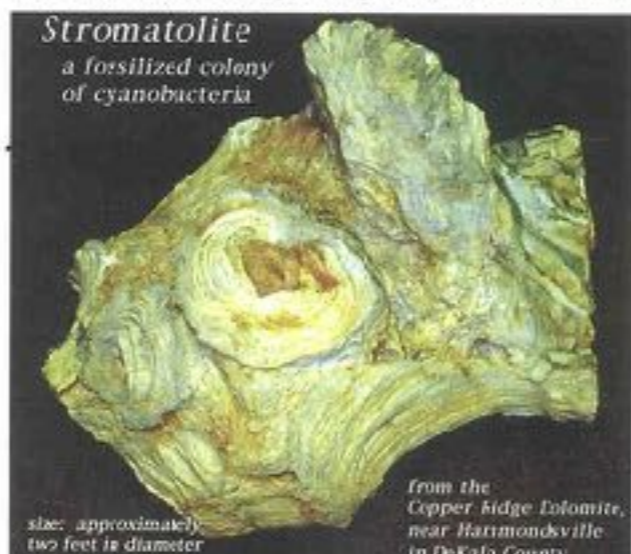
these once deeply buried rocks to the earth's surface, especially in spots where erosion has removed the overlying younger strata. The **Copper Ridge Dolomite**, which is Late Cambrian in age, is one of the major ridge-forming rock units in the Alabama Valley and Ridge province.



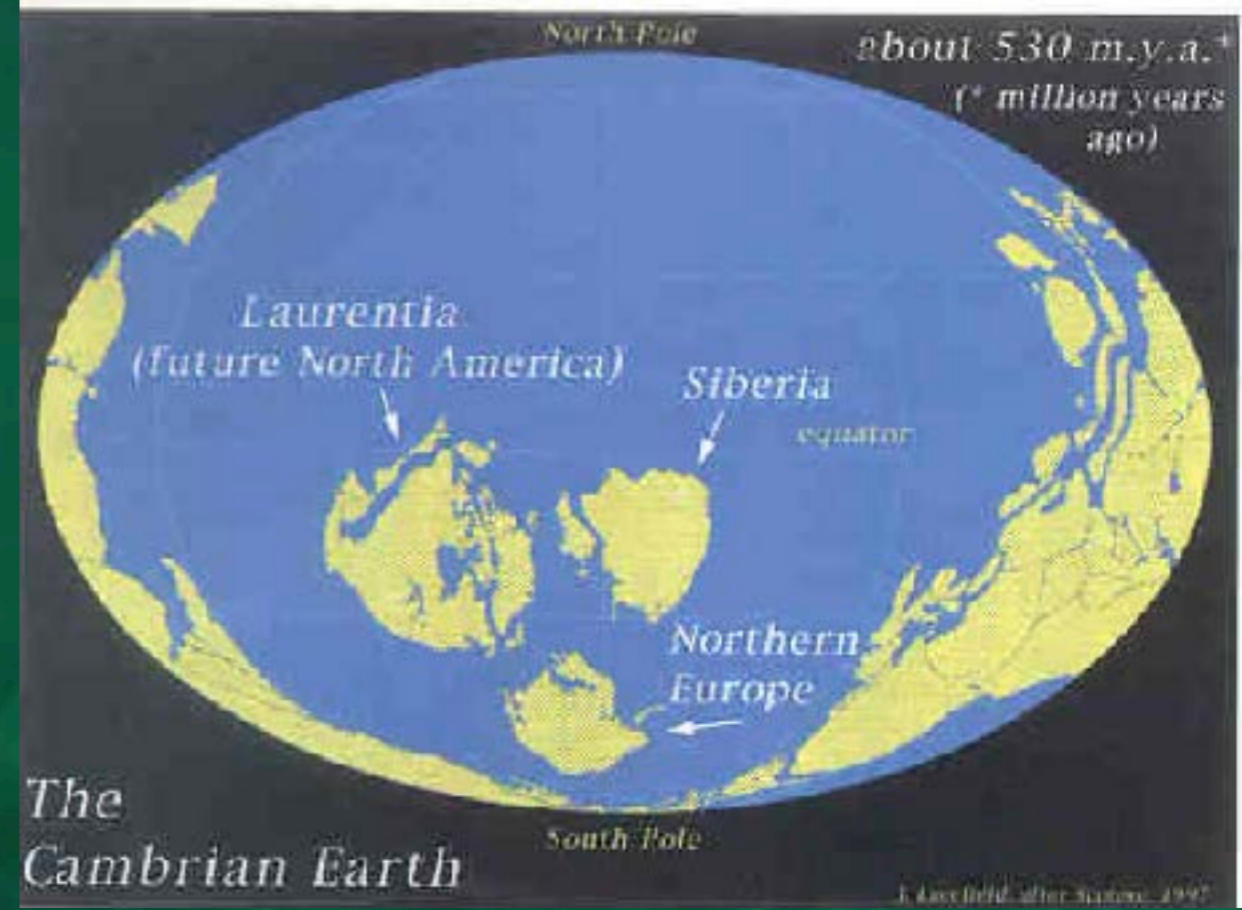
Cambrian-aged limestones and dolostones exposed in a quarry near Helena. The Conasauga Formation and the Keona Dolomite have been mined in Jefferson and Shelby Counties in quarries such as this for many years.



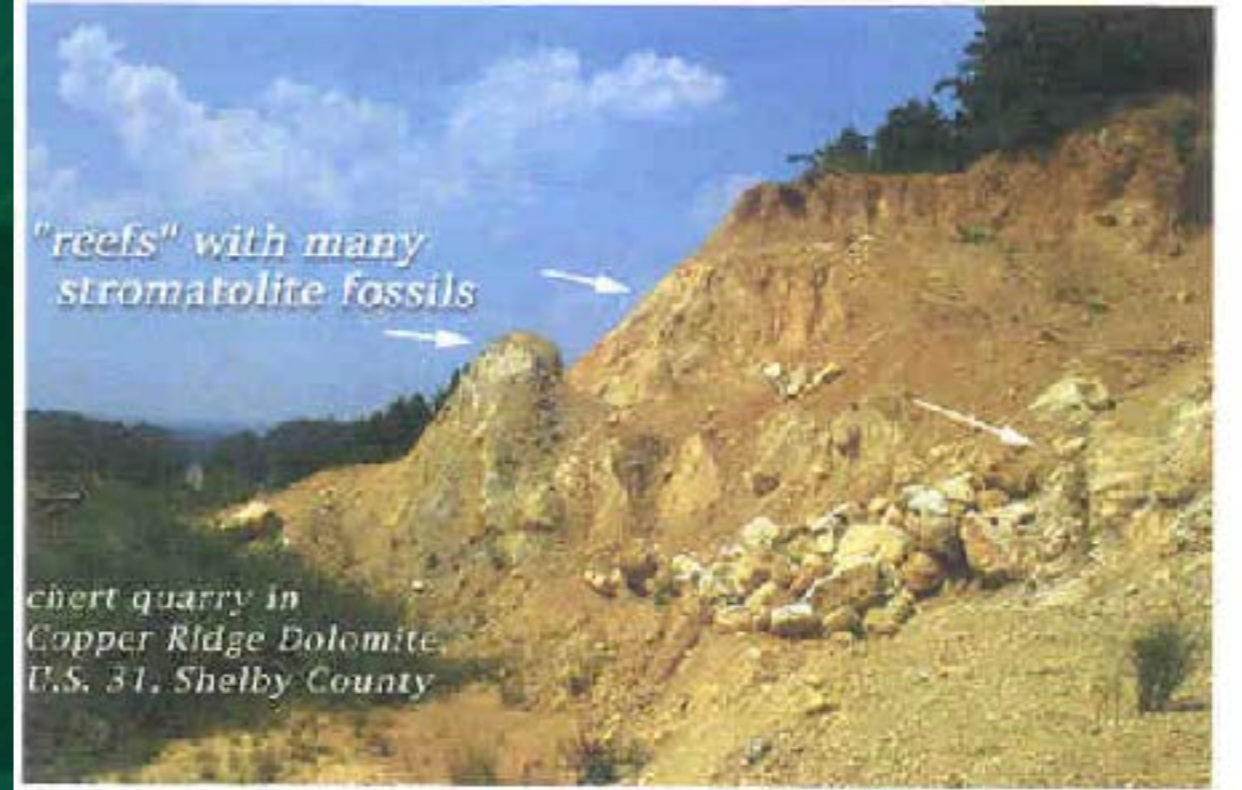
Chert quarry of the Copper Ridge Dolomite near Pellham.



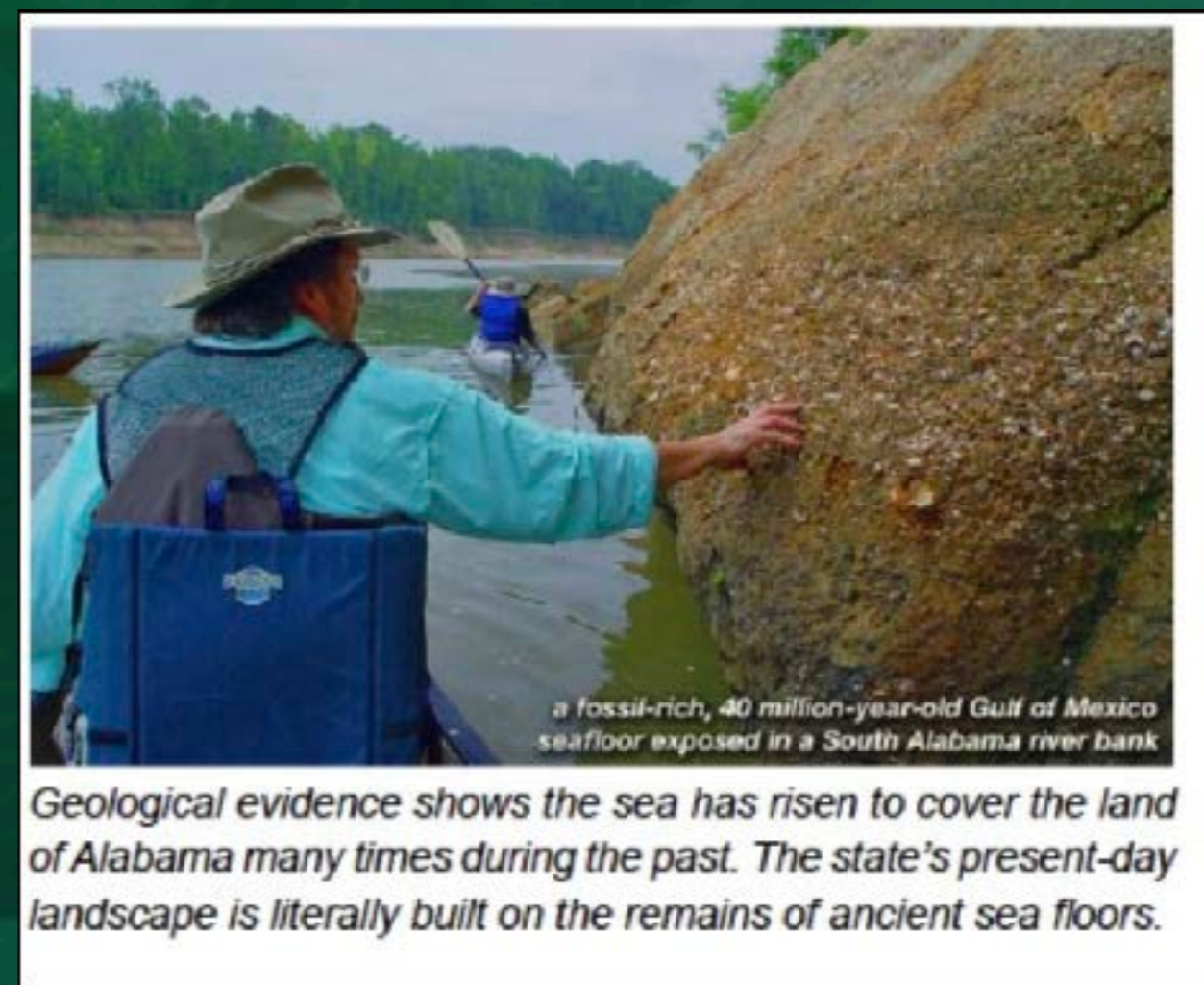
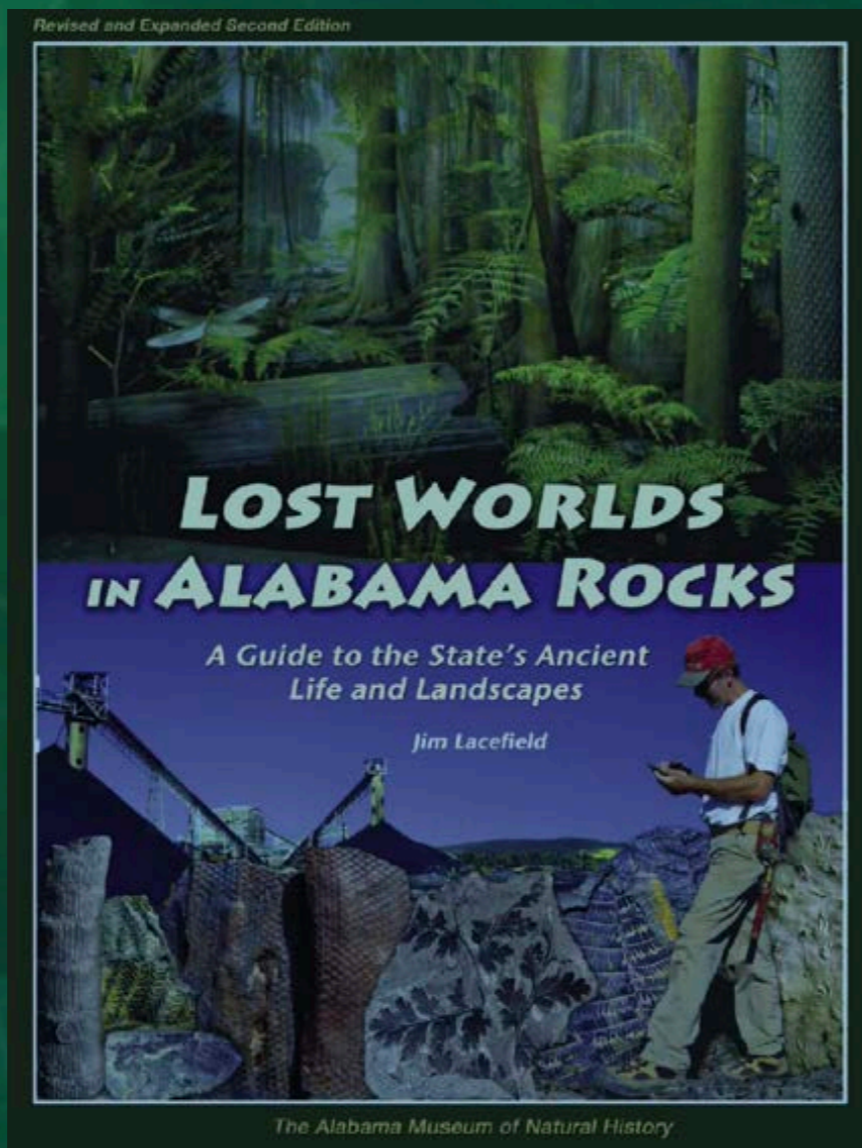
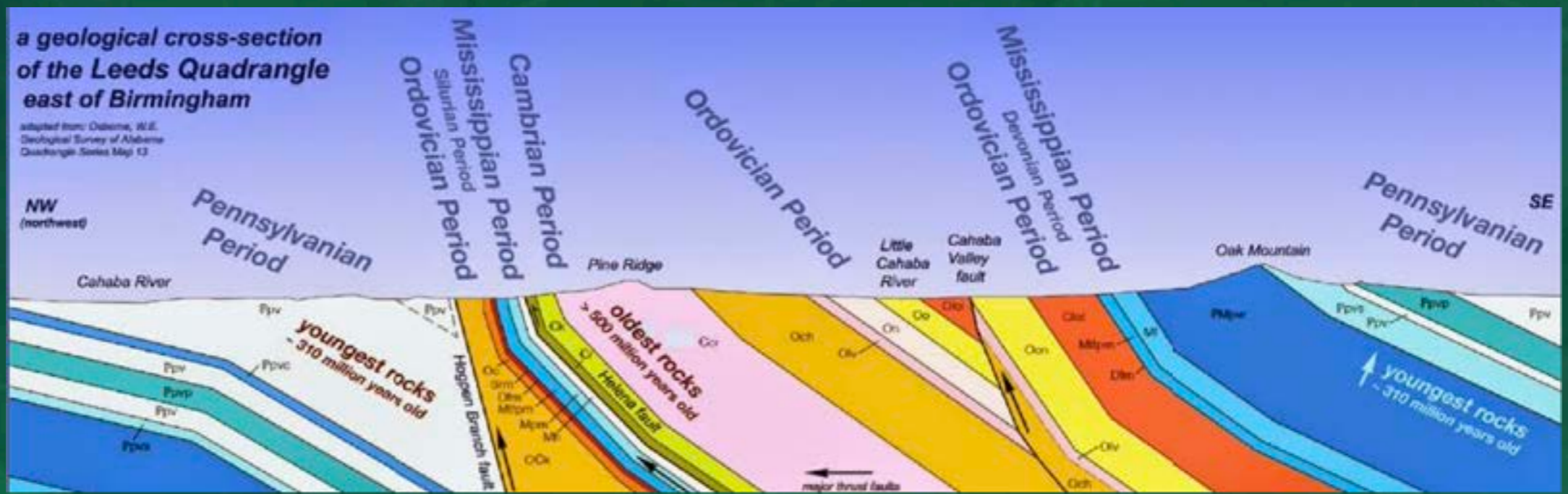
Stromatolite fossils in chert have incorrectly been called "fossil hornets' nests" because of their appearance.

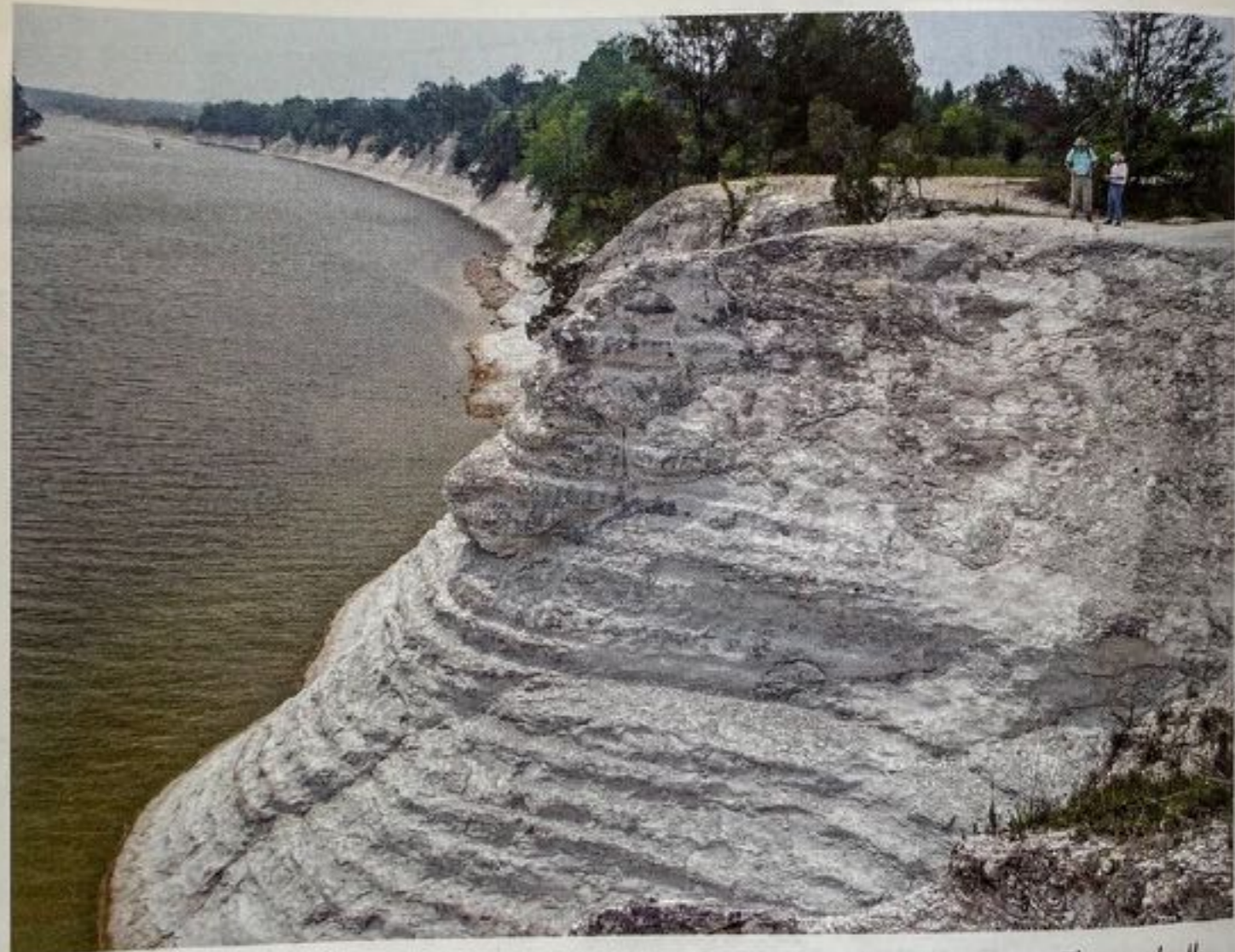
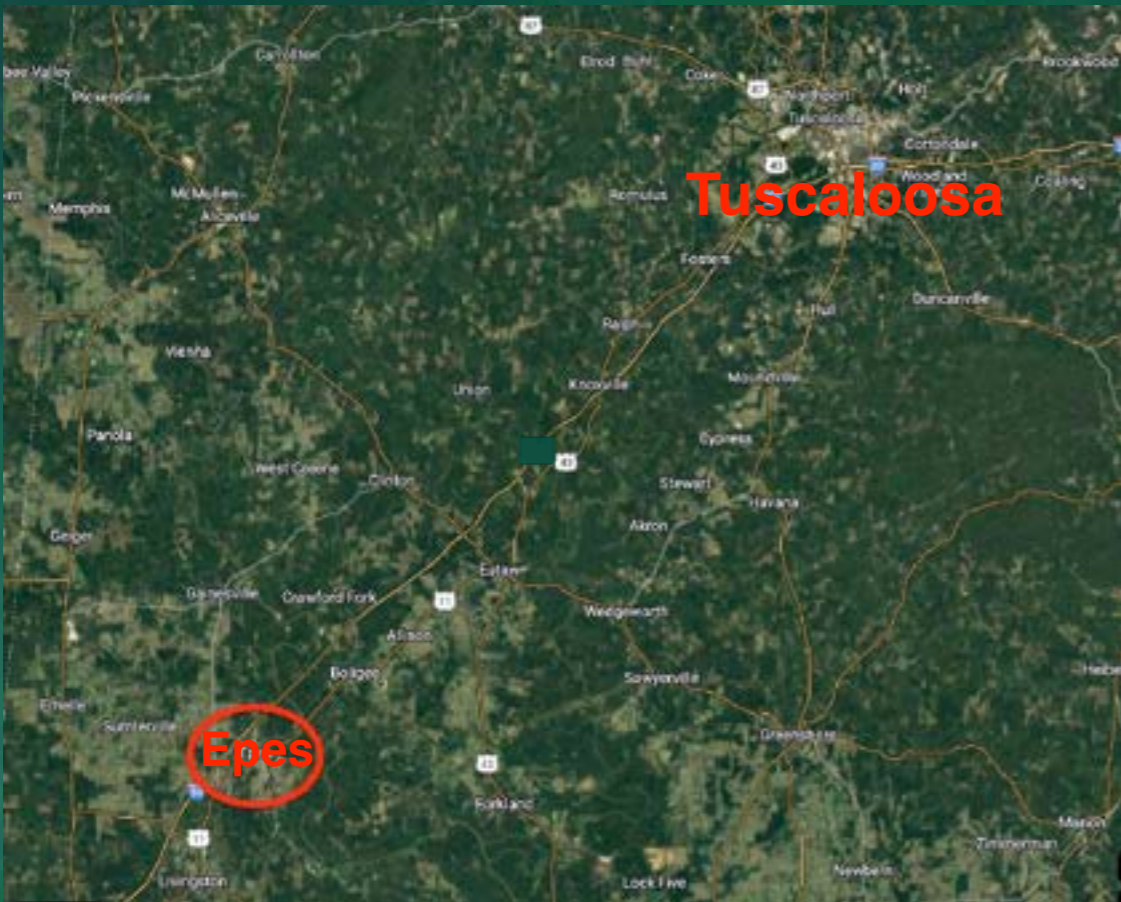


The Cambrian Earth

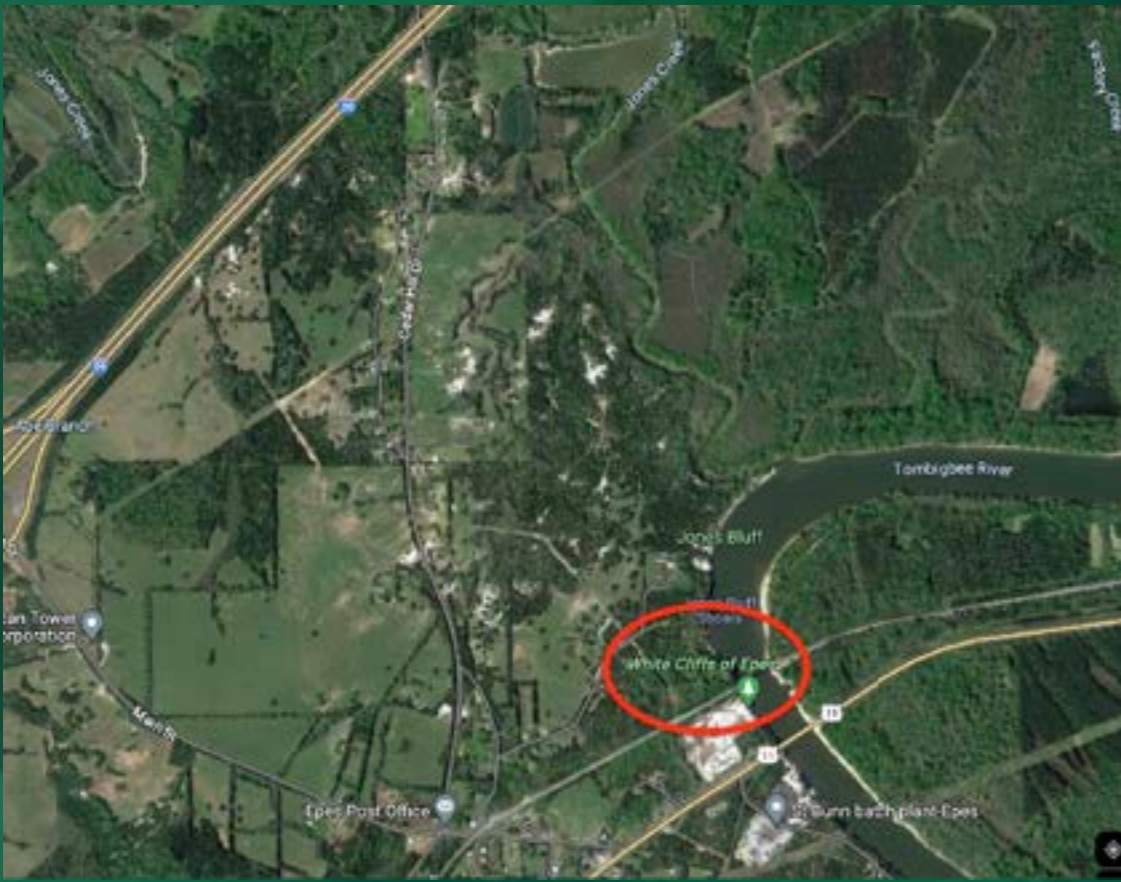


Chert quarry of the Copper Ridge Dolomite near Pellham.





Chalk of the Selma Group is exposed on the Tombigbee River in Epes. These chalk deposits are the same age as the ones exposed famously on England's White Cliffs of Dover. —Courtesy of Jim Laceyfield

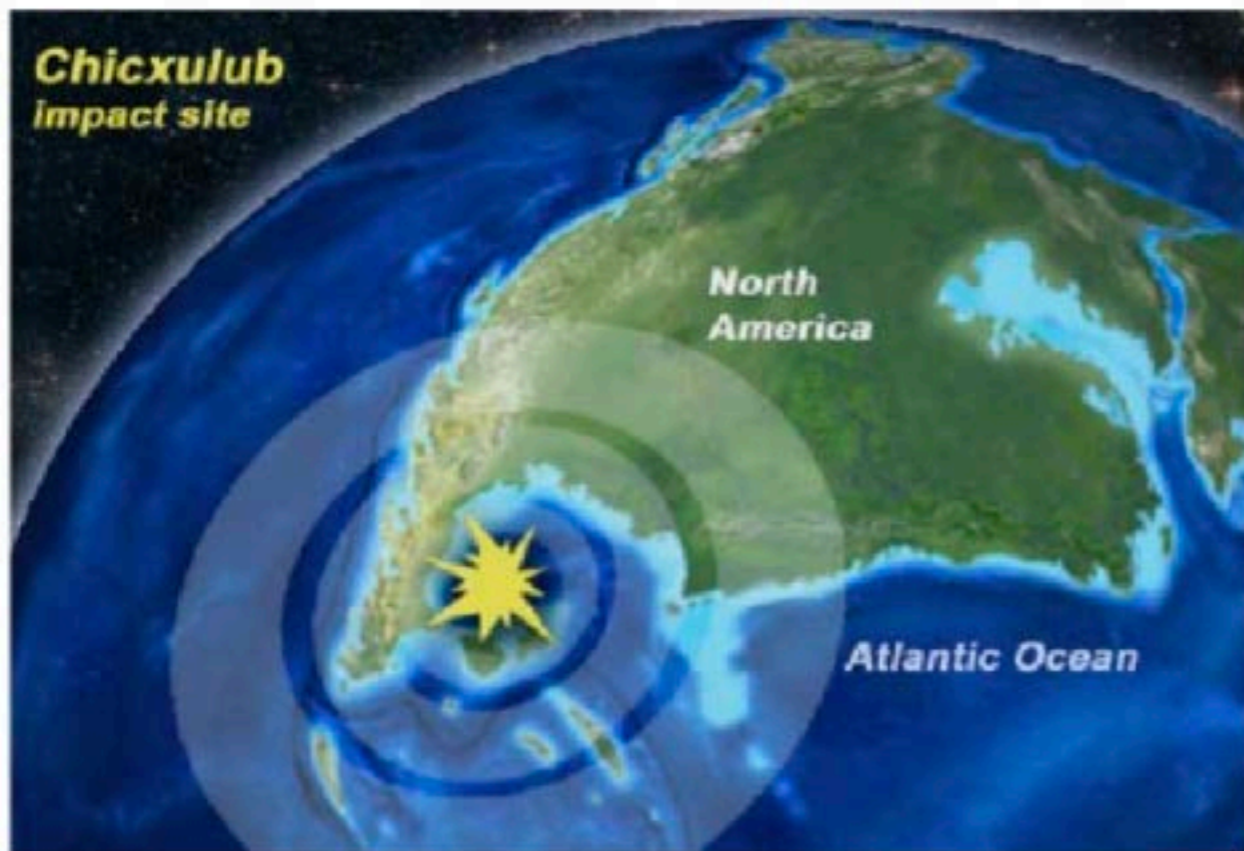


White Cliffs of Epes (!)

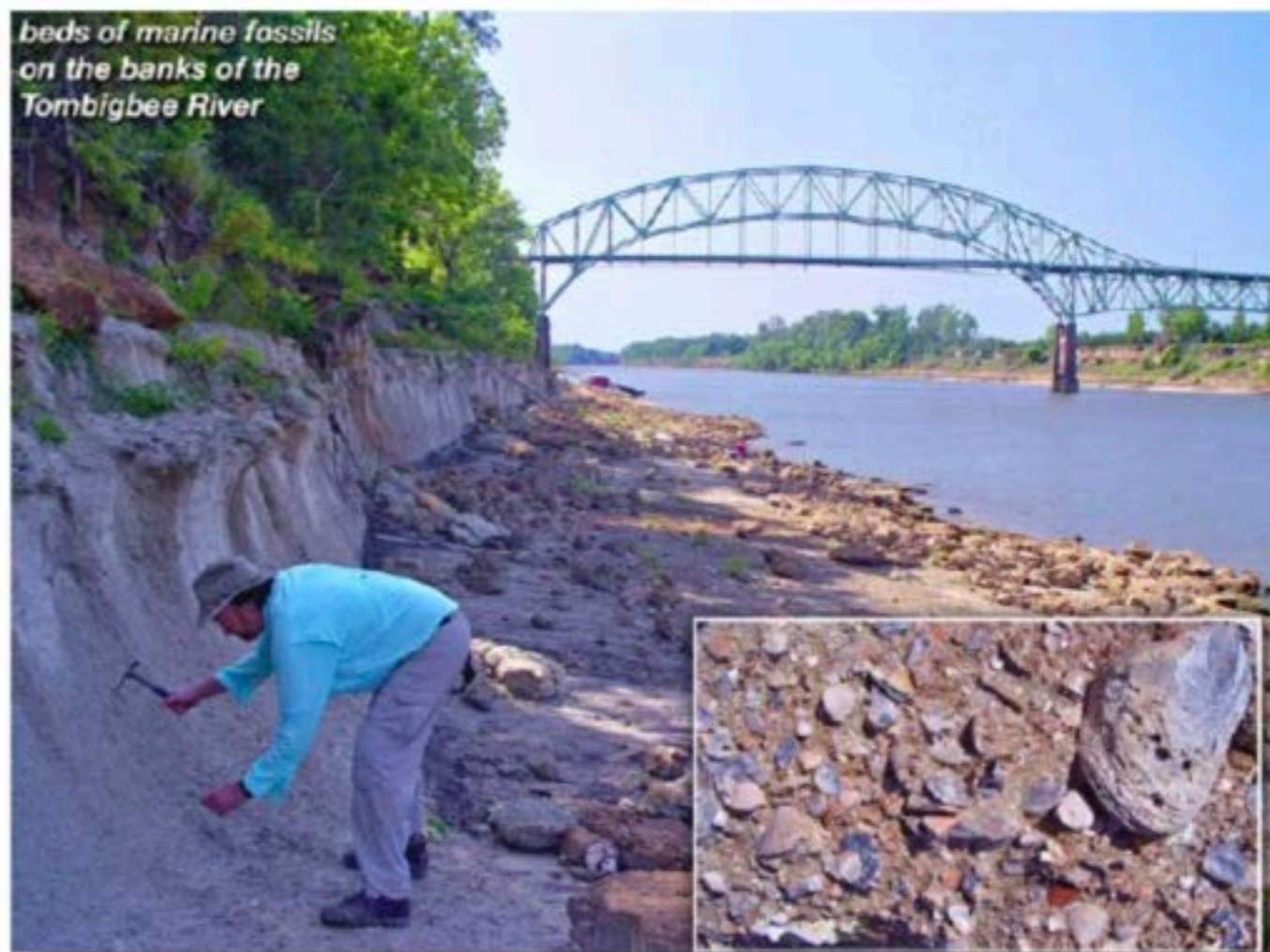


During the Late Cretaceous, sea level was at one of its highest recorded stands. Alabama lay at the southern end of an immense continental seaway that connected the Arctic Ocean and the Gulf of Mexico. —Modified from Lacefield, 2018

The geological evidence pointing to an impact includes a crater approximately 124 miles in diameter, now buried under more than 3,000 feet of limestone deposited since the time of the cataclysm. The impact created huge tsunami, or seismic sea waves hundreds of feet high along the Gulf of Mexico coastline which devastated the Coastal Plain for many miles inland. "Storm" deposits of unprecedented proportions dating to the time of this event are found in Texas and other areas. Tiny beads of glassy rock known as



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The New World of the Cenozoic Era
(65 m.y.a. to Today)

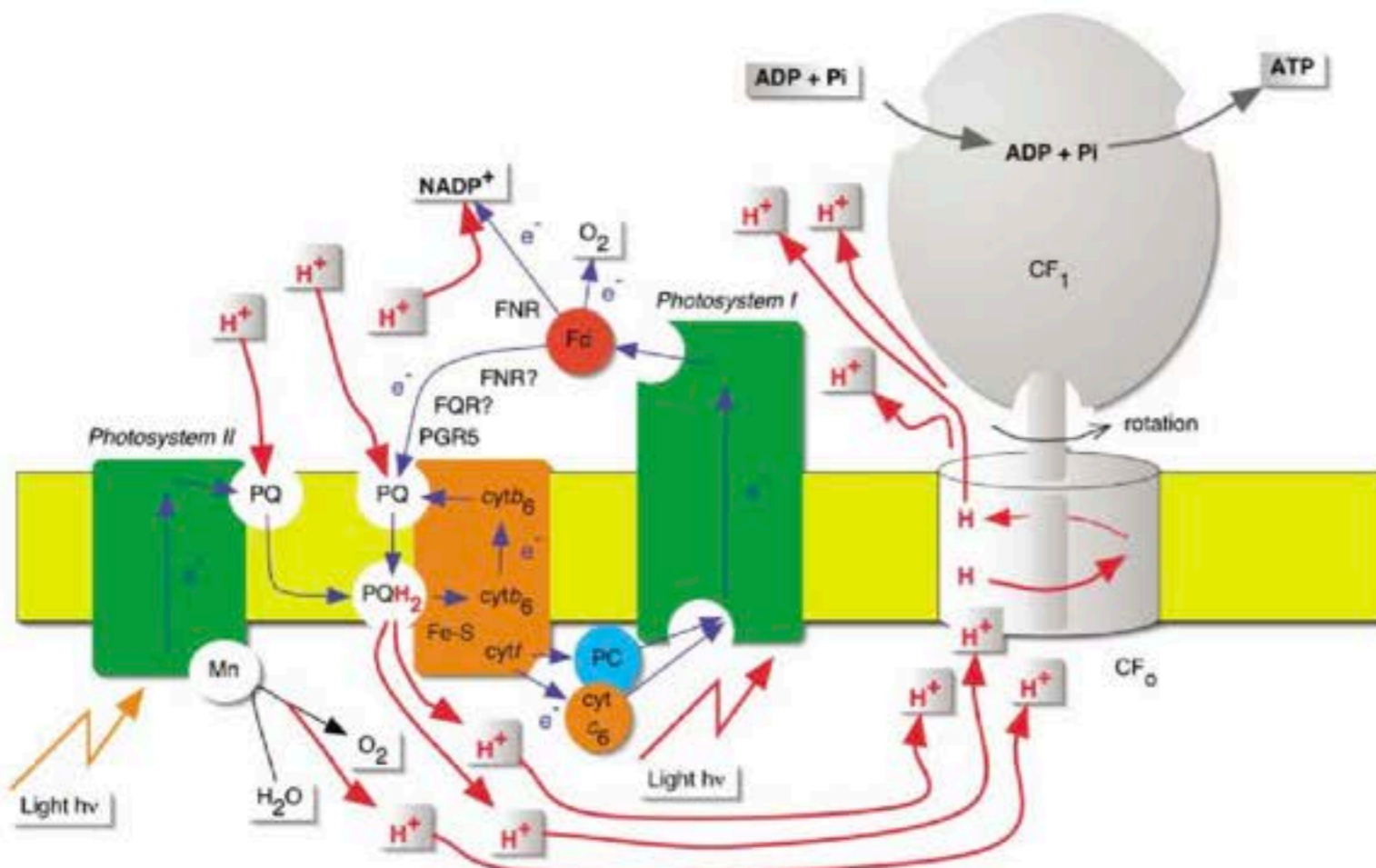
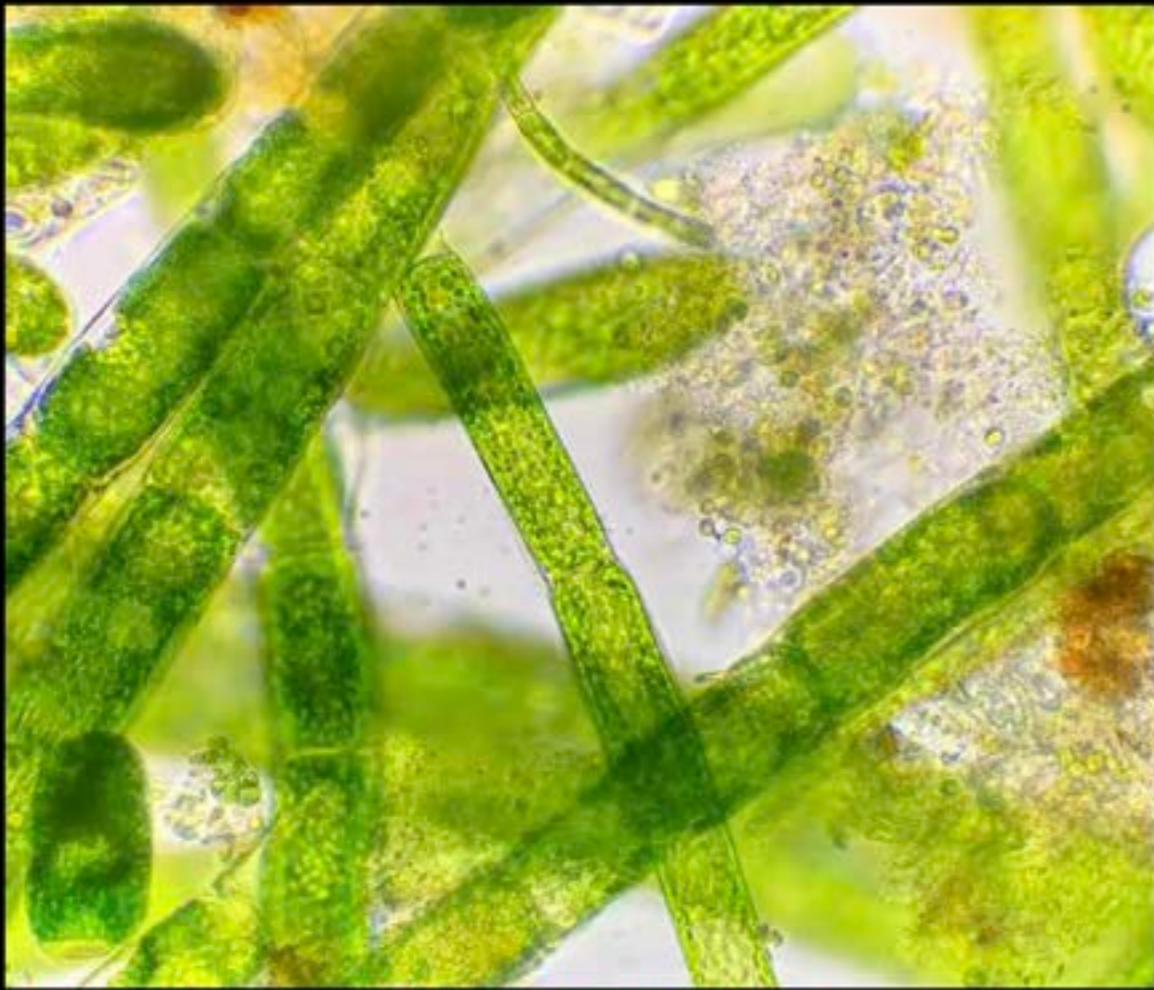
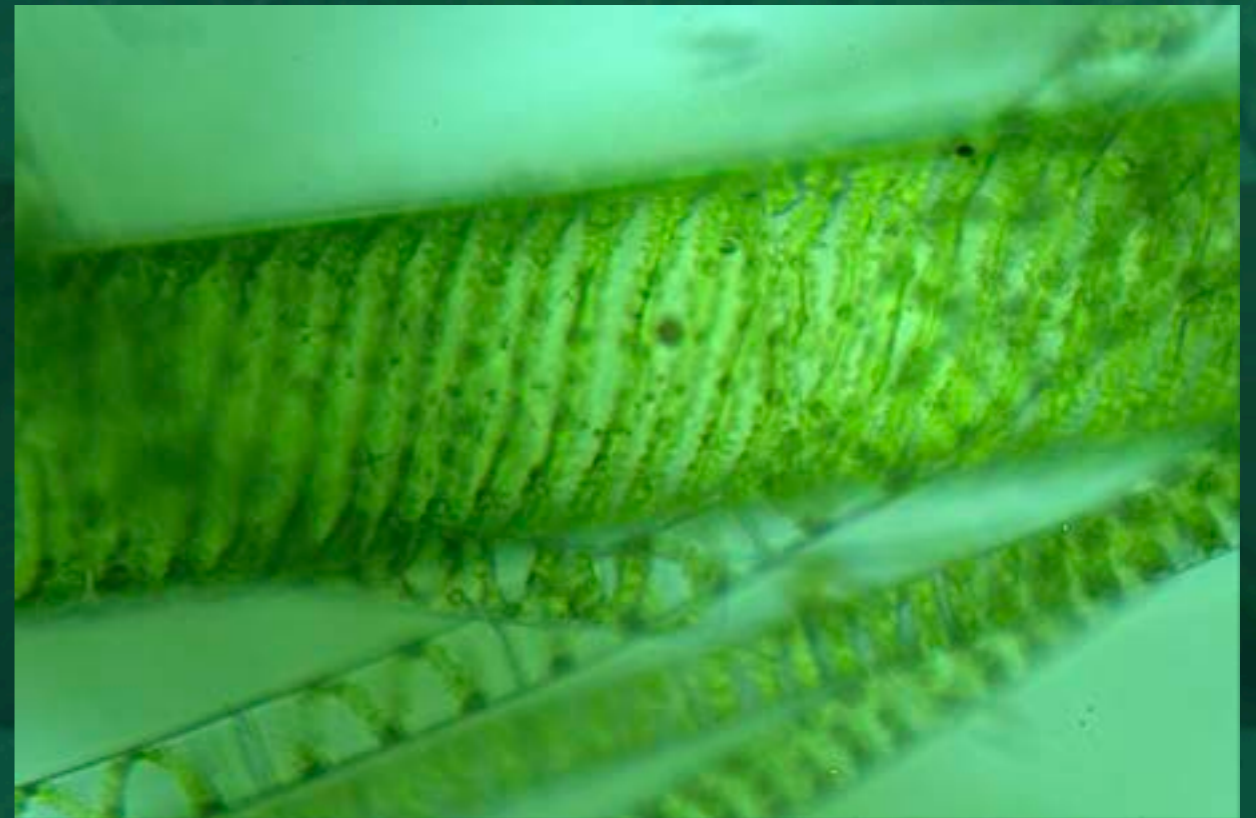
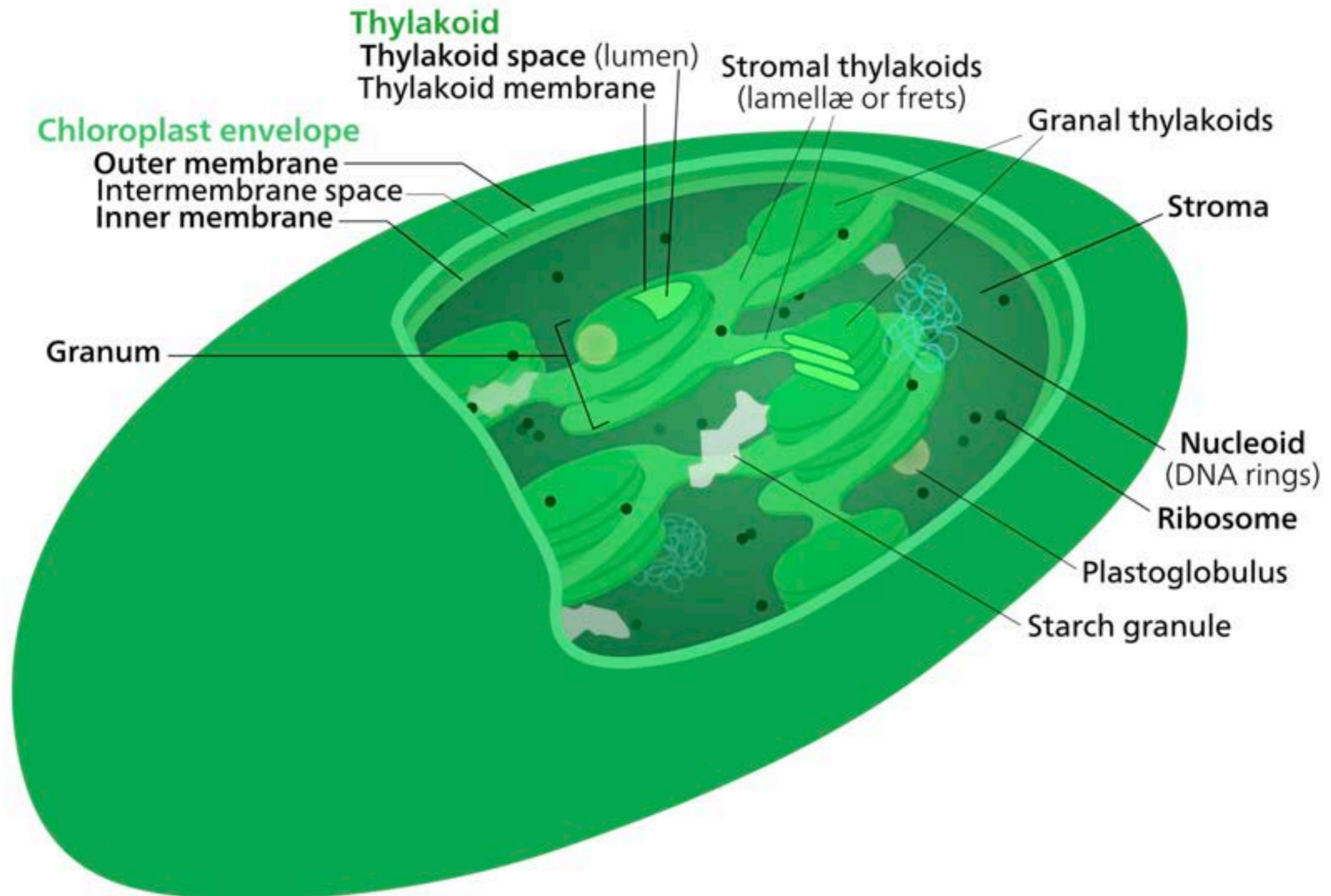


Figure 1. Photosynthesis—From Light to ATP
 Electron transport (e^-) (blue) is arranged vectorially in the chloroplast thylakoid membrane (yellow). Proton (H^+) (red) translocation from the chloroplasts stroma (above the membrane) into the lumen (below the membrane) establishes a proton motive force that couples electron transport to ATP synthesis. The implied stoichiometry $3H^+/e^-$ is for noncyclic electron transport alone (cf. Figure 2). FQR is a hypothetical ferredoxin-quinone-oxidoreductase. Other abbreviations as in text. Junge's animations *Rotary ATP Synthase* and *From Light to ATP* are recommended viewing: <http://www.biologie.uni-osnabrueck.de/Biophysik/Junge/overheads.html>

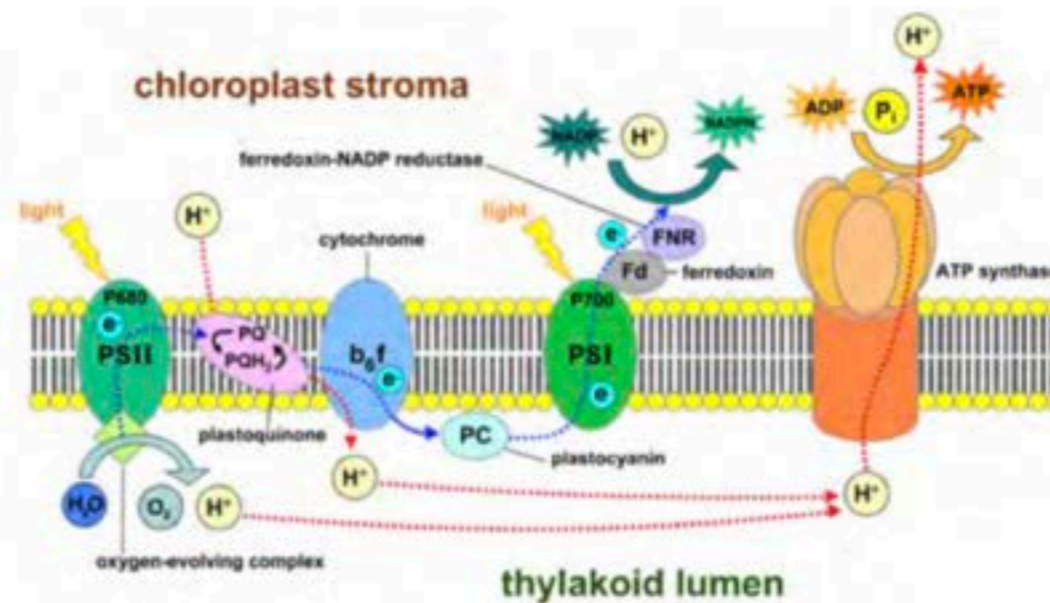
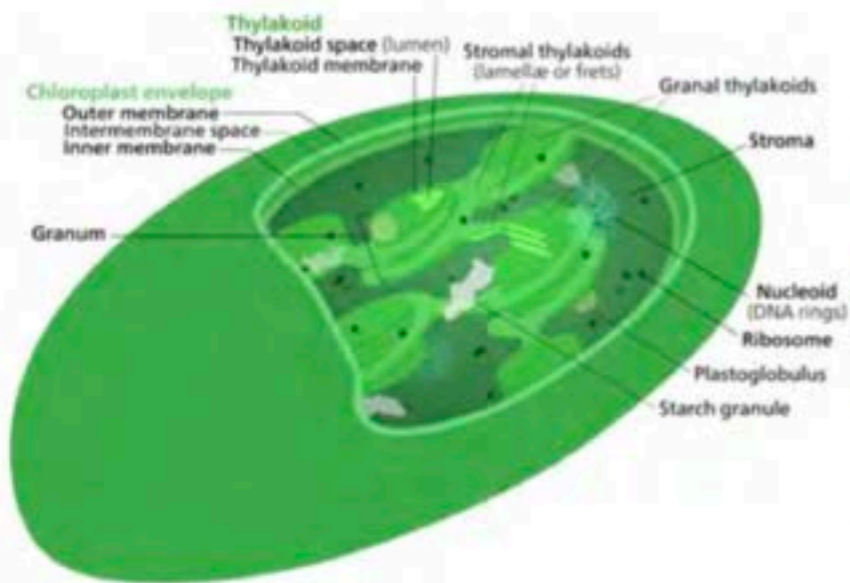


Cedogonium and zoospores ... collected from backyard fountain pond 12/13/21; microphotographs and videos by
Whitsell Boogaerts

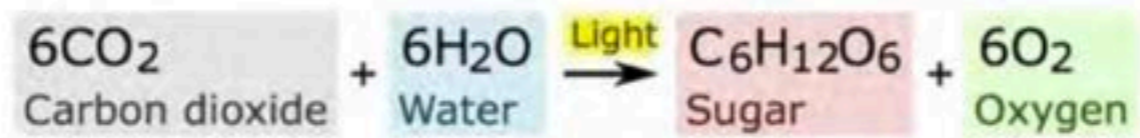
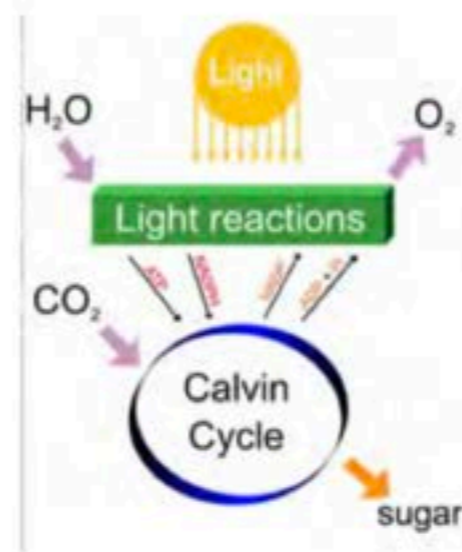
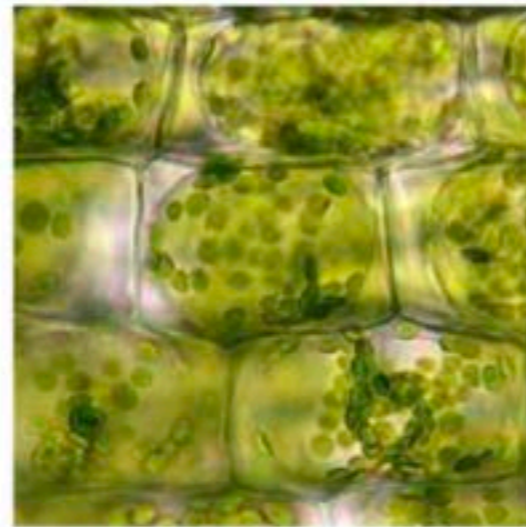




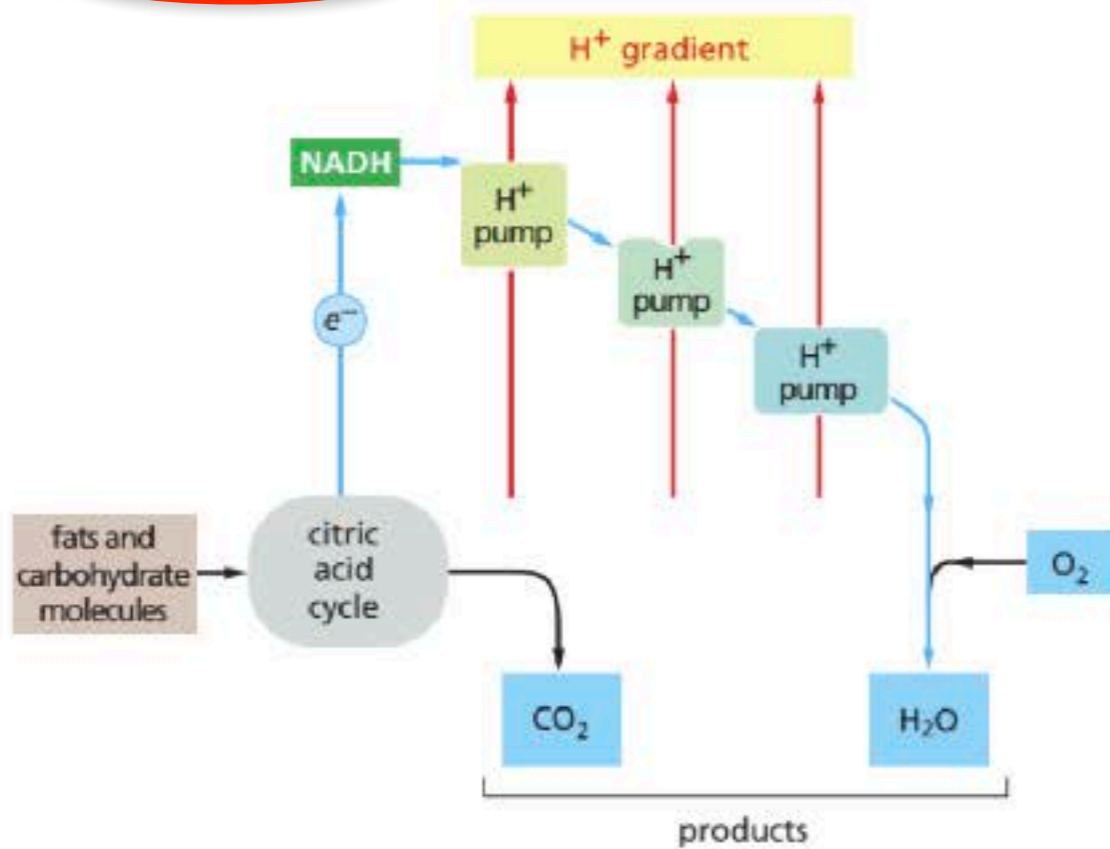
Realize that “*photosynthesis*” is better termed “*photophosphorylation*”, because the energy of light is actually being used *not* to make sugar directly, but rather to *generate an H^+ gradient across a membrane*. This drives phosphorylation of ADP to **ATP**, the energy currency of living systems. In other steps, the **ATP** is used to power the reactions of glucose production. Here’s a view of activity on the chloroplast stromal membrane:



Here is the light-powered reaction sequence by which sugars are made from carbon dioxide and water:



(A) MITOCHONDRION



(B) CHLOROPLAST

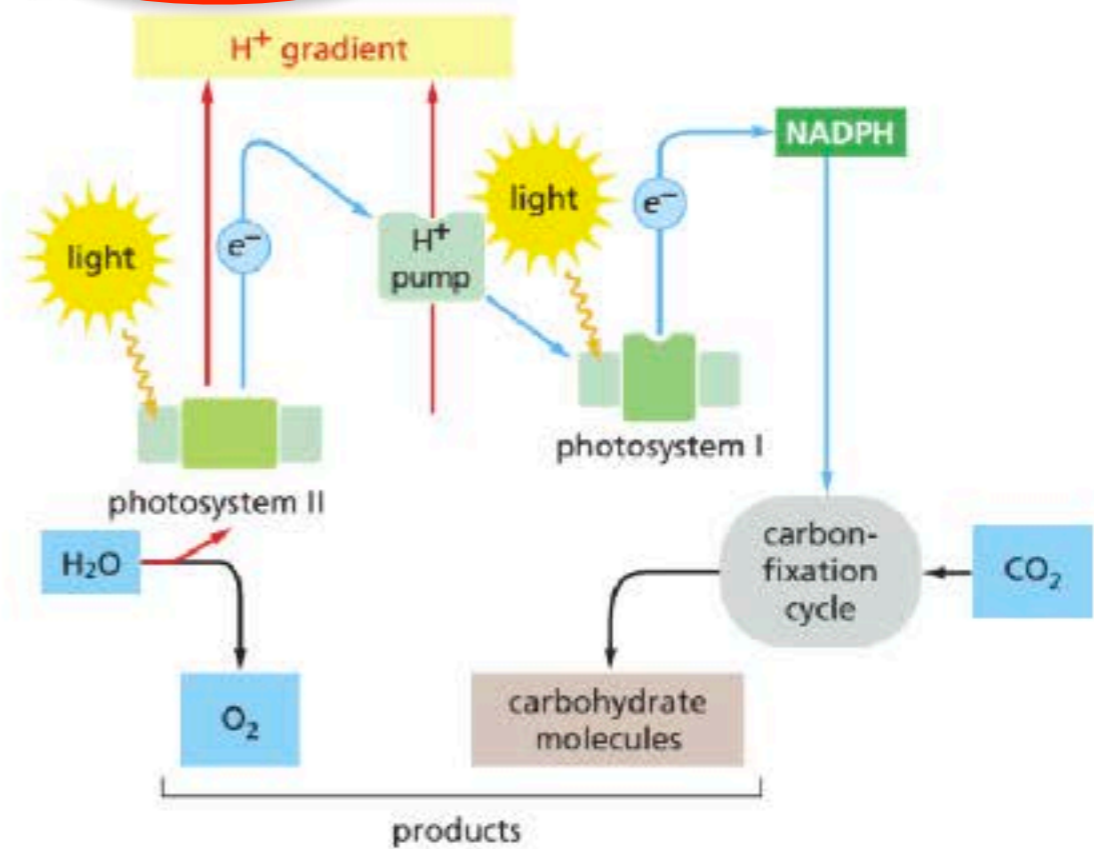
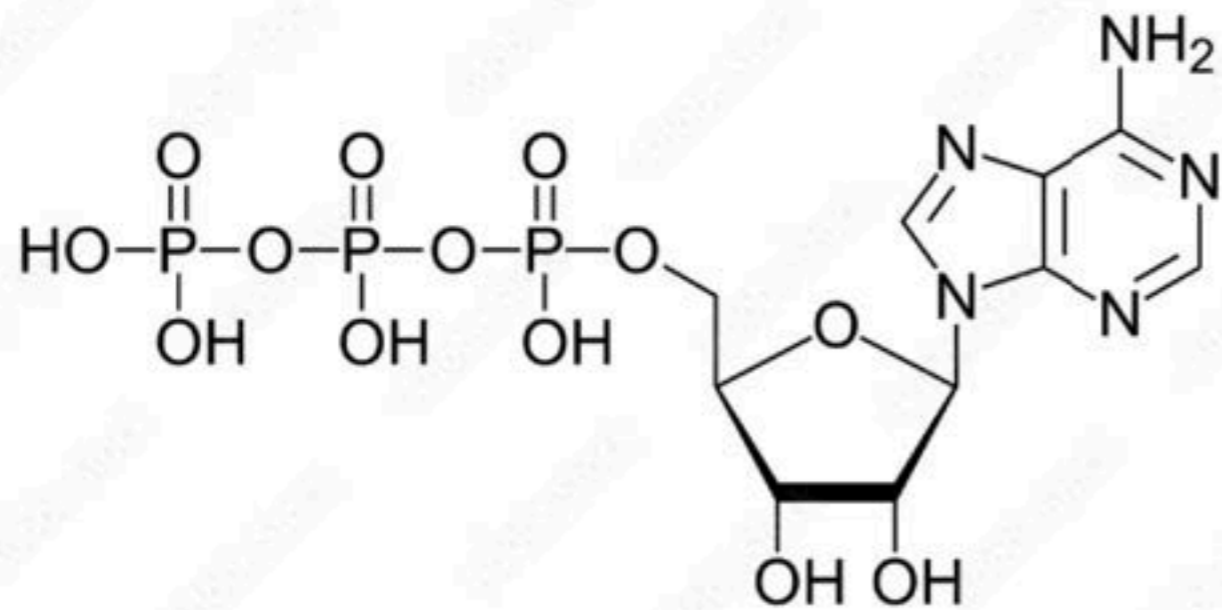
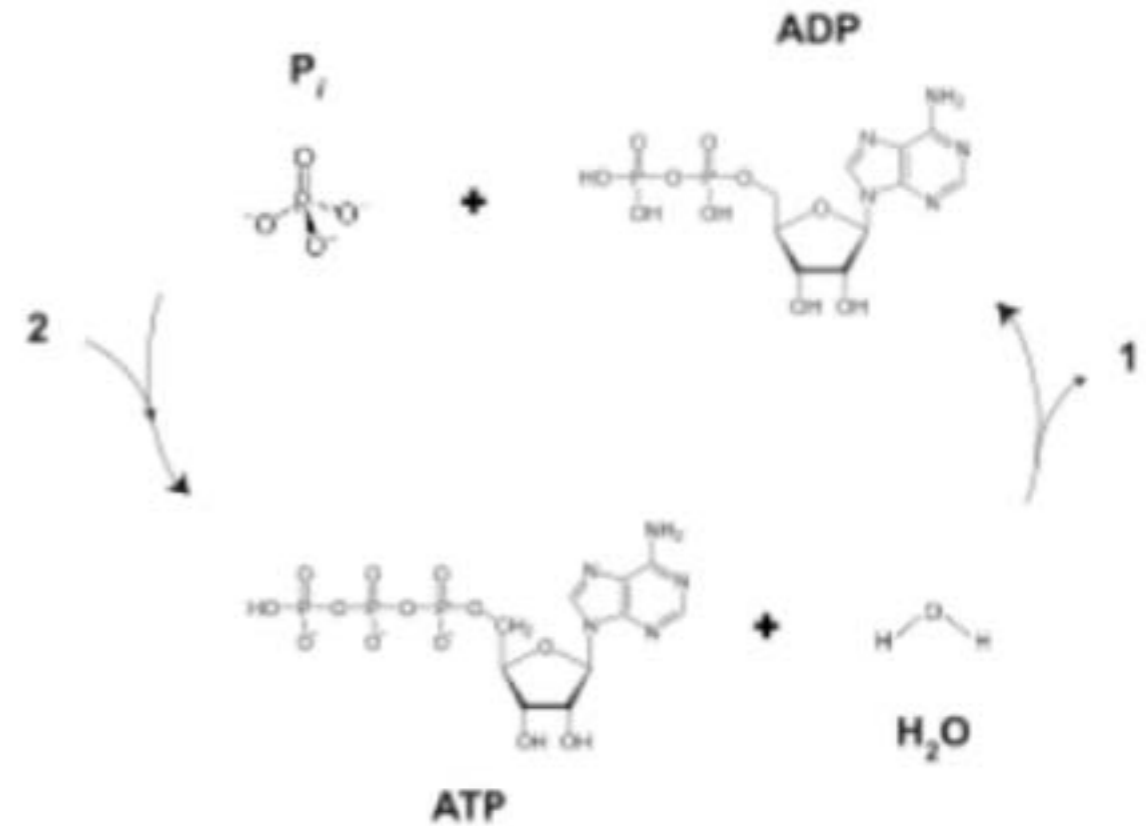


Figure 1-4 Electron-transport processes. (A) The mitochondrion converts energy from chemical fuels. (B) The chloroplast converts energy from sunlight. In both cases, electron flow is indicated by blue arrows. Each of the protein complexes (green) is embedded in a membrane. In the mitochondrion, fats and carbohydrates from food molecules are fed into the citric acid cycle and provide electrons to generate the energy-rich compound NADH from NAD⁺. These electrons then flow down an energy gradient as they pass from one complex to the next in the electron-transport chain, until they combine with molecular O₂ in the last complex to produce water. The energy released at each stage is harnessed to pump H⁺ across the membrane. In the chloroplast, by contrast, electrons are extracted from water through the action of light in the photosystem II complex and molecular O₂ is released. The electrons pass on to the next complex in the chain, which uses some of their energy to pump protons across the membrane, before passing to photosystem I, where sunlight generates high-energy electrons that combine with NADP⁺ to produce NADPH. NADPH then enters the carbon-fixation cycle along with CO₂ to generate carbohydrates.

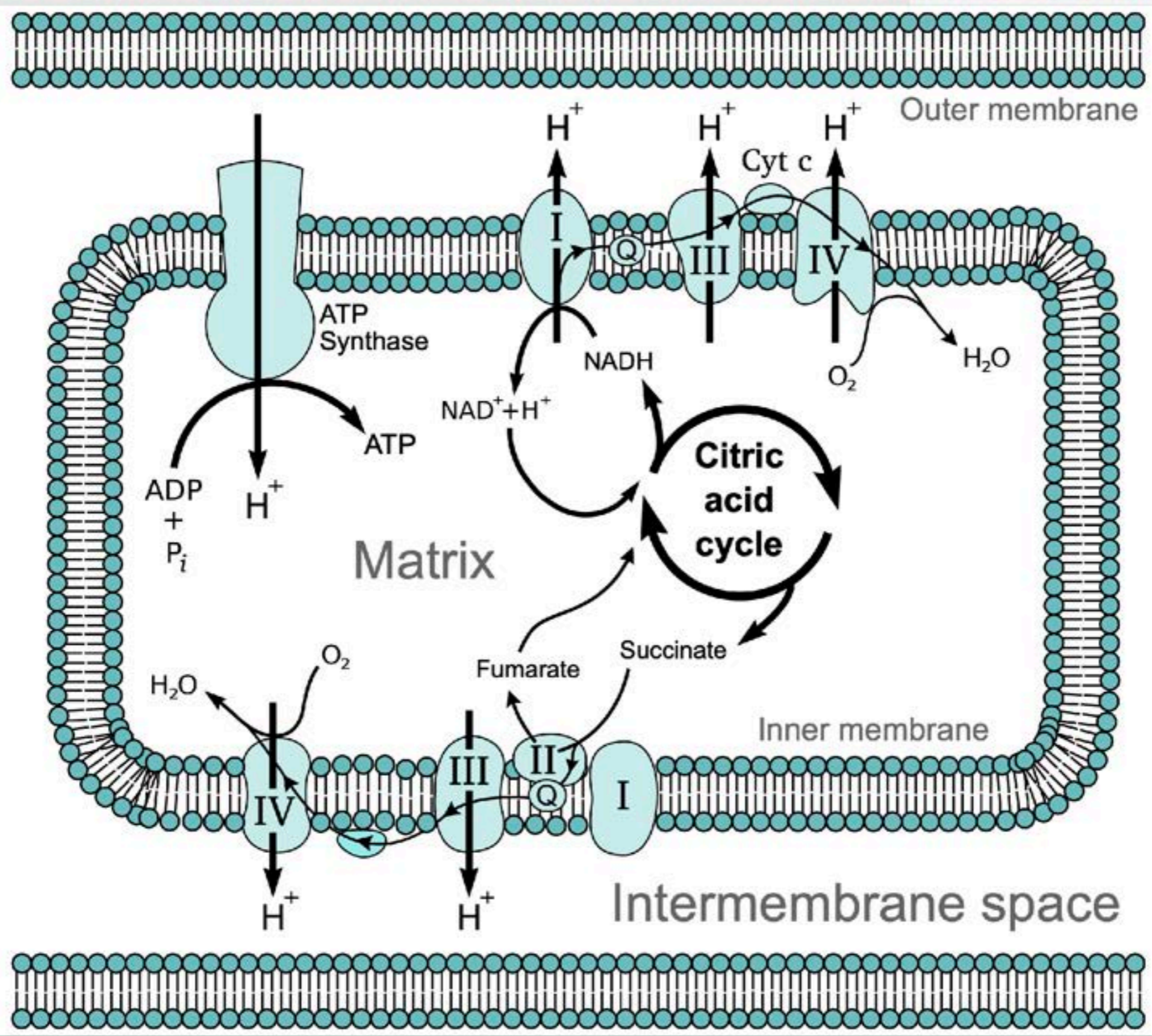


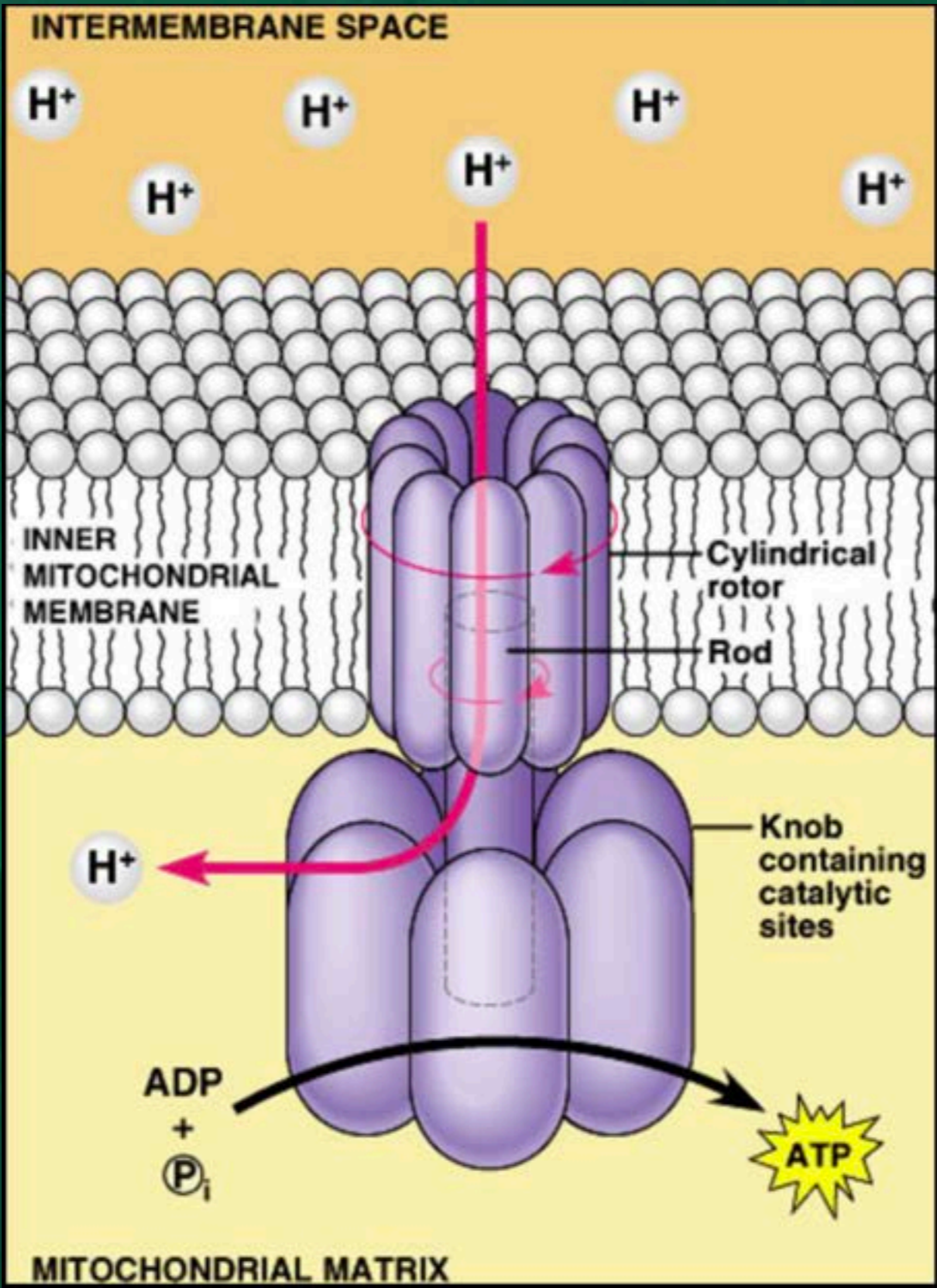
ATP

Adenosine triphosphate



The cycles of synthesis and degradation of ATP; 2 and 1 represent input and output of energy, respectively.





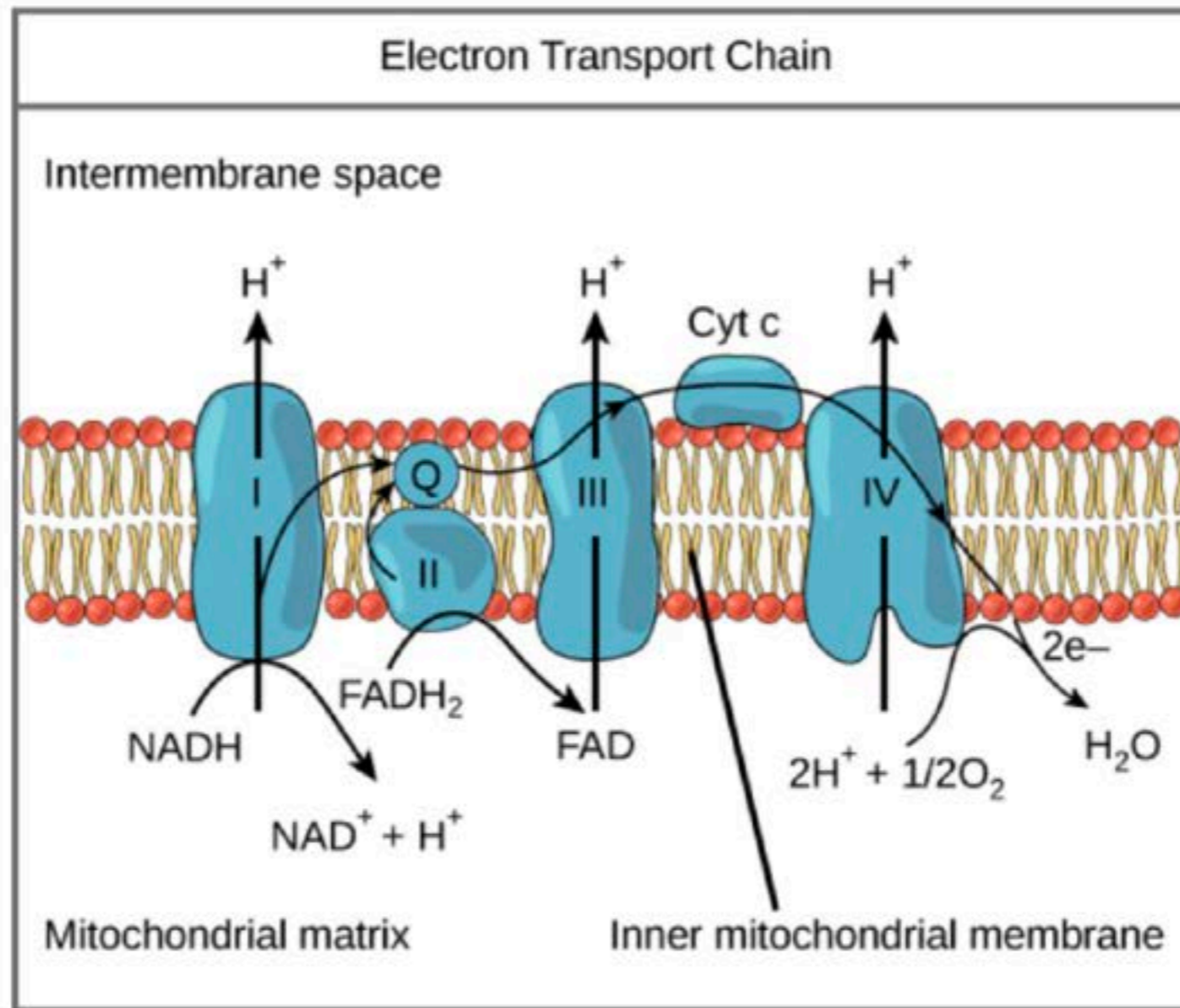
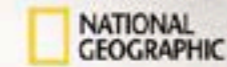


Figure 1. The electron transport chain is a series of electron transporters embedded in the inner mitochondrial membrane that shuttles electrons from NADH and FADH₂ to molecular oxygen. In the process, protons are pumped from the mitochondrial matrix to the intermembrane space, and oxygen is reduced to form water.

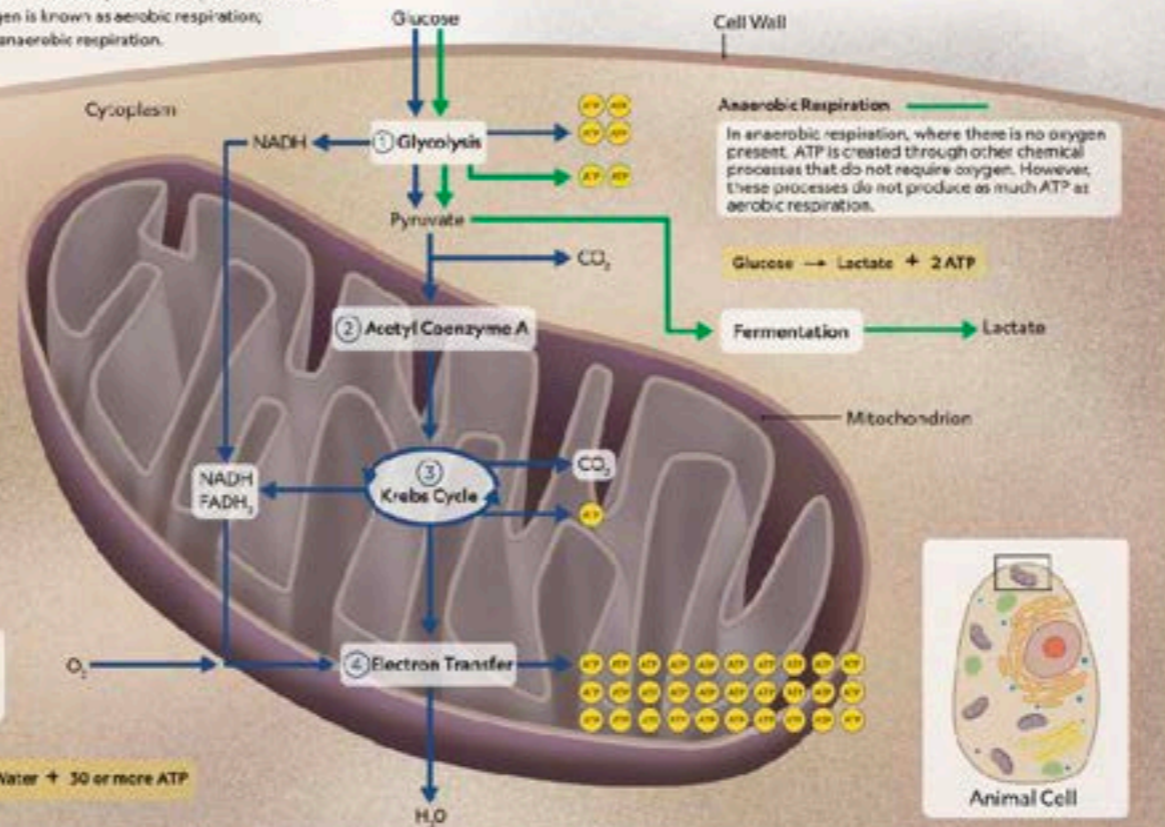
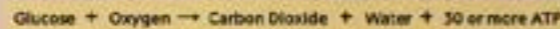
CELLULAR RESPIRATION



Cellular respiration is the process by which food, in the form of sugar (glucose), is transformed into energy within cells. This energy is stored in ATP molecules, which then power all sorts of cellular processes. Respiration that requires oxygen is known as aerobic respiration; respiration that occurs without oxygen is called anaerobic respiration.

Aerobic Respiration

- 1 The first stage of aerobic respiration is **glycolysis**, where **glucose** molecules are broken down to create **ATP** in a cell's cytoplasm. Although the process consumes two ATP molecules, it produces four more, as well as two other substances: **pyruvate** and **NADH**.
- 2 In the second stage, which occurs in the **mitochondria** of a cell, pyruvate is used to create **acetyl coenzyme A** and **carbon dioxide**.
- 3 The third stage is known as the **citric acid cycle**, or **Krebs cycle**. In this stage, acetyl coenzyme A is used to create more **NADH**, as well as **FADH₂**, carbon dioxide, and an additional **ATP** molecule.
- 4 In the final stage, **NADH**, **FADH₂**, and **oxygen** are used to create massive amounts of **ATP** through **electron transfer**. This stage also creates **water** molecules.



Anaerobic Respiration

In anaerobic respiration, where there is no oxygen present, ATP is created through other chemical processes that do not require oxygen. However, these processes do not produce as much ATP as aerobic respiration.

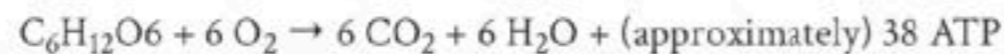


Fermentation → Lactate

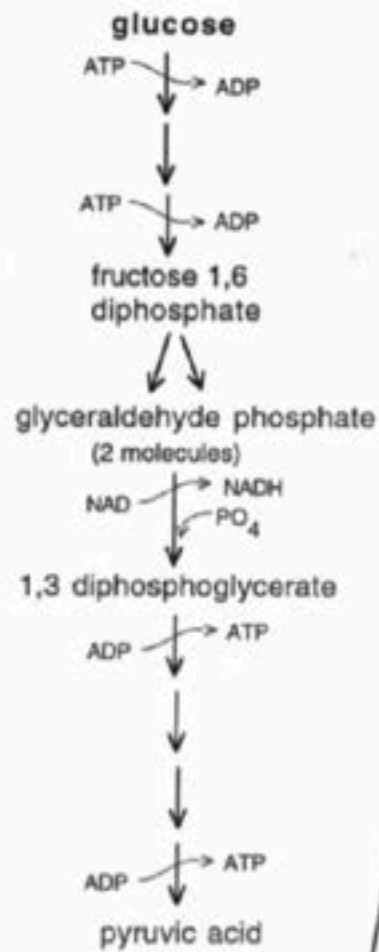
SOURCE

AEROBIC RESPIRATION

Aerobic respiration requires oxygen. This is the reason why we breathe oxygen in from the air. This type of respiration efficiently releases a large amount of energy from glucose that can be stored as ATP. Aerobic respiration happens all the time in animals and plants, where most of the reactions occur in the mitochondria. Even some prokaryotes can perform aerobic respiration (although since prokaryotes don't contain mitochondria, the reactions are slightly different). The overall chemical formula for aerobic respiration can be written as:

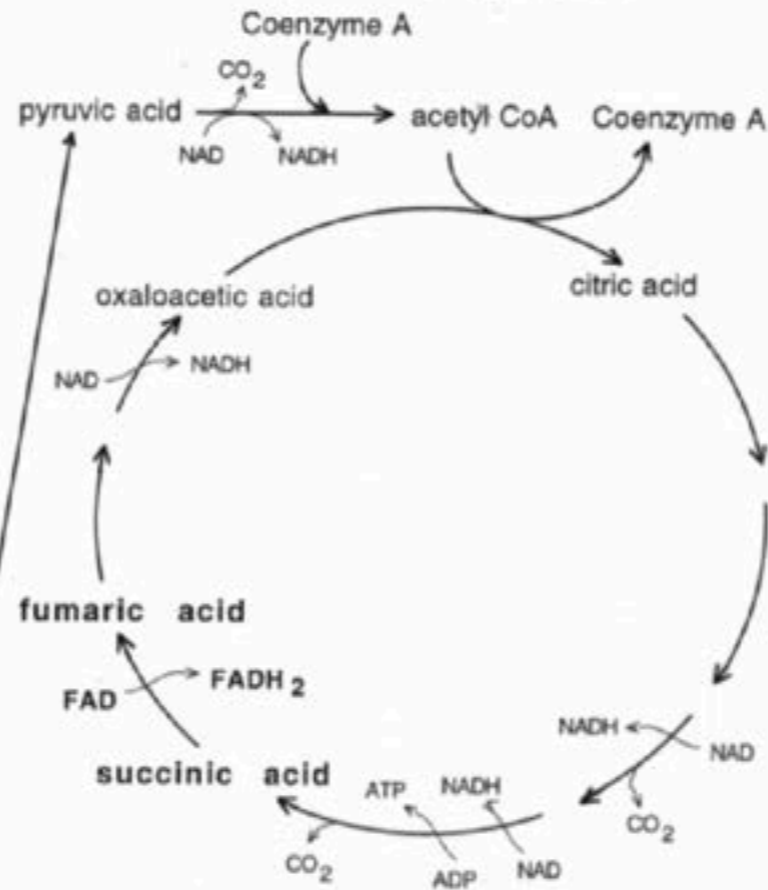


GLYCOLYSIS

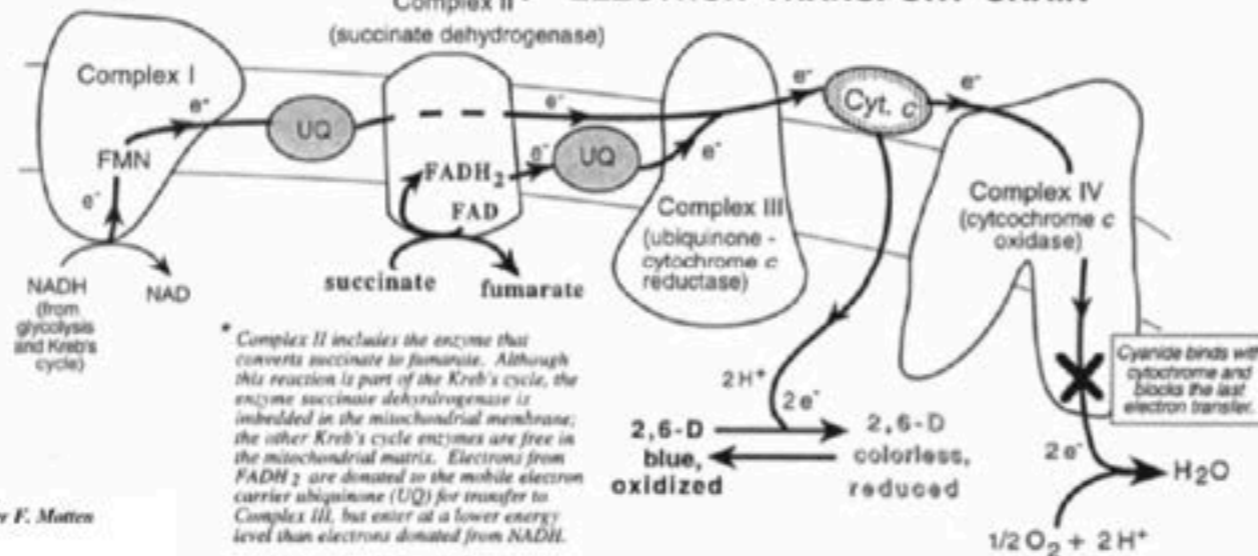


Abbreviated, diagrammatic summary of glycolysis and respiration

KREBS (CITRIC ACID) CYCLE



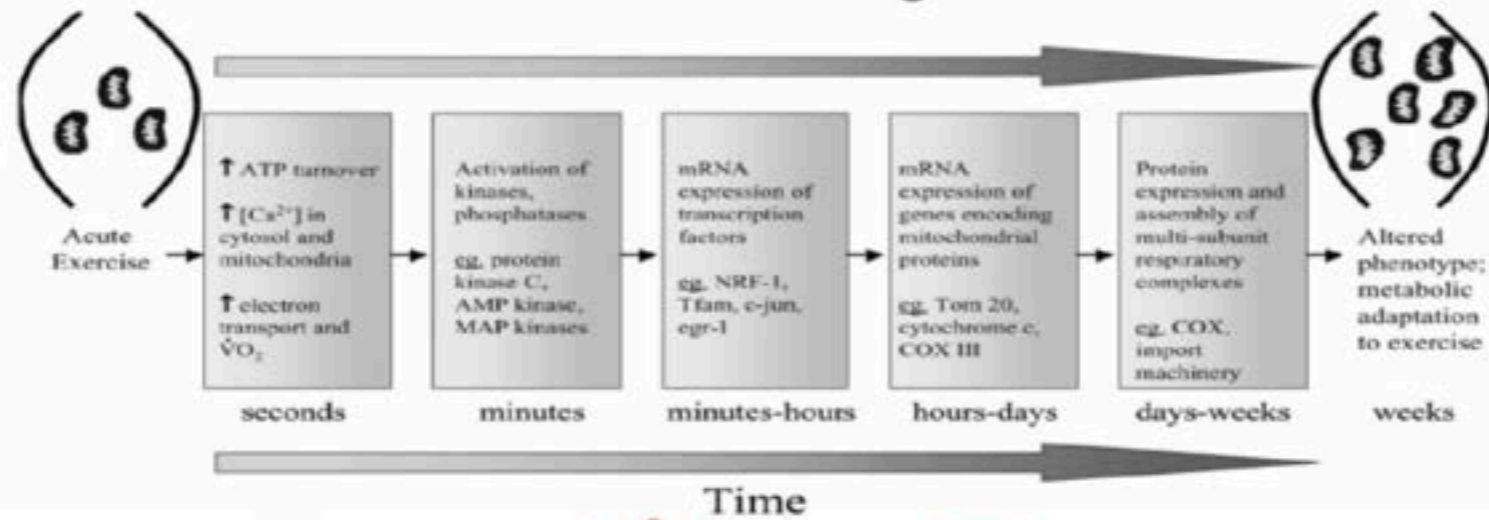
ELECTRON TRANSPORT CHAIN



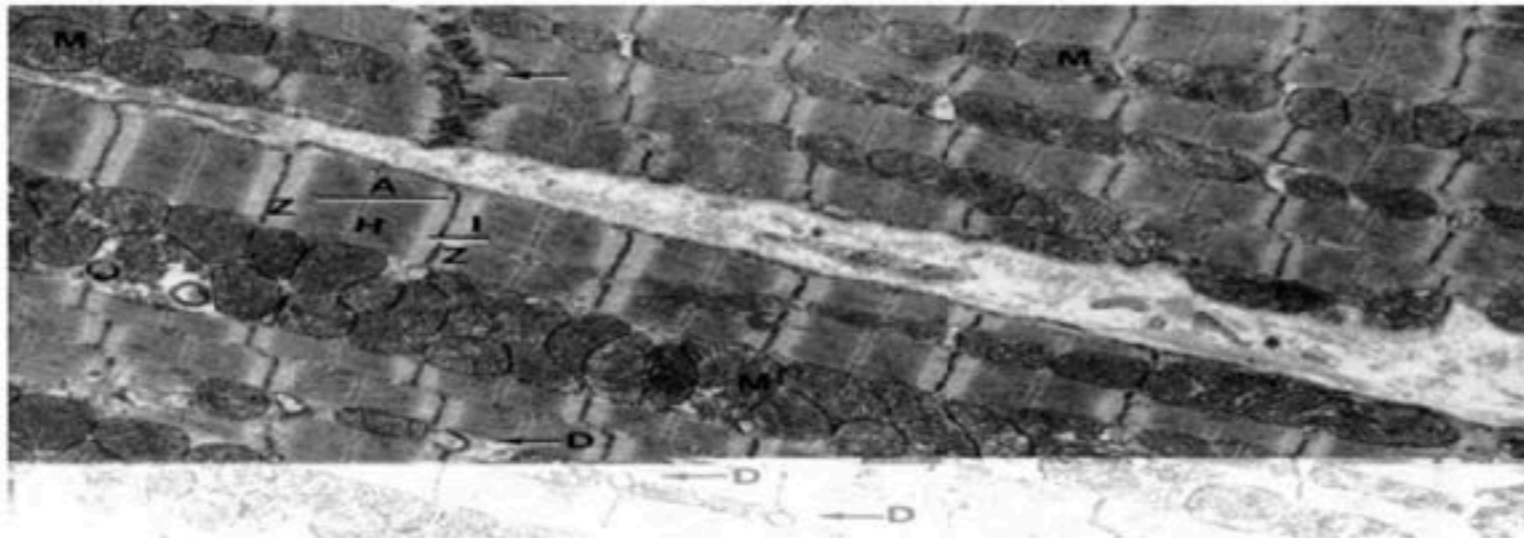
Alexander F. Motten

Department of Zoology
Duke University

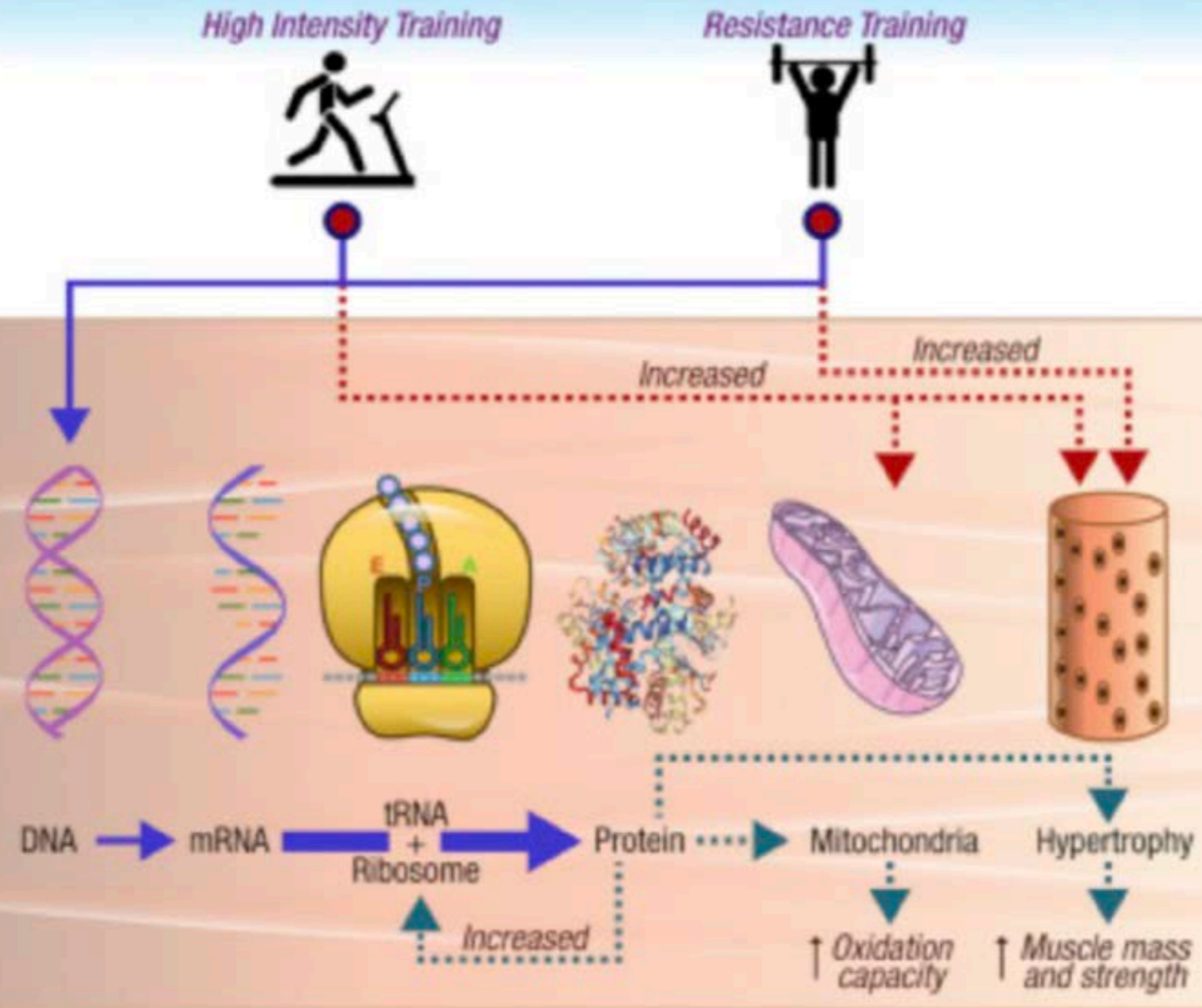
Established sequence of exercise-induced events leading to mitochondrial biogenesis



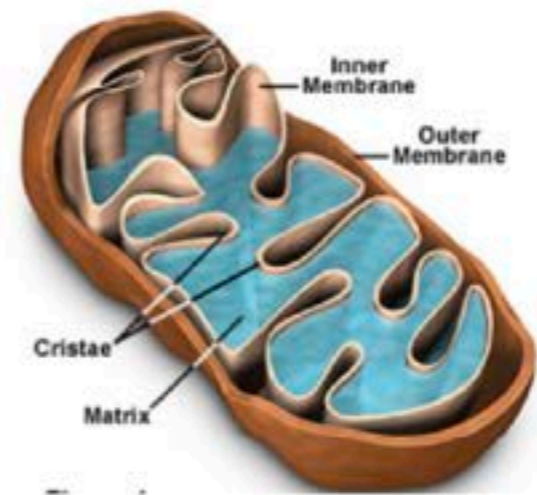
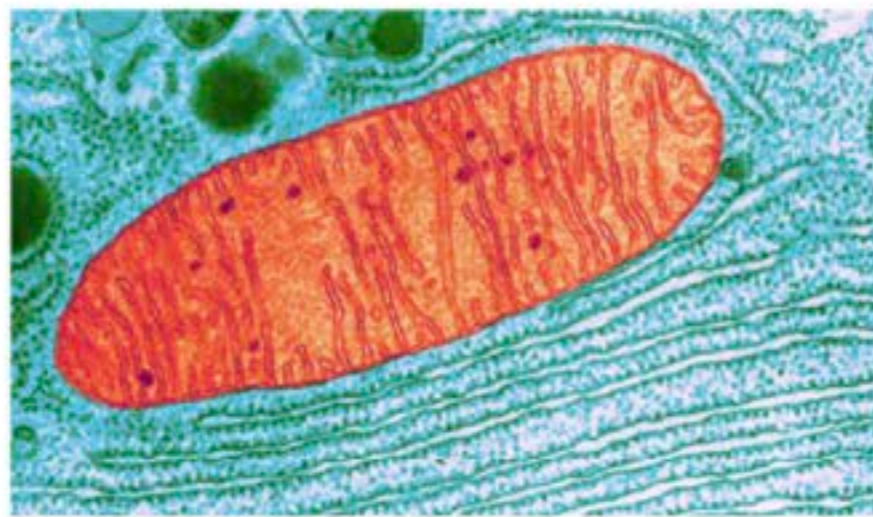
It is well known that endurance training, employing an appropriate duration per day, frequency per week, and submaximal intensity per exercise bout, can produce an increase in mitochondrial content, usually ranging from 50 to 100% within a 6 wk period. This directly results in improved endurance performance, largely independent of the much smaller training-induced changes in maximal oxygen consumption. J Appl Physiol 90: 1137-1157, 2001

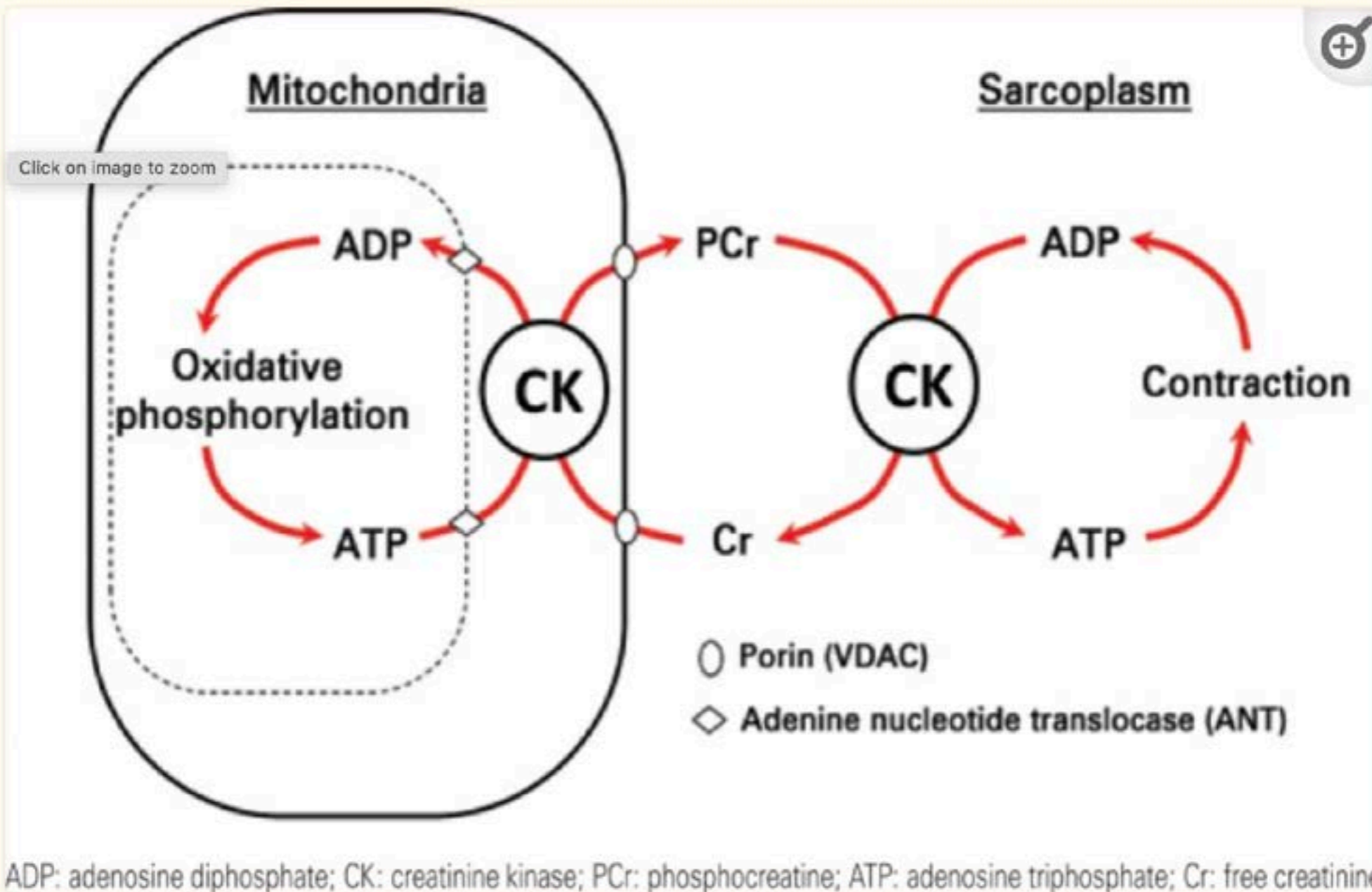


12 Weeks Exercise Training in Younger and Older People



Skeletal Muscle Adaptation to Exercise Training

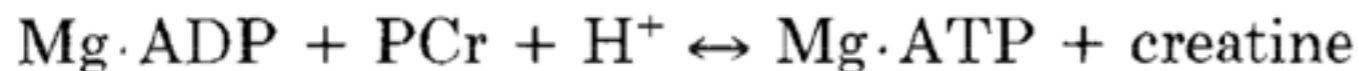




[Figure 1](#)

Phosphocreatine "shuttle" system

CREATINE KINASE catalyzes the reversible transfer of phosphate between phosphocreatine (PCr) and ATP



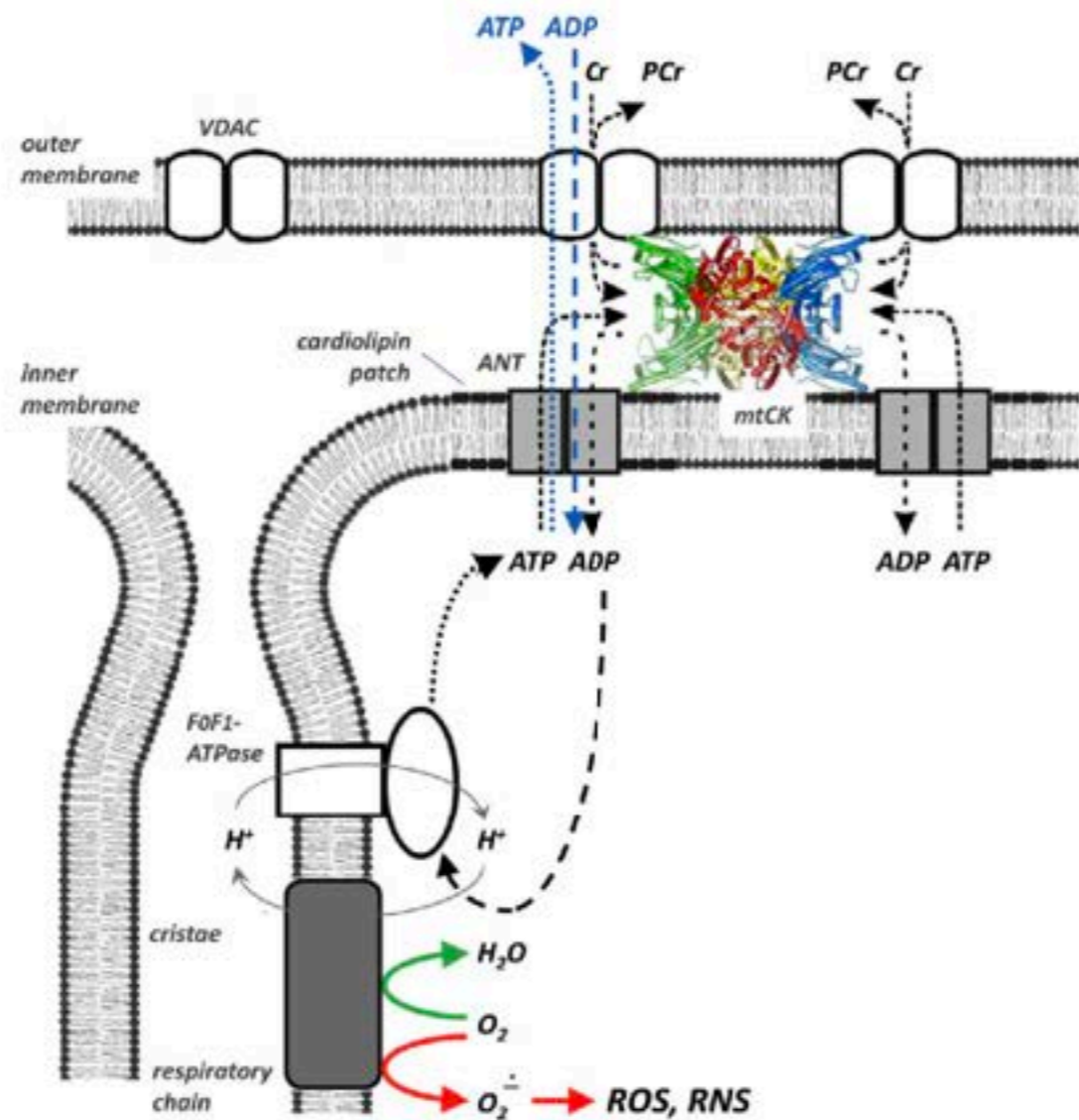
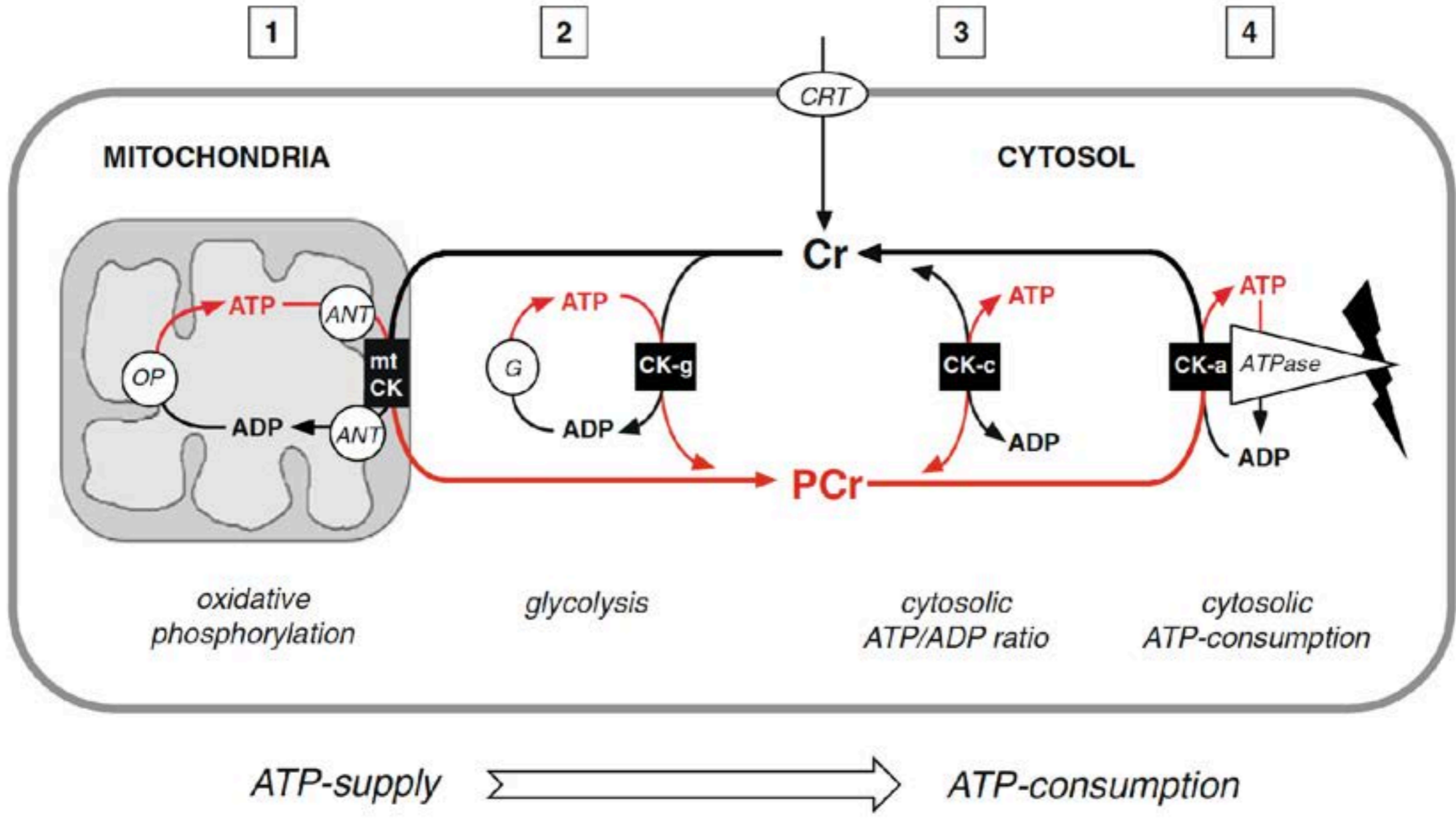
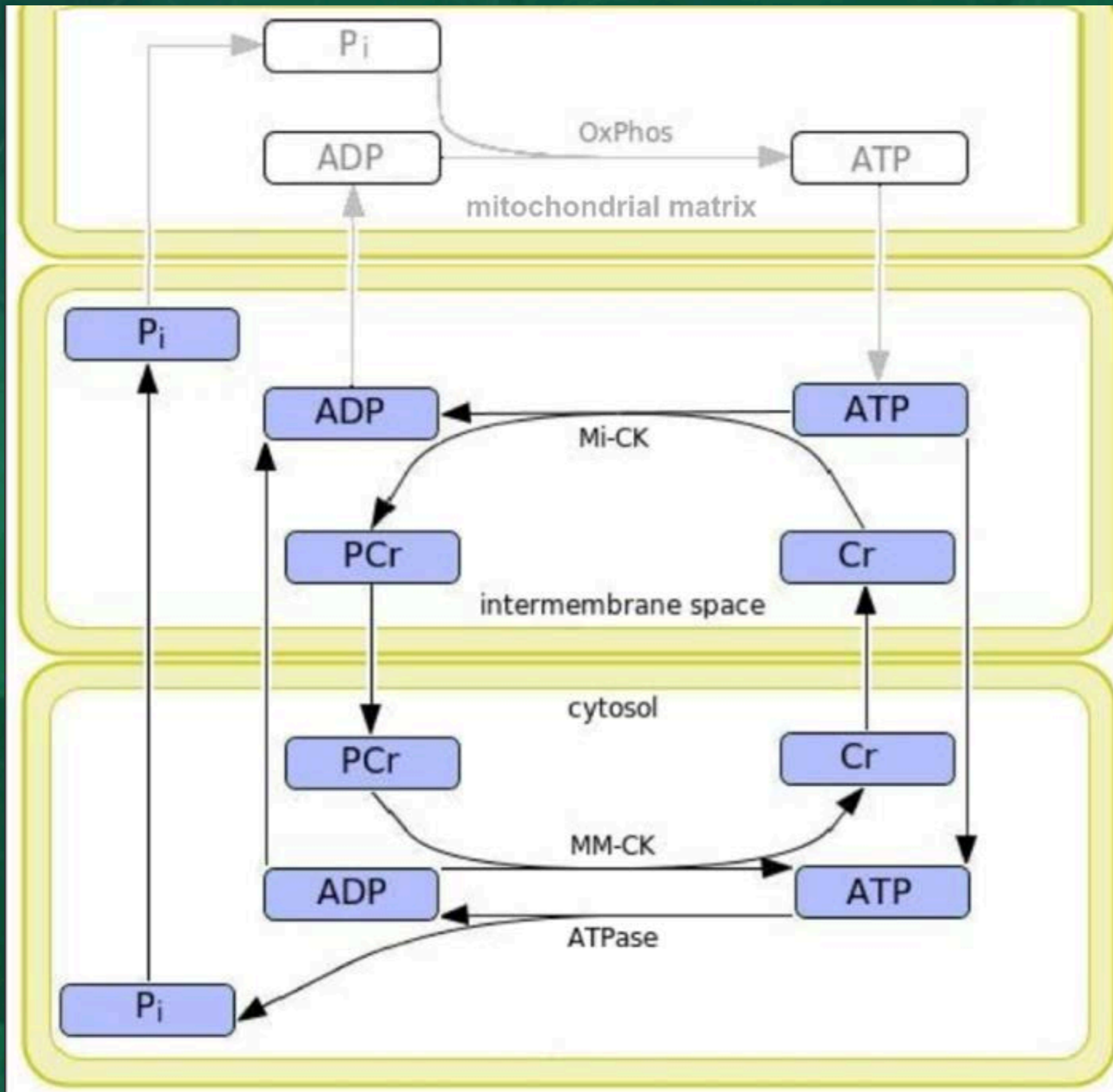
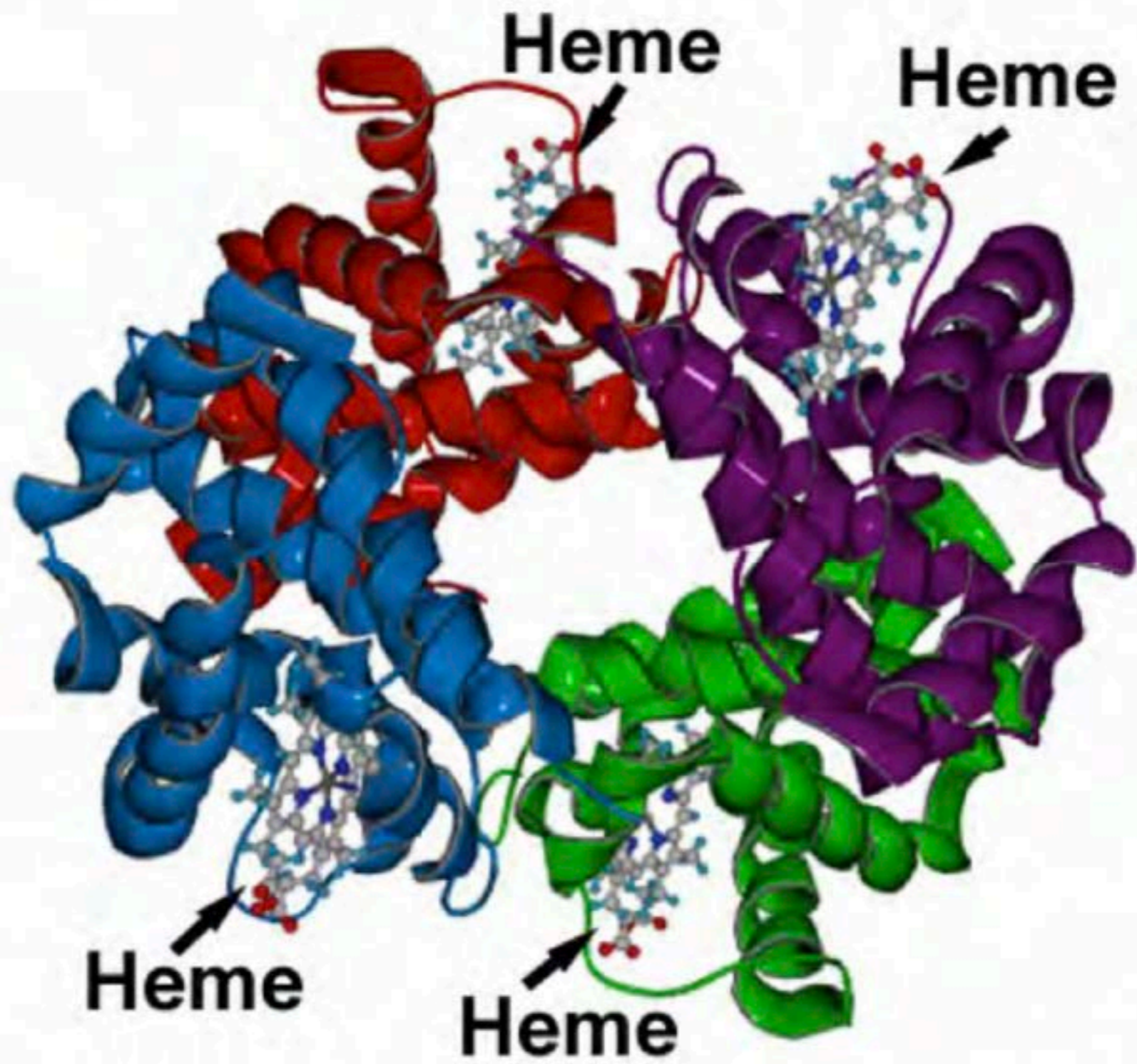


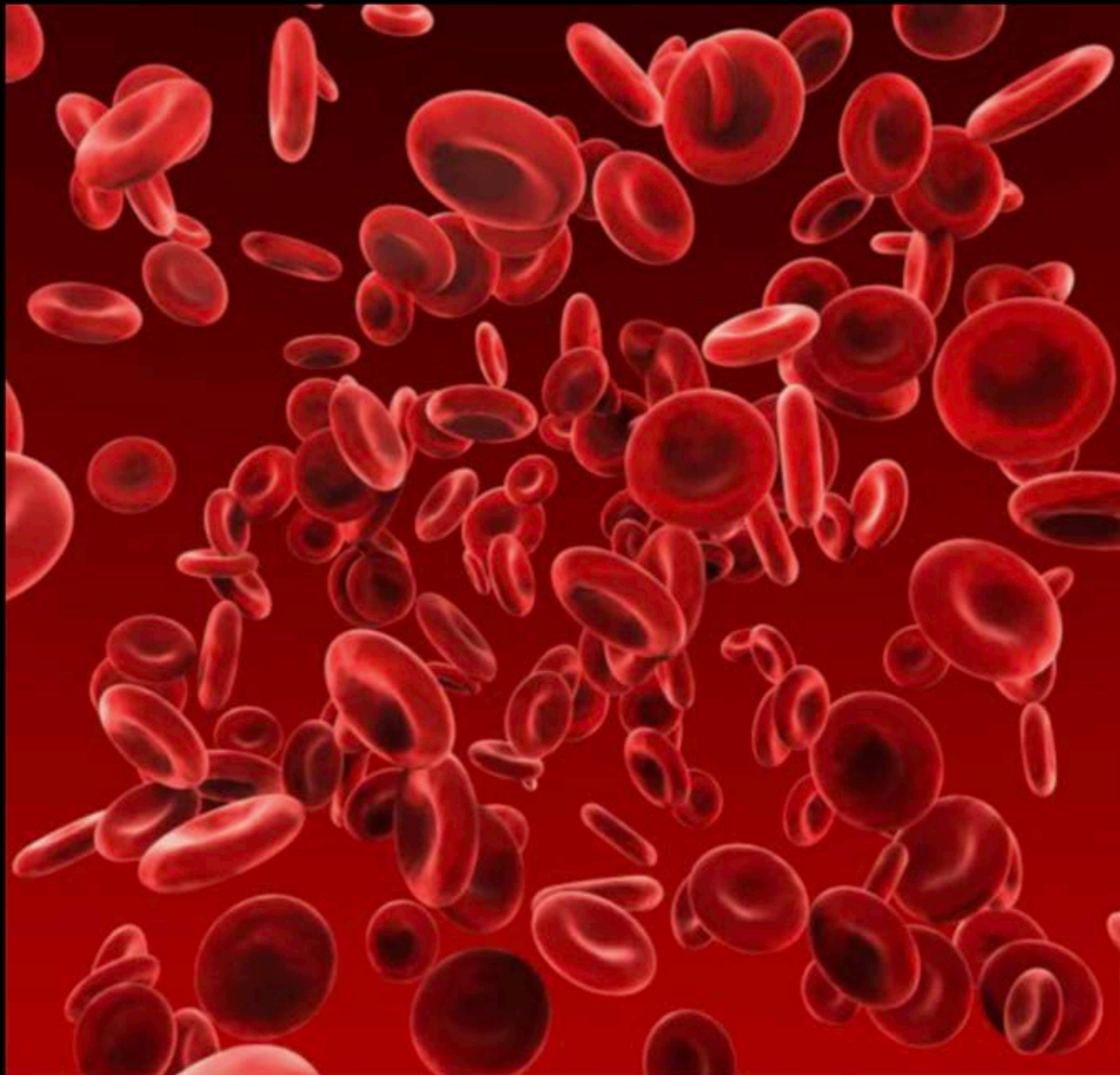
Fig. 3 Mitochondrial mtCK functions for high-energy metabolite channelling in mitochondria. In cells with oxidative metabolism, respiration (green arrow), ATP synthesis and ATP export through the inner mitochondrial membrane via adenine nucleotide transporter (ANT) are tightly coupled to trans-phosphorylation of ATP to PCr by mtCK and export of PCr into the cytosol by the outer membrane voltage-dependent anion channel (VDAC) as indicated by black arrows. In turn, Cr stimulates respiration by favoring constant supply of ADP to the matrix (black arrows), which also lowers ROS/RNS production in the intra-mitochondrial space (red arrows) and inhibits mitochondrial permeability transition. The tight coupling of substrate and product fluxes (black arrows) allows a so-called channelling of "high-energy" metabolites, with PCr being the one released into the cytosol, and ATP/ADP being mainly recycled within the

mitochondria. The structural basis of these mtCK microcompartments are proteolipid complexes containing either VDAC, octameric mtCK and ANT in the peripheral intermembrane space (as shown) or octameric mtCK and ANT in the cristae (not shown). These proteolipid complexes are maintained by mtCK interactions with anionic phospholipids and VDAC in the outer membrane, and with cardiolipin and thus indirectly with cardiolipin-associated ANT in the inner membrane (see cardiolipin patches). In cases of a less coupled mtCK microcompartment, e.g. after impairment of mtCK function by oxidative damage, there is partial direct ATP/ADP exchange with the cytosol (blue arrows). (Figure adapted from Kaldis et al. 1997; Meyer et al. 2006; Schlattner et al. 2006a; Schlattner et al. 2011) (The different fluxes are indicated by coloured arrows in the figure)





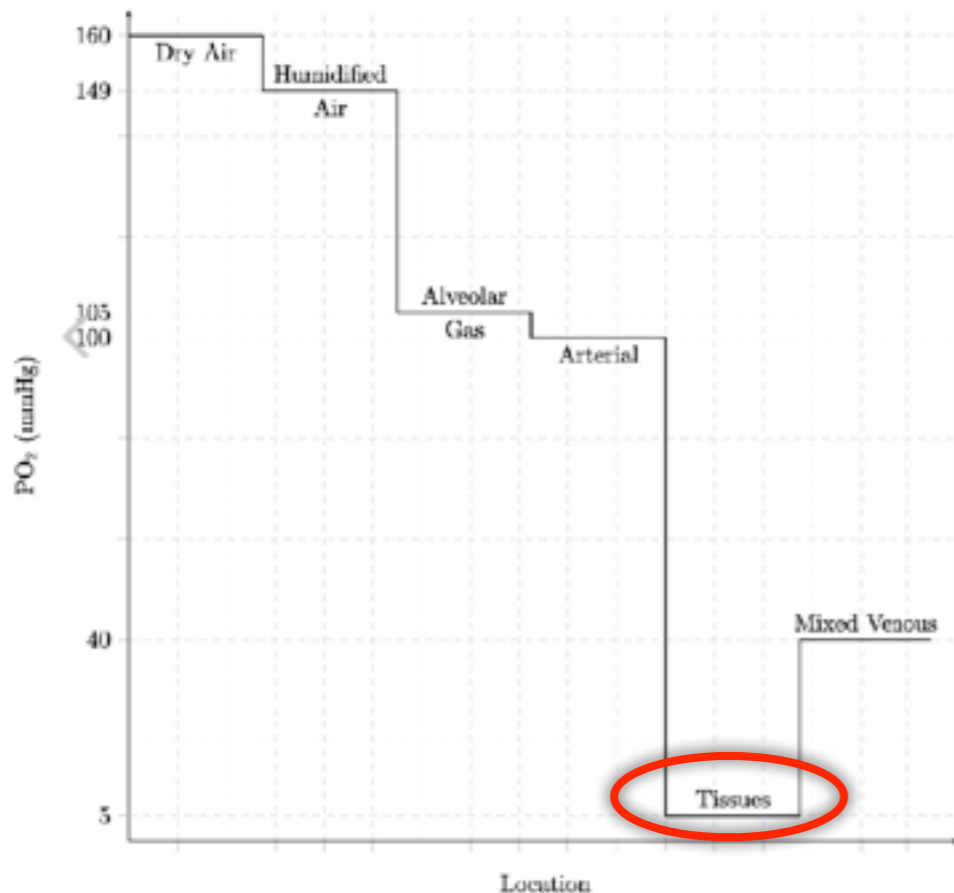




Oxygen Cascade

The **oxygen cascade** describes the transfer of oxygen from air to mitochondria.

- In each step of the cascade the P_{aO_2} falls. It demonstrates that oxygen delivery to tissues relies on the **passive transfer** of gas down **partial pressure gradients**.
- The steps of the cascade are:
 - Dry atmospheric gas
 - Humidified tracheal gas
 - Alveolar gas
 - Arterial blood
 - Mitochondria
 - Venous blood



Atmospheric Gas

Atmospheric partial pressure of oxygen is a function of barometric pressure and the F_{iO_2} :

- $PO_2 = P_B \times F_{iO_2}$, where:
 - P_B is 760mmHg
 - F_{iO_2} is 0.21
- Therefore, $PO_2 = 160\text{mmHg}$

P_{iN_2} : 590 mmHg
 P_{iO_2} : 160 mmHg
 P_{iAr} : 7 mmHg
 P_{iCO_2} : 0.3 mmHg
 P_{iO_2} : 160 mmHg

Alveolar Gas

Ideal alveolar PO_2 is calculated using the alveolar gas equation:

$$P_{AO_2} = P_{iO_2} - \frac{P_aCO_2}{R} + F$$

- P_{AO_2} is the alveolar partial pressure of oxygen
- P_{iO_2} is the inspired partial pressure of oxygen
- P_aCO_2 is the arterial partial pressure of carbon dioxide
- R is the respiratory quotient, where $R = \frac{\text{Volume of } CO_2 \text{ produced}}{\text{Volume of } O_2 \text{ consumed}}$

↓
 tracheal humidity
 149 mmHg
 ↓
 respiratory PaCO₂
 → ↓ PaO₂

Arterial Blood

- Normal arterial PO_2 is 100mmHg
 P_{aO_2} : 100 mmHg

Mitochondria

- PO_2 varies with metabolic activity, but typically quoted as 5mmHg
- The **Pasteur point** is the partial pressure of oxygen at which oxidative phosphorylation ceases, and is ~1mmHg

P_{aO_2} : 5 mmHg

Venous Blood

- PO_2 is greater than mitochondrial PO_2 . Mixed venous blood typically quoted as 40mmHg.
- Higher than mitochondria as not all arterial blood travels through capillary beds

P_{aO_2} : 40mmHg

The Oxygen Cascade During Exercise in Health and Disease



Paolo B. Dominelli, PhD; Chad C. Wiggins, PhD; Tuhin K. Roy, PhD, MD;
Timothy W. Secomb, PhD; Timothy B. Curry, PhD, MD; and Michael J. Joyner, MD

Abstract

The oxygen transport cascade describes the physiological steps that bring atmospheric oxygen into the body where it is delivered and consumed by metabolically active tissue. As such, the oxygen cascade is fundamental to our understanding of exercise in health and disease. Our narrative review will highlight each step of the oxygen transport cascade from inspiration of atmospheric oxygen down to mitochondrial consumption in both healthy active males and females along with clinical conditions. We will focus on how different steps interact along with principles of homeostasis, physiological redundancies, and adaptation. In particular, we highlight some of the parallels between elite athletes and clinical conditions in terms of the oxygen cascade.

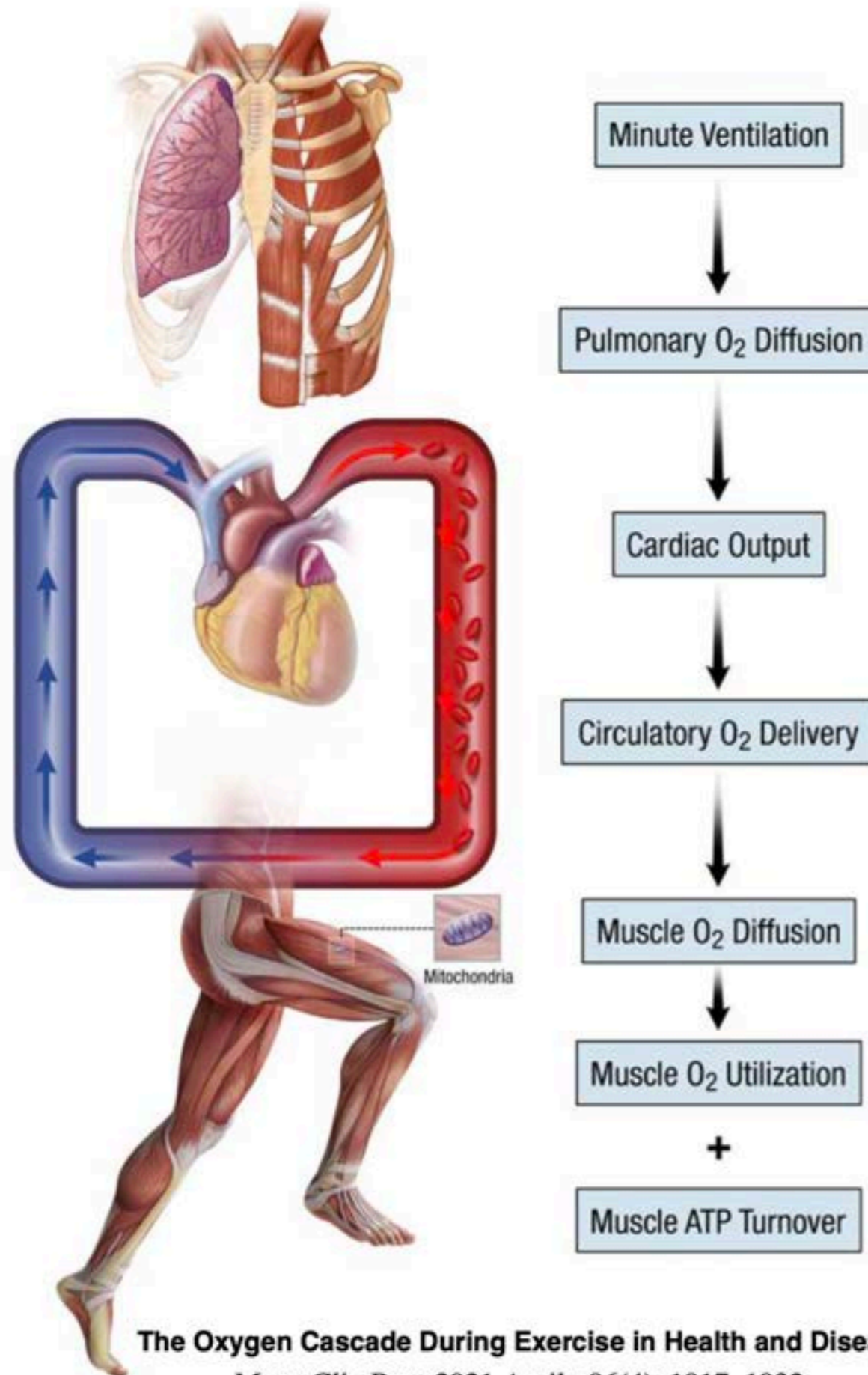
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In the era of molecular biology it is easy to overlook the central role that the oxygen molecule plays in life. In complex organisms, where most cells are anatomically remote from atmospheric oxygen, a transport and gas exchange system is required to move oxygen from the air to the tissues and supports the continuous generation of adenosine triphosphate via oxidative metabolism. To defend whole body homeostasis, this system must be robust enough to sustain vast increases in oxidative metabolism during exercise, survive at high altitude, and — at the opposite end of the homeostatic spectrum — withstand substantial insults to key elements of the system associated with disease. In this review, we will follow the movement of oxygen from the air to the tissues and use examples ranging from elite athletes, rare patients, and comparative biology to show key principles of oxygen transport in humans. The impressive adaptive nature of the cardiopulmonary system will be emphasized and the redundant nature of physiological control mechanisms and related anatomical design features will be highlighted.

THE PROBLEM

The partial pressure of oxygen in air at sea level is ~ 150 mm Hg, but in the mitochondria of exercising skeletal muscle the partial pressure of oxygen can be ~ 100 -fold lower without significant engagement of anaerobic energy metabolism. Thus, the question is, how does this happen and what systems are engaged as it occurs? In this context, it is also important to consider the range of oxygen consumption that can be seen in humans. In healthy young adults, resting metabolic rate is approximately $3.5 \text{ mL O}_2 \cdot \text{kg}^{-1}$ of body weight $\cdot \text{min}^{-1}$ and it can increase to more than $90 \text{ mL O}_2 \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in at least some of the most aerobically trained elite athletes.¹ At the opposite end of the O_2 uptake spectrum, even modest metabolic rates require physiological redundancies to be engaged in patients with diseases that hinder the ability to take up, transfer, and utilize oxygen. Notable examples include marked tachypnea or tachycardia even during very modest levels of exercise in patients with diseases, such as chronic obstructive pulmonary disease or congestive heart failure, along with a marked redistribution of blood flow away from inactive tissues to the active muscles.²

From the Department of Kinesiology, University of Waterloo, Ontario, Canada (P.B.D.); Department of Anesthesiology and Perioperative Medicine, Mayo Clinic, Rochester, MN (C.C.W., T.K.R., T.W.S., M.J.J.); and the Departments of Physiology and Pharmacology, University of Arizona, Tucson, (T.W.S.).

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Mayo Clin Proc. 2021 April ; 96(4): 1017–1032.

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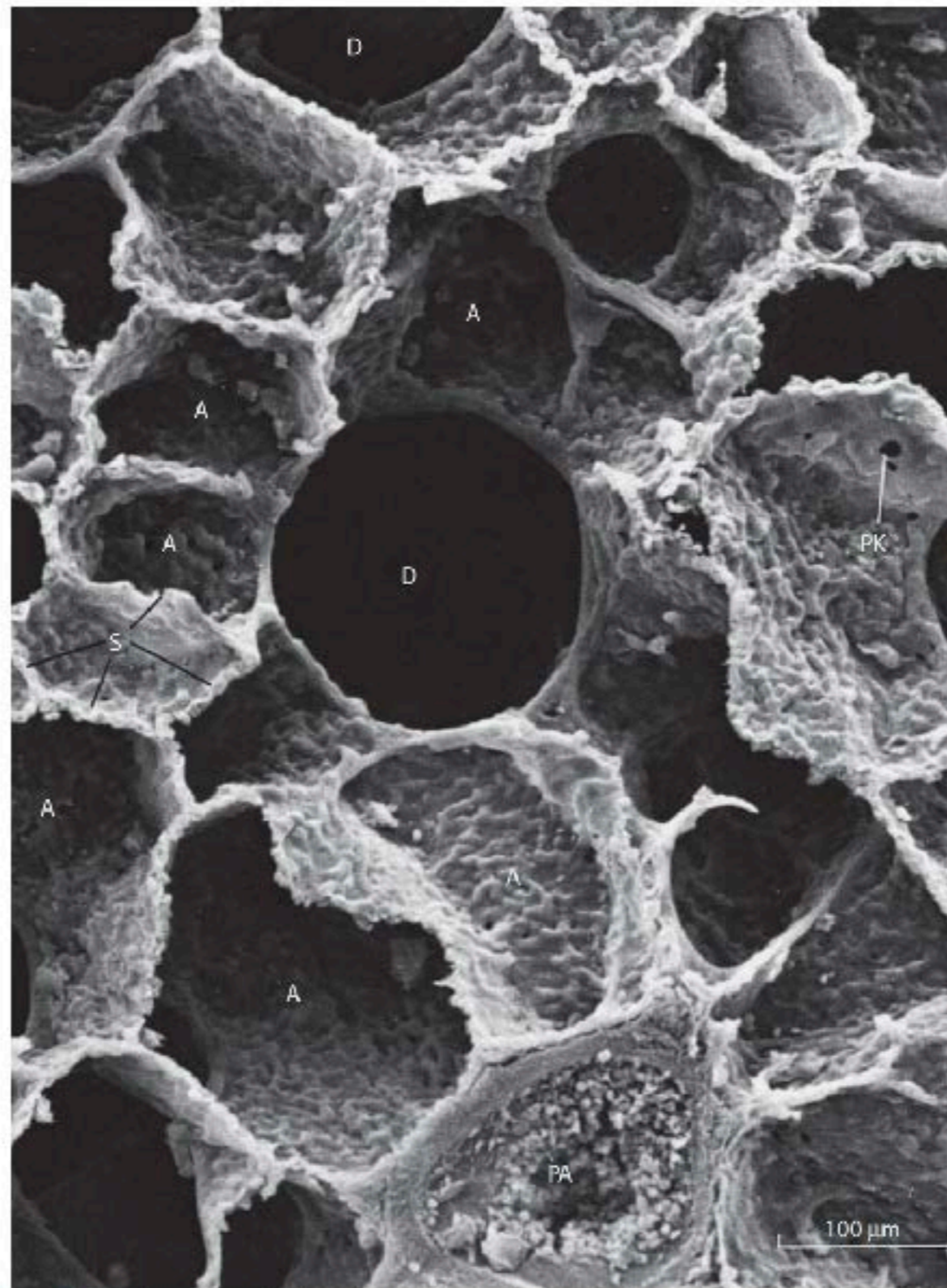


Figure 1-3. Scanning electron micrograph of human lung parenchyma. A = alveolus; S = alveolar septa; D = alveolar duct; PK = pore of Kohn; PA = small branch of the pulmonary artery. (Reproduced with permission from Fishman AP, Kaiser LR, Hahnman JA, et al: *Pulmonary Diseases and Disorders*, 3rd ed. New York: McGraw-Hill; 1998.)

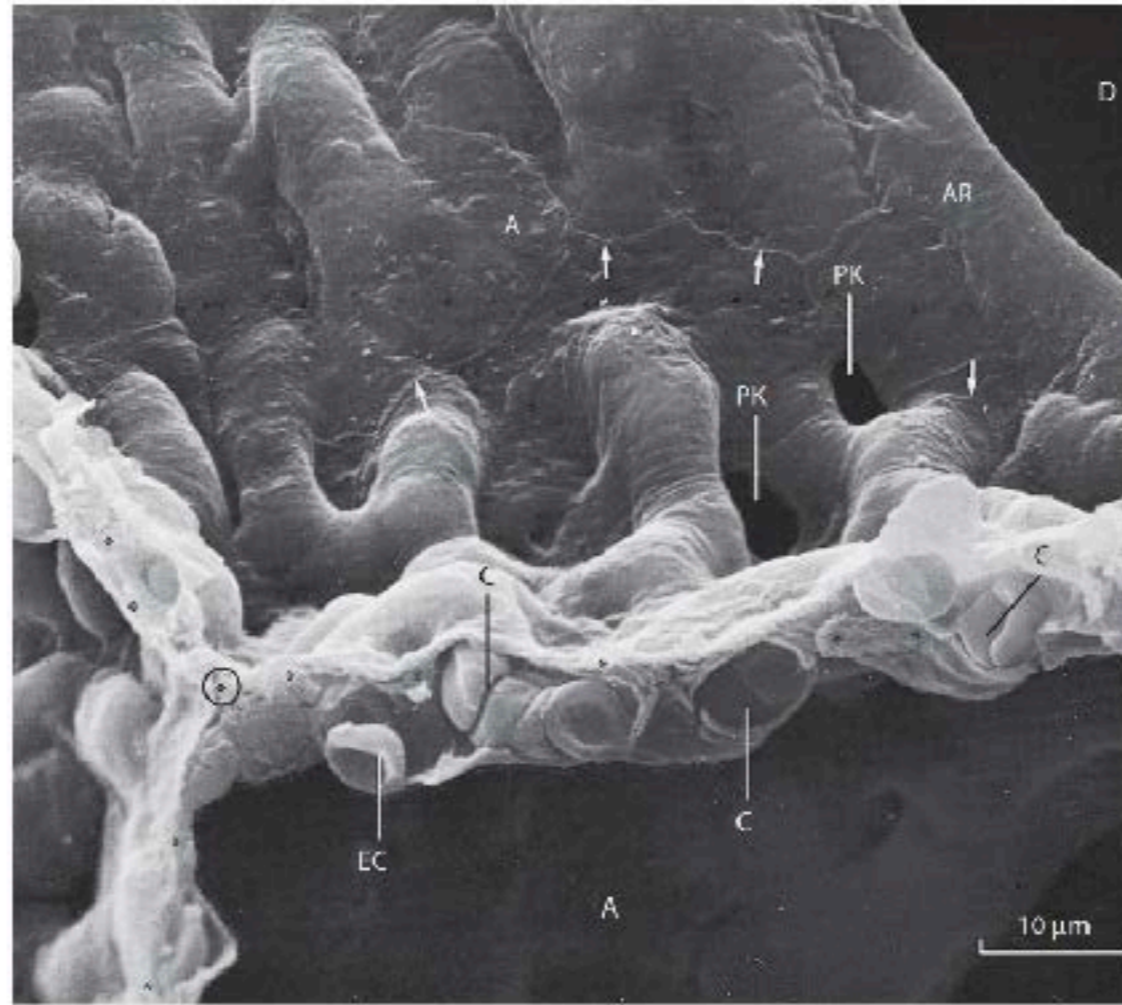


Figure 1-4. Scanning electron micrograph of the surface and cross section of an alveolar septum. Capillaries (C) are seen sectioned in the foreground, with erythrocytes (EC) within them. A = alveolus; D = alveolar duct; PK = pore of Kohn; AR = alveolar entrance to duct; * = connective tissue fibers. The encircled asterisk is at a junction of 3 septa. The arrows indicate the edges of a type I alveolar epithelial cell. (Reproduced with permission from Fishman AP, Kaiser LR, Fishman JA, et al: *Pulmonary Diseases and Disorders*, 3rd ed. New York: McGraw-Hill; 1998.)

In Figure 1–4 the alveolar septum appears to be almost entirely composed of pulmonary capillaries.

Red blood cells (erythrocytes) can be seen inside the capillaries at the point of section.

Elastic and connective tissue fibers, not visible in the figure e, are found between the capillaries in the alveolar septa.

Also shown in these figures are the pores of Kohn or interalveolar communications.

	Generation		Diameter, cm	Length, cm	Number	Total cross-sectional area, cm ²		
Conducting zone	Trachea		0	1.80	12.0	1	2.54	
	Bronchi		1	1.22	4.8	2	2.33	
	Bronchioles		2	0.83	1.9	4	2.13	
			3	0.56	0.8	8	2.00	
			4	0.45	1.3	16	2.48	
			5	0.35	1.07	32	3.11	
Terminal bronchioles		16	0.06	0.17	6×10^4	180.0		
Transitional and respiratory zones	Respiratory bronchioles		17	↓	↓	↓	↓	
			18	↓	↓	↓	↓	
			19	0.05	0.10	5×10^5	10^3	
	Alveolar ducts		T ₃	20	↓	↓	↓	↓
			T ₂	21	↓	↓	↓	↓
			T ₁	22	↓	↓	↓	↓
Alveolar sacs		T	23	0.04	0.05	8×10^6	10^4	

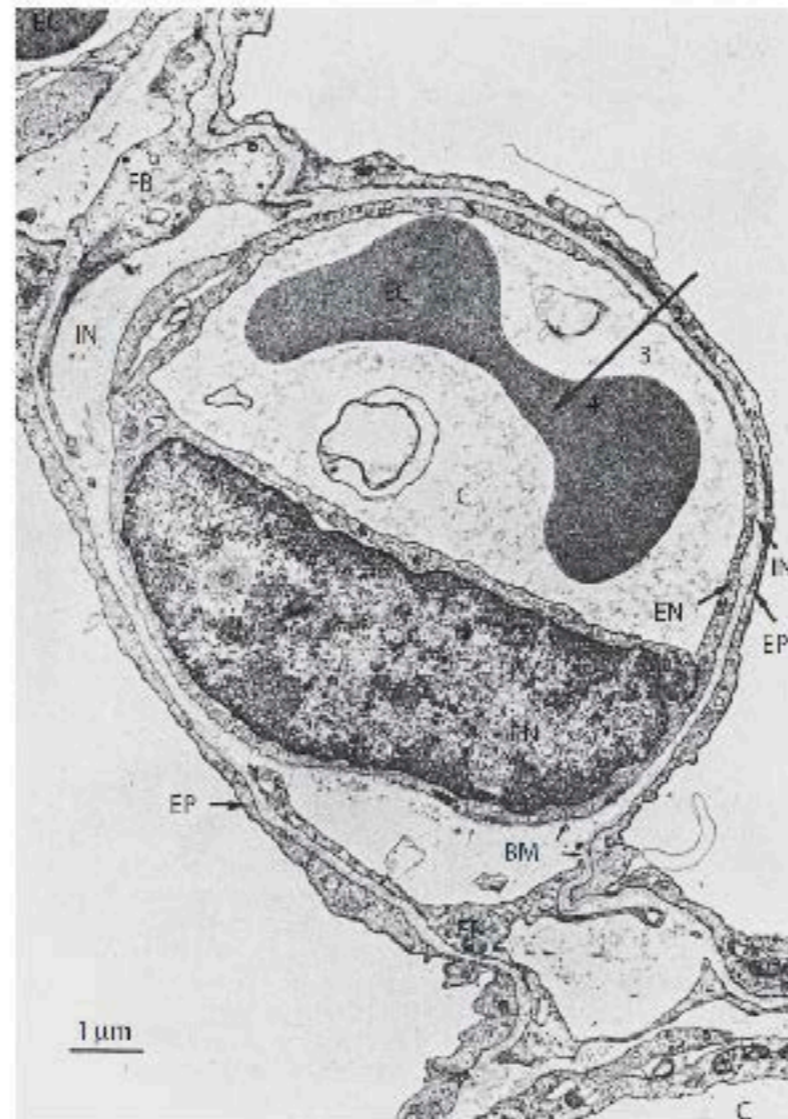


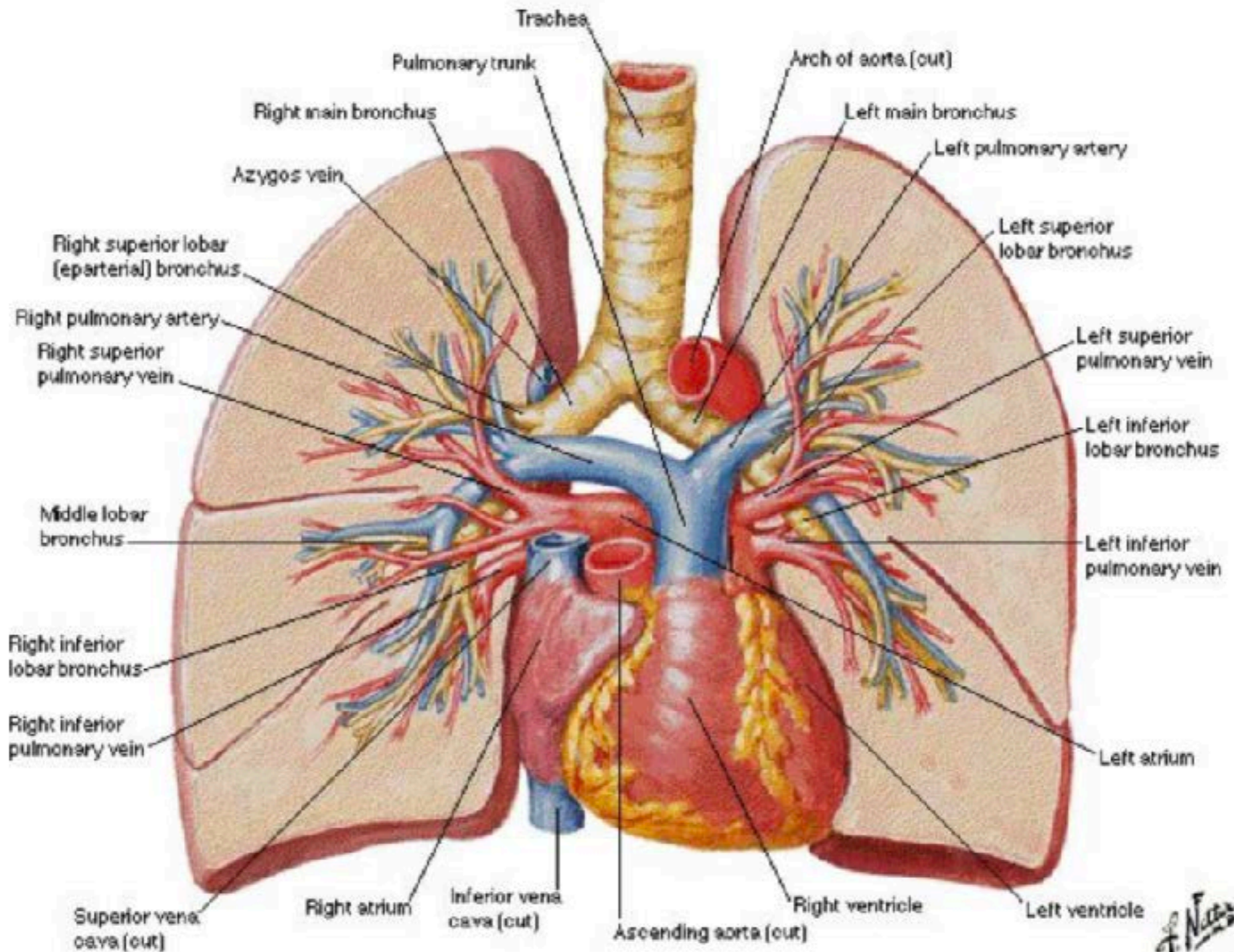
Figure 1-5. Transmission electron micrograph of a cross section of a pulmonary capillary. C = capillary; EN = capillary endothelial cell (note its large nucleus); EP = alveolar epithelial cell; IN = interstitial space; BM = basement membrane; FB = fibroblast processes; 1, 2, 3 = diffusion pathway through the alveolar capillary barrier, the plasma, and the erythrocyte, respectively. Note that the alveolar capillary barrier appears to have a thin side and a thick side that has a greater interstitial space and more connective tissue. (Reproduced with permission from Weibel ER. Morphometric estimation of pulmonary diffusion capacity. I. Model and method. *Respir Physiol*. 1970;4:54-75.)

The barrier to gas exchange between the alveoli and pulmonary capillaries can also be seen in Figure 1-5.

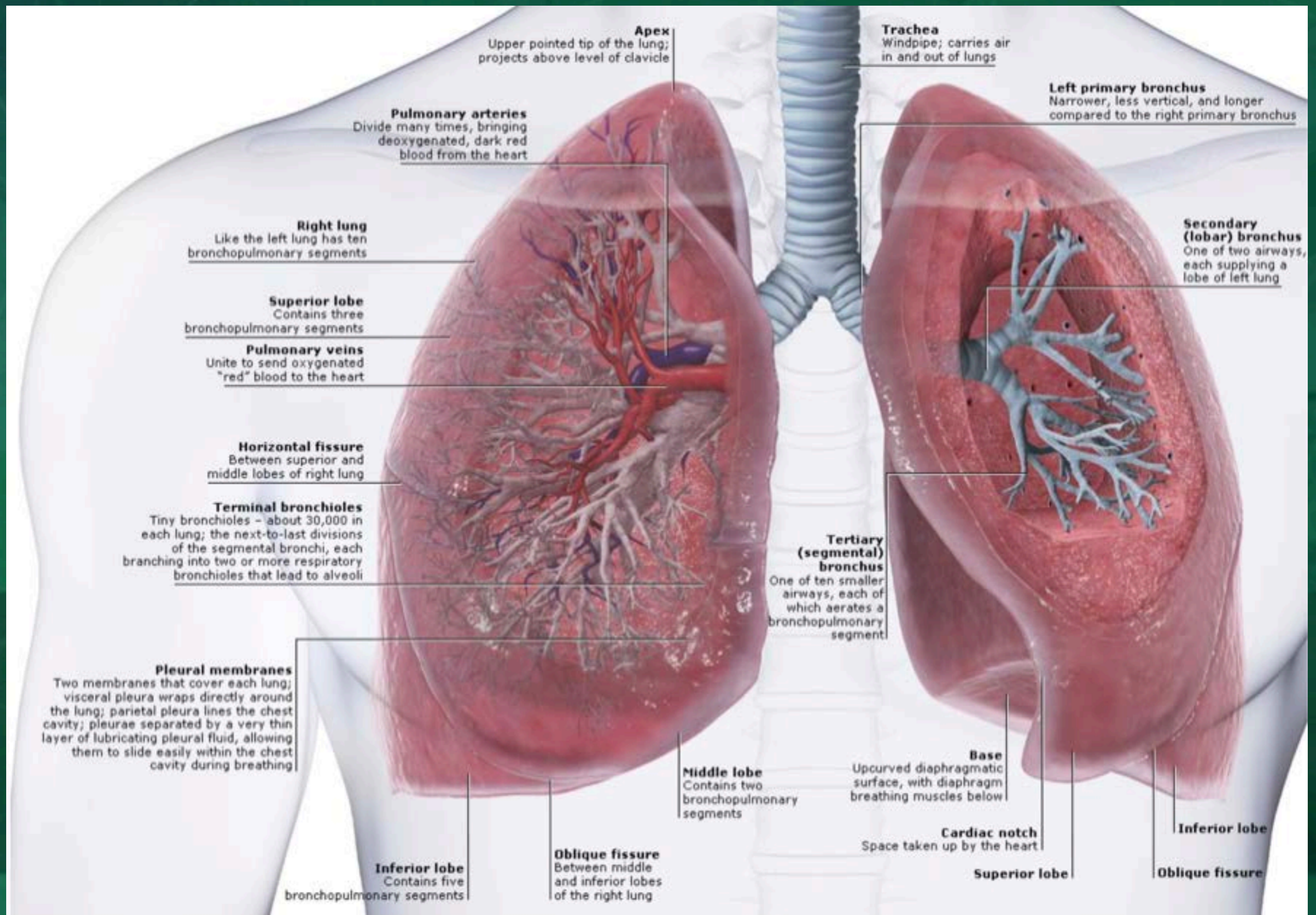
It consists of the alveolar epithelium, the capillary endothelium, and the interstitial space between them. Gases must also pass through the fluid lining the alveolar surface (not visible in Figure 1-5) and the plasma in the capillary.

The barrier to diffusion is normally 0.2- to 0.5-μm thick.

Pulmonary Arteries and Veins



F. Netter
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We shall not cease from exploration

And the end of all our exploring

Will be to arrive where we started

And know the place for the first time.

T.S. Eliot --- "Little Gidding" ... *Four Quartets*





