Intervention: The importance of physics in the biological sciences

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Radiative laws

-- Wien's displacement law

$$\lambda_m T = \frac{h_c}{4.965114k} = 2.897791 \times 10^{-3}\ (\mathrm{m \cdot K})$$

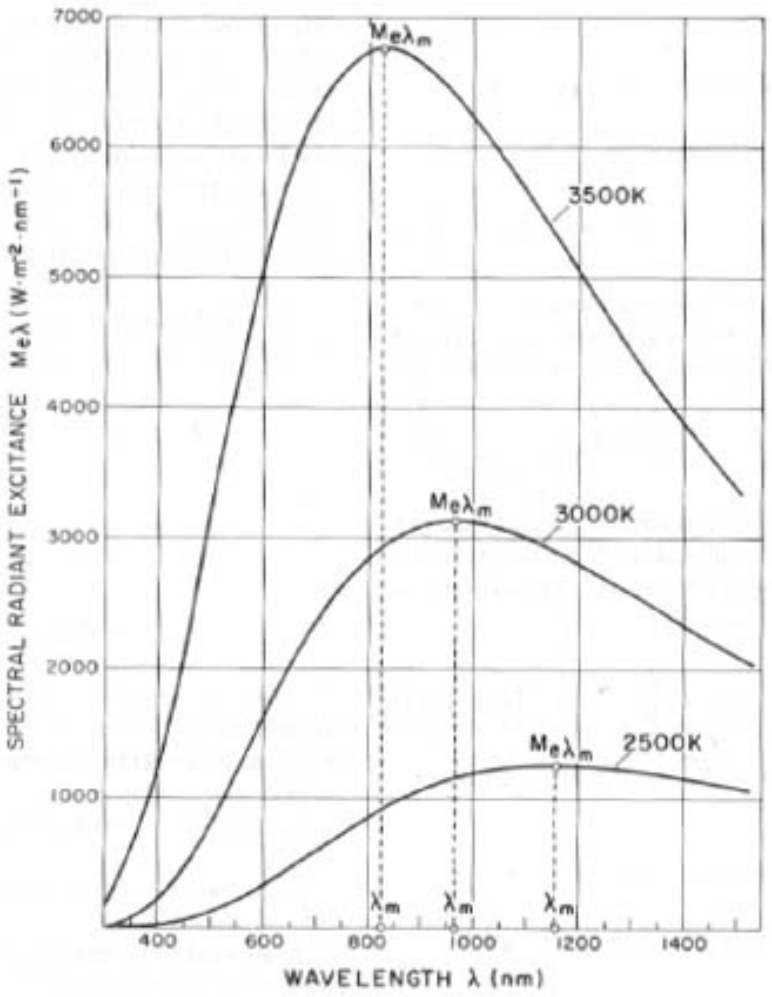
$$M_{e\lambda_m} T^{-5} = 1.286673 \times 10^{-5}\ (\mathrm{W \cdot m^{-3} \cdot K^{-5}})$$

-- Total Radiant Exitance, Stephan-Boltzmann law

$$M_e = \int_0^\infty M_{e\lambda}\, d\lambda = \sigma T^4\ (\mathrm{W \cdot m^{-2}})$$

$$\sigma = \frac{2\pi^5 k^4}{15 h^3 c^2} = 5.67032 \times 10^{-8}\ (\mathrm{W \cdot m^{-2} \cdot K^{-4}})$$

Stephan-Boltzmann constant



Energetics of metabolism

$$Rs_{j\to N-1} = \alpha \sum_{i\neq j}^{N-1} \frac{R_j^2}{r_{j-i}^2} = \alpha R_j^2 \sum_{i\neq j}^{N-1} \frac{1}{r_{j-i}^2}$$

$$Rs_{G\to j} = \alpha \sum_{i\subset G, i\neq j}^{n} \frac{R_i^2}{r_{i-j}^2} \qquad (1)$$

$$\sigma^*_{j\to N-1} = \beta \sum_{i\neq j}^{N-1} \frac{(\chi_j^0 - \chi_i^0) R_j^2}{r_{j-i}^2}$$

$$\sigma^*_{G\to j} = \beta \sum_{i\subset G, i\neq j}^{n} \frac{(\chi_i^0 - \chi_j^0) R_i^2}{r_{i-j}^2} \qquad (2)$$

$$\chi^0_{N-1\to j} = \frac{\sum_{i\neq j}^{N-1} \frac{\chi_i^0 (R_i^2 + R_j^2)}{r_{i-j}^2}}{\sum_{i\neq j}^{N-1} \frac{R_i^2 + R_j^2}{r_{i-j}^2}}$$

$$\chi^0_{N-1\to j} = \frac{\sum_{i\neq j}^{N-1} \frac{\chi_i^0 (R_i^2 + R_j^2)}{r_{i-j}^2}}{\sum_{i\neq j}^{N-1} \frac{R_i^2 + R_j^2}{r_{i-j}^2}} \qquad (3)$$

$$\Delta N_j = Q_j + \gamma \sum_{i\neq j}^{N-1} \frac{(\chi_j - \chi_i)(R_j^2 + R_i^2)}{r_{j-i}^2} \qquad (4)$$

Navier – Stokes equations

$$\rho\left(\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{dy}+w\frac{\partial u}{\partial z}\right)=$$

$$\rho g_x-\frac{\partial p}{\partial x}+\frac{\partial}{\partial x}\left[2\mu\frac{\partial u}{\partial x}+\lambda\nabla\cdot\mathbf{V}\right]+\frac{\partial}{\partial y}\left[\mu\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]+\frac{\partial}{\partial z}\left[\mu\left(\frac{\partial w}{\partial x}+\frac{\partial u}{\partial z}\right)\right]$$

$$\rho\left(\frac{\partial v}{\partial t}+u\frac{\partial v}{\partial x}+v\frac{\partial v}{dy}+w\frac{\partial v}{\partial z}\right)=$$

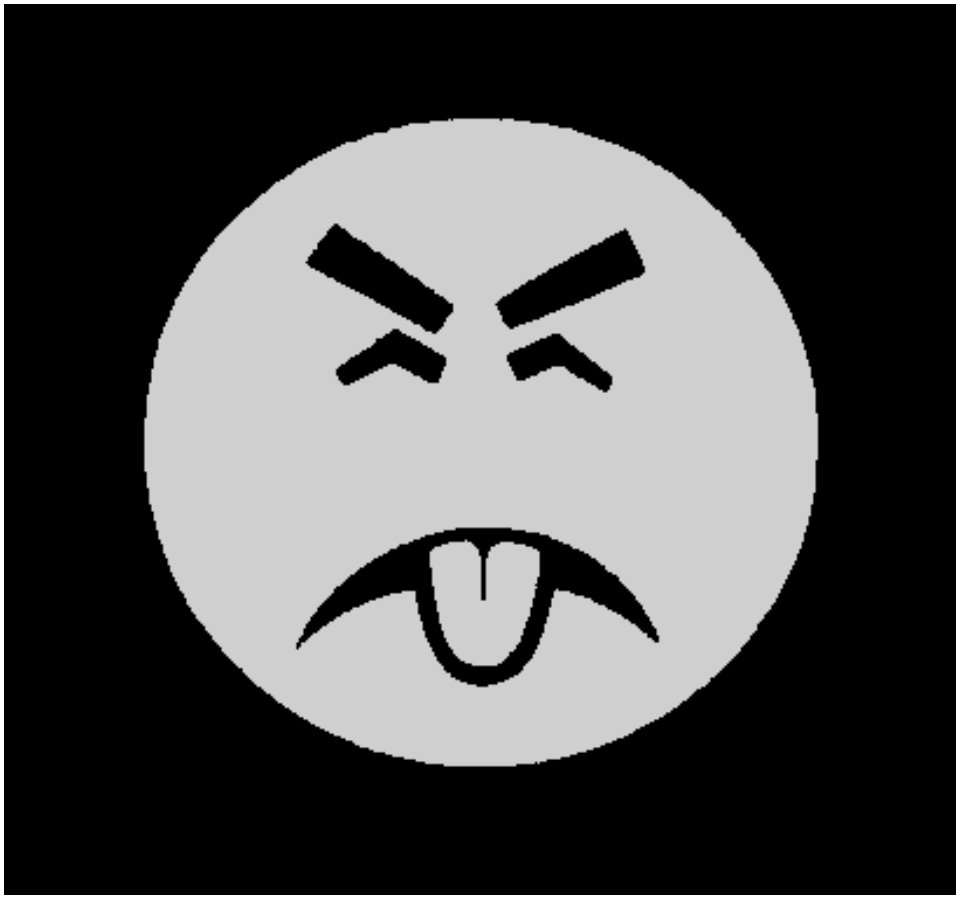
$$\rho g_y-\frac{\partial p}{\partial y}+\frac{\partial}{\partial y}\left[2\mu\frac{\partial v}{\partial y}+\lambda\nabla\cdot\mathbf{V}\right]+\frac{\partial}{\partial z}\left[\mu\left(\frac{\partial v}{\partial z}+\frac{\partial w}{\partial y}\right)\right]+\frac{\partial}{\partial x}\left[\mu\left(\frac{\partial u}{\partial y}+\frac{\partial v}{\partial x}\right)\right]$$

$$\rho\left(\frac{\partial w}{\partial t}+u\frac{\partial w}{\partial x}+v\frac{\partial w}{dy}+w\frac{\partial w}{\partial z}\right)=$$

$$\rho g_z-\frac{\partial p}{\partial z}+\frac{\partial}{\partial z}\left[2\mu\frac{\partial w}{\partial z}+\lambda\nabla\cdot\mathbf{V}\right]+\frac{\partial}{\partial x}\left[\mu\left(\frac{\partial w}{\partial x}+\frac{\partial u}{\partial z}\right)\right]+\frac{\partial}{\partial y}\left[\mu\left(\frac{\partial v}{\partial z}+\frac{\partial w}{\partial y}\right)\right]$$

Sweet dreams…

Many people dislike physics



WHY?

Why people dislike physics

- **Many people think that –**
  - Physics is boring
  - Physics is difficult
  - Physics is irrelevant

Why people dislike physics

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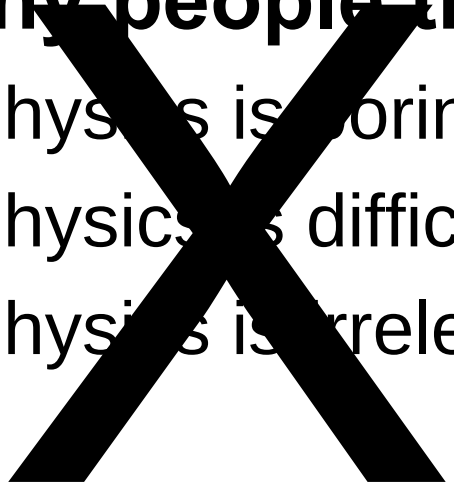
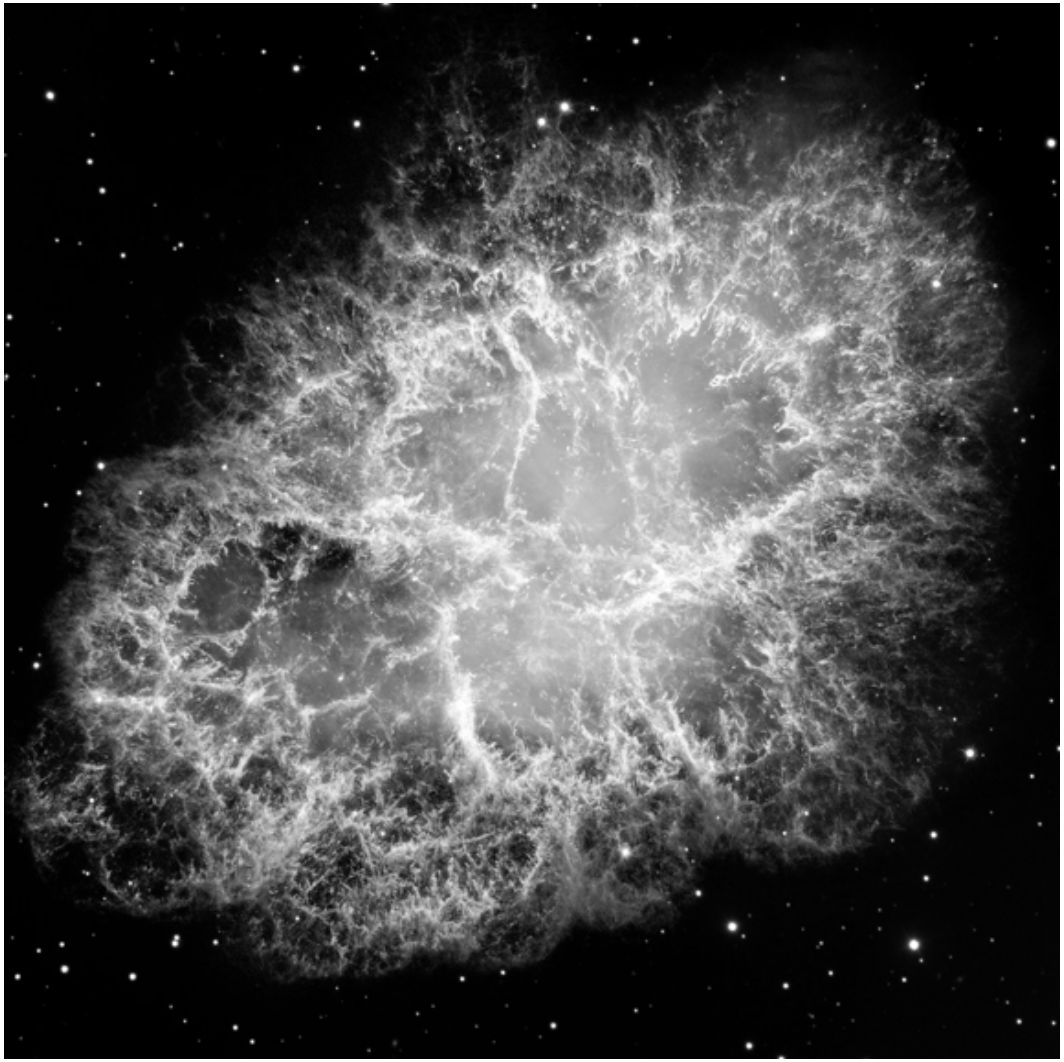
  - Physics is irrelevant

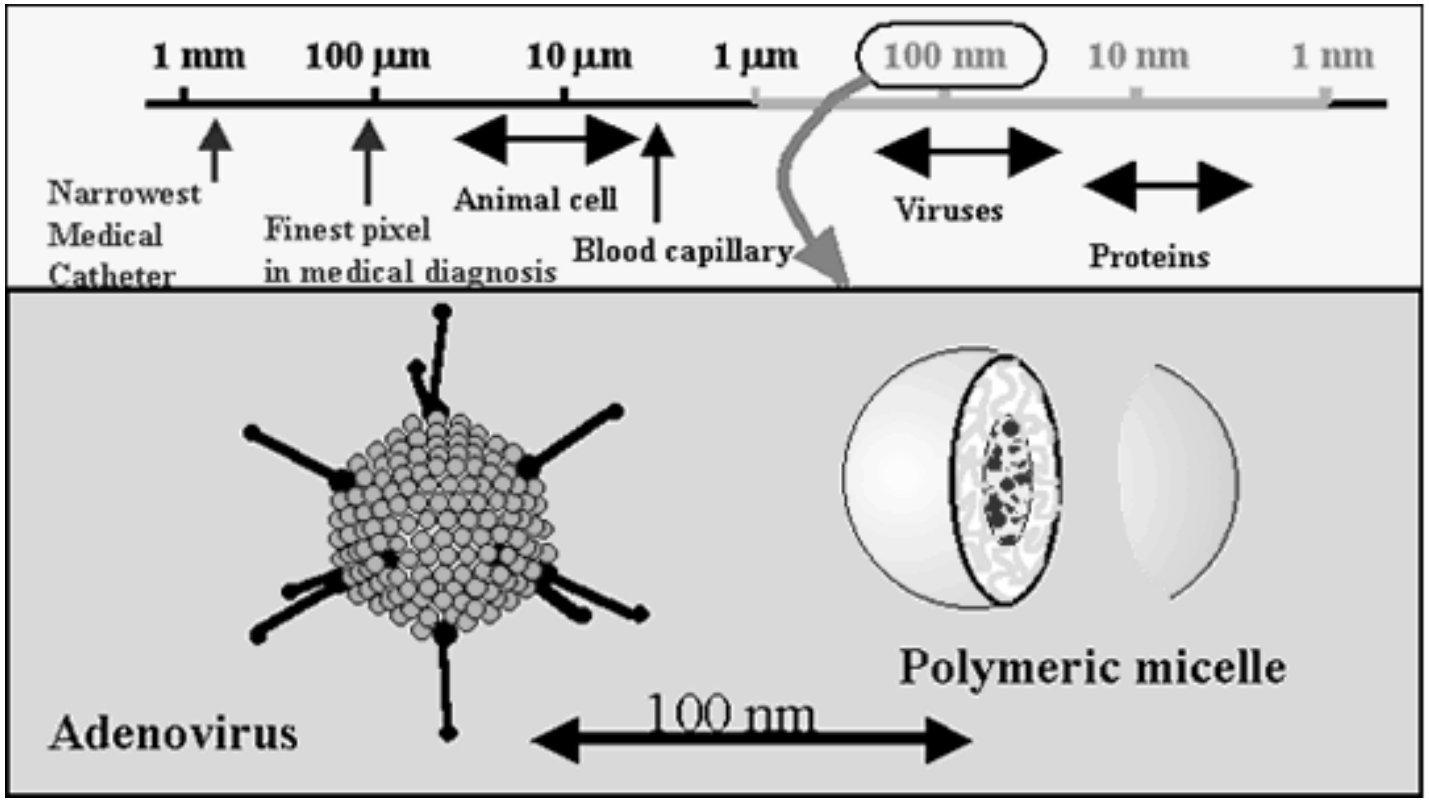


These are not so!

Physics is not boring!



Physics is <u>not</u> boring!



Physics is not boring!

Physics is not difficult!

Physics is not irrelevant!

Physics is not irrelevant!

- **The laws of physics govern the actions and interactions of everything in the natural world**

Physics is not irrelevant!

- **The laws of physics govern the actions and interactions of everything in the natural world**

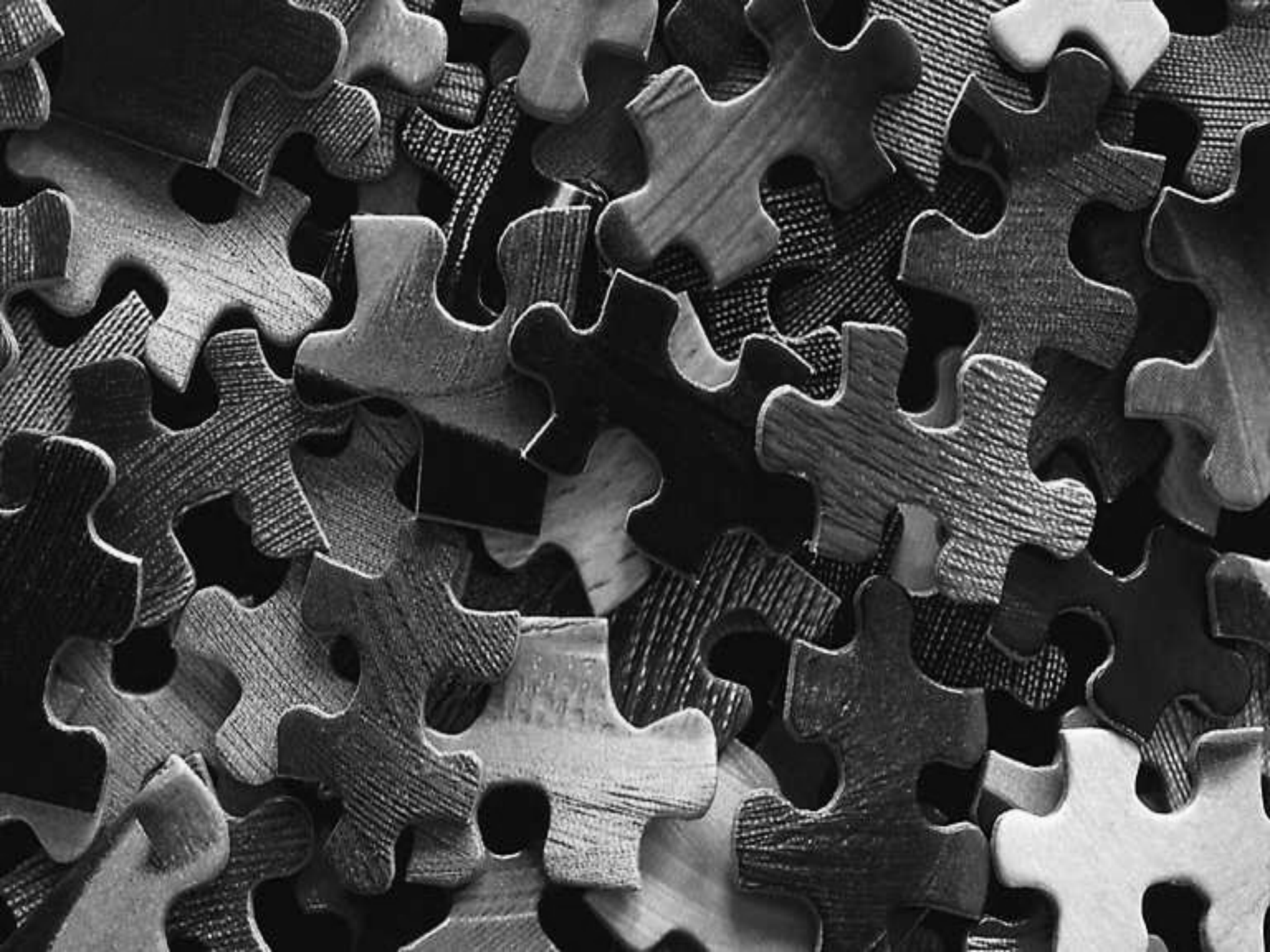
Like it or not, physics is the boss!

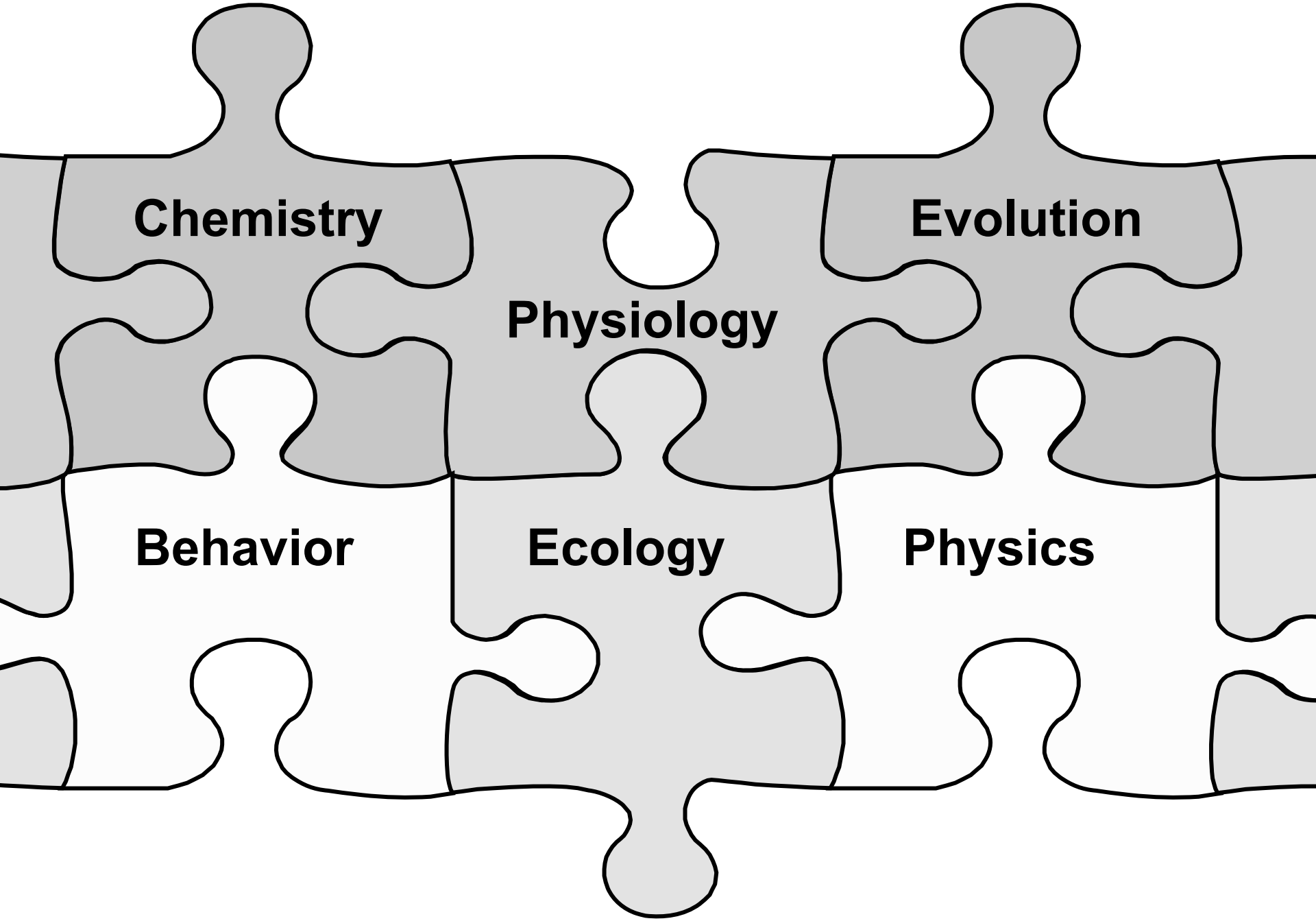
Physics is not irrelevant!

Overview

- **Highlight the importance of physics in biological research**
- **Demonstrate the role of physics in the in clinical and research medicine**
- **Discuss pursuing graduate study in physics-minded biology**

Some laws, you just can't break…

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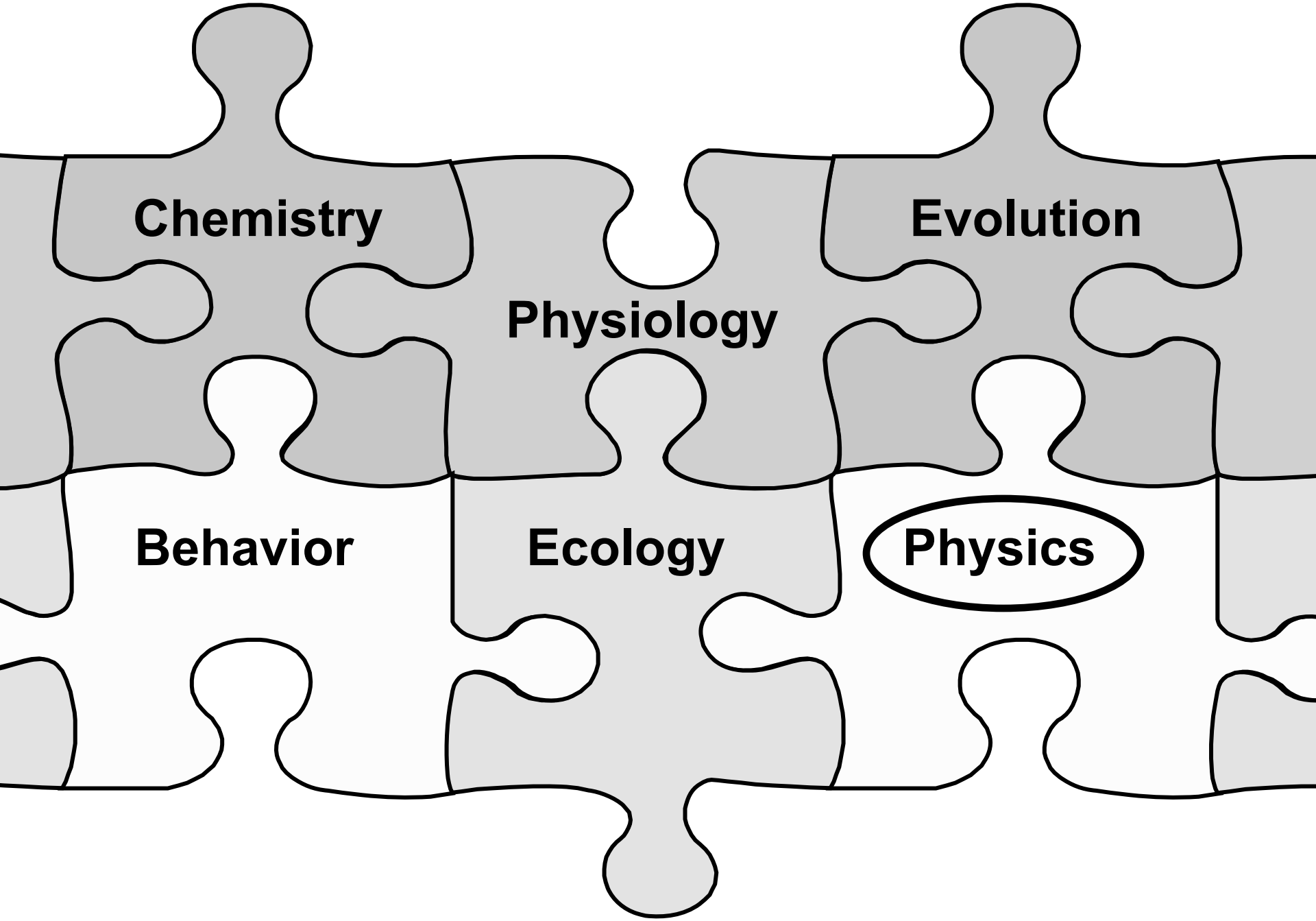
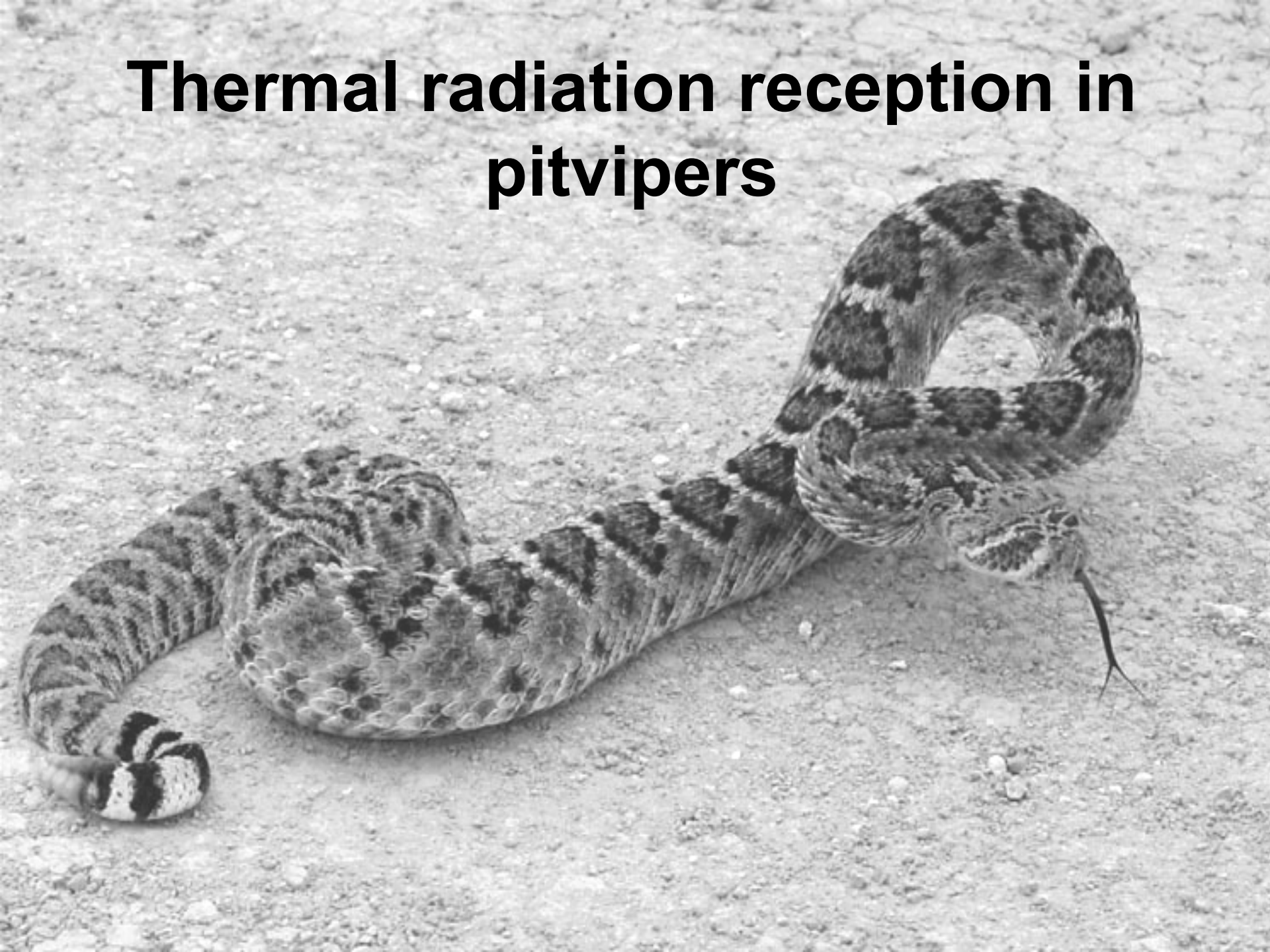
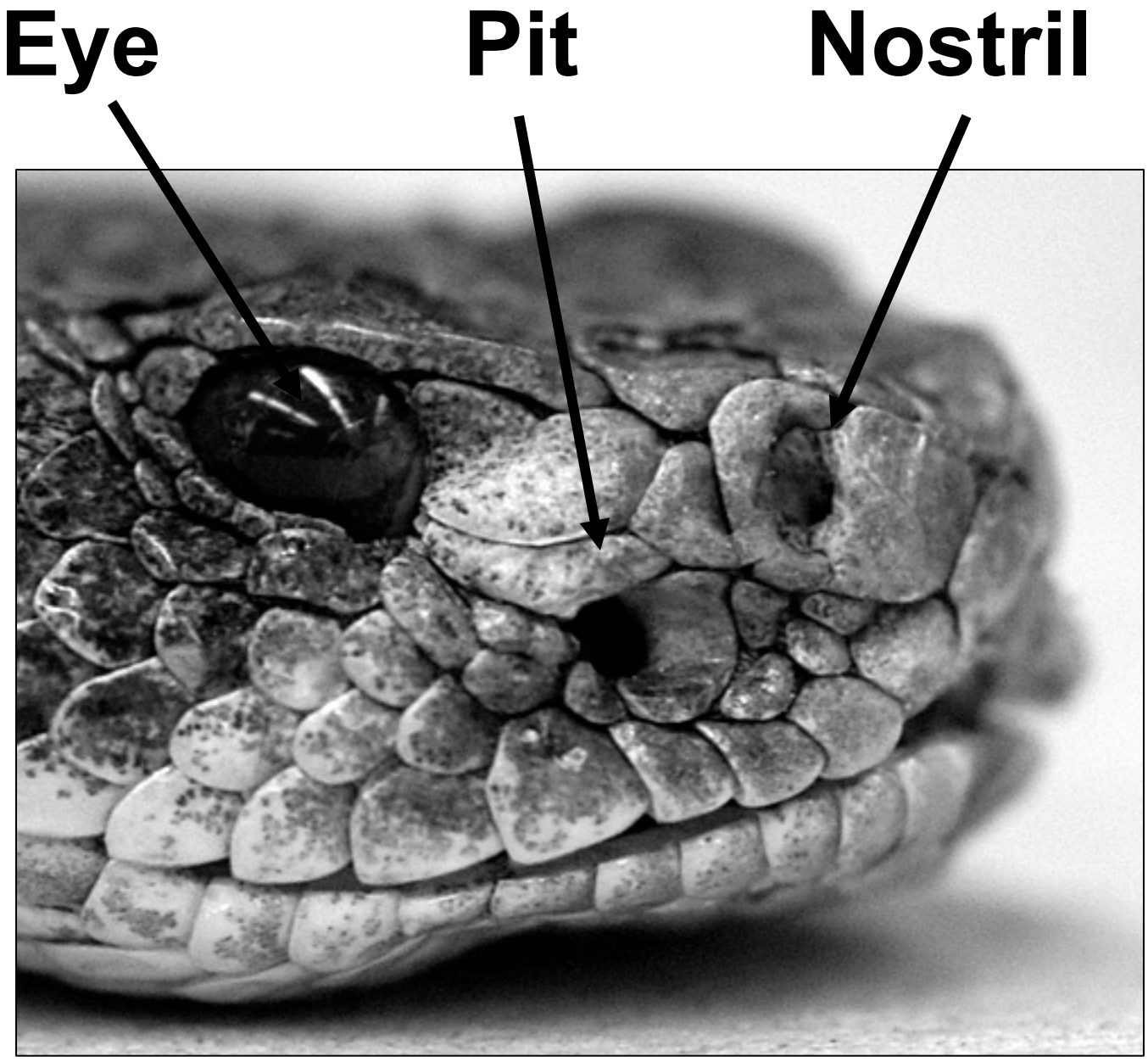
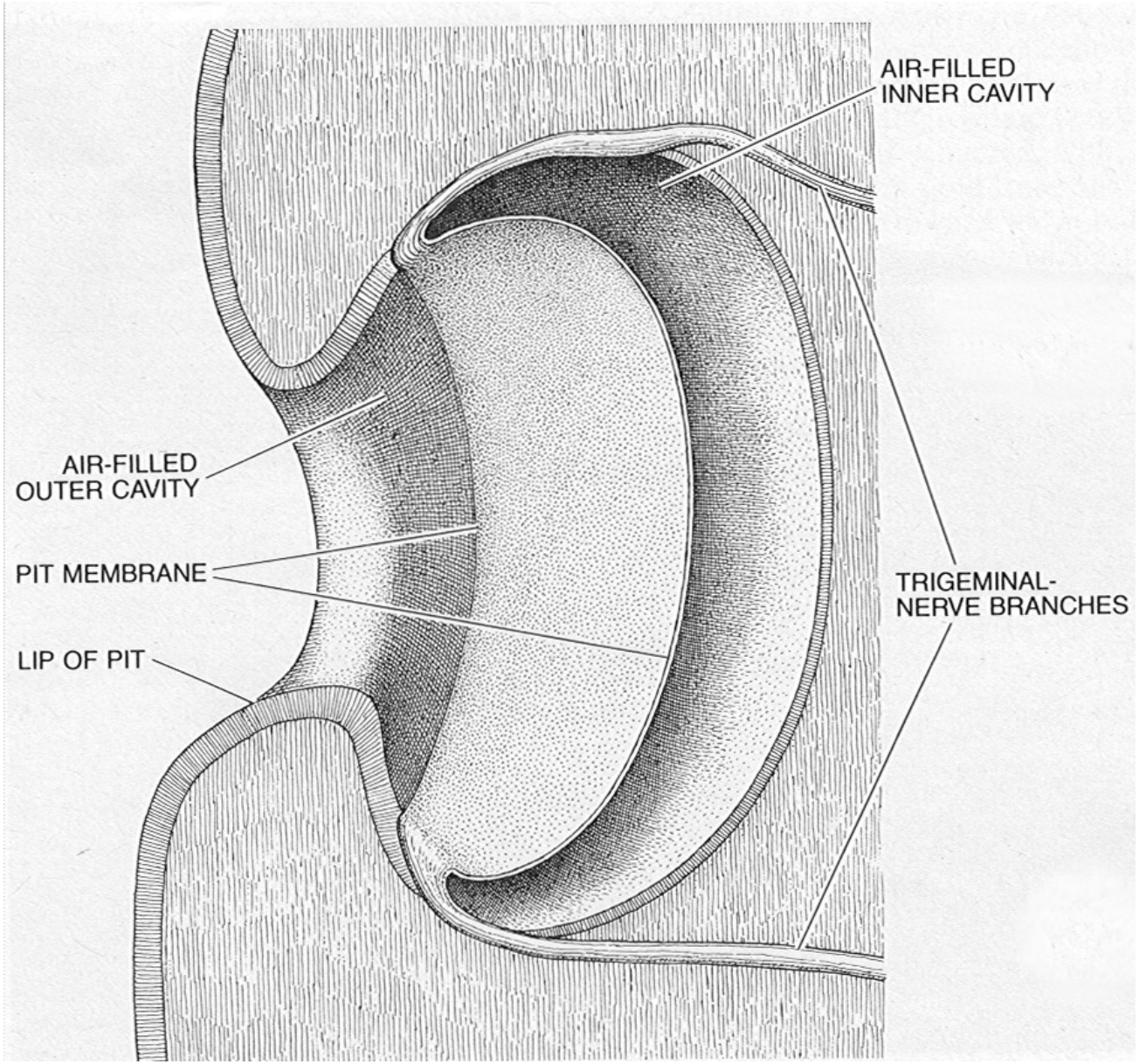
Physiology
Evolution
Behavior
Ecology
Physics


Chemistry
Evolution
Physiology
Behavior
Ecology
Physics

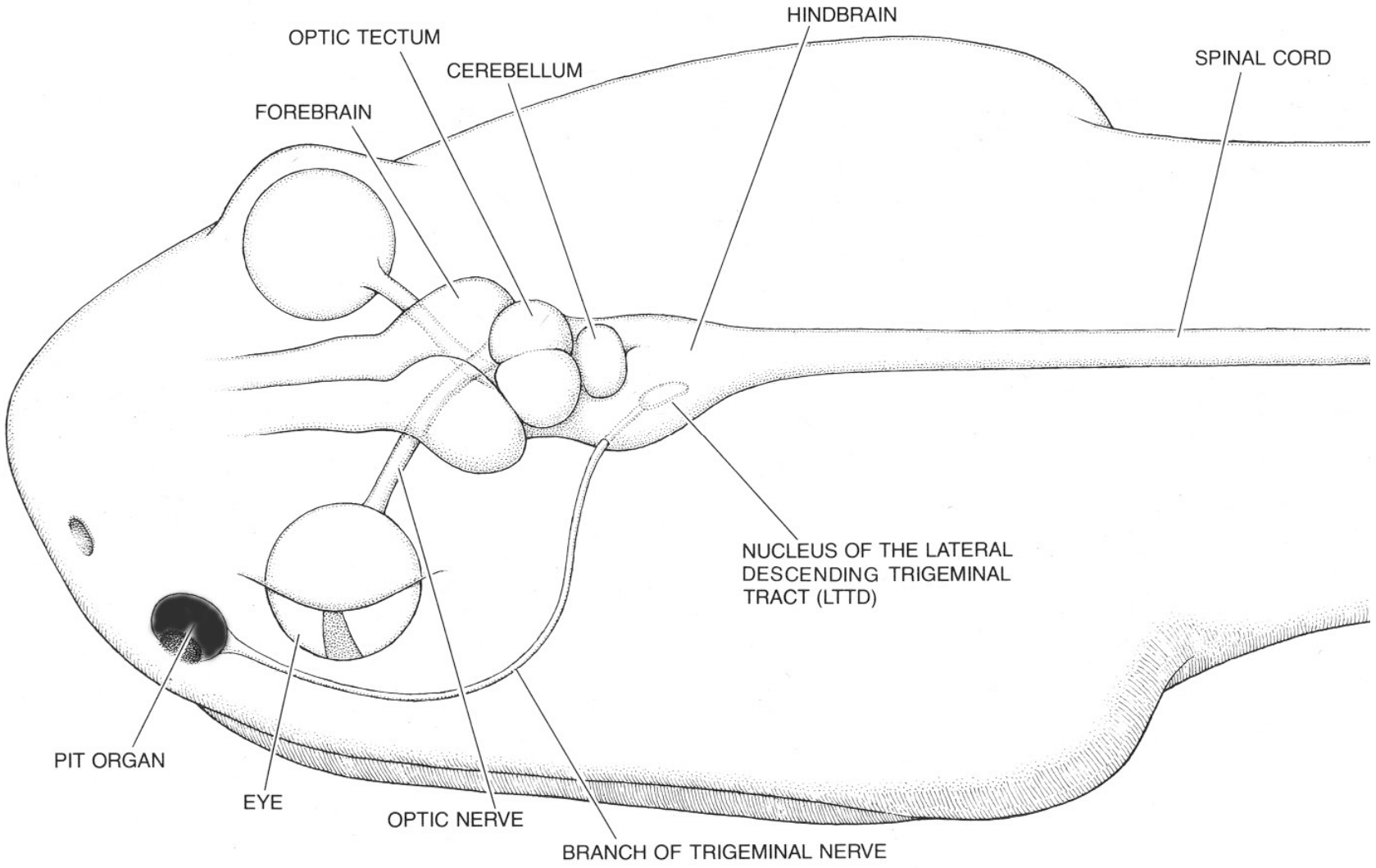
Thermal radiation reception in pitvipers




Eye
Pit
Nostril



From Newman and Hartline, 1982



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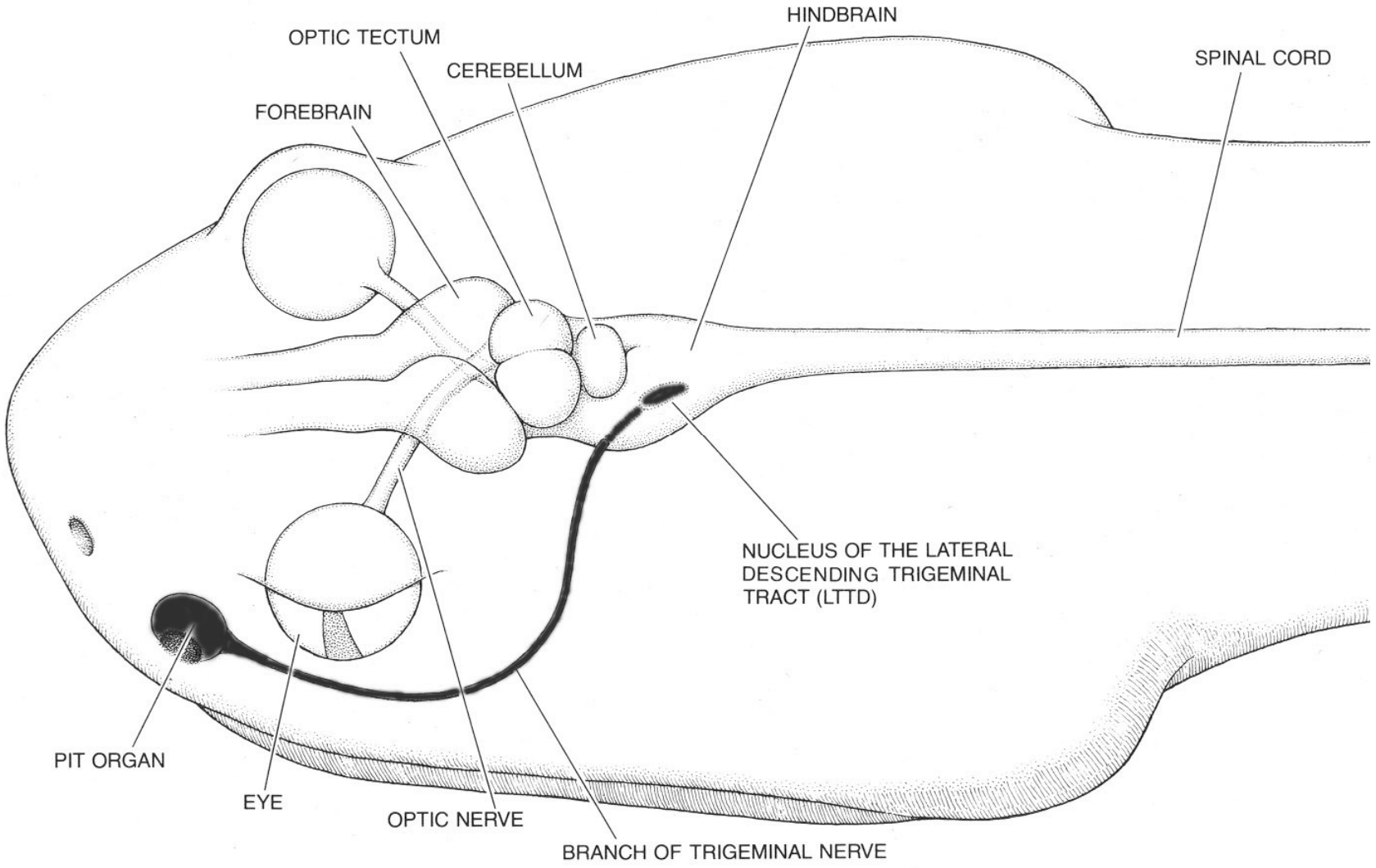

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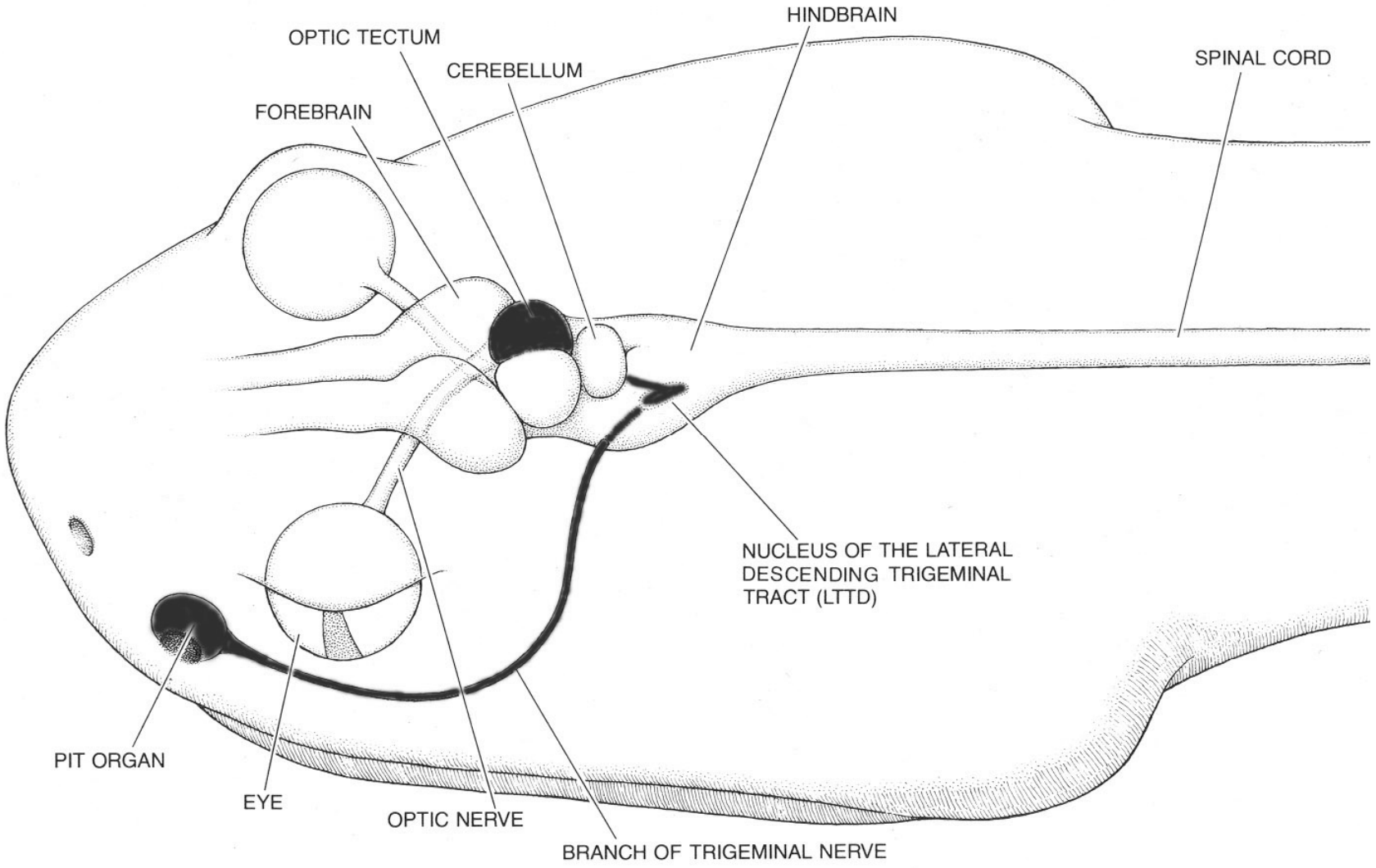

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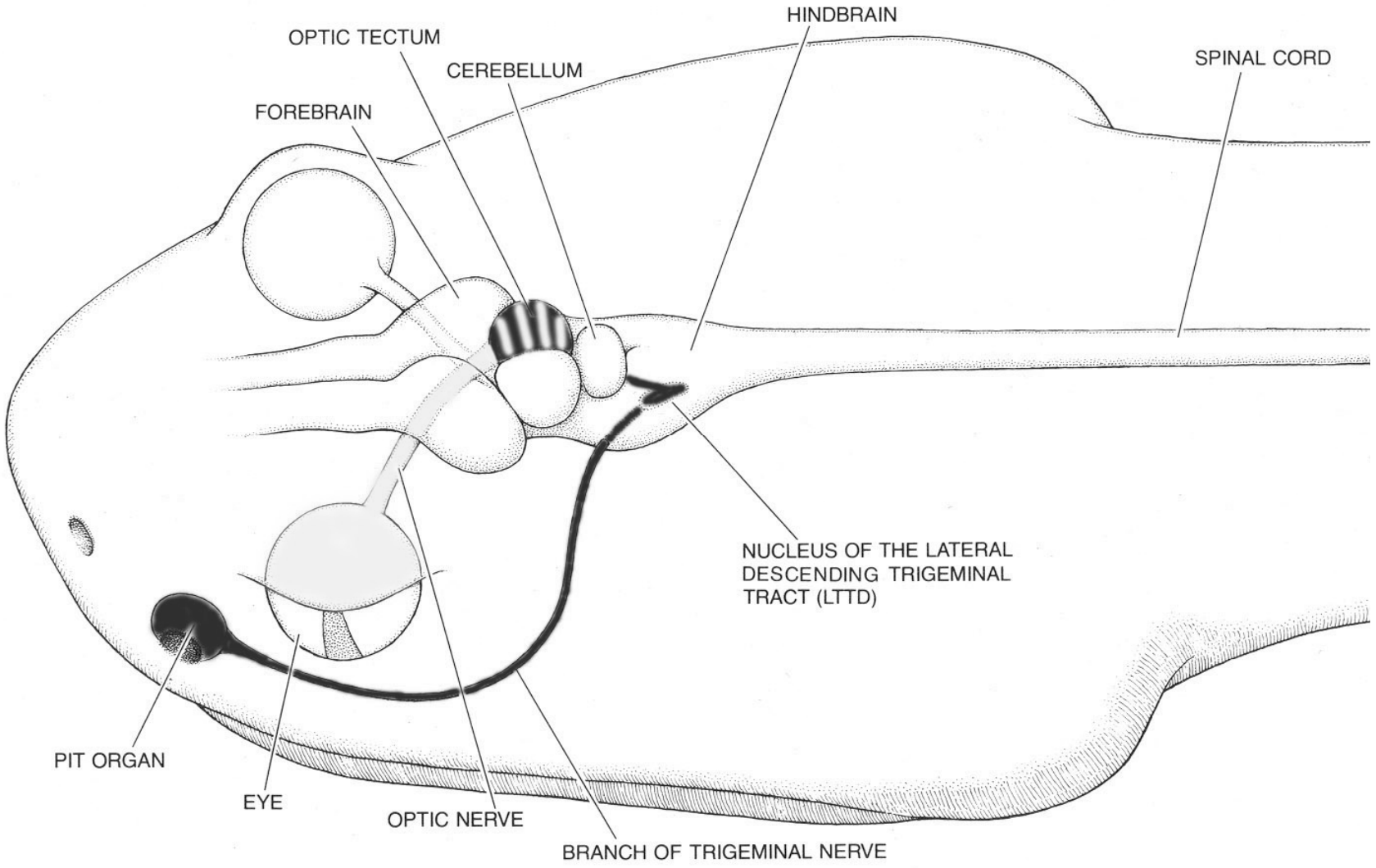
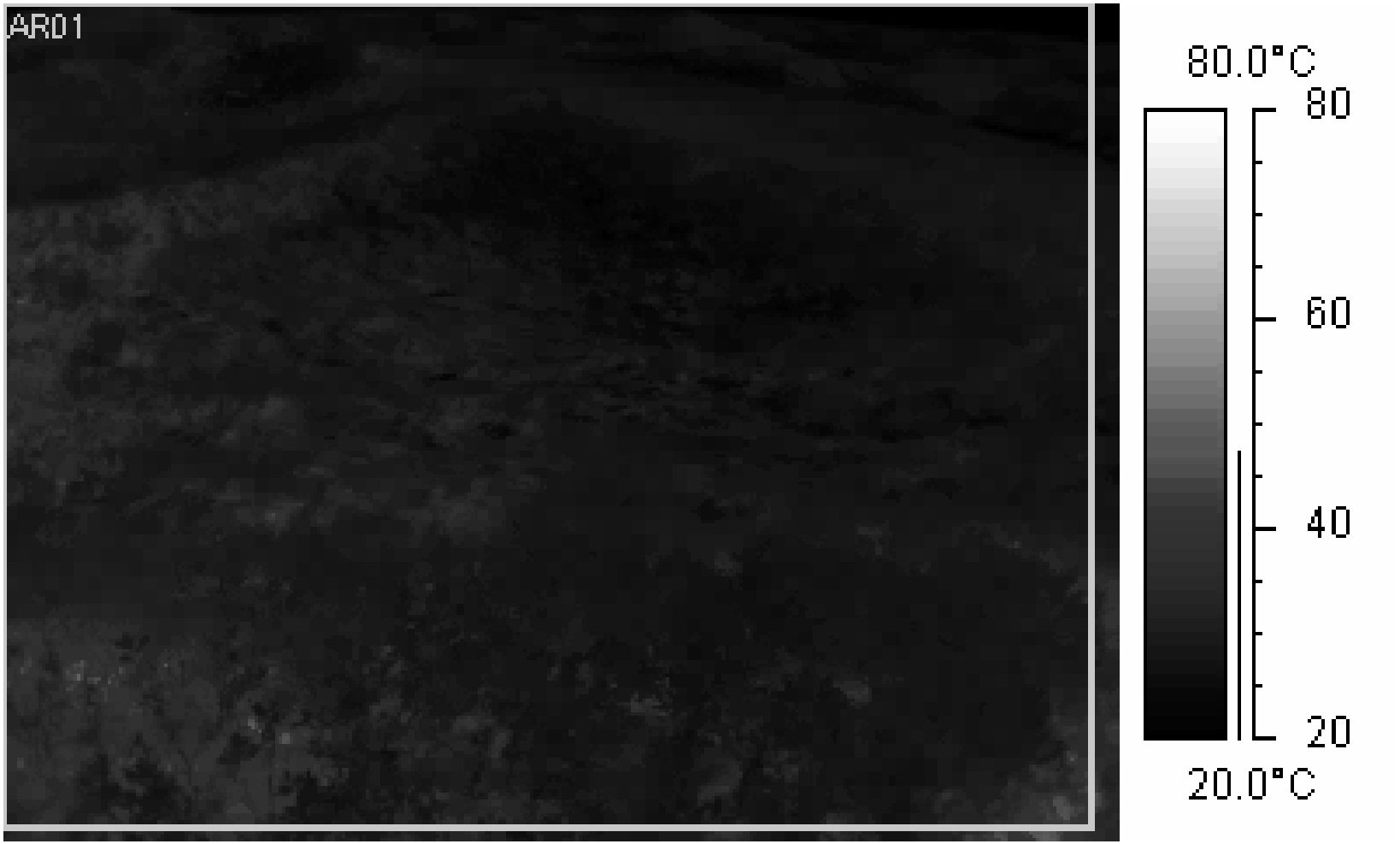


From Newman and Hartline, 1982

Prey acquisition

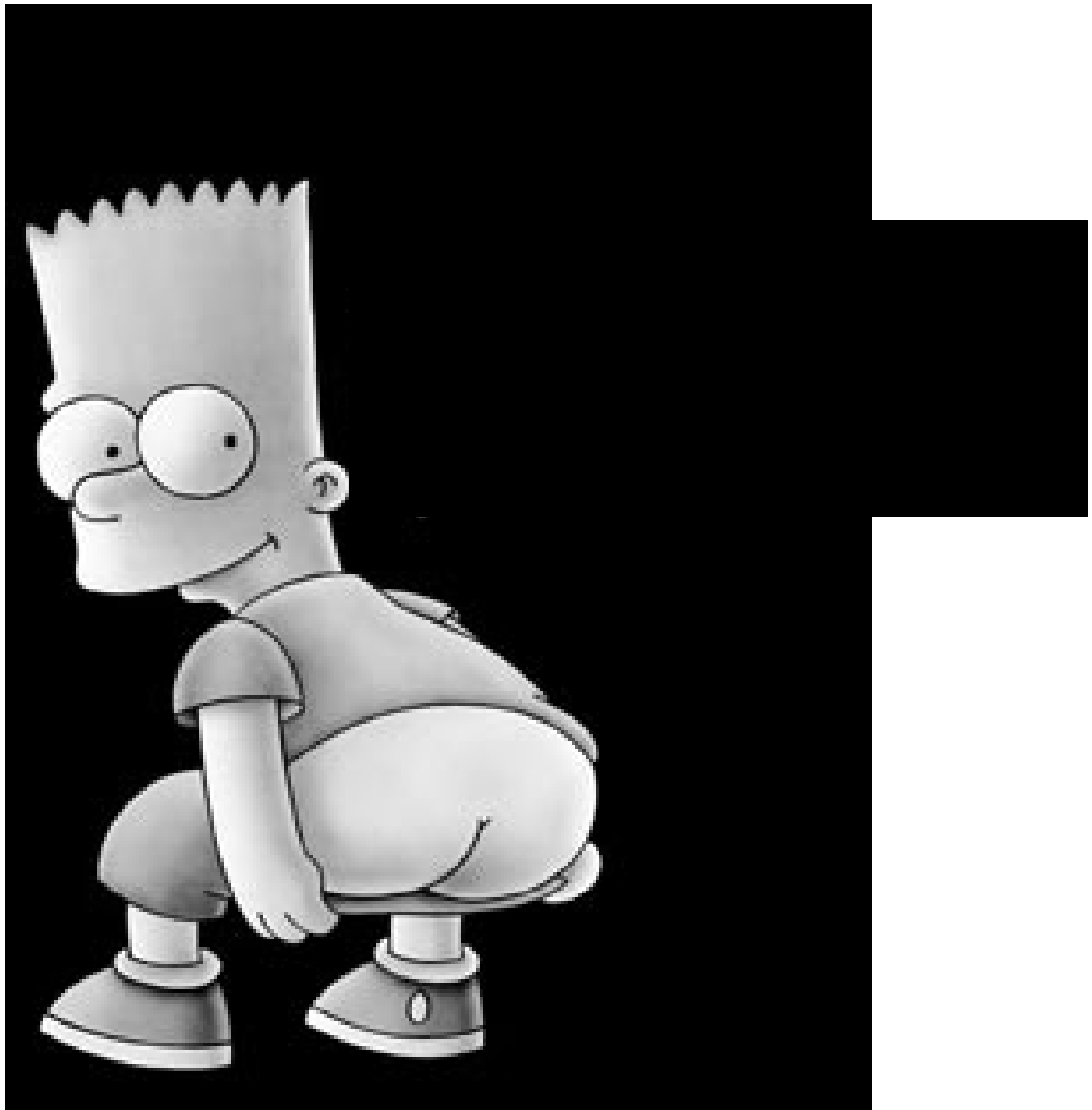
Thermoregulation



Spatial acuity of the facial pits

- **Pitvipers accomplish complex tasks with high accuracy using the facial pits**

BUT…

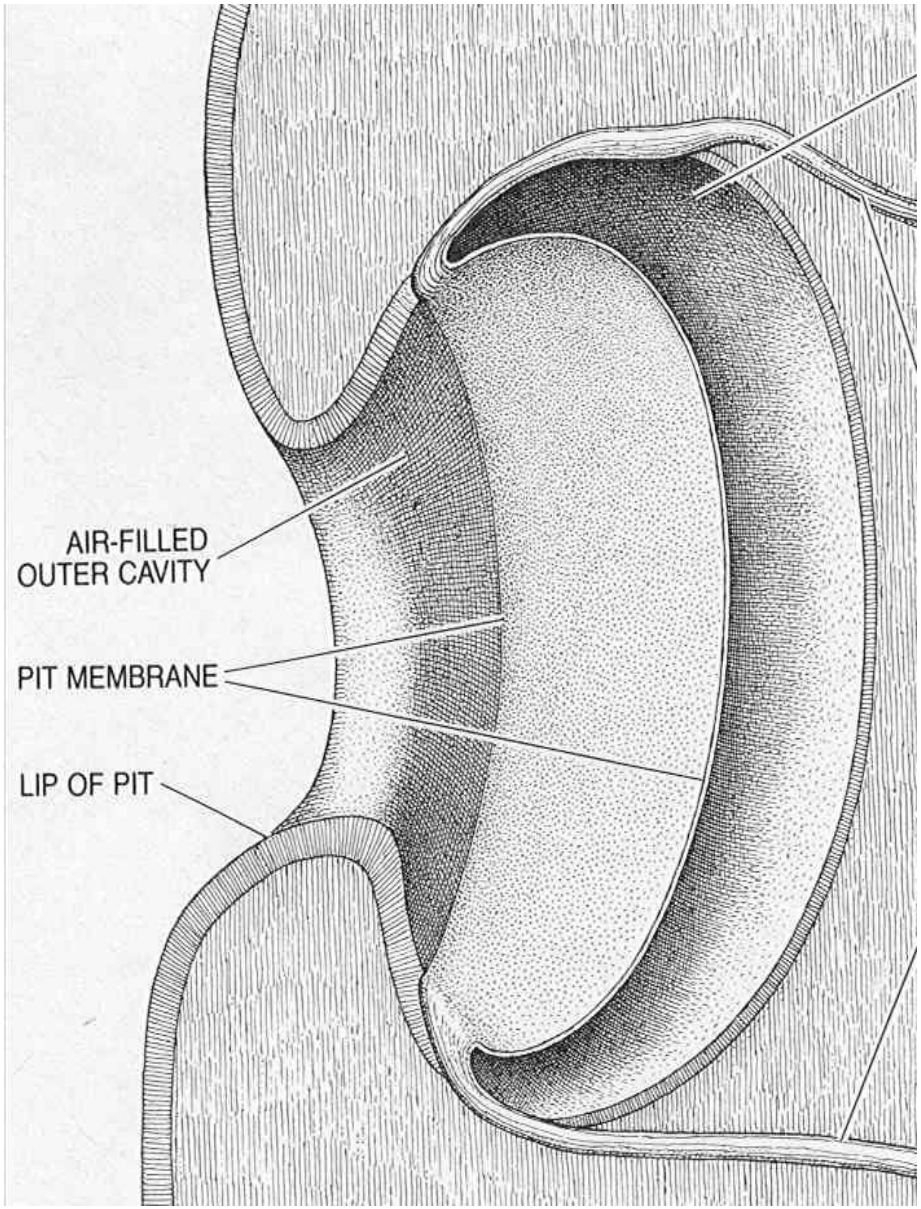


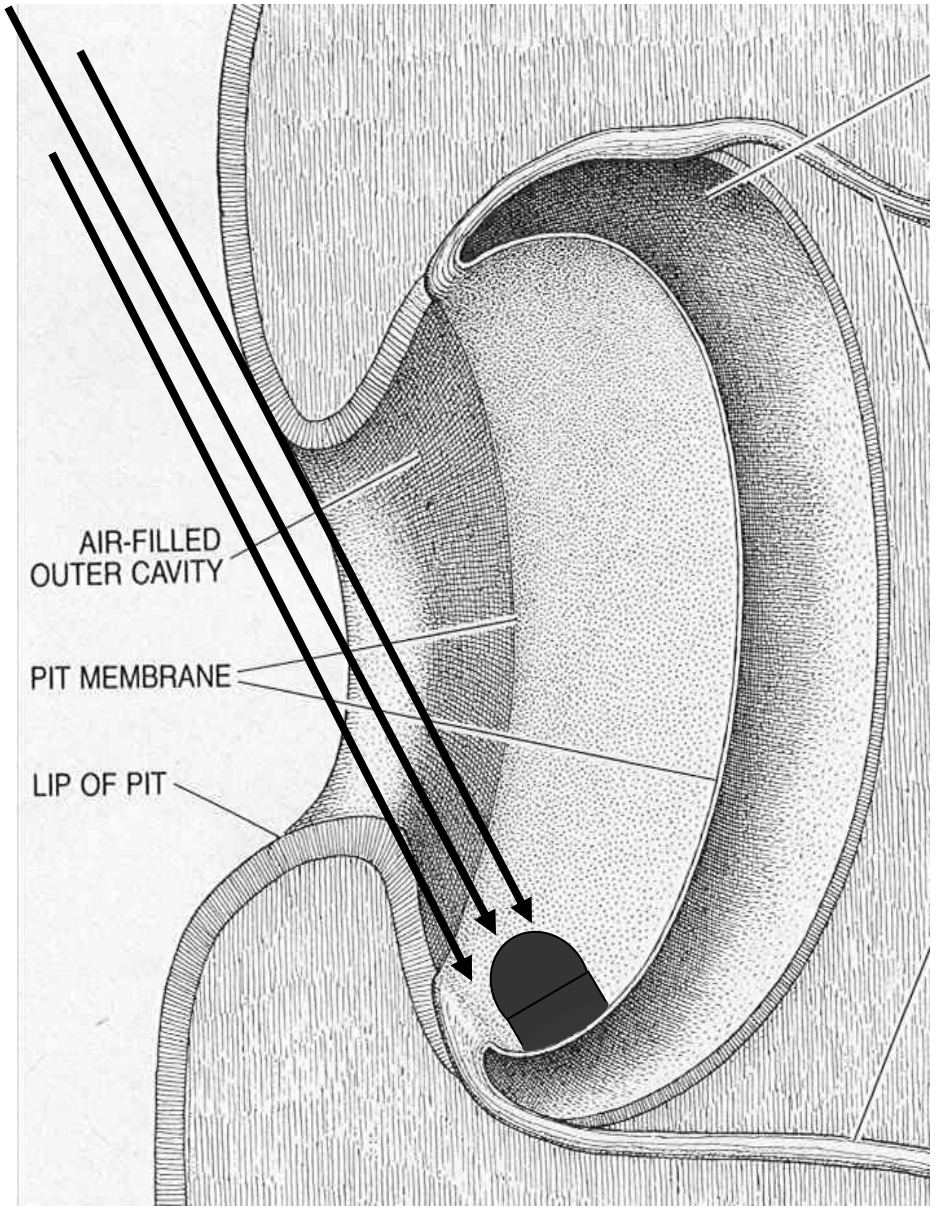
Spatial acuity of the facial pits

- **Pitvipers accomplish complex tasks with high accuracy using the facial pits**

But

- **The facial pit itself is incapable of forming a sharp image**


AIR-FILLED
OUTER CAVITY
PIT MEMBRANE
LIP OF PIT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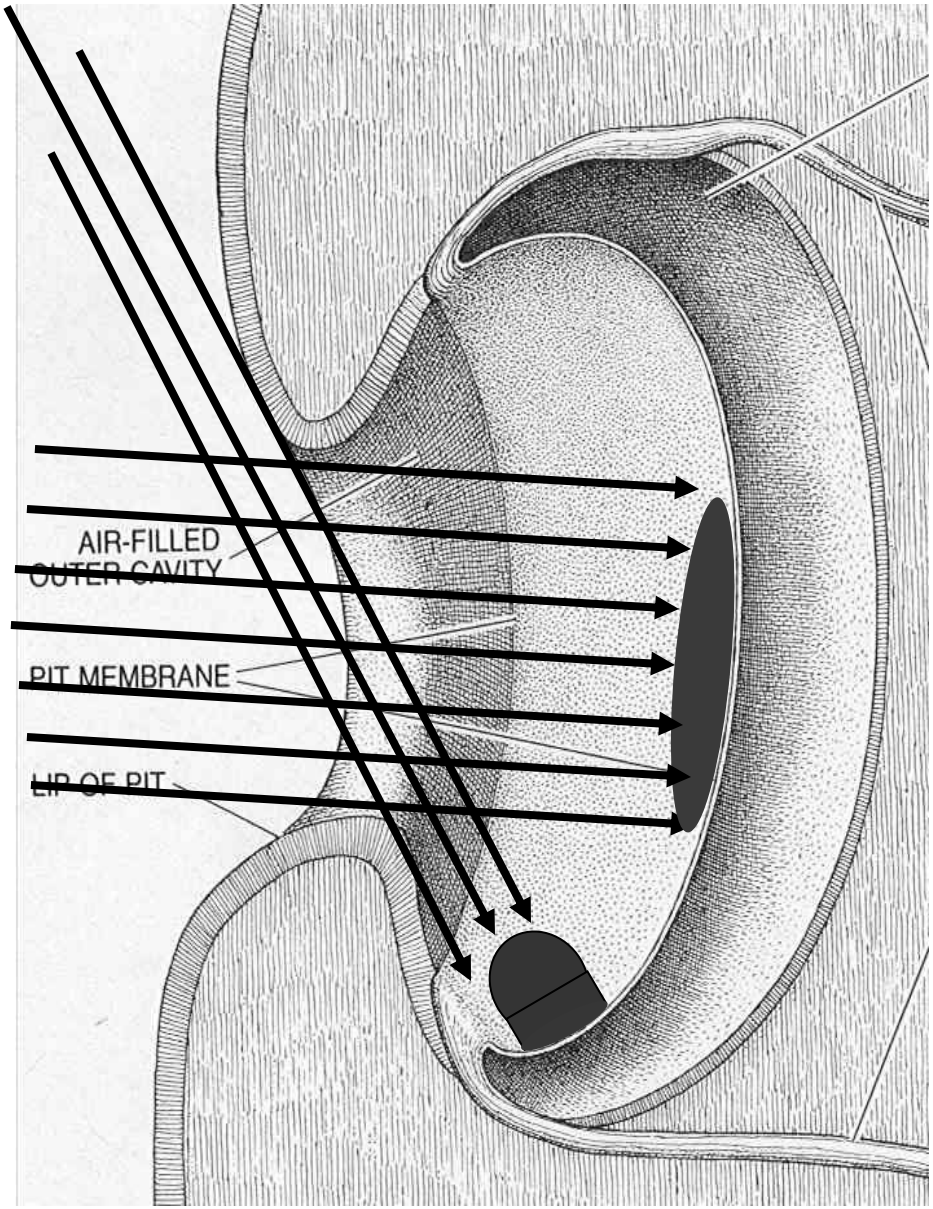
AIR-FILLED
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Spatial acuity of the facial pits

- **Observation: Pit cannot form sharp image on its own**

- **Observation: Snakes behave as if image is sharp**

Spatial acuity of the facial pits

- **Hypothesis:**

Spatial acuity of the facial pits

- **Hypothesis: Pitvipers use CNS to sharpen blurred images**

Spatial acuity of the facial pits

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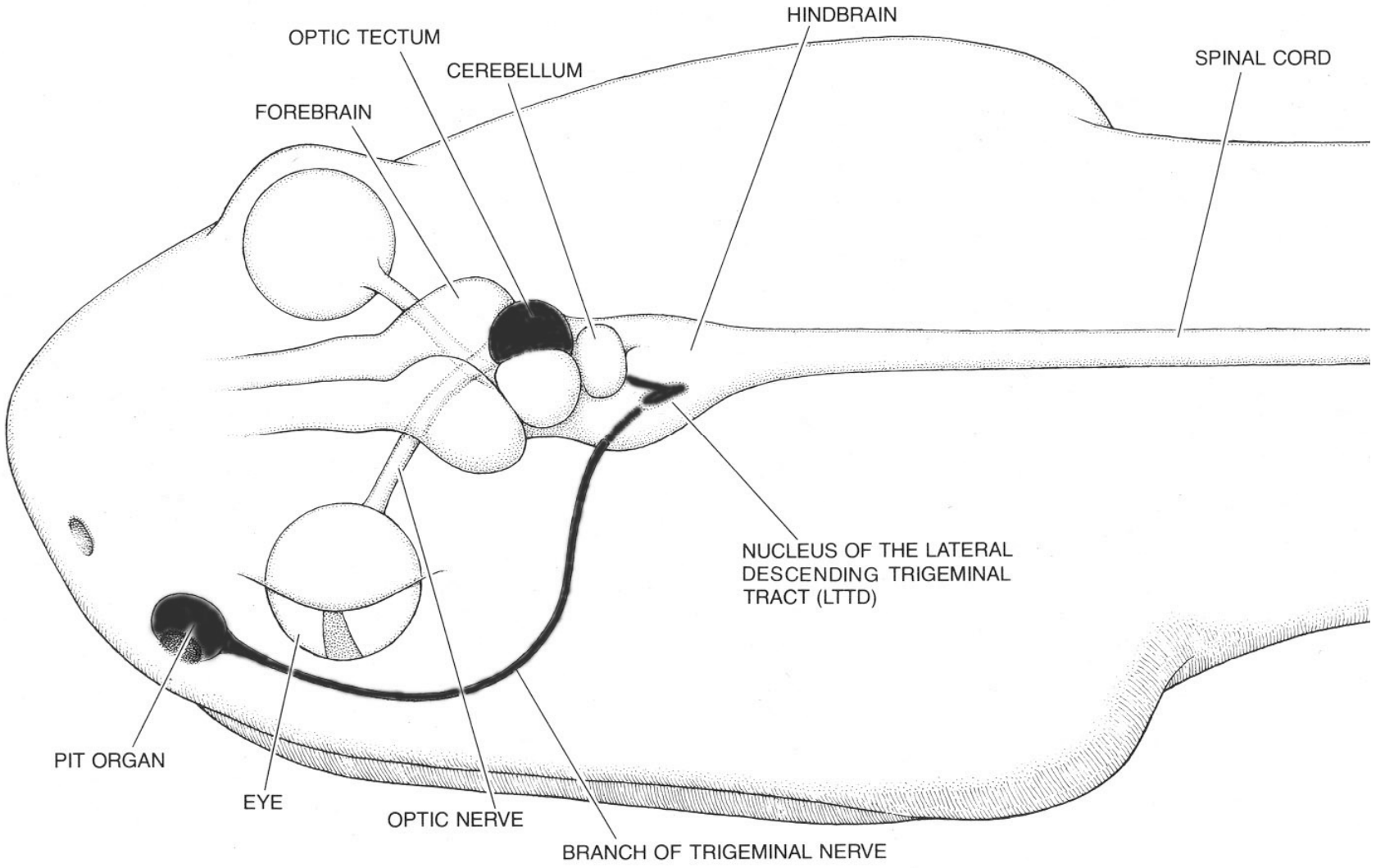
- **Prediction 1:**

Spatial acuity of the facial pits

- **Hypothesis: Pitvipers use CNS to sharpen blurred images**

- **Prediction 1: IF pitvipers use CNS to sharpen blurred images, THEN there must be an area for such calculations**

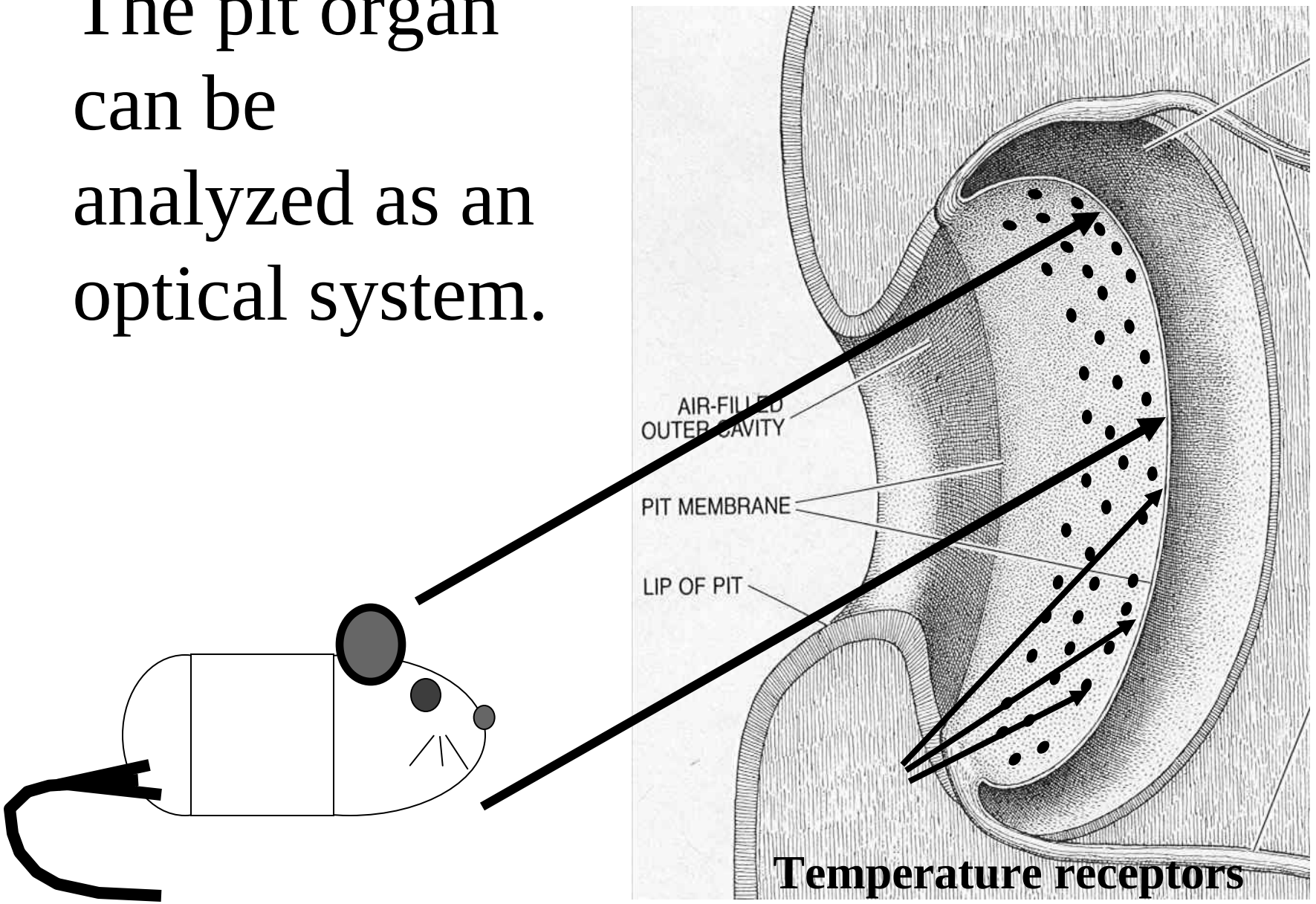


From Newman and Hartline, 1982

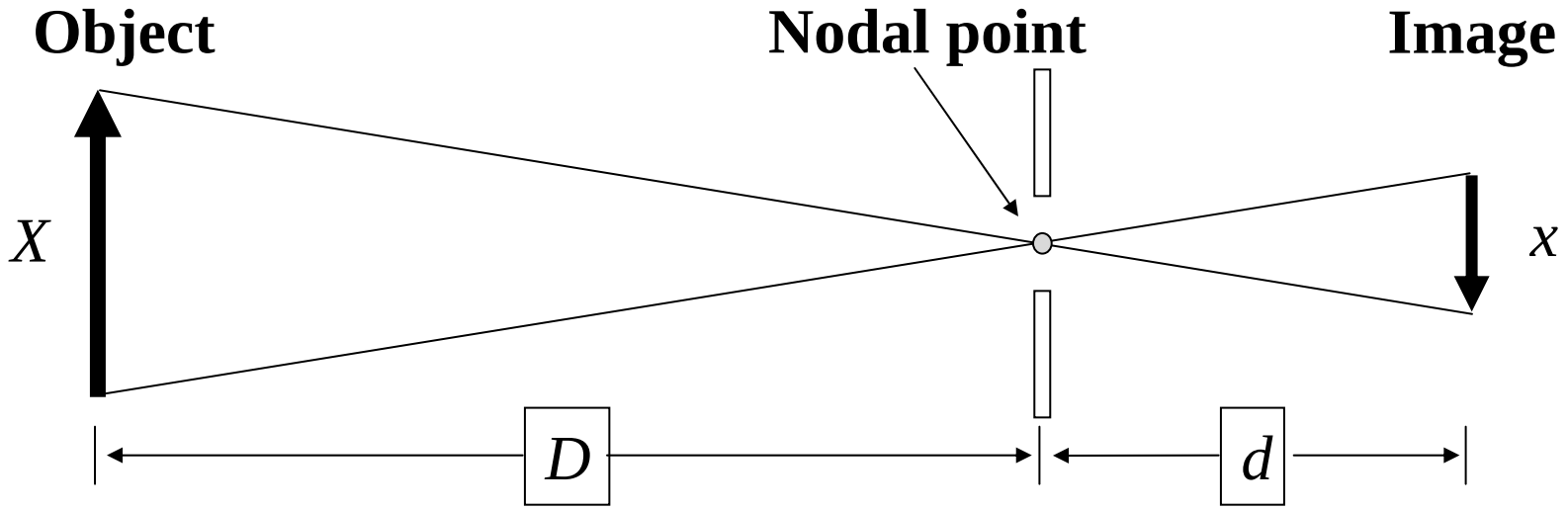
Spatial acuity of the facial pits

- **Prediction 2: IF the blur can be quantified, THEN the LTTD might be able to reverse engineer a crisp image**

The pit organ can be analyzed as an optical system.

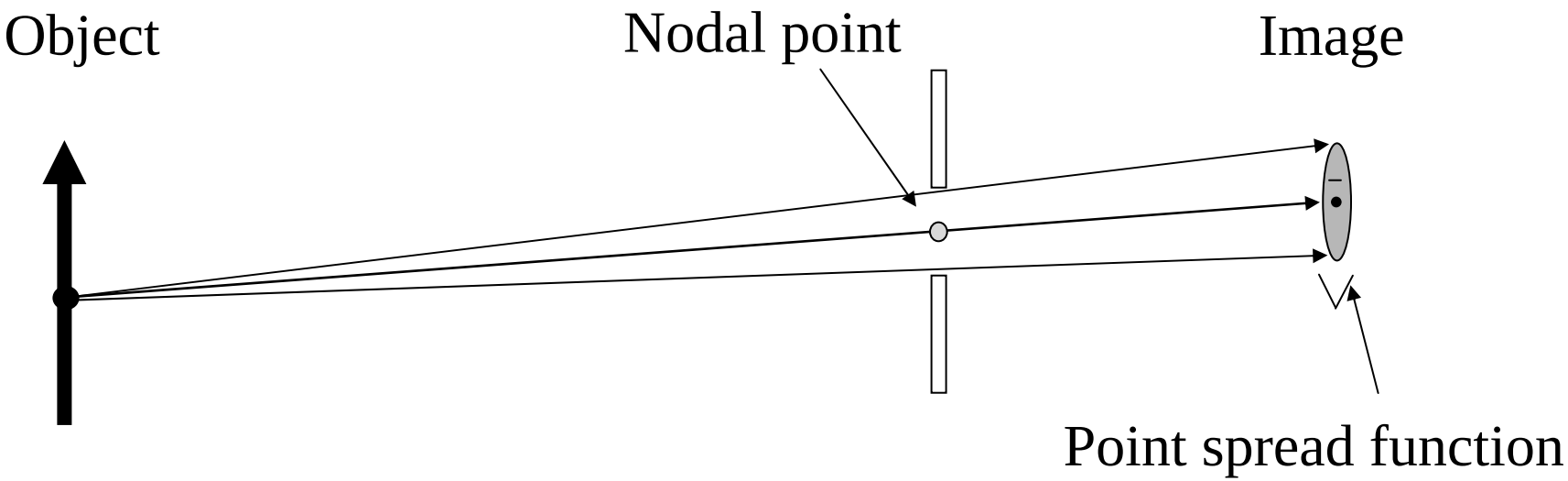


Magnification – Simple Geometry

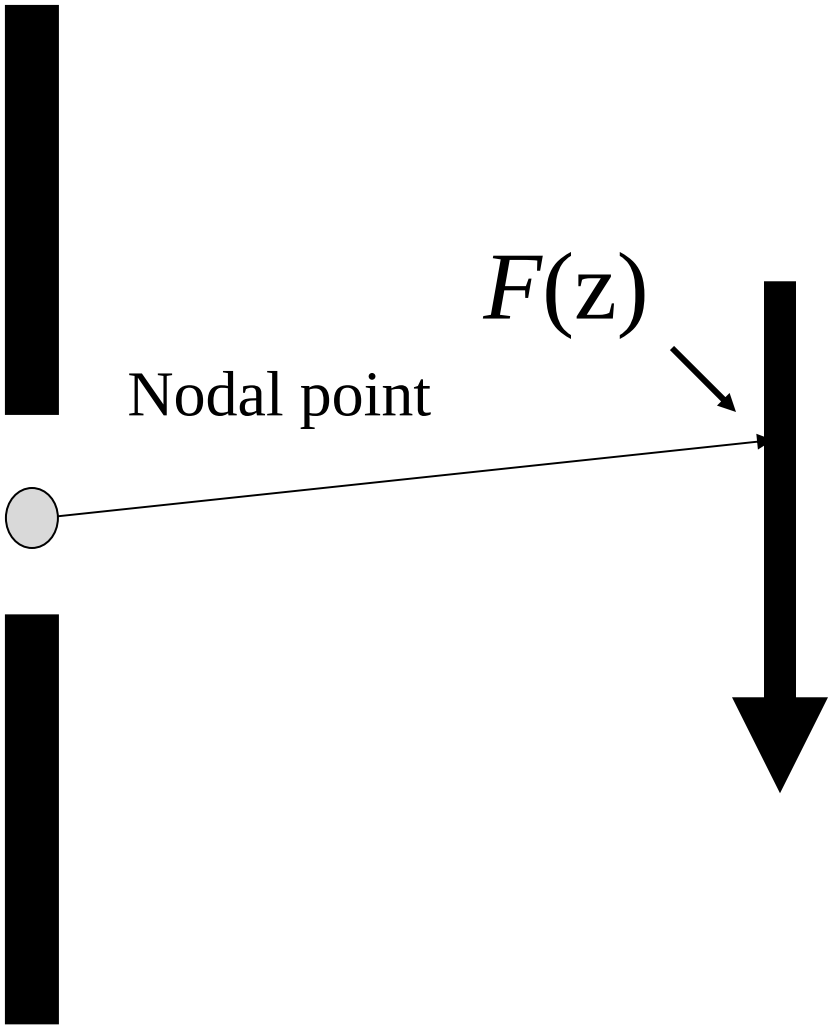


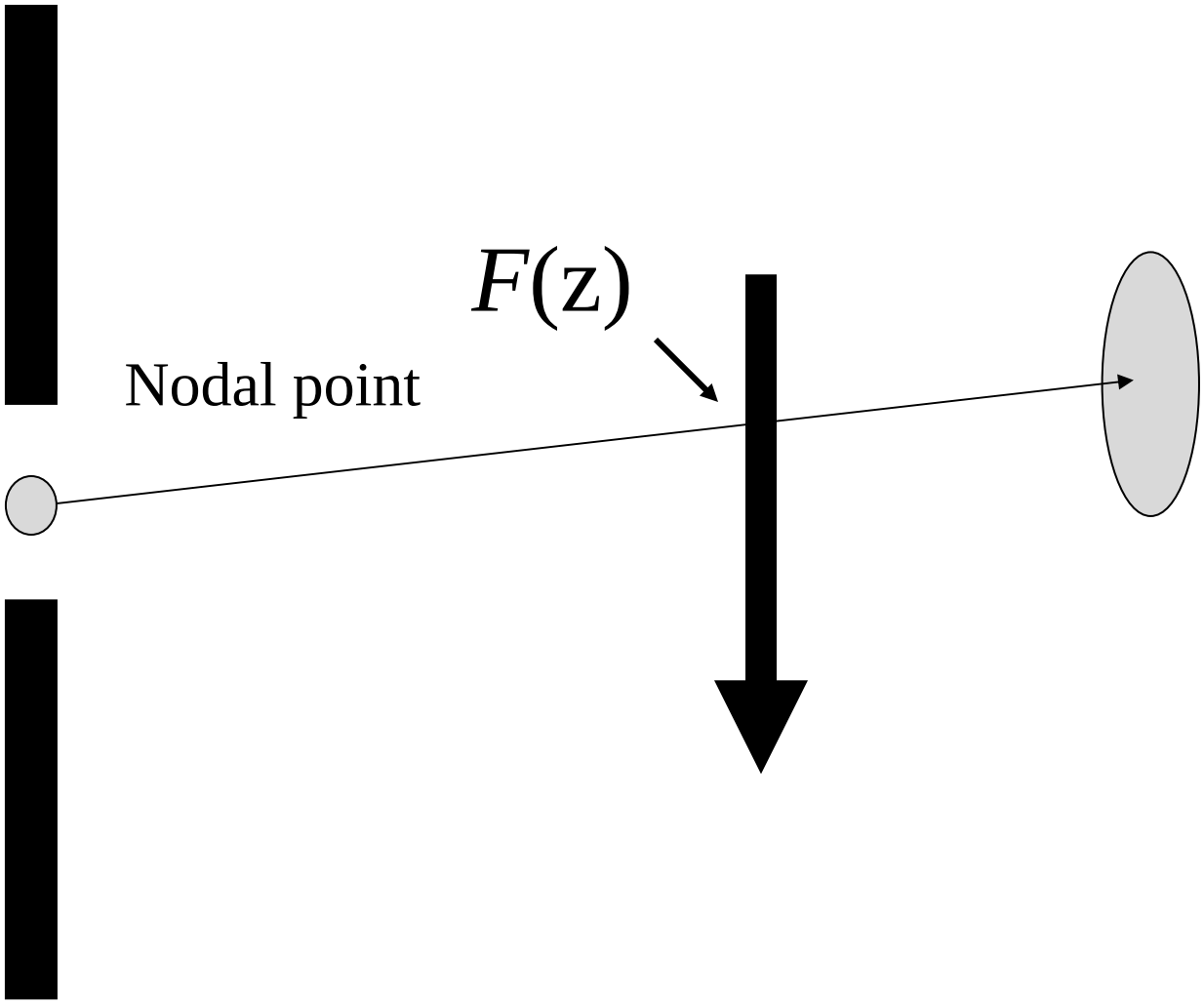
Similar triangles, so $X/D = x/d$;

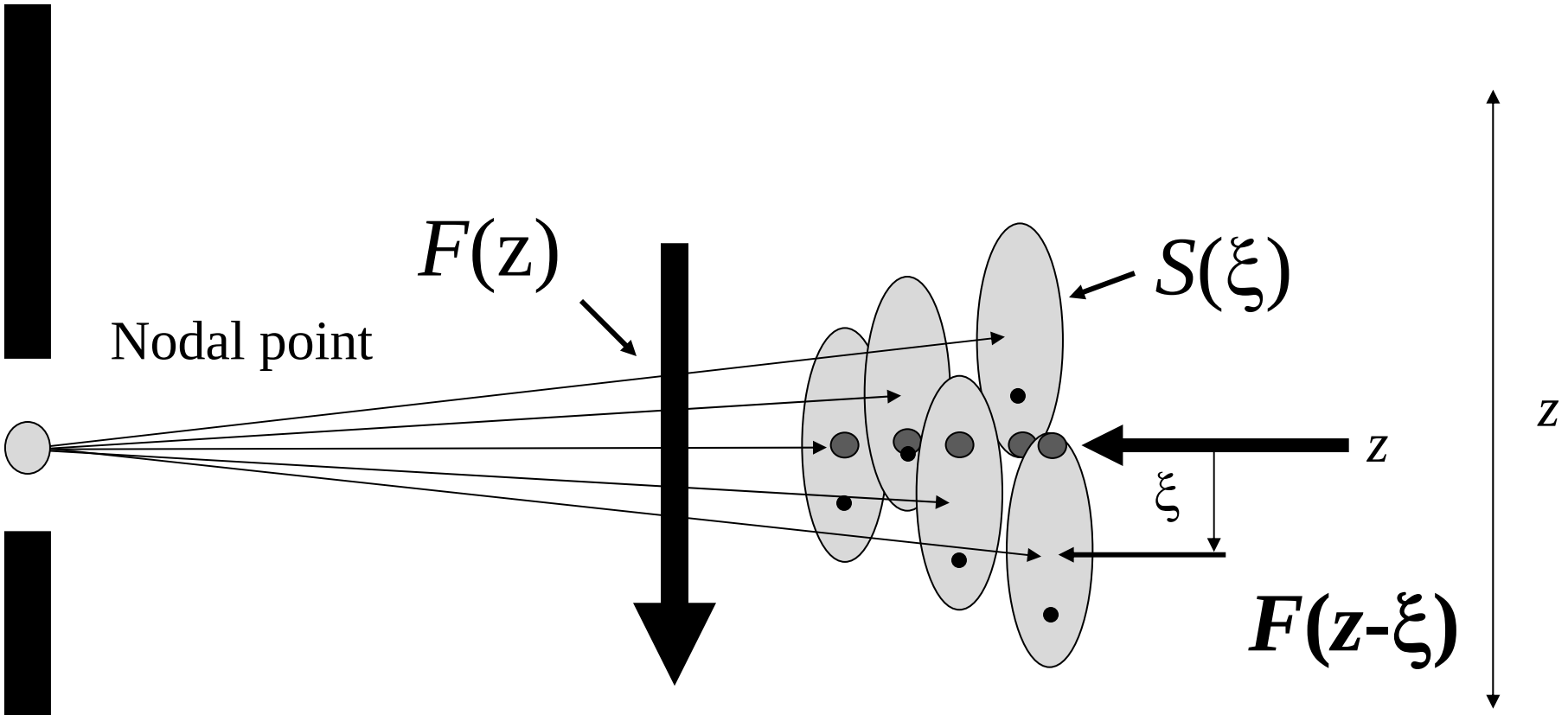
Therefore $M = x/X = d/D$



The point spread function describes the way light from a point ● on the object is distributed over the image plane. For a pinhole camera, the point spread function is a disk centered on the corresponding point of the image.


F(z)
Nodal point


F(z)
Nodal point



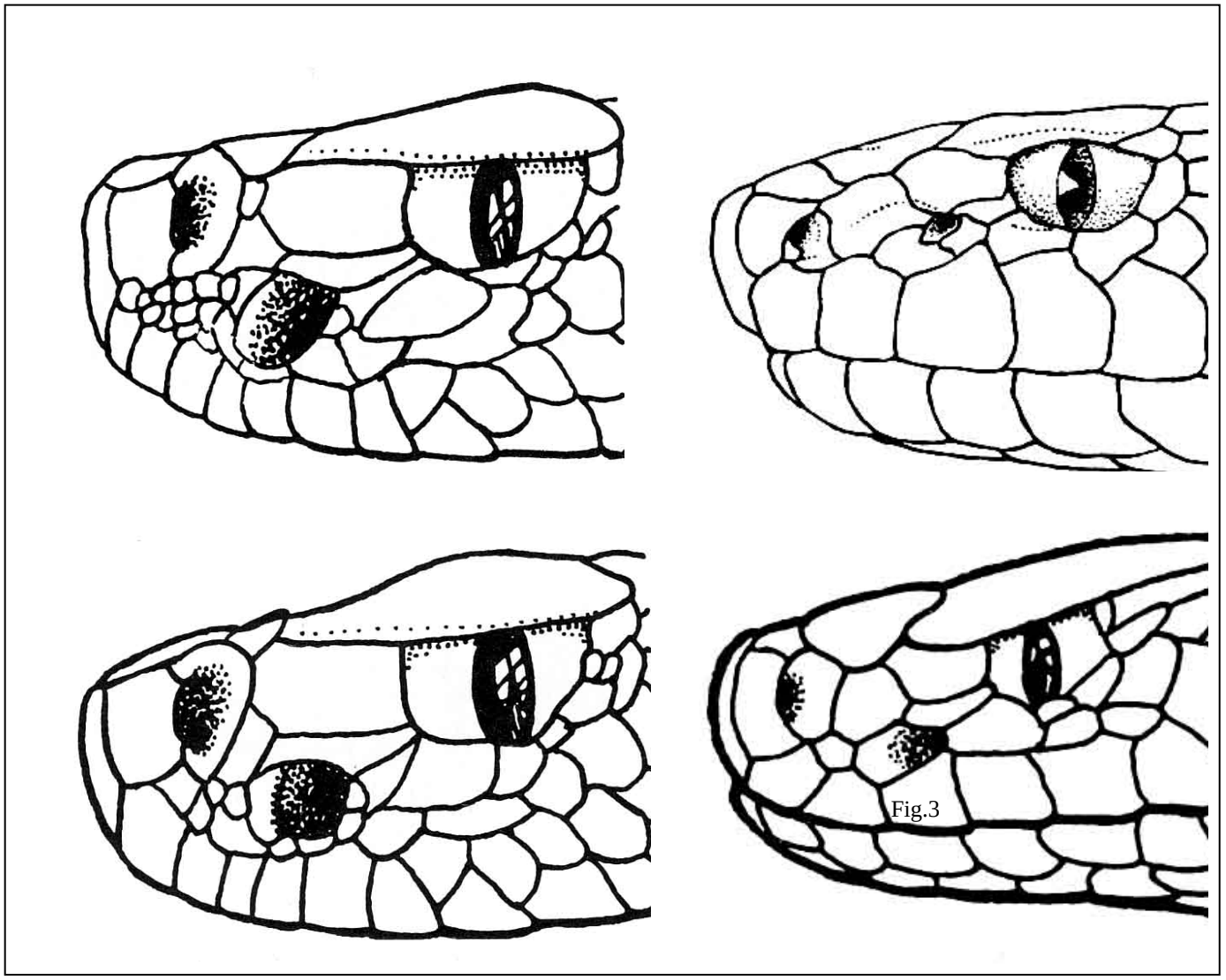
$$I(z) = \int S(\xi)F(z-\xi)\, d\xi \,/\, \int S(\xi)d\xi$$

$I(z)$ = image irradiance at point z, $F(z)$ = ideal image irradiance, $S(\xi)$ = spread function. This is called a *convolution.*

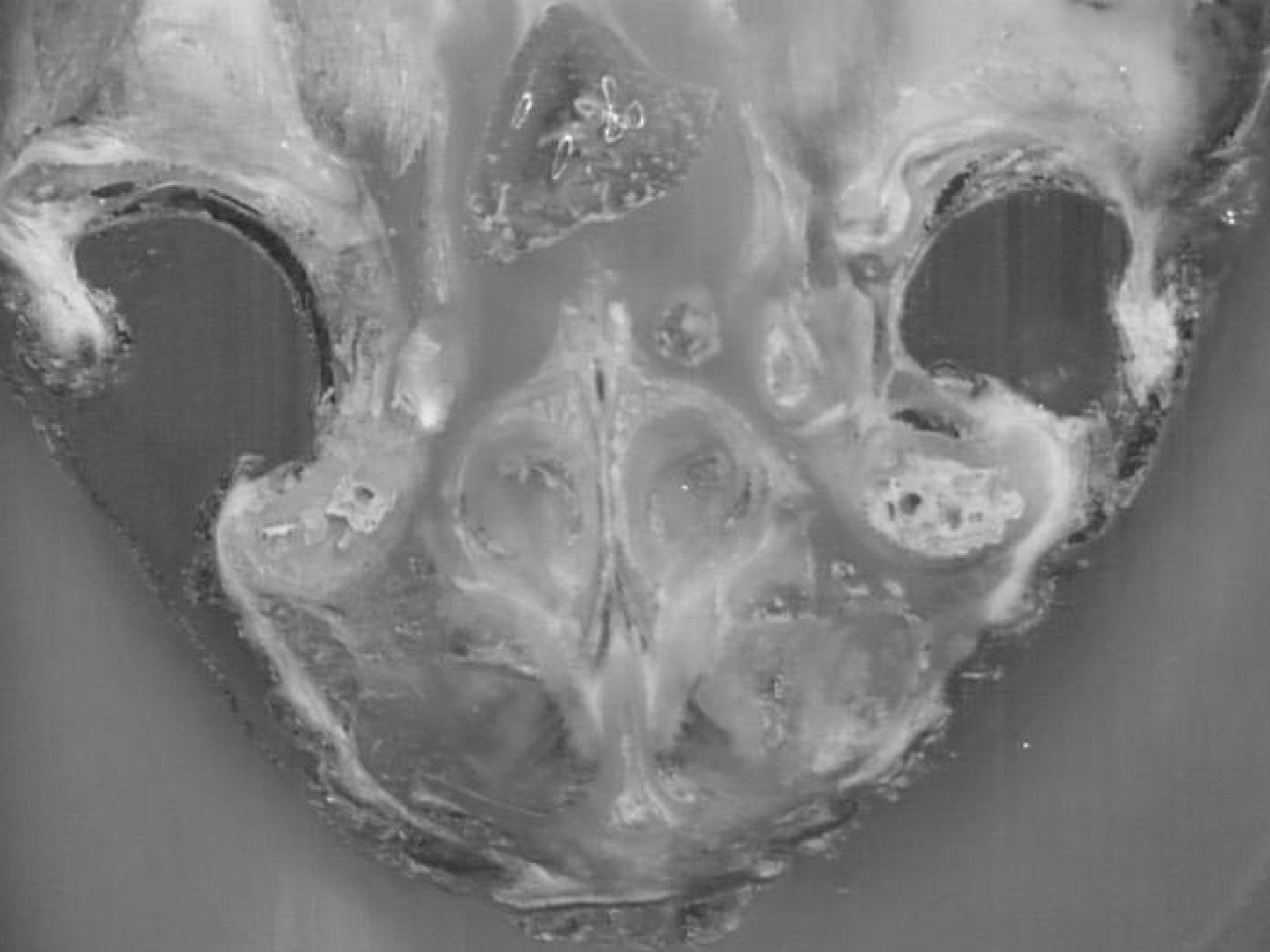
Spatial acuity of the facial pits

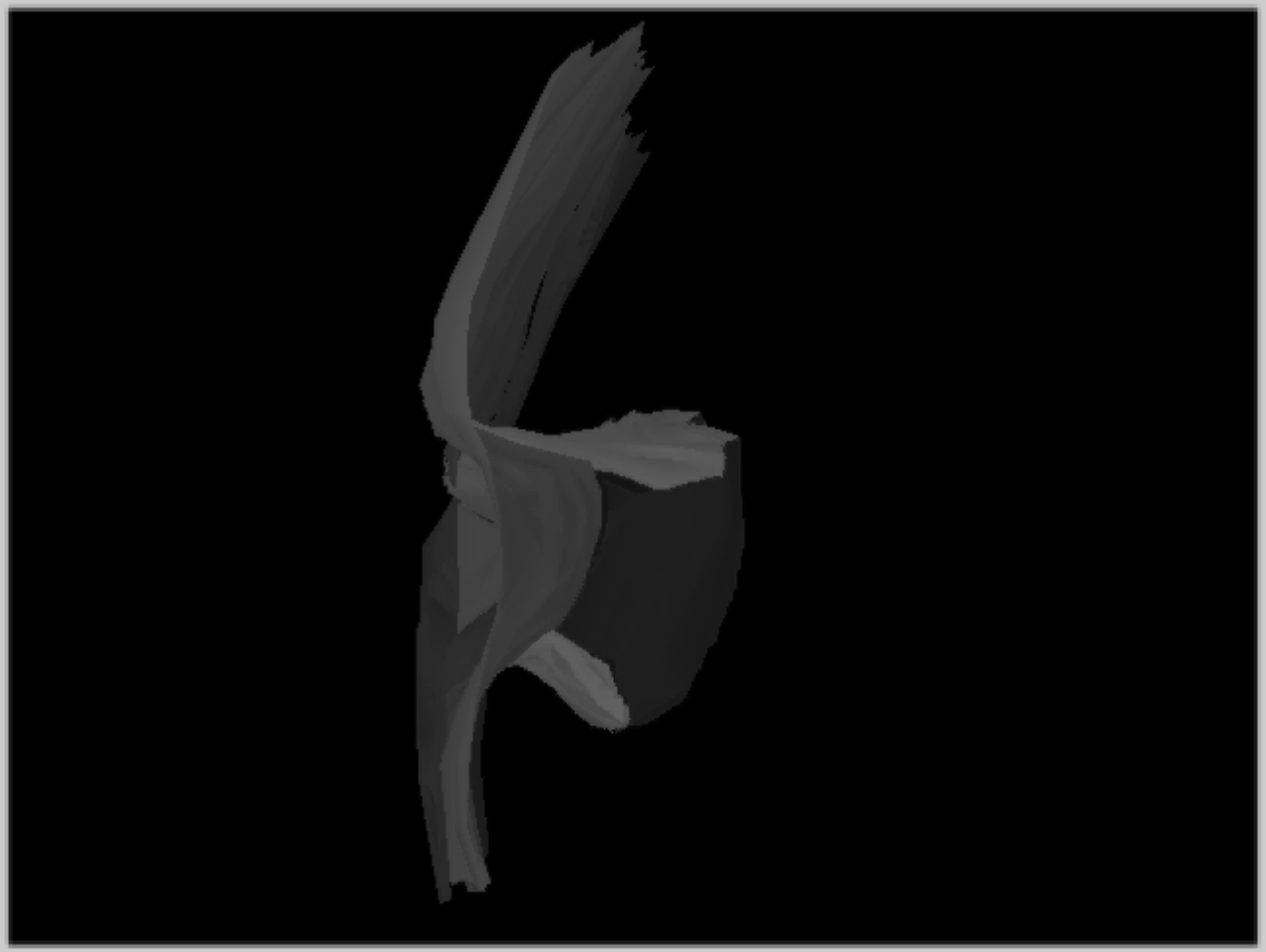
- **Is geometry dependent**
  - Total aperture; effective aperture
  - Internal geometry

Externally pit geometry is variable



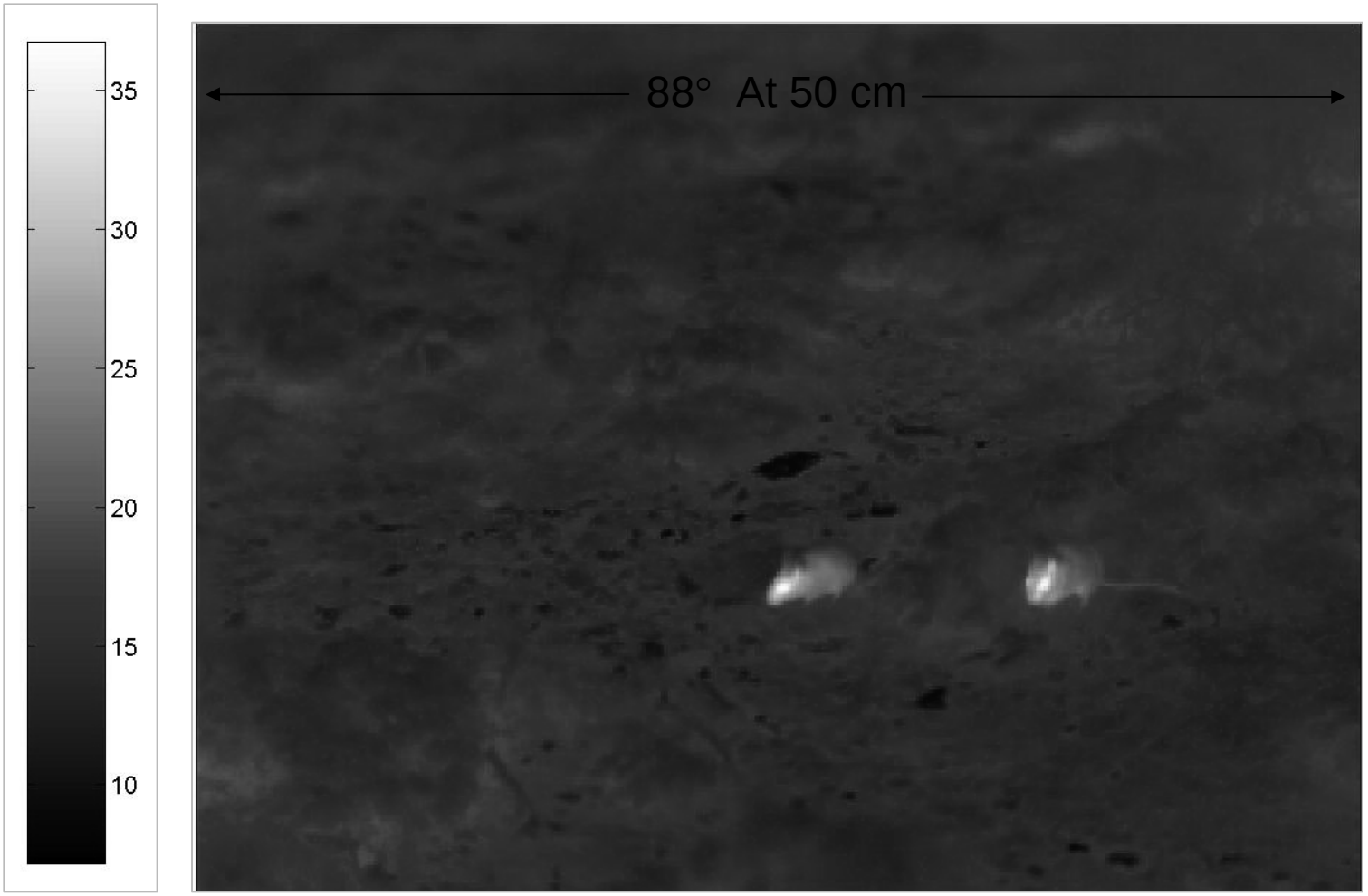
Klauber, 1972

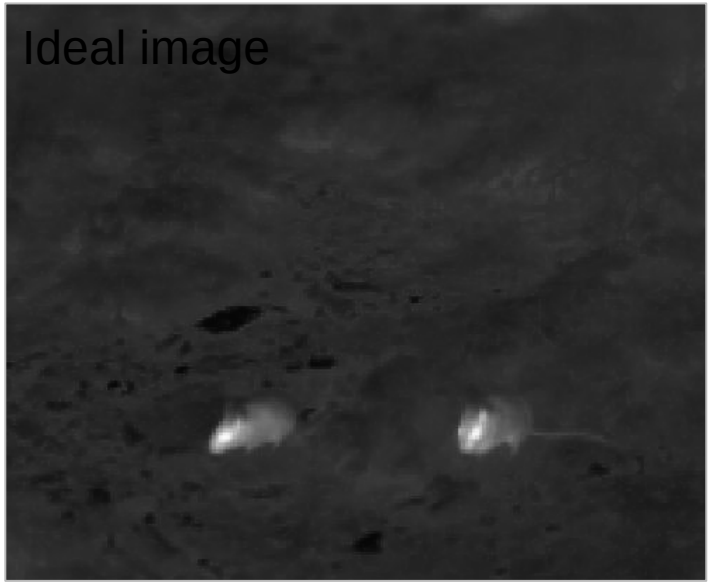




Insert calculus here…

Night: Peromyscus sp, 2300h, Ta=15°C




Ideal image

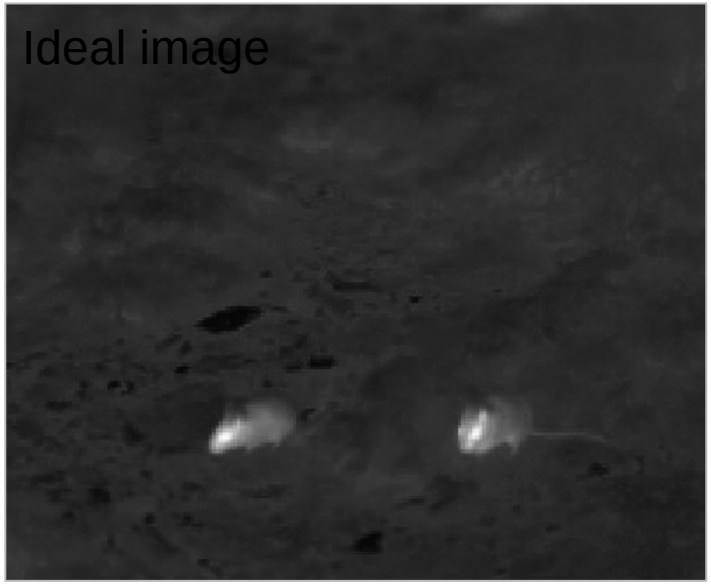

Ideal image


Image $\theta = 2.5$ °

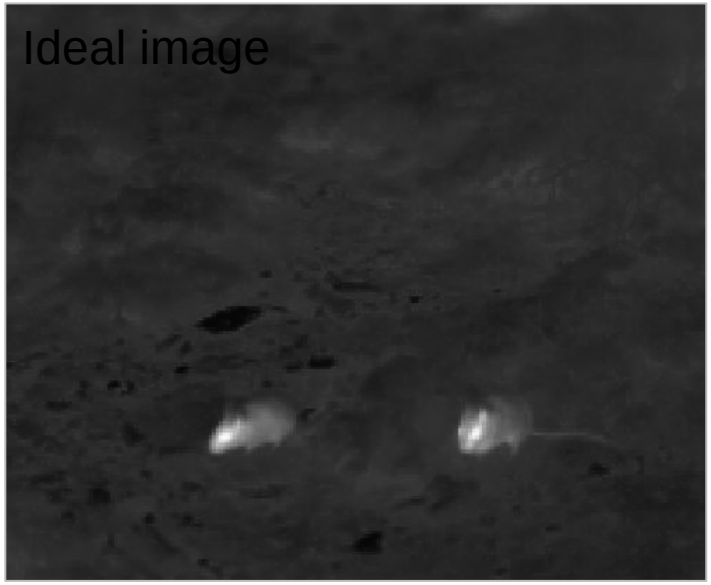

Ideal image


Image θ = 2.5 °

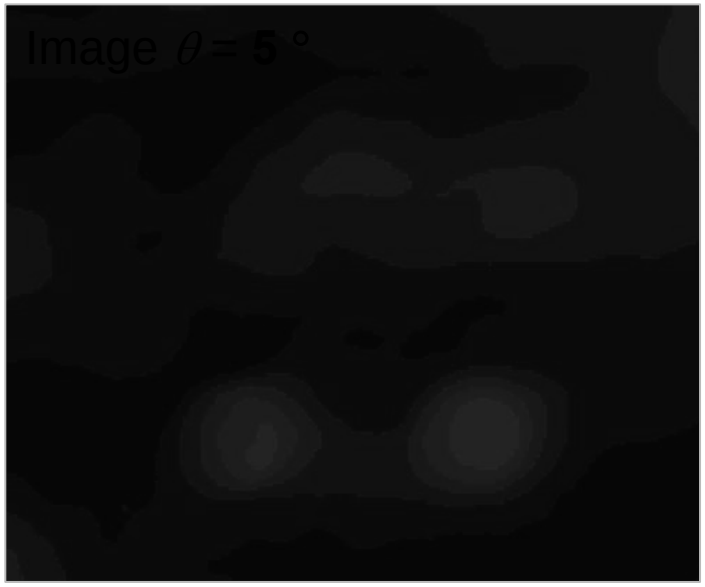


Image θ = **5** °

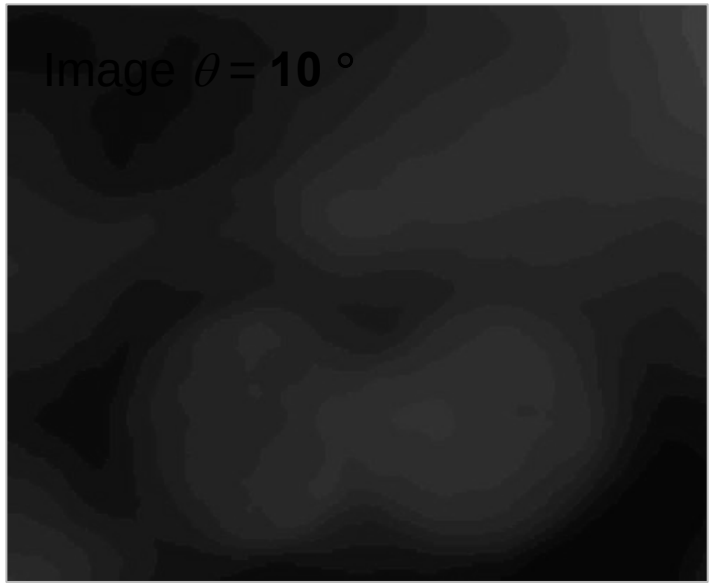
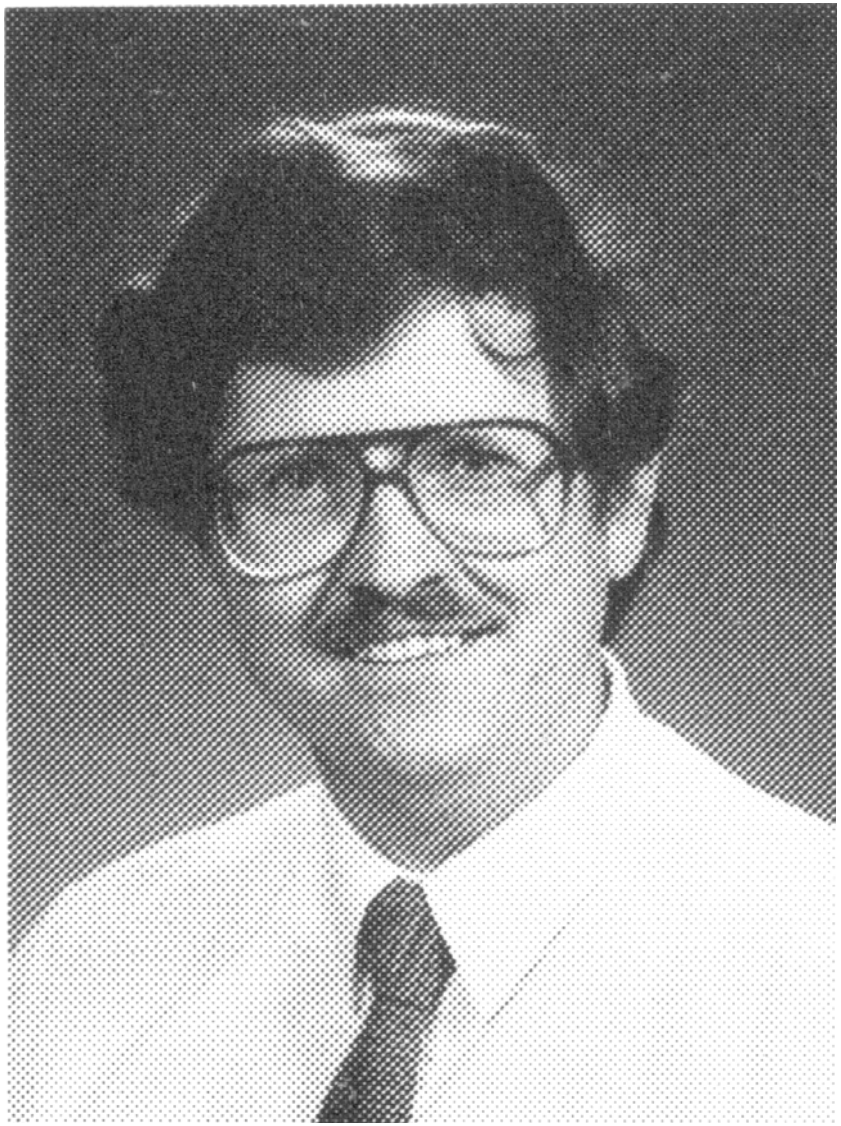
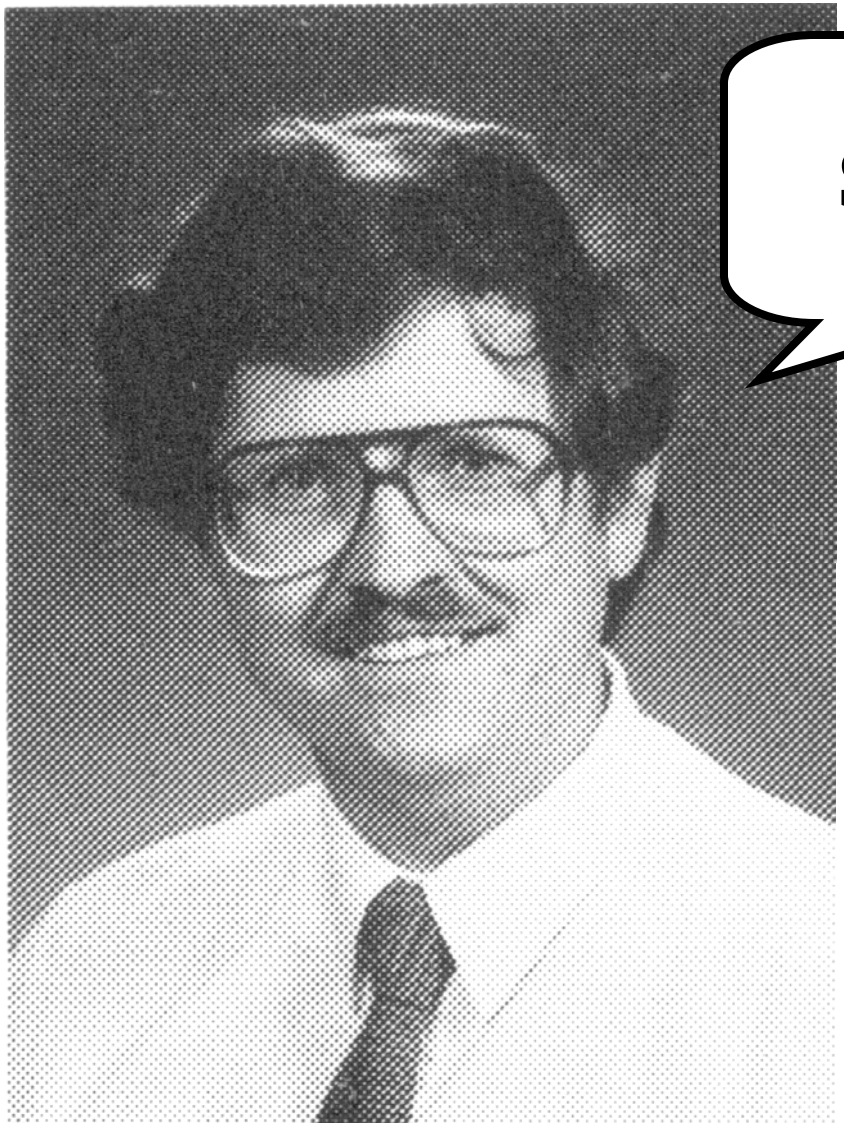
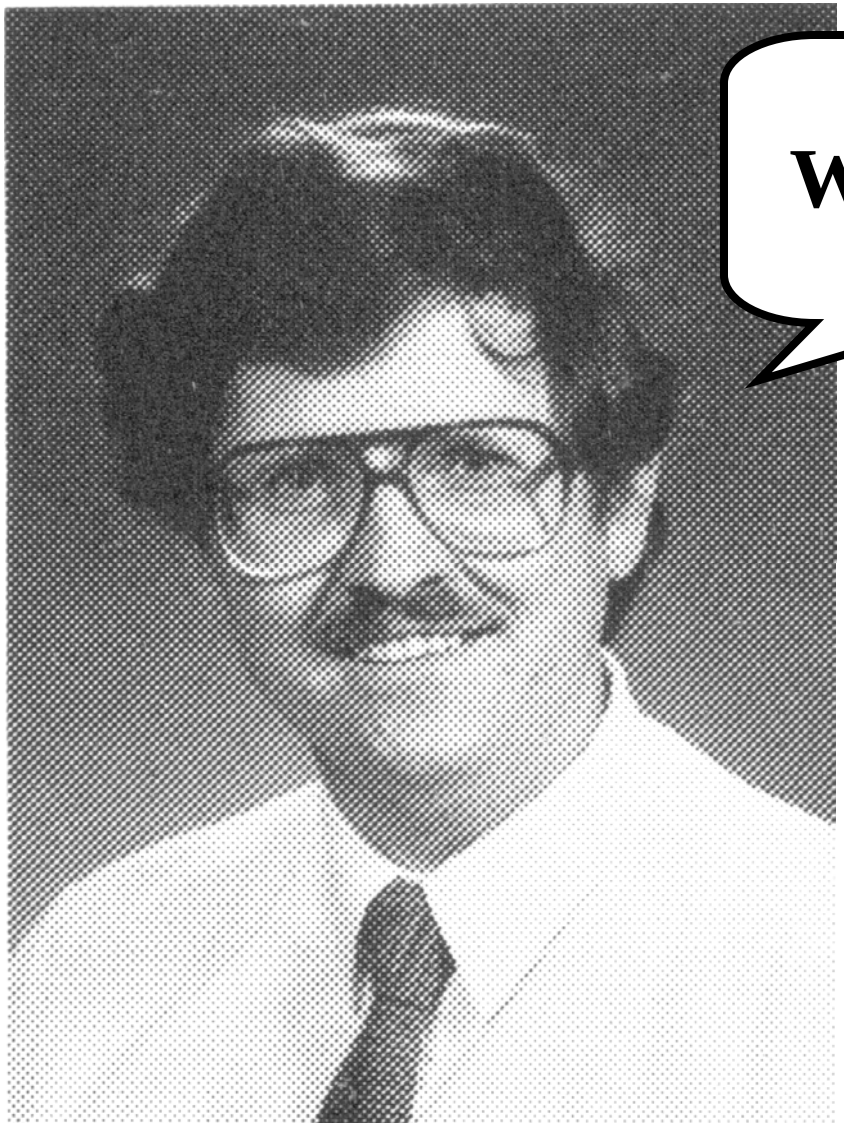
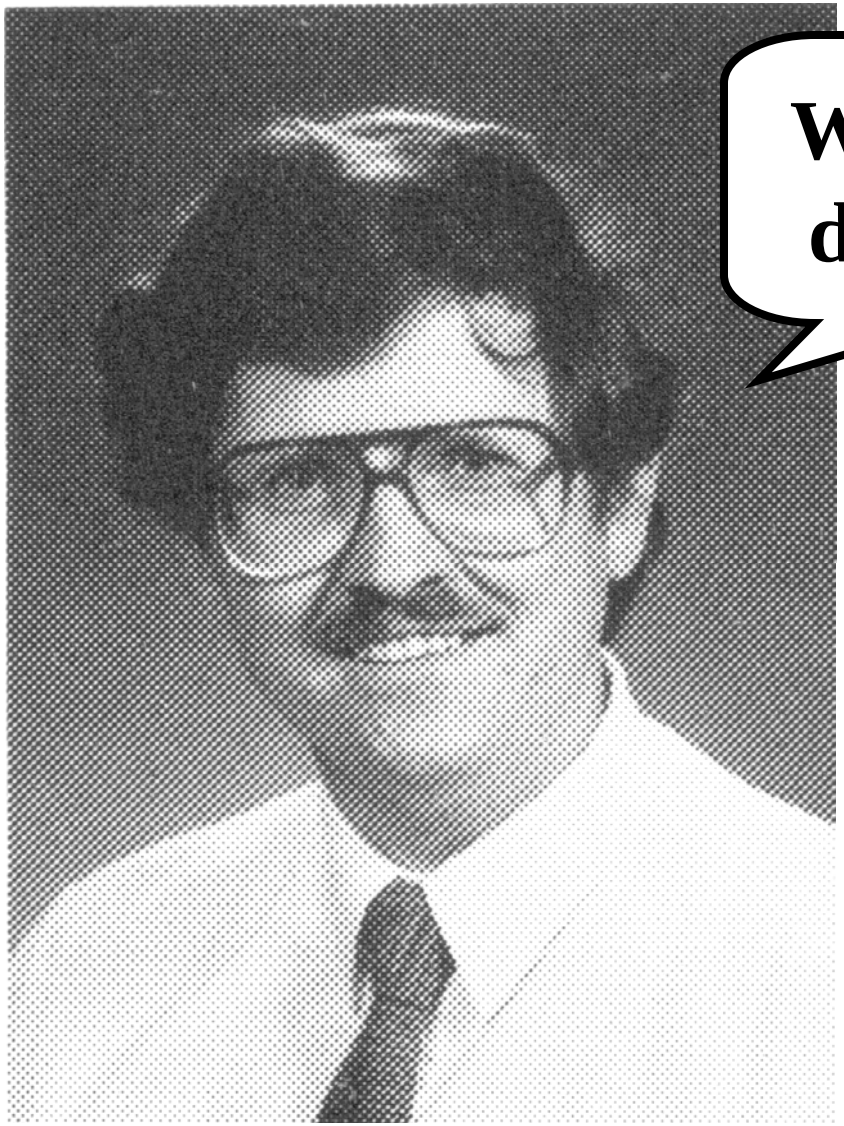


Image θ = **10** °




So what?

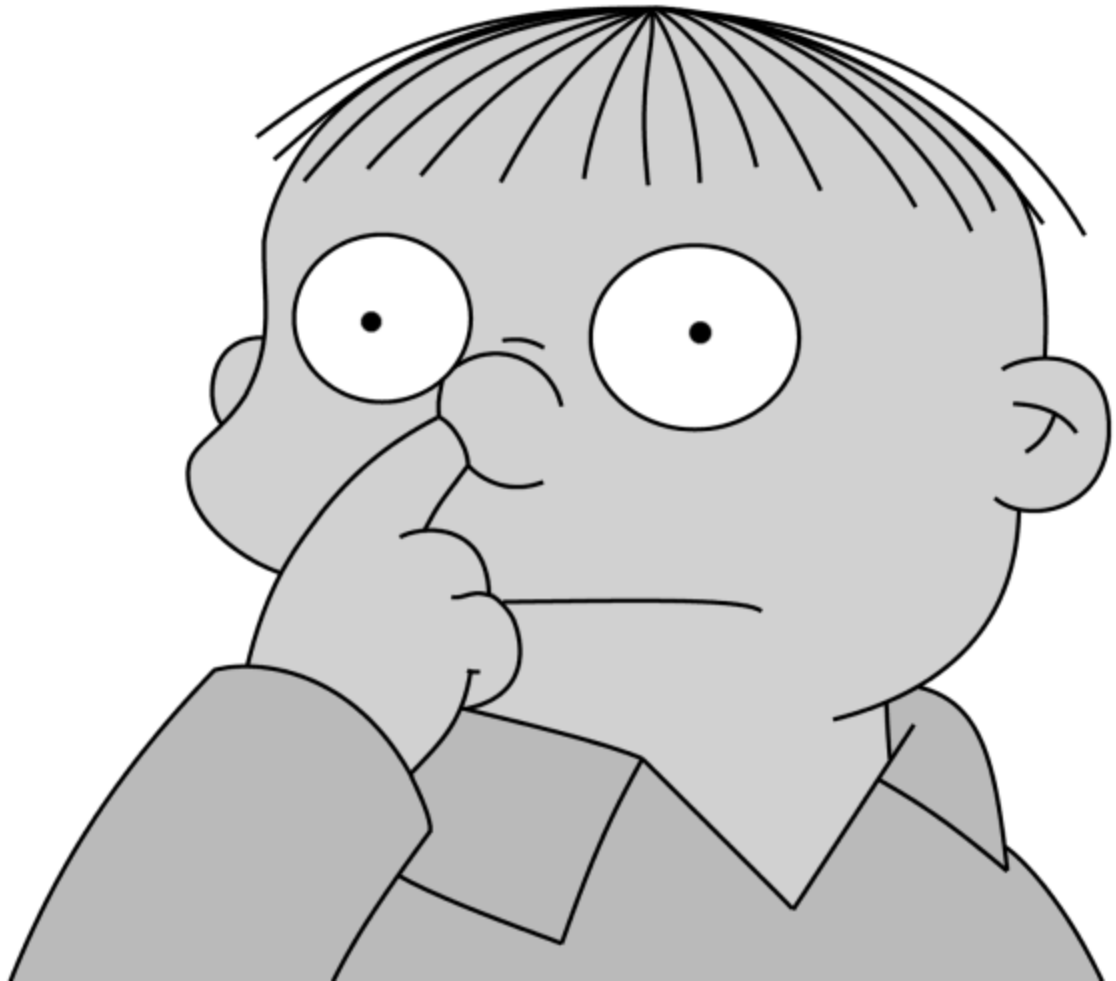

Who cares?


Why are we doing this?

The big picture

- **Evolution of sensory system**
- **Evolution of neural computations**
- **Restoration of human eyesight**

But you’re special…



Physics is everywhere!

But *I* don't need physics…

How to know if you need physics

How to know if you need physics

- **Does your research discipline focus on part of the physical, natural world?**

How to know if you need physics

- **Is your study system made of matter or energy?**

How to know if you need physics

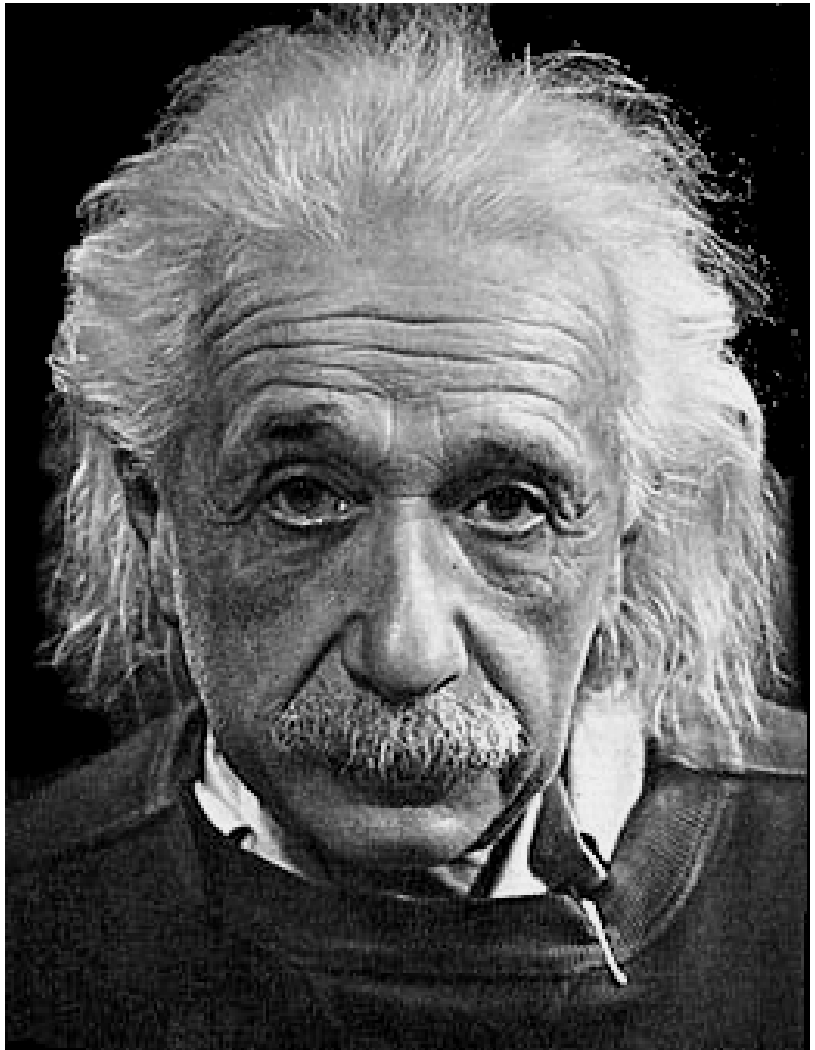
- Do you use any physical equipment in your research?

If you answered yes to any of these questions, then you need physics!

Physics is not irrelevant!

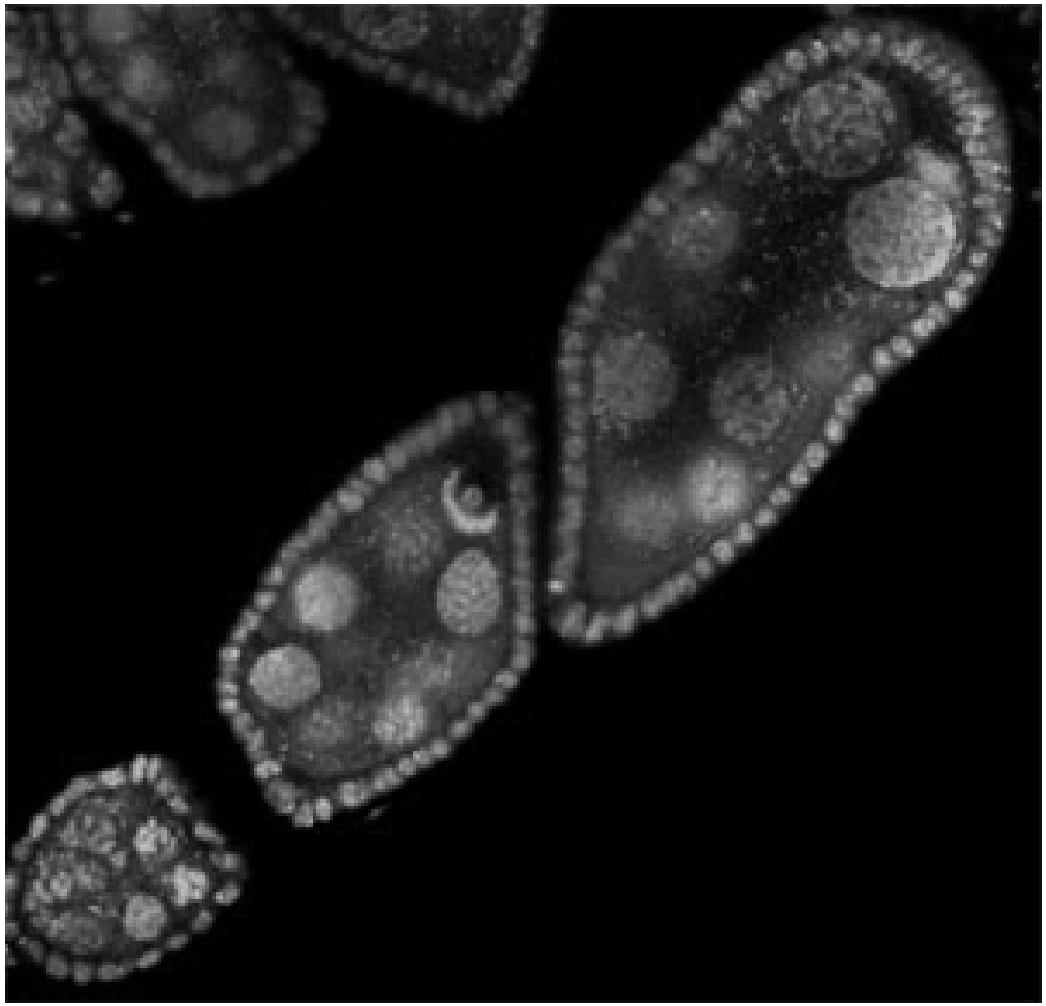
- **The laws of physics govern the actions and interactions of everything in the natural world**

PHYSICS CHALLENGE!

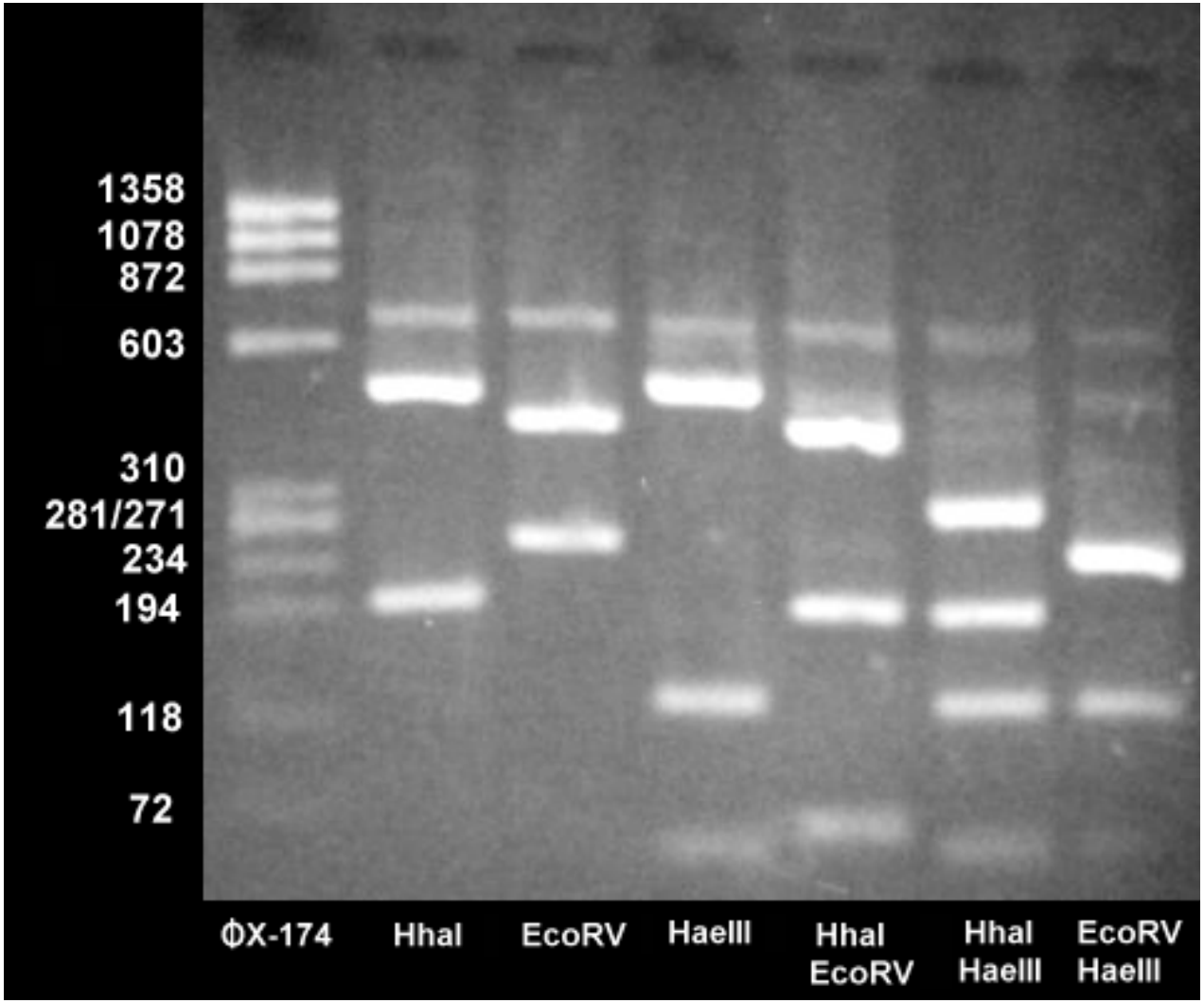


Bring it!

Cell biologist



Molecular geneticist



Agriculture specialist

Microbiologist

Mammalogist

Physics in biological research

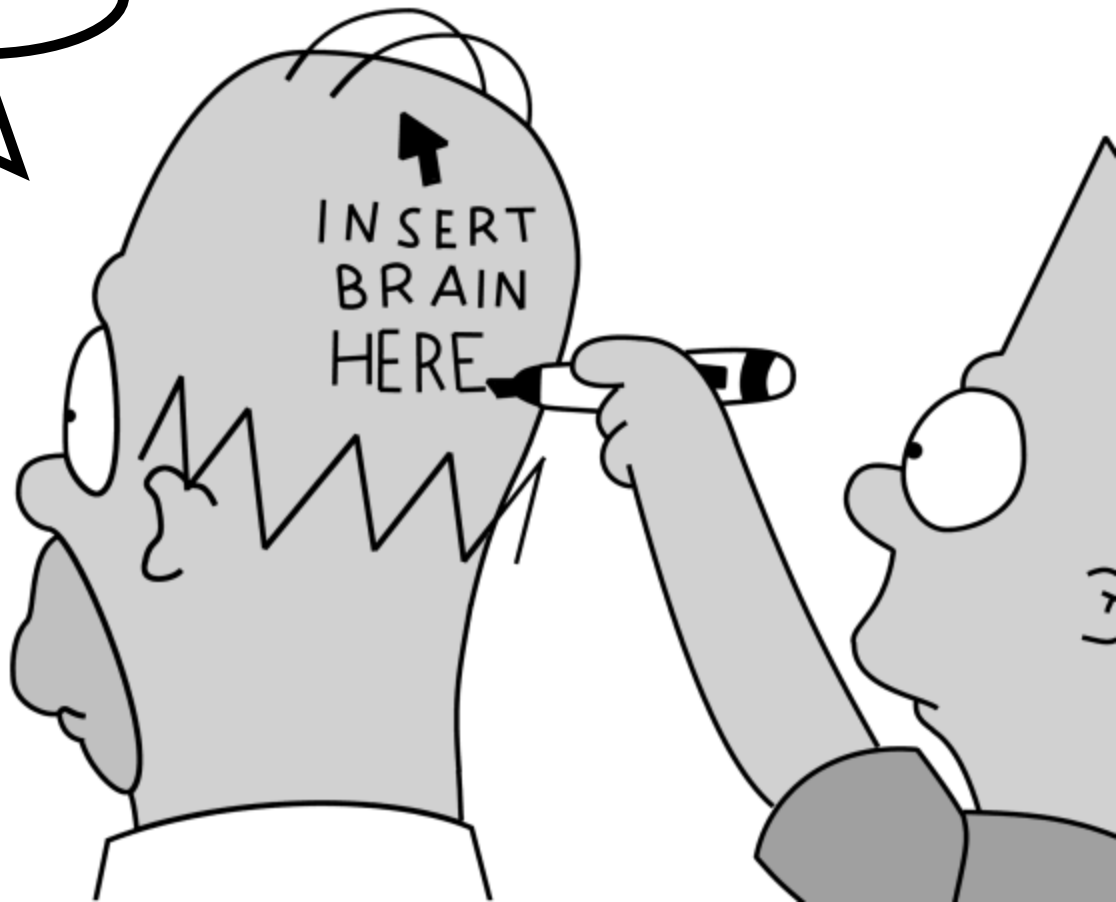
- **Governs physical interactions between all molecules**

- **Dictates the movement of all energy forms**

Physics in biological research

- Governs how your equipment works
- Explains what your machine is telling you
- Allows you to more completely interpret result

But me no so smart, Dr. K…



Ignorance of physics can lead to

- Failure to obtain usable results
- Limits on experimental design
- Inability to troubleshoot
- Errant rejection of results
- Errant acceptance of results

It takes a big man to apologize…


Luke, I am your doctor…

Medicine – issues and misconceptions

- **Medicine is the default career for science students**

When I grow up, I'm going to doctor school!

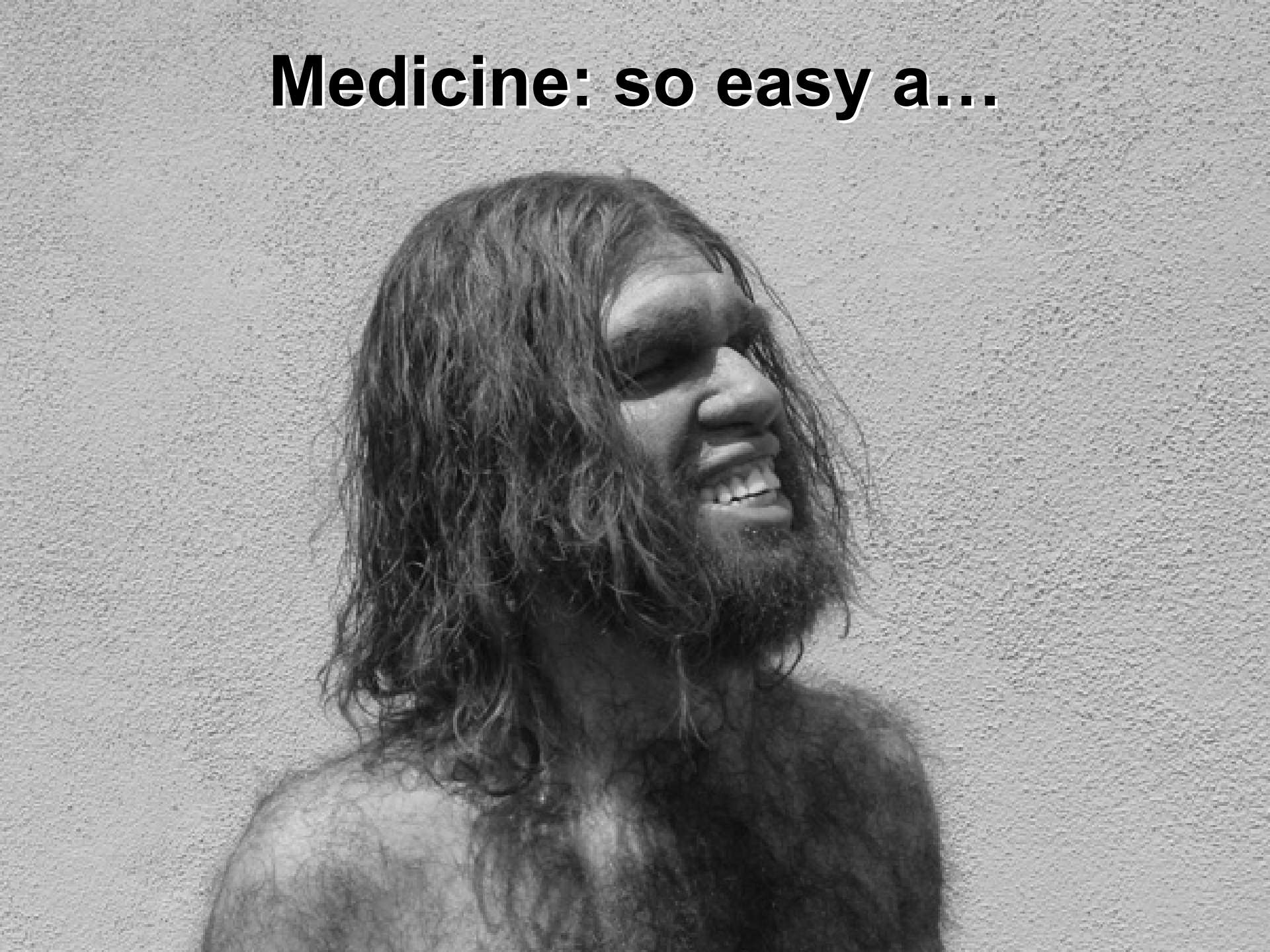
Medicine – issues and misconceptions

- **A successful career in hinges in an encyclopedic fluency in biology and *ONLY* biology.**

Medicine – issues and misconceptions

- **Medicine is not a scientific discipline**

Medicine: so easy a…



The truth behind medicine

- **Success as a physician actually requires**
  - Proficiency in the hypotheticdeductive method
  - Fluency in multiple scientific disciplines, including physics!

A personal tale…

Initial case facts and symptoms

- **A 32 year old male, 5’8, 180 lbs, enters the ER complaining of difficulty breathing, tightness in chest and numbness in the extremities**

- **No history of respiratory issue, cardiovascular illness or allergy**

Initial case facts and symptoms

- **Patient spent recently 4 days at altitude in Sandy, UT**

- **Patient flew recently (2, 4 hr flights, 4 days apart)**

Scientific inquiry and medicine

- **Observation: patient has difficulty breathing, tightness in chest and numbness in the extremities**

Scientific inquiry and medicine

- **Observation: patient has difficulty breathing, tightness in chest and numbness in the extremities**

- **Hypothesis:**

Scientific inquiry and medicine

- **Observation: patient has difficulty breathing, tightness in chest and numbness in the extremities**

- **Hypothesis: Patient has an obstruction in the pulmonary vasculature precluding normal gas exchange**

Scientific inquiry and medicine

- **Hypothesis: Patient has an obstruction in the pulmonary vasculature precluding normal gas exchange**

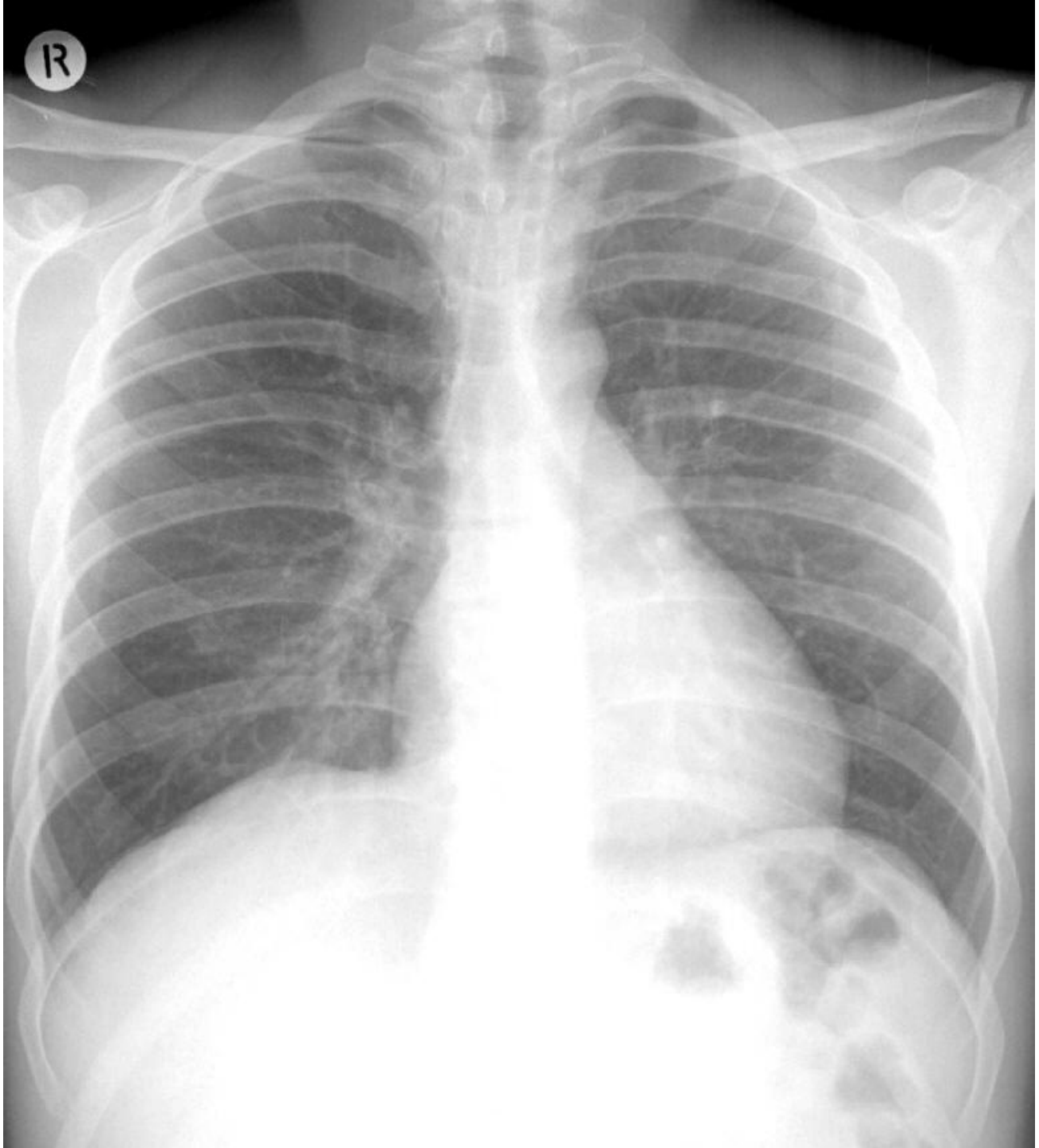
- **Prediction: *IF* the patient has an obstruction, *THEN* it should be visible with proper imaging techniques**

What test do we do first?

X-ray

X-ray

- **Use λ 10 to 0.01nm (30 x 10^{15}- 30 10^{18} Hz)**
- **Penetrate lung tissue, absorbed by bones**
- **Expose a photographic plate**


R

Scientific inquiry and medicine

- **Hypothesis: Patient has an obstruction in the pulmonary vasculature preclude normal gas exchange**

- **Prediction: *IF* the patient has an obstruction, *THEN* it should be visible with proper imaging techniques**

What can we conclude from our test results?

- **Conclusion:**

What can we conclude from our test results?

- **Conclusion: The patient does not have an obstruction in the pulmonary vasculature preclude normal gas exchange**

What can we conclude from our test results?

- Conclusion: The patient does not have an obstruction in the pulmonary vasculature preclude normal gas exchange

What can we conclude from our test results?

What can we conclude from our test results?

Not

What can we conclude from our test results?

Not a

What can we conclude from our test results?

Not a DAMN

What can we conclude from our test results?

Not a DAMN thing

Shortcomings of X-rays

- **Wavelength**
- **Intensity**
- **Variability in penetration**
- **Spatial resolution**

What test should we do instead?

- High spatial resolution
- More broad tissue penetration
- Differential tissue absorbency

CT with contrast

CT with contrast

- **Uses contrast dye**
  - **Generally iodine-based dyes**
- **Allows fine-level distinguishing among tissues**
- **Increases spatial resolution, detail**

Actual CT-contrast data

Scientific inquiry and medicine

- **Hypothesis: Patient has an obstruction in the pulmonary vasculature preclude normal gas exchange**

- **Prediction: *IF* the patient has an obstruction, *THEN* it should be visible with proper imaging techniques**

What can we conclude from our test results?

- **Conclusion:**

What can we conclude from our test results?

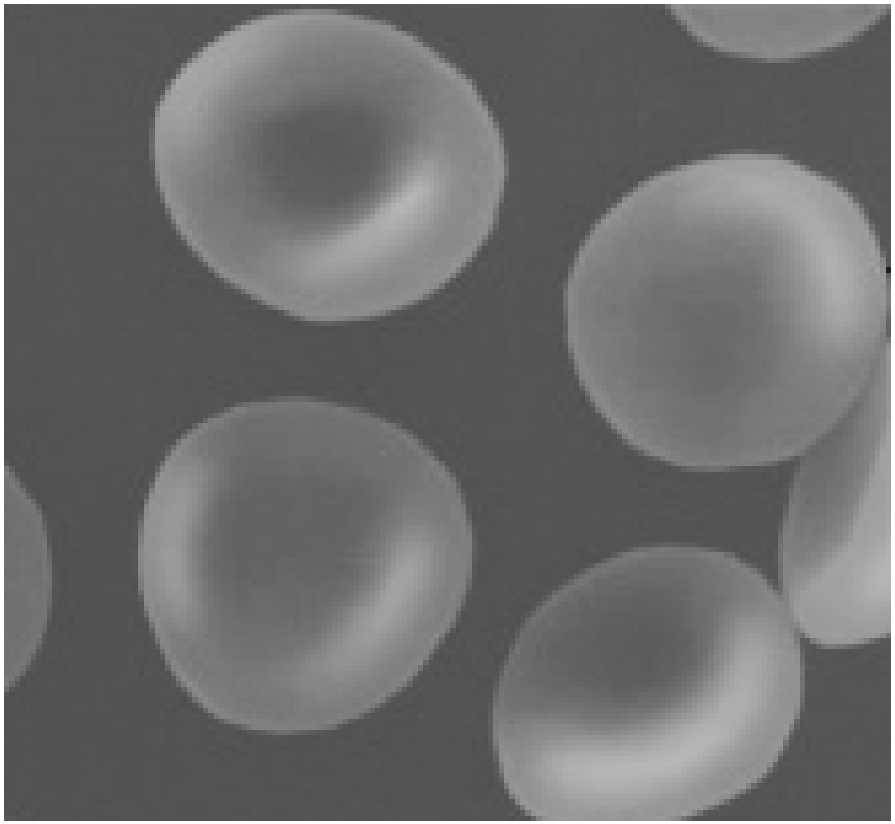
- **Conclusion: The patient does not have an obstruction in the pulmonary vasculature preclude normal gas exchange**

What can we conclude from our test results?

- **Conclusion: The patient does not have an obstruction in the pulmonary vasculature preclude normal gas exchange**

So where / what might the pathology be?

Blood



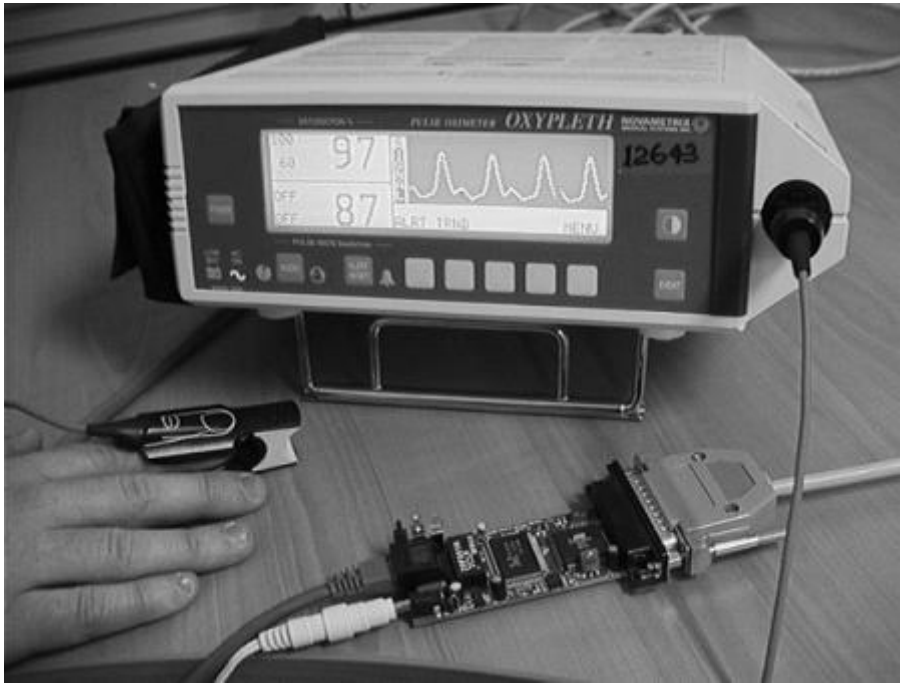
Scientific inquiry and medicine

- **Hypothesis: Patient's difficulty breathing results from decreased O_2 carrying capacity of blood**

- **Prediction: *IF* the patient has a decrease in O_2 carrying capacity of blood, *THEN* his blood should have low O_2 levels**

How can we measure O_2 in blood?

Pulse oximeter



Pulse oximeter

- **Measures O_2 saturation using LEDs**
  - One LED is red (660 nm), the other is infrared, (905 - 940 nm)

- **Compares absorption in both wavelengths to calculate % bound hemoglobin**

Pulse oximeter - results

- **The pulse oximeter results indicate that the patient's blood is 98%-100% saturated with O_2.**

Scientific inquiry and medicine

- **Hypothesis: Patient's difficulty breathing results from decreased O_2 carrying capacity of blood**

- **Prediction: *IF* the patient has a decrease in O_2 carrying capacity of blood, *THEN* his blood should have low O_2 levels**

What can we conclude from our test results?

- **Conclusion:**

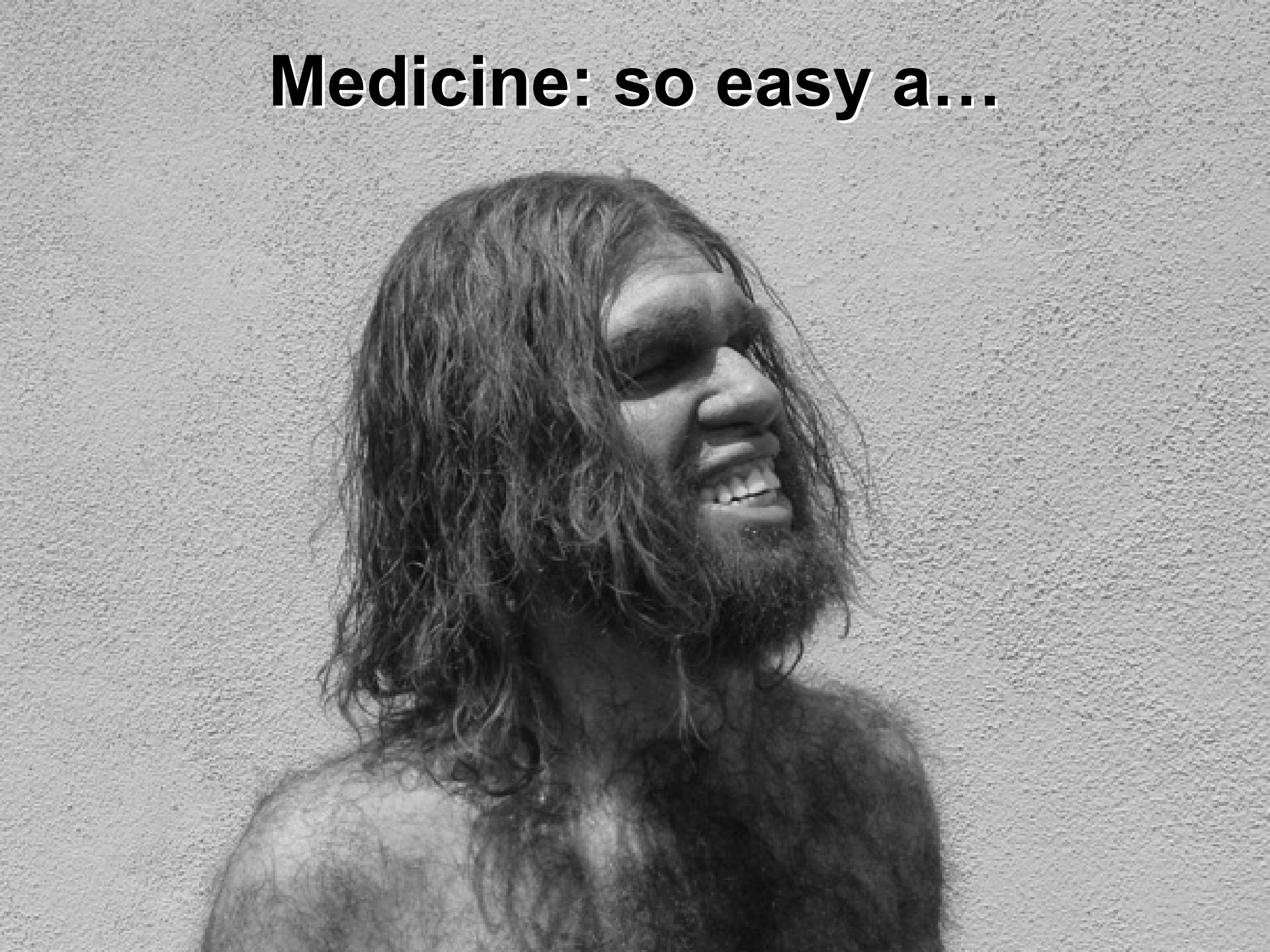
What can we conclude from our test results?

- **Conclusion: Patient's difficulty breathing <u>is not</u> a result of decreased O_2 carrying capacity of blood**

What can we conclude from our test results?

- Conclusion: Patient's difficulty breathing is <u>not</u> a result of decreased O_2 carrying capacity of blood

Medicine: so easy a…



What can we conclude from our test results?

- We want to know how much O_2 is in the blood

What can we conclude from our test results?

- We want to know how much O_2 is in the blood

- We use light to measure how much Hb is bound.

What can we conclude from our test results?

- We want to know how much O_2 is in the blood

- We measure bound Hb, not O_2!

What can we conclude from our test results?

- We want to know how much O_2 is in the blood

- We measure bound Hb, not O_2!

What else could Hb be bound to?

What do we do now?

Blood gas

- **Take blood sample from patient**
- **Make direct measurement of O_2 in blood**

Blood gas

- **Take blood sample from patient**
- **Make direct measurement of O_2 in blood**

Blood gas measurements read

100% saturated!

What can we conclude from our test results?

- **Conclusion: Patient's difficulty breathing <u>is not</u> a result of decreased O_2 carrying capacity of blood**

What can we conclude from our test results?

- **Conclusion: Patient's difficulty breathing <u>is not</u> a result of decreased O_2 carrying capacity of blood**

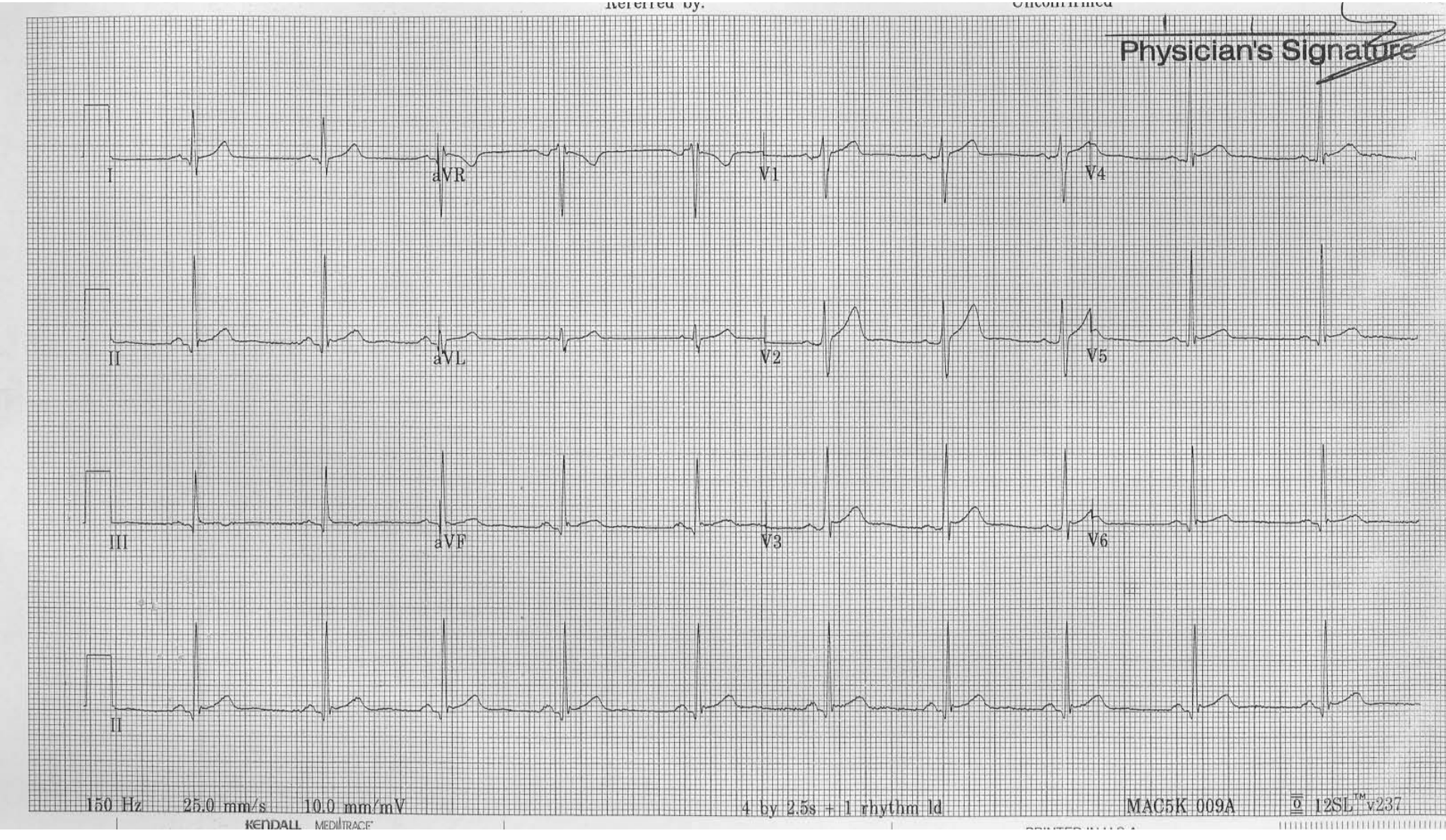
So where / what might the pathology be?

Scientific inquiry and medicine

- **Hypothesis: Cardiac pathology is responsible for symptoms**

- **Prediction: *IF* the patient has a cardiac pathology, *THEN* it should be visible with proper imaging techniques**

Electrocardiogram



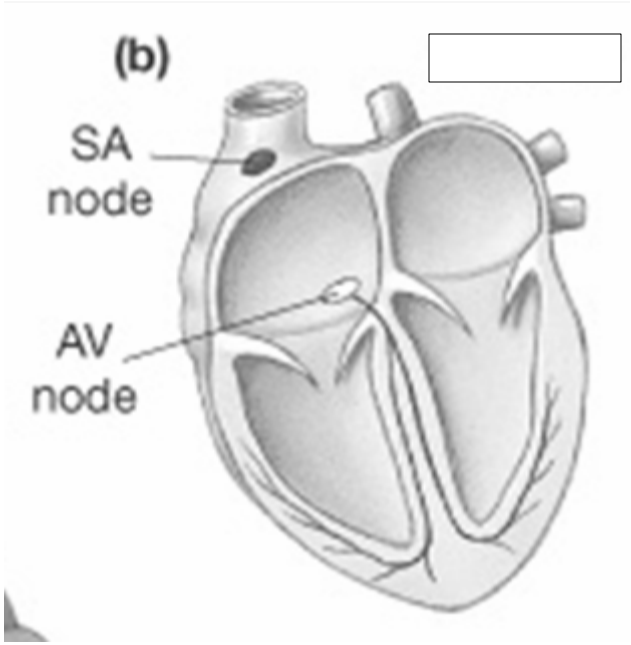
Heartbeat is electrical!

Heartbeat is electrical!

- **Electrical stimulation**
  - Drives heartbeat
  - Originates in heart itself
    - Autorhythmic cells

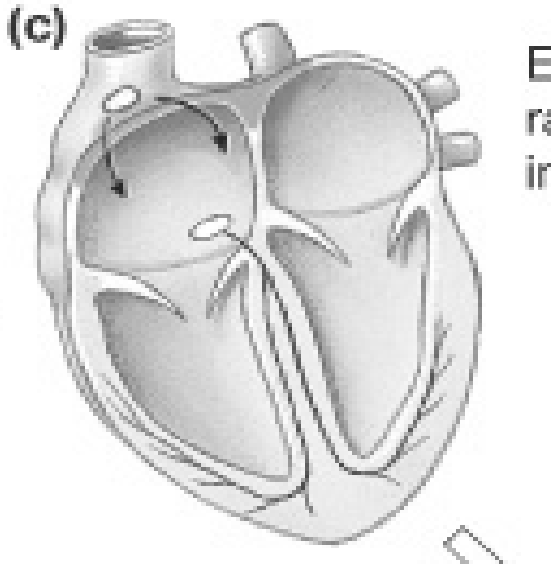
Steps in Electrical Conduction

- **Sinoatrial (SA) node depolarizes**



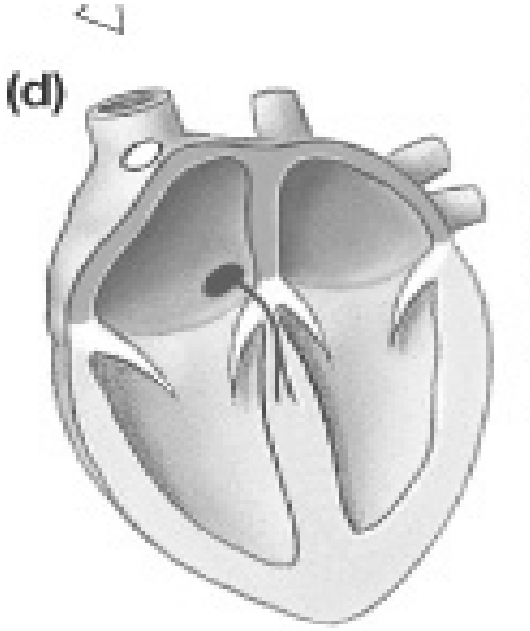
Steps in Electrical Conduction

- **Depolarization travels through internodal pathway**



Steps in Electrical Conduction

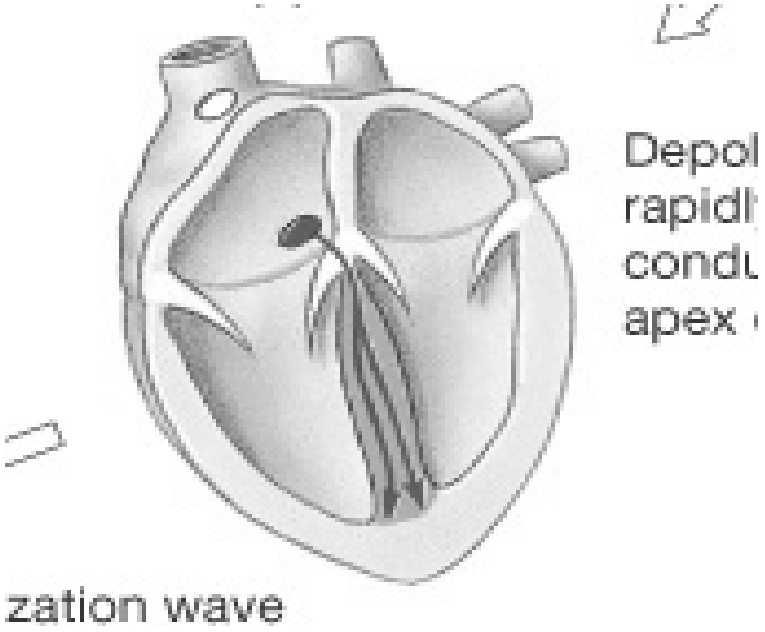
- **Depolarization reaches atrioventricular (AV) node**



ATRIA CONTRACT

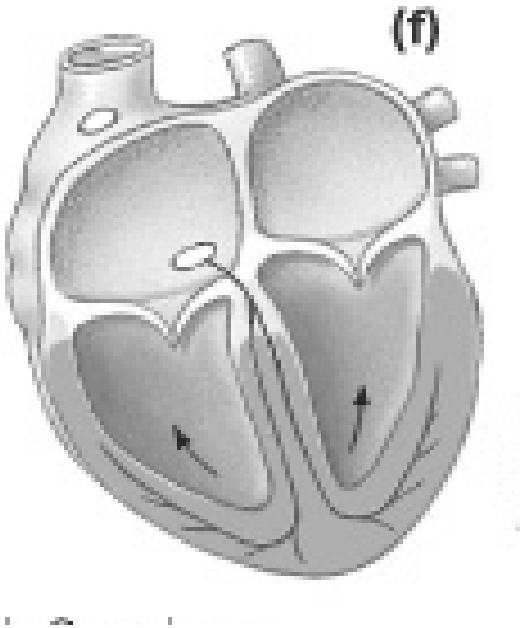
Steps in Electrical Conduction

- **Depolarization enters bundle of His**



Steps in Electrical Conduction

- **Depolarization enters purkinje fibers**
  - **Envelop apex of ventricles**

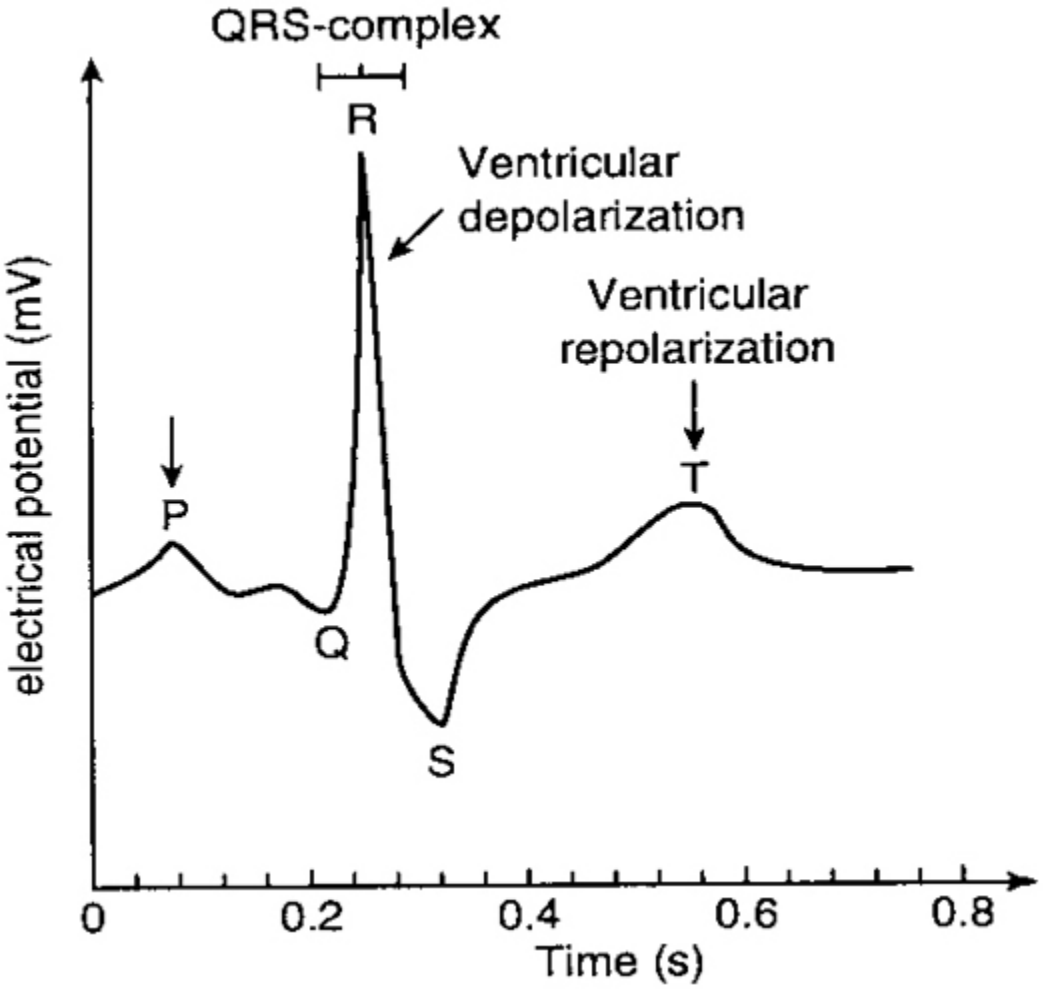


VENTRICLES CONTRACT

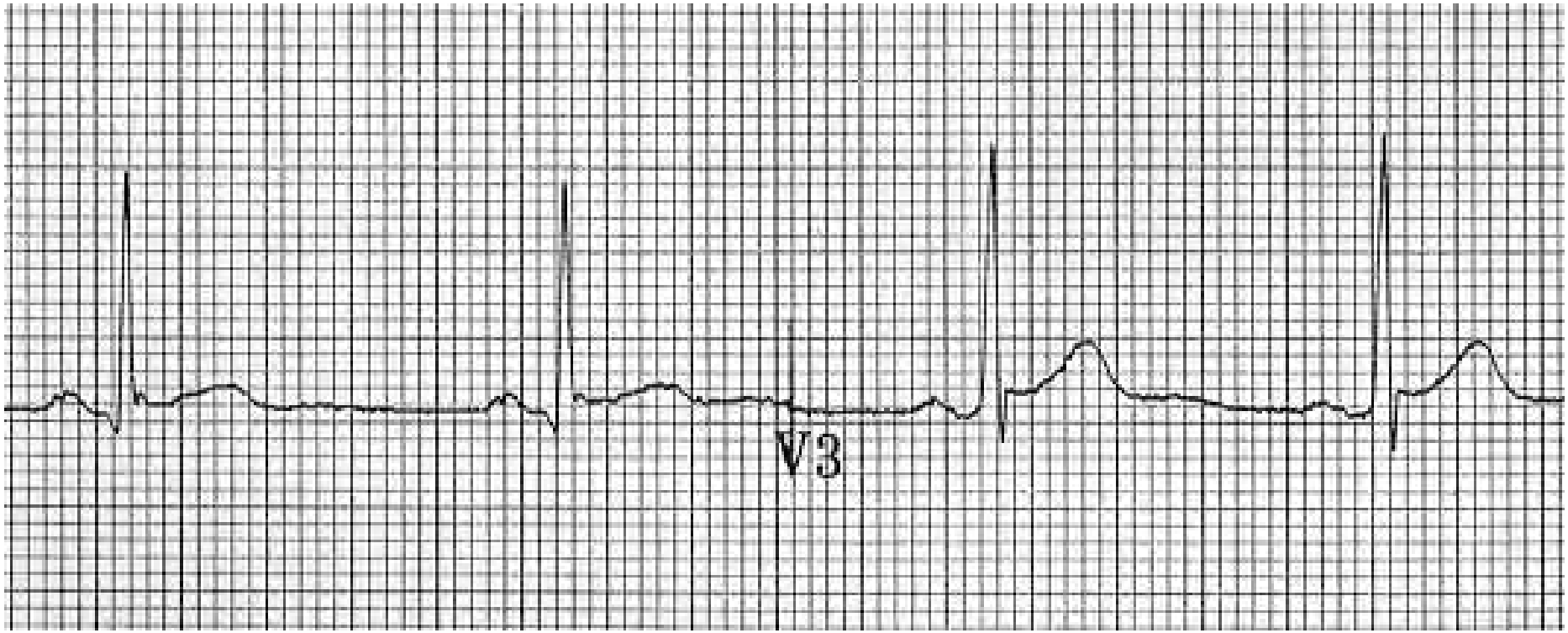
Electrocardiogram

- **Measures voltage differences across the heart throughout cycle of contractions**
- **Takes on characteristic wave form**
- **Can be used to indirectly observe pathological cardiac function**

Electrocardiogram explained



Electrocardiogram results



Vent. rate	63 bpm
PR interval	144 ms
QRS duration	88 ms
QT/QTc	374/382 ms
P-R-T axes	56 66 37

Normal sinus rhythm
ST elevation, consider early repolarization, pericarditis, (
Abnormal ECG

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KROCHMAL, AARON R
M 032Y DOB 09/11/74
04/26/07
GINDY ADEL M

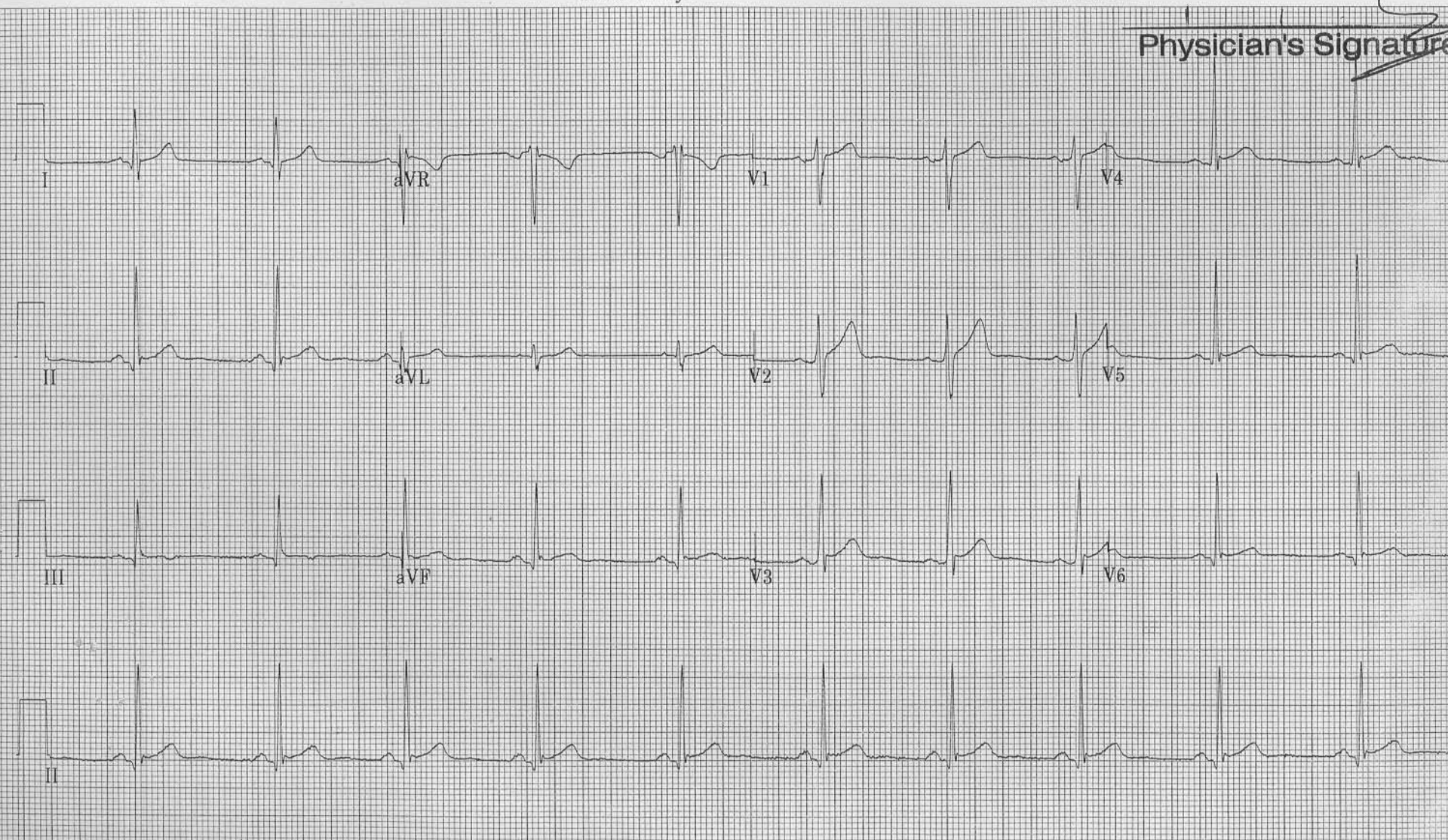
Technician:
Test ind:

(Final Report When Sign

Referred by:

Unconfirmed

Physician's Signature

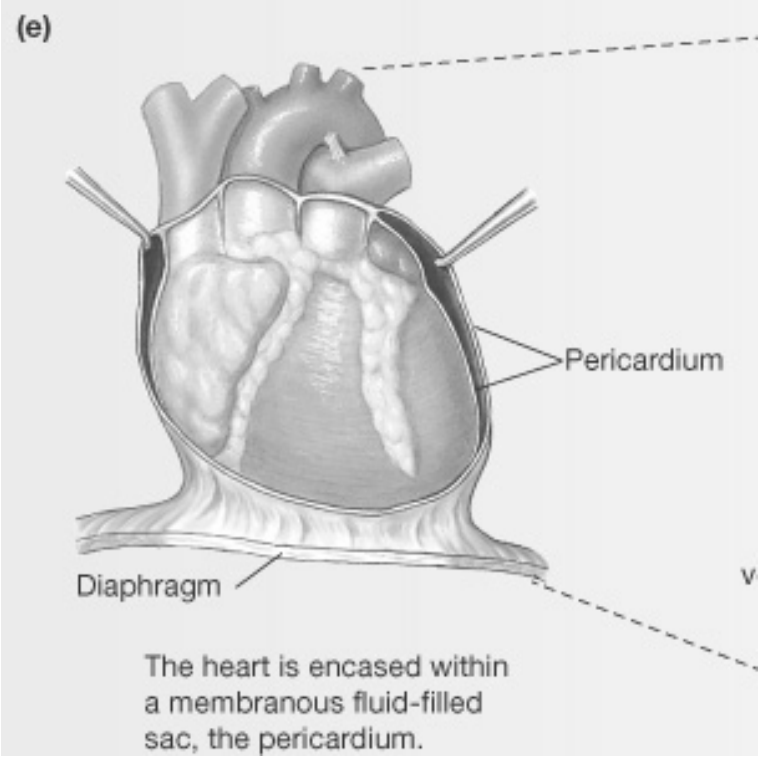


Electrocardiogram results

- **Readout indicates possible pericarditis**

Cardiac Anatomy – an aside

- **Pericardium**
  - Membranous sac containing heart



Electrocardiogram results

- Readout indicates possible pericarditis
- CT; X-ray rule out pericarditis


Whut duh hell?

Scientific inquiry and medicine

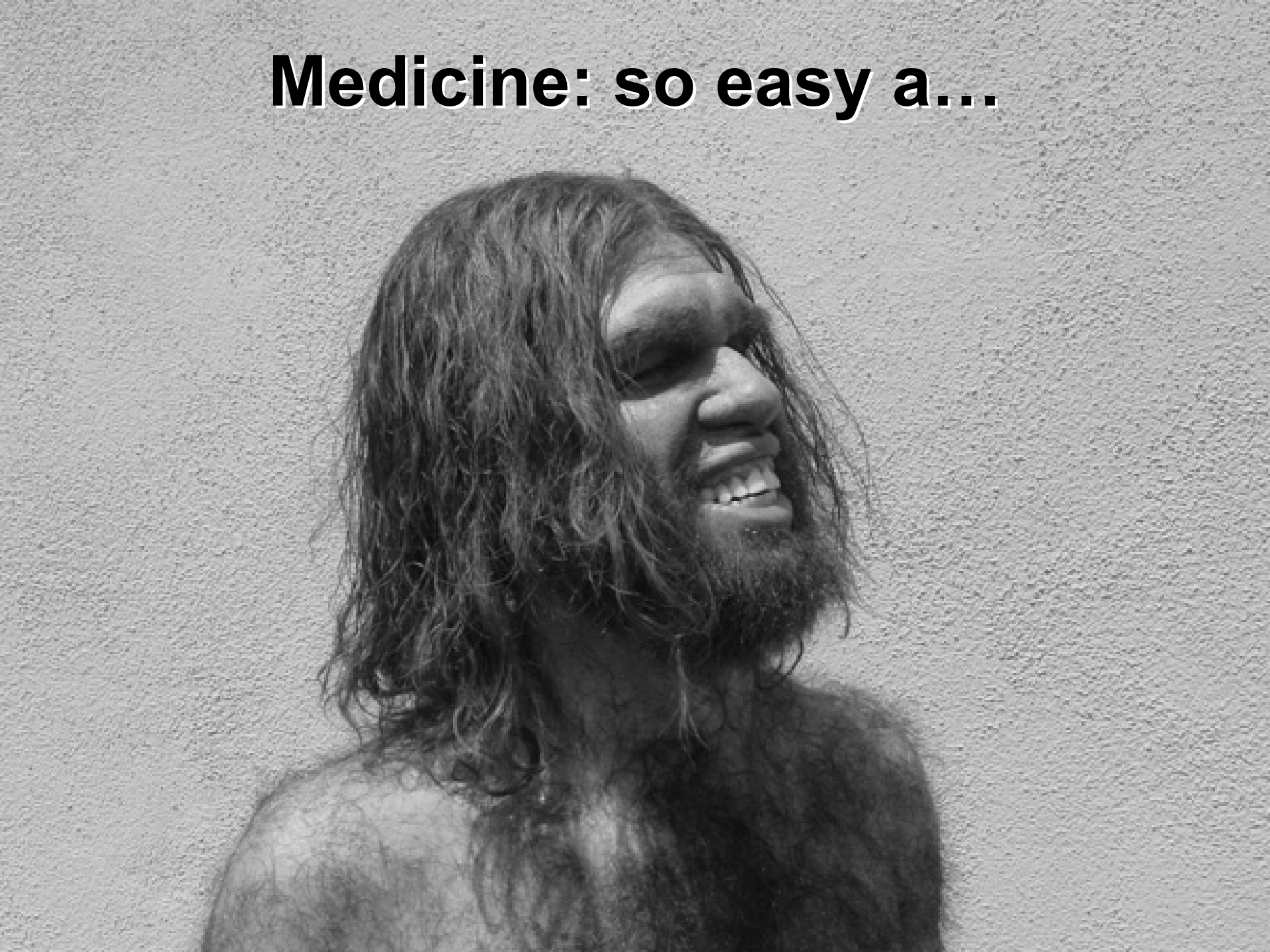
- **Hypothesis: Cardiac pathology is responsible for symptoms**

- **Prediction: *IF* the patient has a cardiac pathology, *THEN* it should be visible with proper imaging techniques**

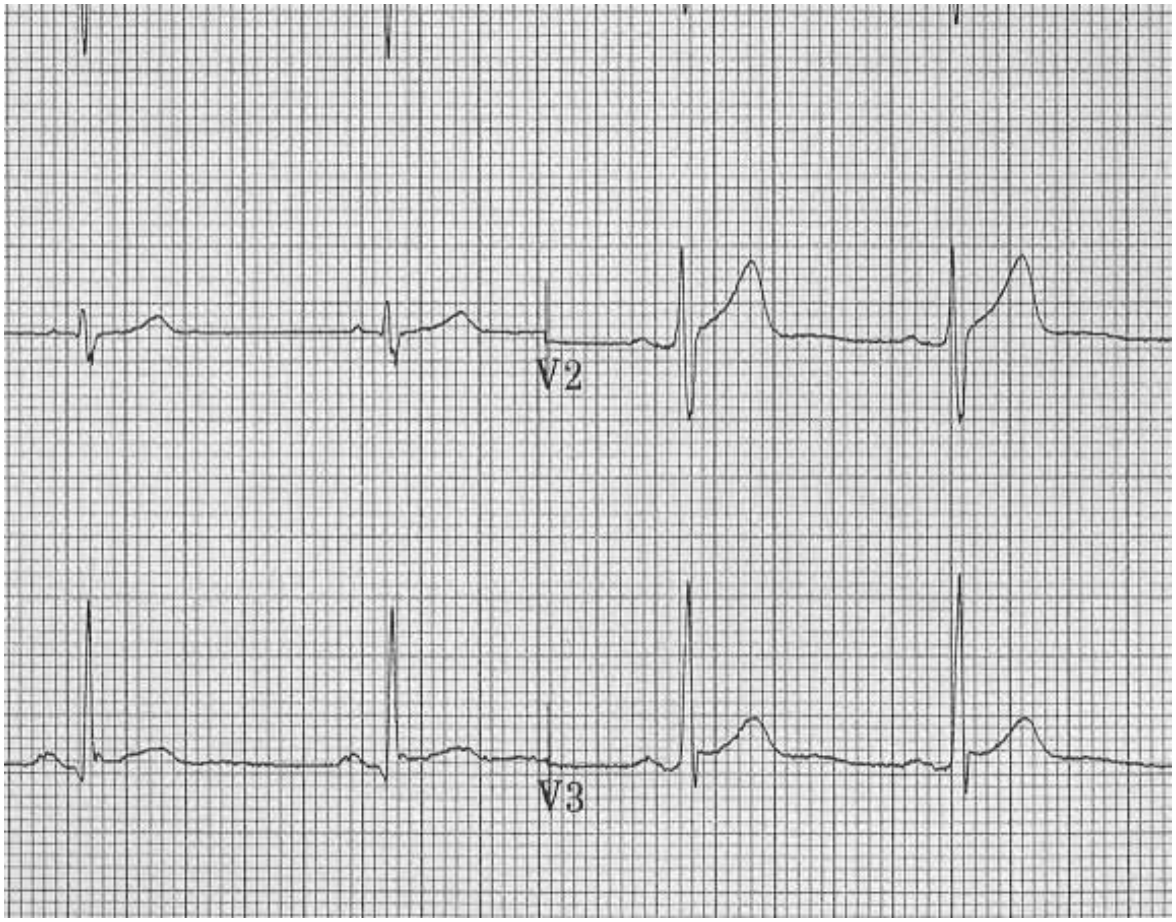
What can we conclude from our test results?

- **Conclusion: Patient's pathology**
- **<u>is not</u> a result of cardiac issue**

Medicine: so easy a…



Electrocardiogram results



Electrocardiogram – revisited

- **Voltage – the potential energy of an electric field**
- **Current –**
- **Resistance –**

Electrocardiogram – revisited

- **Voltage – the potential energy of an electric field**
- **Current – the flow of electric charge; the potential energy of an electric field**
- **Resistance –**

Electrocardiogram – revisited

- **Voltage – the potential energy of an electric field**
- **Current – the flow of electric charge; the potential energy of an electric field**
- **Resistance – the degree to which an object opposes an electric current**

Electrocardiogram – revisited

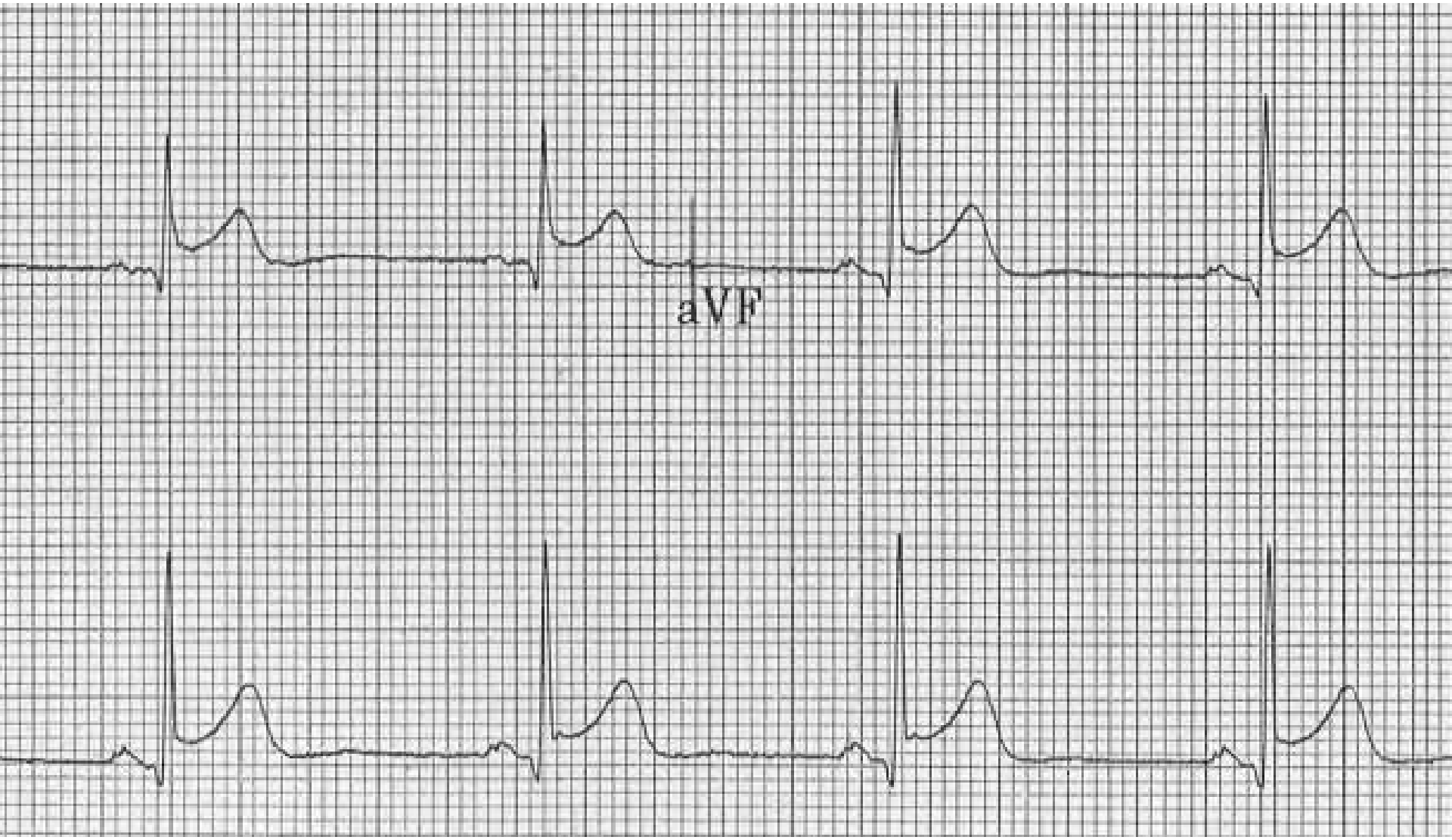
$$V = I \times R$$

Electrocardiogram – revisited

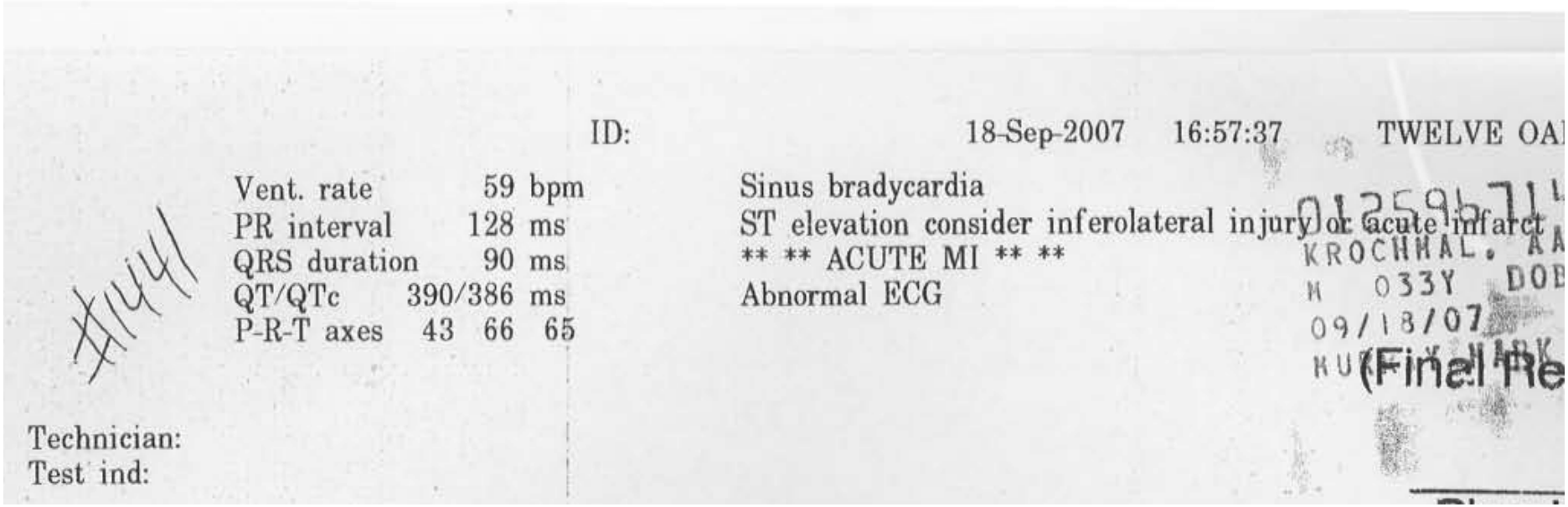
$$V = I \times R$$

How do we see an increase in voltage?

Electrocardiogram results - 2



Electrocardiogram results - 2



ID:

18-Sep-2007 16:57:37 TWELVE OA

Vent. rate	59 bpm
PR interval	128 ms
QRS duration	90 ms
QT/QTc	390/386 ms
P-R-T axes	43 66 65

Sinus bradycardia
ST elevation consider inferolateral injury or acute infarct
** ** ACUTE MI ** **
Abnormal ECG

KROCHHAL. AA
M 033Y DOB
09/18/07
(Final Re

Technician:
Test ind:

Scientific inquiry and medicine

- **Hypothesis: Patient's is experiencing inferolateral cardiac injury / infarction**

- **Prediction: *IF* the patient is experiencing inferolateral cardiac injury / infarction *THEN* a vascular blockage must be present**

Angiogram

- **Is a medical imaging technique in which an X-ray picture is taken to visualize the lumen of vasculature**

- **Uses contrast die to highlight blood flow or lack thereof F**

Angiogram results

Scientific inquiry and medicine

- **Hypothesis: Patient's is experiencing inferolateral cardiac injury / infarction**

- **Prediction: *IF* the patient is experiencing inferolateral cardiac injury / infarction *THEN* a vascular blockage must be present**

What can we conclude from our test results?

- **Conclusion: Patient's pathology is a experiencing inferolateral cardiac injury / infarction**


AW CRAP!

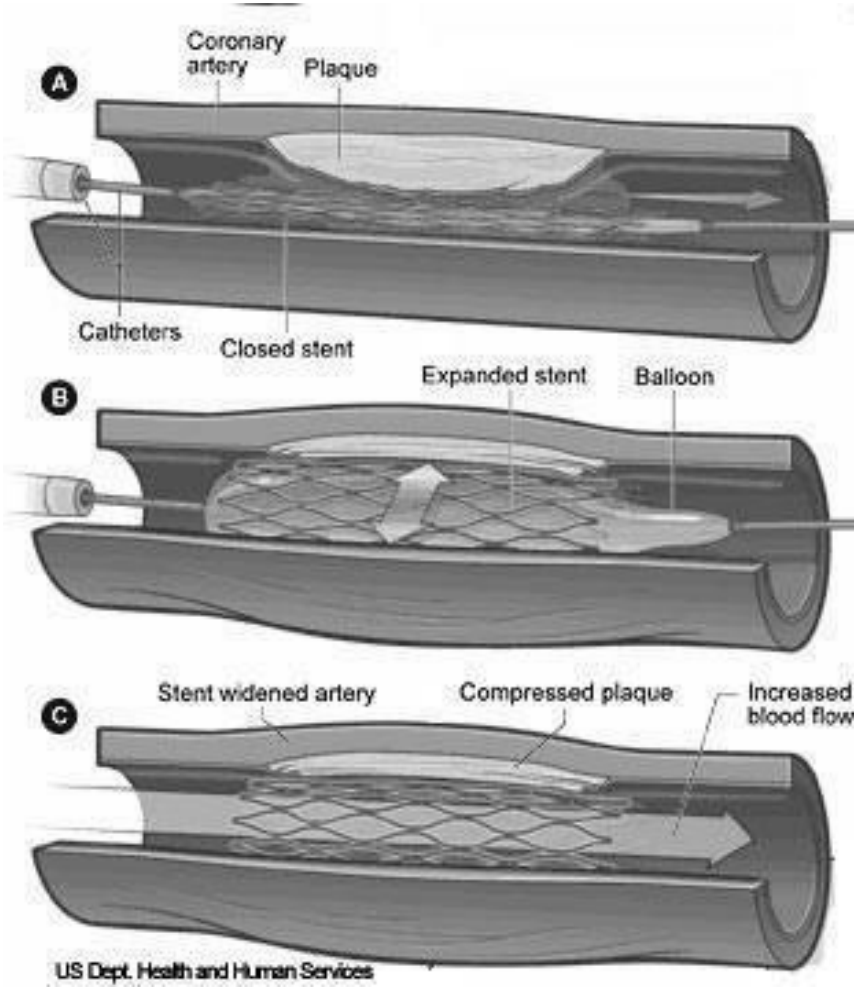
Scientific inquiry and medicine

- **Hypothesis: Patient's is experiencing inferolateral cardiac injury / infarction**

- **Prediction 2: *IF* the patient is experiencing inferolateral cardiac injury / infarction *THEN* removing the blockage will reverse the pathology**

PTCA - Stent

- Percutaneous Transluminal Coronary Angioplasty
  - Catheter inserted into blood vessel in legs and snaked into coronary vasculature
  - Plaques in coronary areteries “removed” via balloon inflation
  - Stent implanted to maintain open aretry


A
Coronary artery
Plaque
Catheters
Closed stent
B
Expanded stent
Balloon
C
Stent widened artery
Compressed plaque
Increased blood flow
US Dept. Health and Human Services

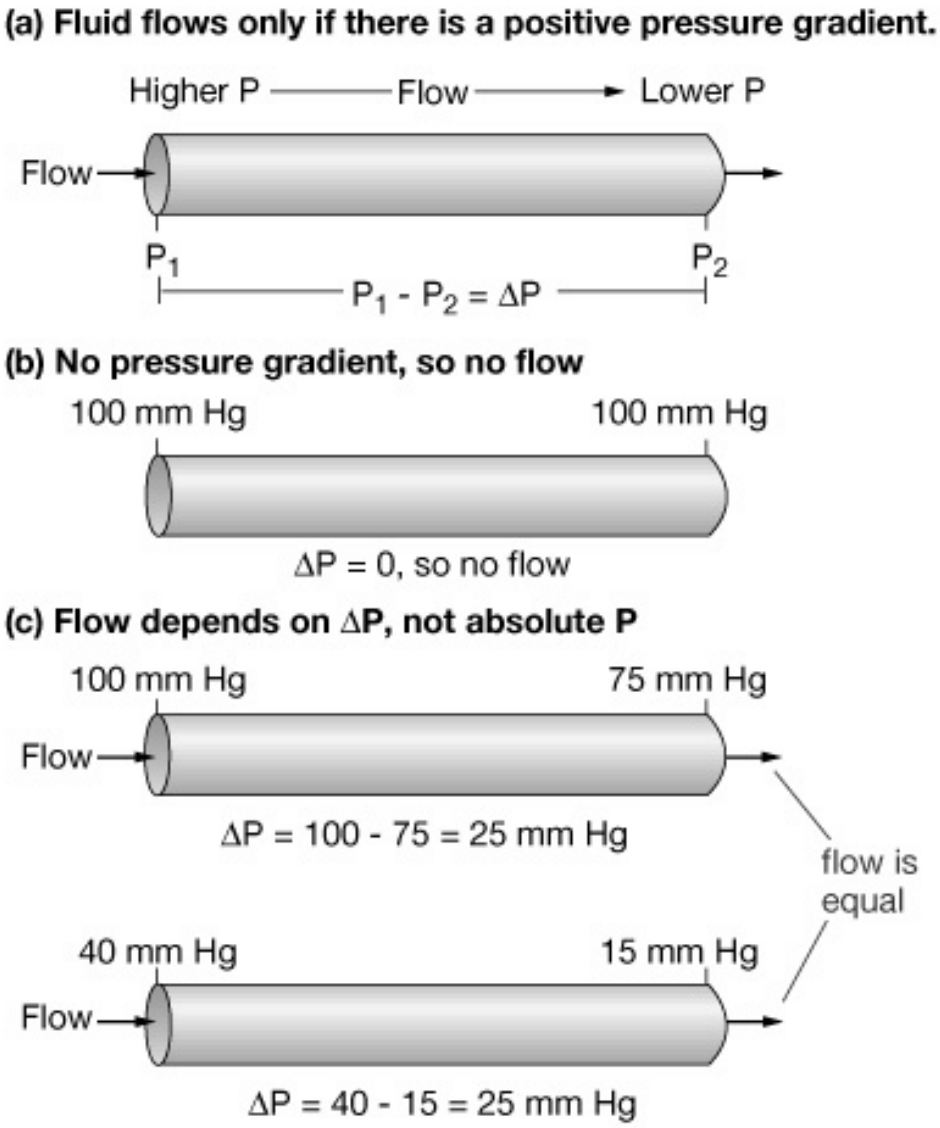
Resistance Opposes Flow

Resistance Opposes Flow

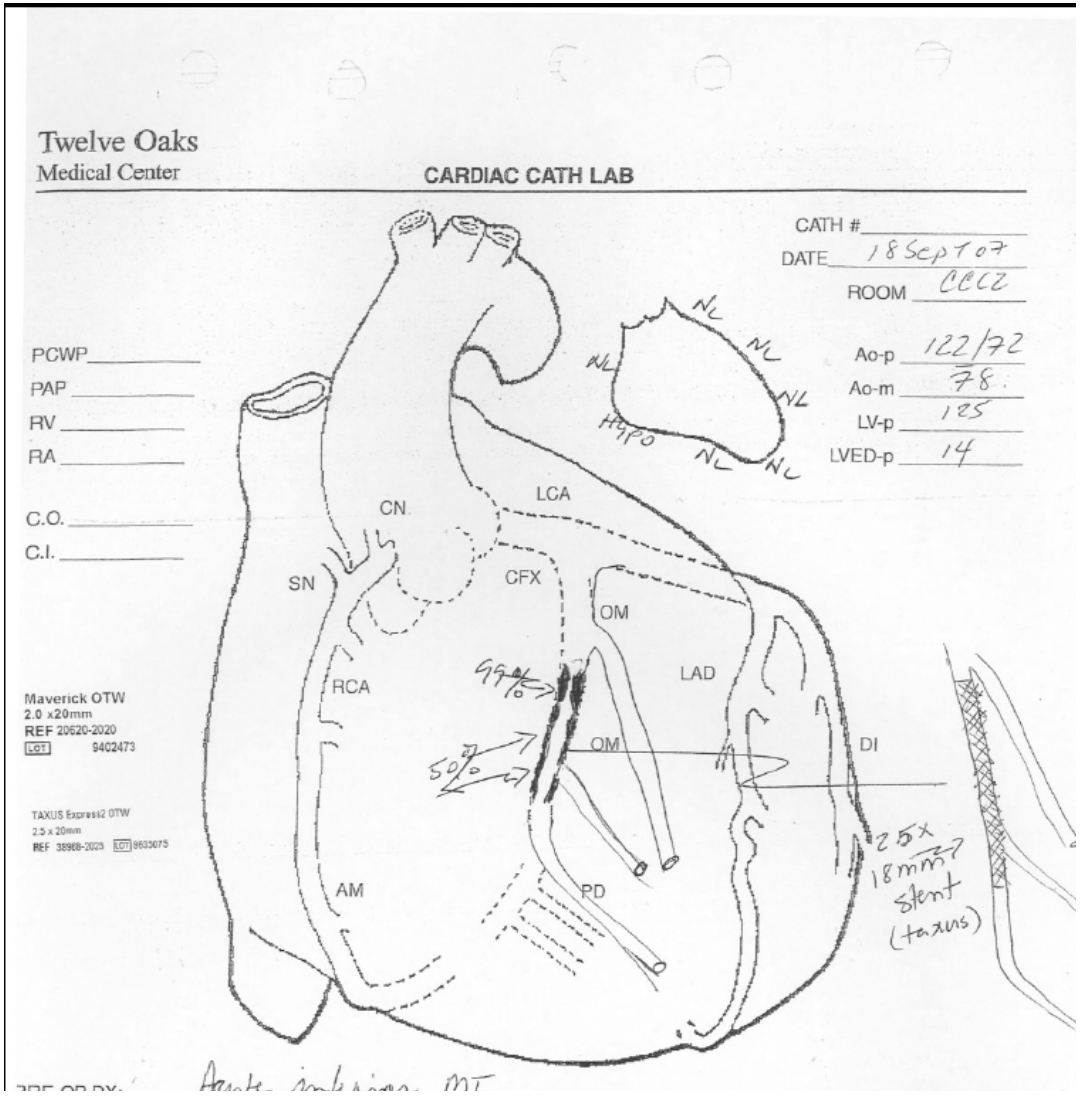
- **Flow α Δ Pressure**
- **Flow α 1 / Resistance**
- **Resistance α L / r^4**
  - L= tube length (uniform for us)
  - r = tube radius

Flow α Δ Pressure / Resistance

Pressure gradient drives flow



PTCA – Stent results



Scientific inquiry and medicine

- **Hypothesis: Patient's is experiencing inferolateral cardiac injury / infarction**

- **Prediction 2: *IF* the patient is experiencing inferolateral cardiac injury / infarction *THEN* removing the blockage will reverse the pathology**

What can we conclude from our test results?

- **Conclusion: Removing blockage reverses patient's pathology**

DT0085

ST. LUKE'S Episcopal Hospital

CORONARY ANGIOGRAPHY

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zmbs01

DATE OF CATH: 2/28/08 CATH #: INDICATIONS: Angina, (+) CAD

RECOMMENDATIONS:
Continue medical management

EF 50 %

HEMODYNAMICS	SAT %
RA: a: ___ V: ___ X: ___	___
RV: ___ / ___	___
PA: ___ / ___ X ___	___
PCP: a: ___ V ___ X: ___	___
AO: 120 / 67 / 94	
LV: 121 / EDP 2-8	
CI: ___ BSA ___	

COMMENTS:
Patent Omniflex stent
No other significant obstructive CAD.

SIGNATURE: [signature] DATE: 2/28/08 TIME: 5PM

SIGNATURE: [signature] DATE: 2/28/8 TIME: 8A

PS-2513 04/07

Conclusions

- **Physics is everywhere!**
- **Knowledge of physics enhances the quality of research, medical care**
- **Ignorance of knowledge can cost data, lives**

Physics in biology education