On the Development of Predictive Models of Light Interaction with Organic and Inorganic Materials

Lecture Series

Gladimir V. G. Baranoski

Natural Phenomena Simulation Group

School of Computer Science

University of Waterloo, Canada

National Institute of Informatics -Tokyo - 2012

Schedule of Lectures

- ✓ Predictability: Benefits and Costs
- ✓ Data Collection: Finding the Pieces of Jigsaw Puzzles
- ✓ Model Design: Balancing Reality and Abstraction
- ✓ Evaluation: The Key for Assessing “Real” Contributions
- ❑ Interdisciplinary Applications: Technical and Political Barriers

Interdisciplinary Applications: Technical and Political Barriers

Lecture 5

Gladimir V. G. Baranoski

Natural Phenomena Simulation Group

School of Computer Science

University of Waterloo, Canada

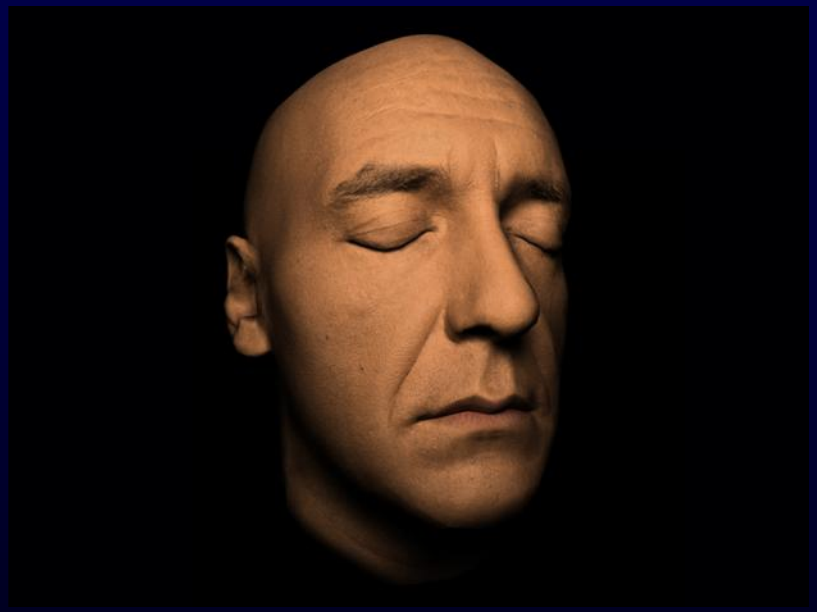
National Institute of Informatics -Tokyo - 2012

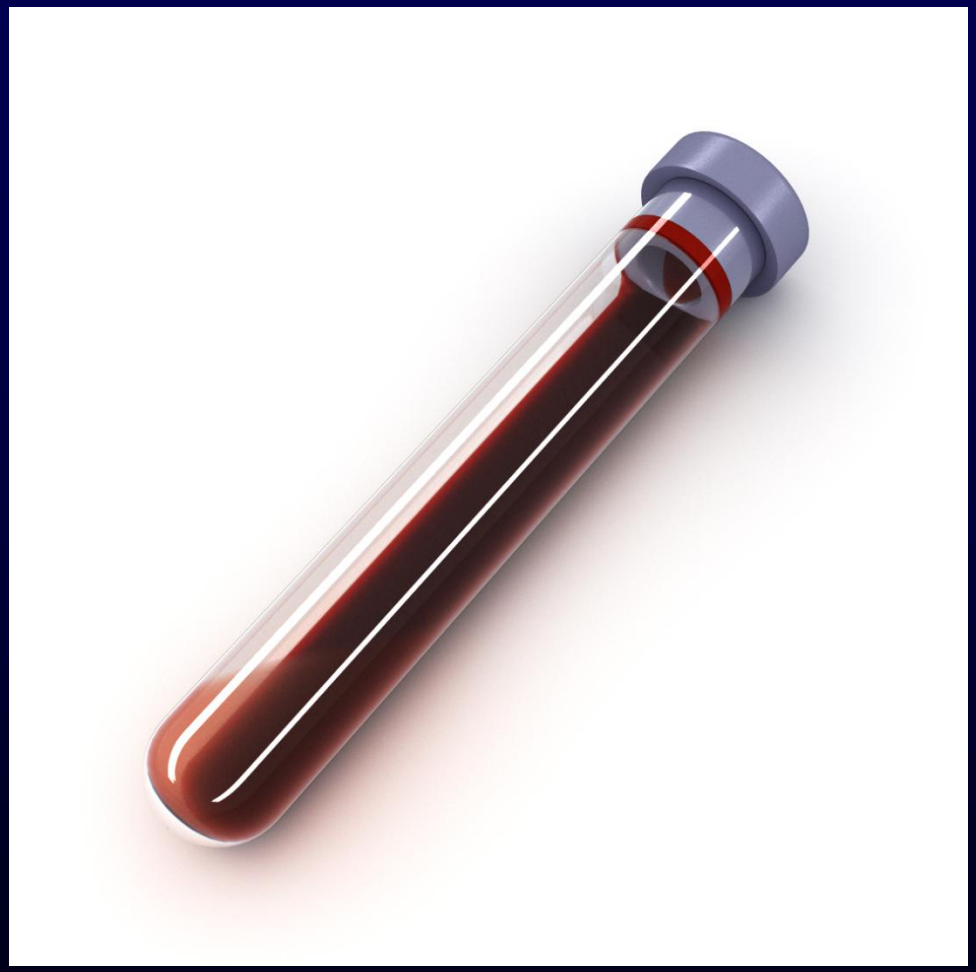
Outline

- Scope of Applications
- Case 1: Iridal Pigmentation
- Case 2: Relocation of Chloroplasts
- Case 3: Dysfunctional Hemoglobins
- Theoretical and Practical Perspectives

Scope of Applications

- From realistic image synthesis …





➢ … and biomedical optics …

- Investigation of photobiological processes triggered by light exposure:

Tanning

Melanoma

- Screening, treatment and monitoring of medical conditions

Jaundice

- Screening, treatment and monitoring of medical conditions

Jaundice

Phototherapy

- Screening, treatment and monitoring of medical conditions

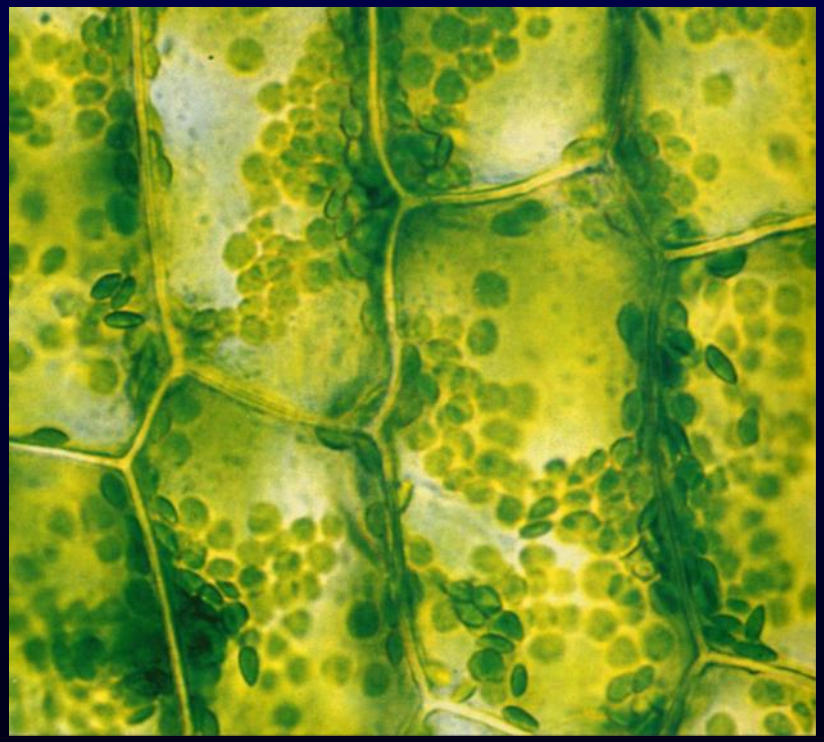
Jaundice

Phototherapy

Pulse Oximetry

➢ … to systems biology, …

- Investigation of biophysical processes (*e.g.*, chloroplast movements) triggered by environmental stimuli



- … remote sensing of natural resources …

What condition(s) and/or parameter(s) are responsible for the color of these leaves**?**

Landsat Image

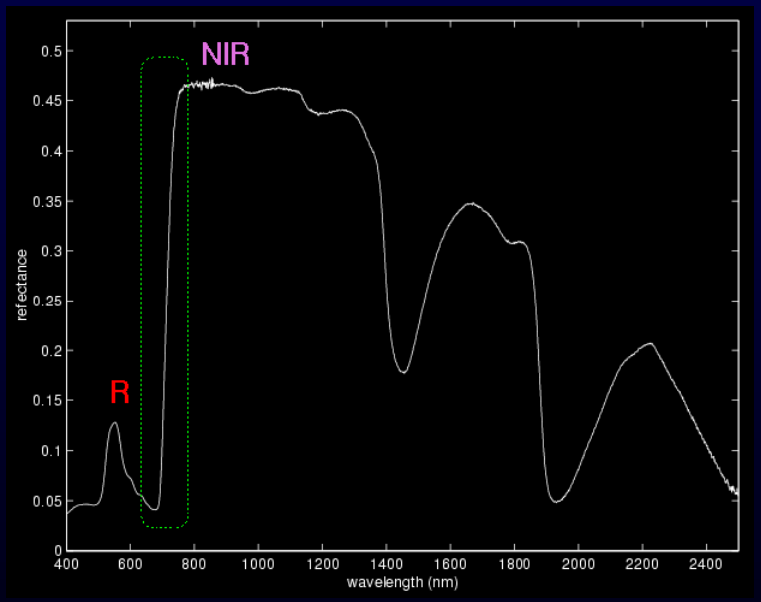
Photograph - ISS Crew Earth Observations Experiment

Negro-Solimoes River Confluence at Manaus, Brazil

… and exobiology

- Use of vegetation red edge (VRE) as a biosignature in the search for extraterrestrial life

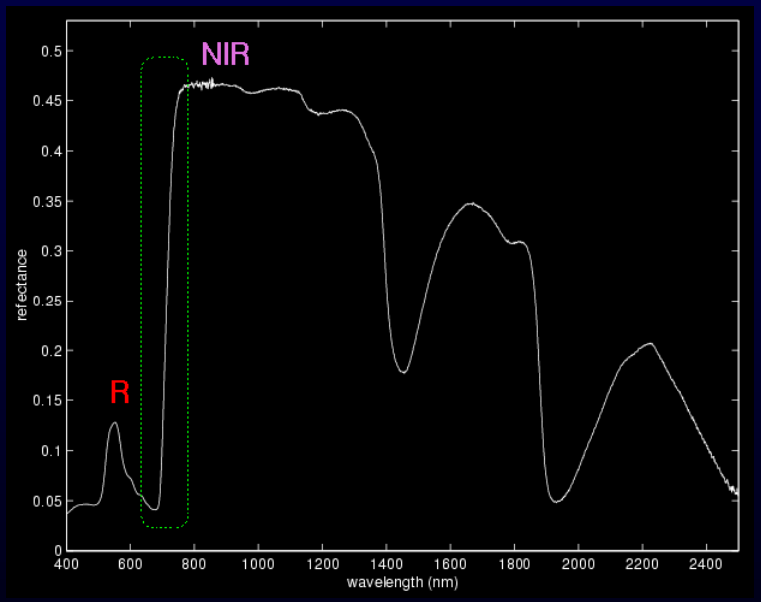
Leaf Reflectance

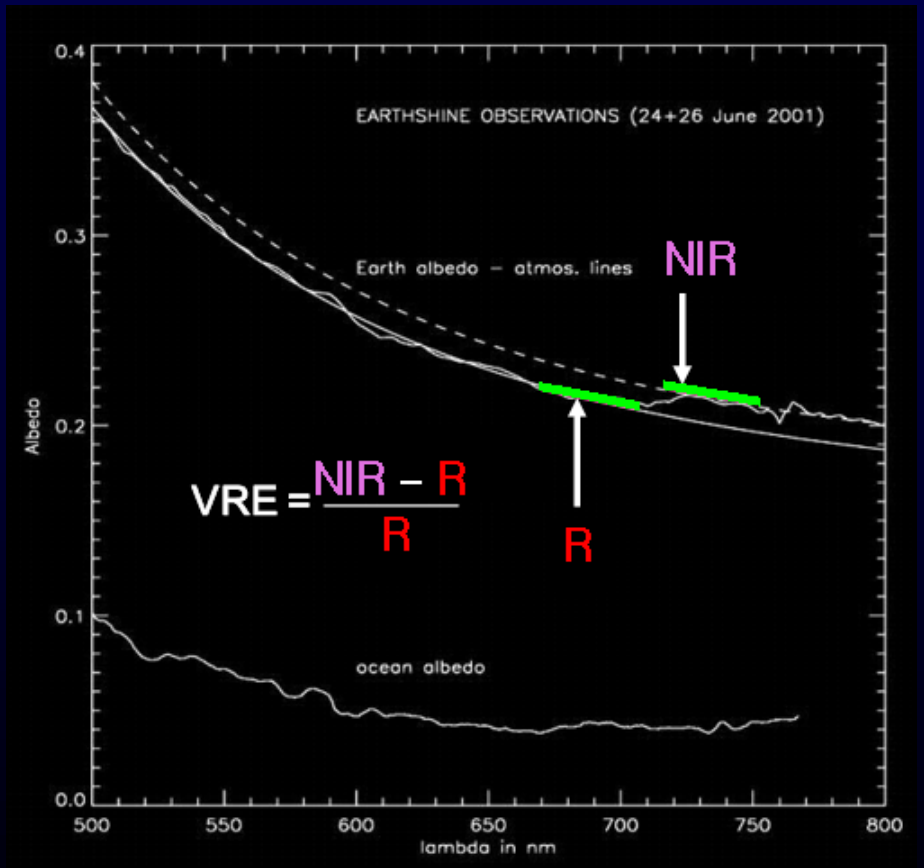


➢ … and exobiology

- Use of vegetation red edge (VRE) as a biosignature in the search for extraterrestrial life

Leaf Reflectance





(Arnold *et al.*, Astronomy and Astrophysics 2002)

- Effects of extraterrestrial environments on living things

SPACE SCIENCE

The Color of Plants on Other Worlds

Green aliens are so passé.

On other worlds, plants could be red, blue, even black

BY NANCY Y. KIANG

KEY CONCEPTS

- What color will alien plants be? The question matters scientifically because the surface color of a planet can reveal whether anything lives there—specifically, whether organisms collect energy from the parent star by the process of photosynthesis.
- Photosynthesis is adapted to the spectrum of light that reaches organisms. This spectrum is the result of the parent star's radiation spectrum, combined with the filtering effects of the planet's atmosphere and, for aquatic creatures, of liquid water.
- Light of any color from deep violet through the near-infrared could power photosynthesis. Around stars hotter and bluer than our sun, plants would tend to absorb blue light and could look green to yellow to red. Around cooler stars such as red dwarfs, planets receive less visible light, so plants might try to absorb as much of it as possible, making them look black.

—*The Editors*

The prospect of finding extraterrestrial life is no longer the domain of science fiction or UFO hunters. Rather than waiting for aliens to come to us, we are looking for them. We may not find technologically advanced civilizations, but we can look for the physical and chemical signs of fundamental life processes: "biosignatures." Beyond the solar system, astronomers have discovered more than 200 worlds orbiting other stars, so-called extrasolar planets. Although we have not been able to tell whether these planets harbor life, it is only a matter of time now. Last July astronomers confirmed the presence of water vapor on an extrasolar planet by observing the passage of starlight through the planet's atmosphere. The world's space agencies are now developing telescopes that will search for signs of life on Earth-size planets by observing the planets' light spectra.

Photosynthesis, in particular, could produce very conspicuous biosignatures. How plausible is it for photosynthesis to arise on another planet? Very. On Earth, the process is so successful that it is the foundation for nearly all life. Although some organisms live off the heat and methane of oceanic hydrothermal vents, the rich ecosystems on the planet's surface all depend on sunlight.

Photosynthetic biosignatures could be of two kinds: biologically generated atmospheric gases such as oxygen and its product, ozone, and surface colors that indicate the presence of specialized pigments such as green chlo-

RED EARTH, GREEN EARTH, BLUE EARTH: Type M stars (red dwarfs) are feeble, so plants on an orbiting Earth-like world might need to be black to absorb all the available light (*first panel*). Young M stars fry planetary surfaces with ultraviolet flares, so any organisms must be aquatic (*second*). Our sun is type G (*third*). Around F stars, plants might get too much light and need to reflect much of it (*fourth*).

"The intrusion of computational biology into 'wet' laboratories is producing a quite revolution wherein simulation tools are used to complement experiments and accelerate the hypothesis generation and validation cycle of research."

Di Ventura *et al.*
"From *in vivo* to *in silico* biology and back", Nature 2006

Outline

- ✓ Scope of Applications
- ❑ Case 1: Iridal Pigmentation
- ❑ Case 2: Relocation of Chloroplasts
- ❑ Case 3: Dysfunctional Hemoglobins
- ❑ Theoretical and Practical Perspectives

Case 1: Iridal Pigmentation

- Science question:
  - Why blue irides with lower melanin content appear darker than blue irides with higher melanin content? (Measurements by Wielgus and Sarna, Pig. Cell Res. 2005)

Case 1: Iridal Pigmentation

- Science question:
  - Why blue irides with lower melanin content appear darker than blue irides with higher melanin content? (Measurements by Wielgus and Sarna, Pig. Cell Res. 2005)

- Importance:
  - Correlation between lightly pigmented irides and the occurrence of iridal pathologies (*e.g.*, uveal melanoma)

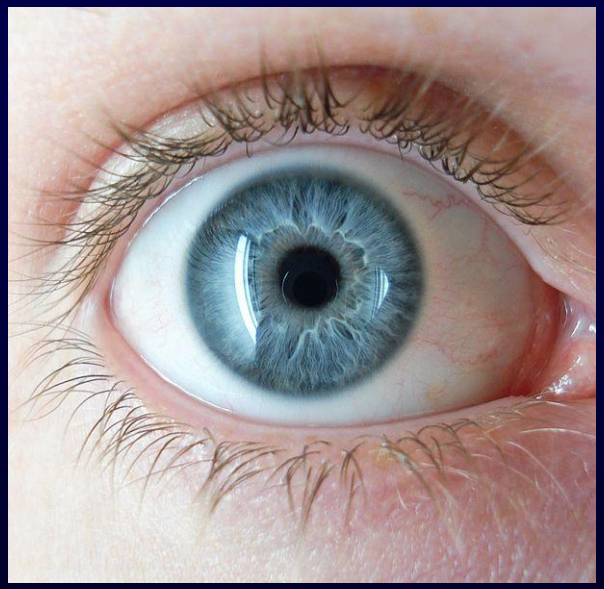
Case 1: Iridal Pigmentation

- Science question:
  - Why blue irides with lower melanin content appear darker than blue irides with higher melanin content? (Measurements by Wielgus and Sarna, Pig. Cell Res. 2005)

- Importance:
  - Correlation between lightly pigmented irides and the occurrence of iridal pathologies (*e.g.*, uveal melanoma)

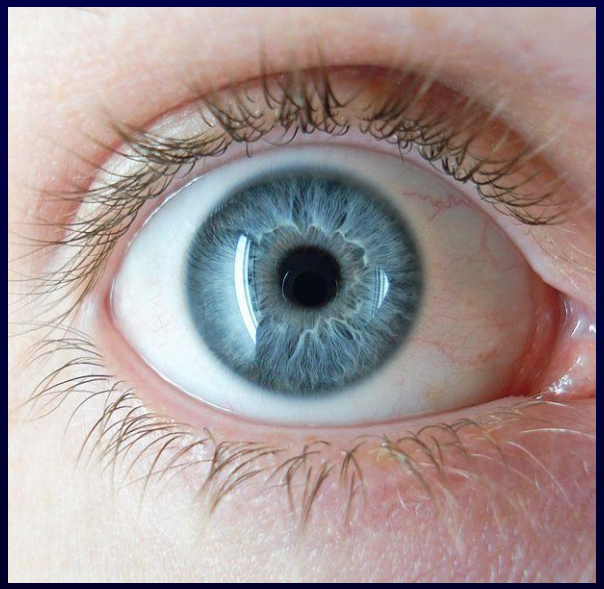
➢ Challenges:

- Unfeasibility of *in loco* investigations of iridal tissues



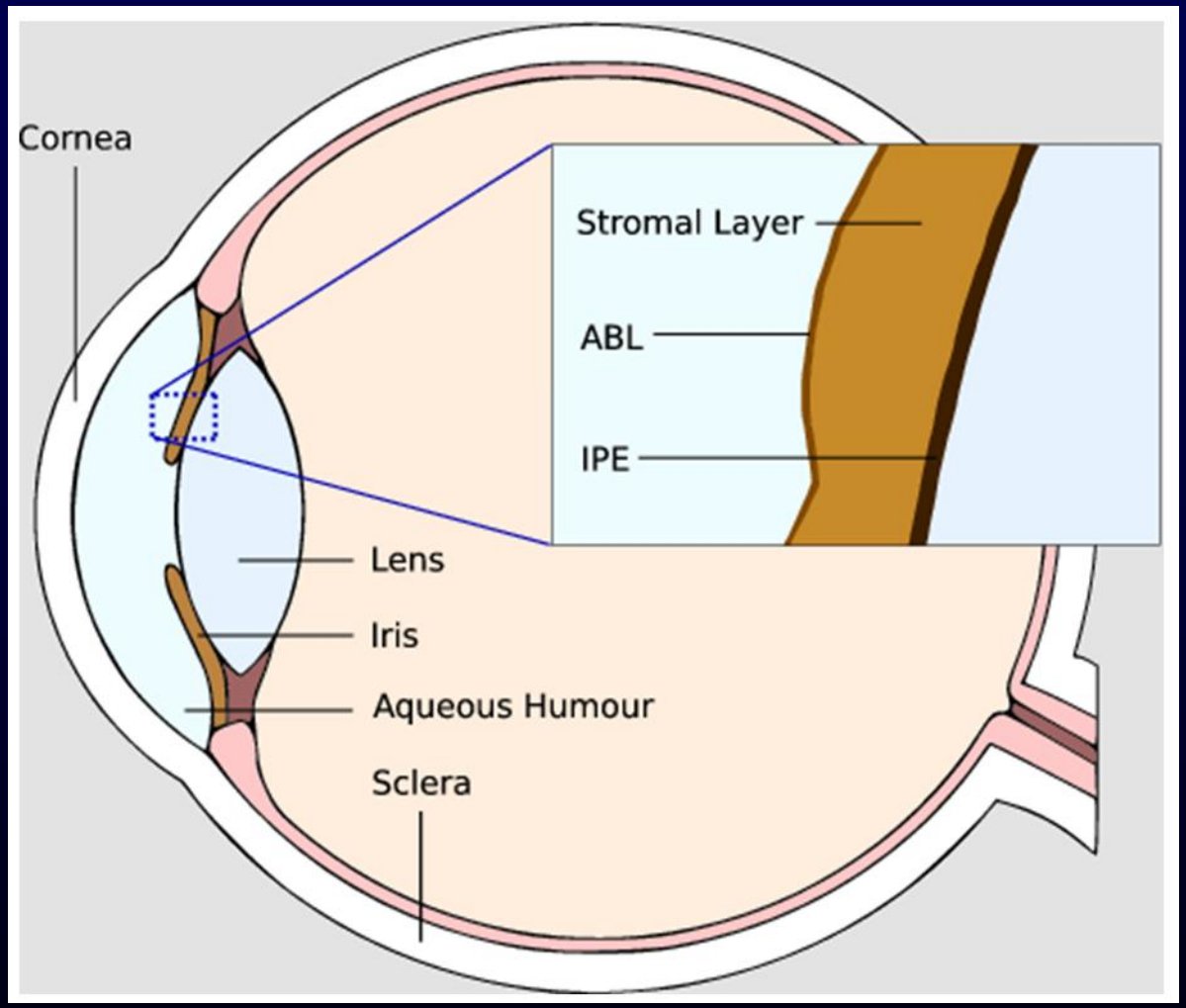
➢ Challenges:

- Unfeasibility of *in loco* investigations of iridal tissues

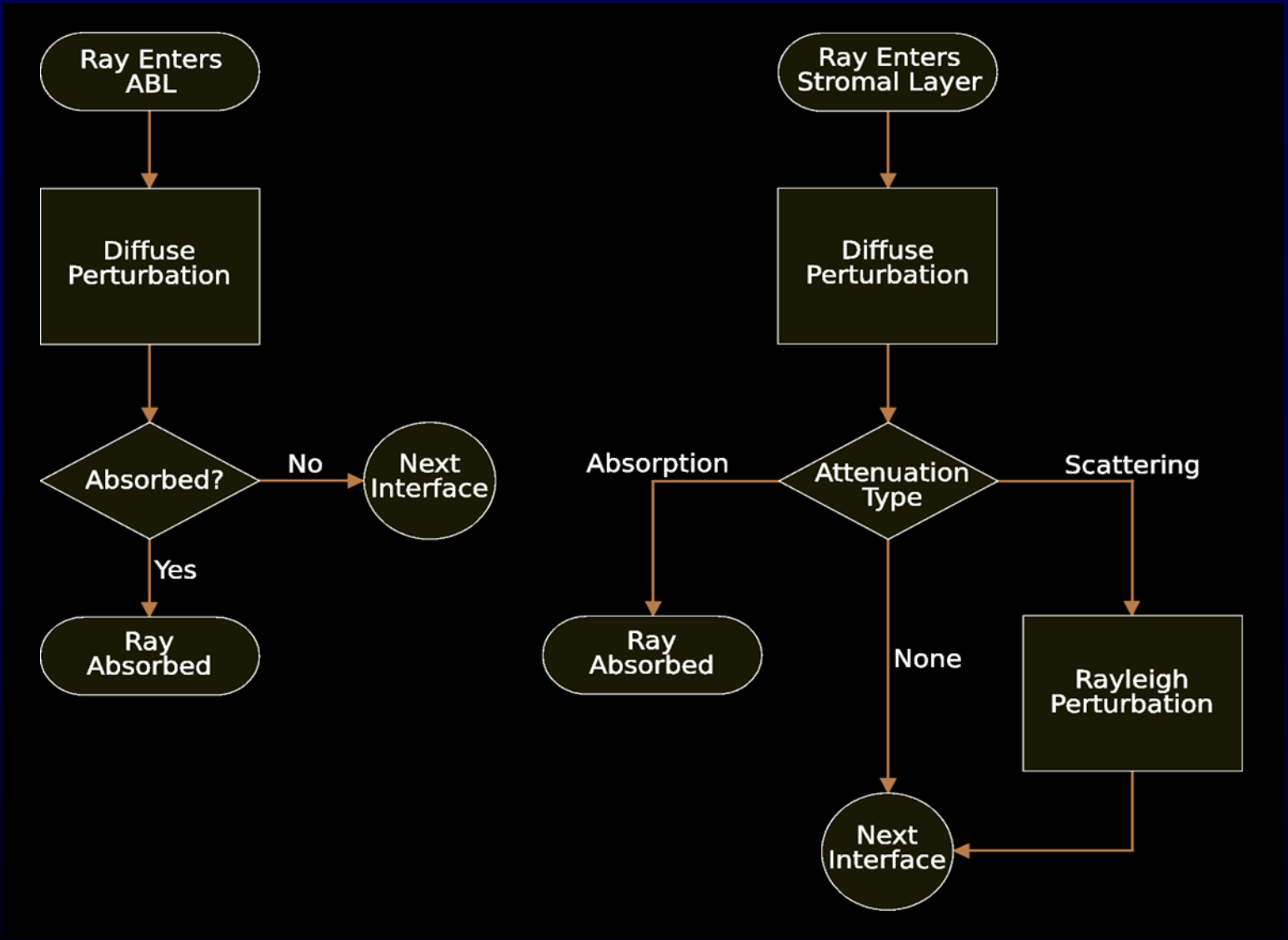


- Changes in the optical properties of extracted specimens

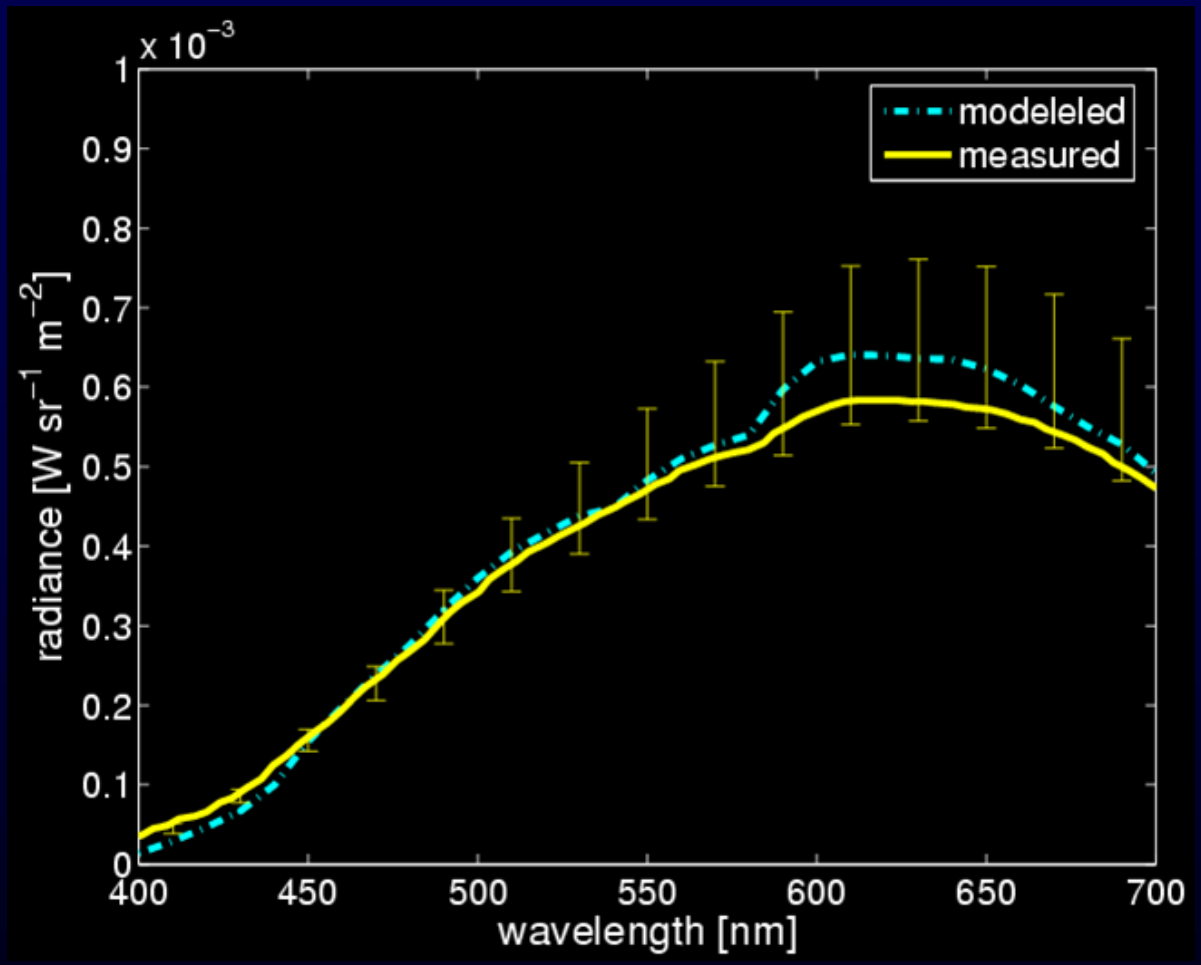
- Recall the presence of melanin in the iridal tissues



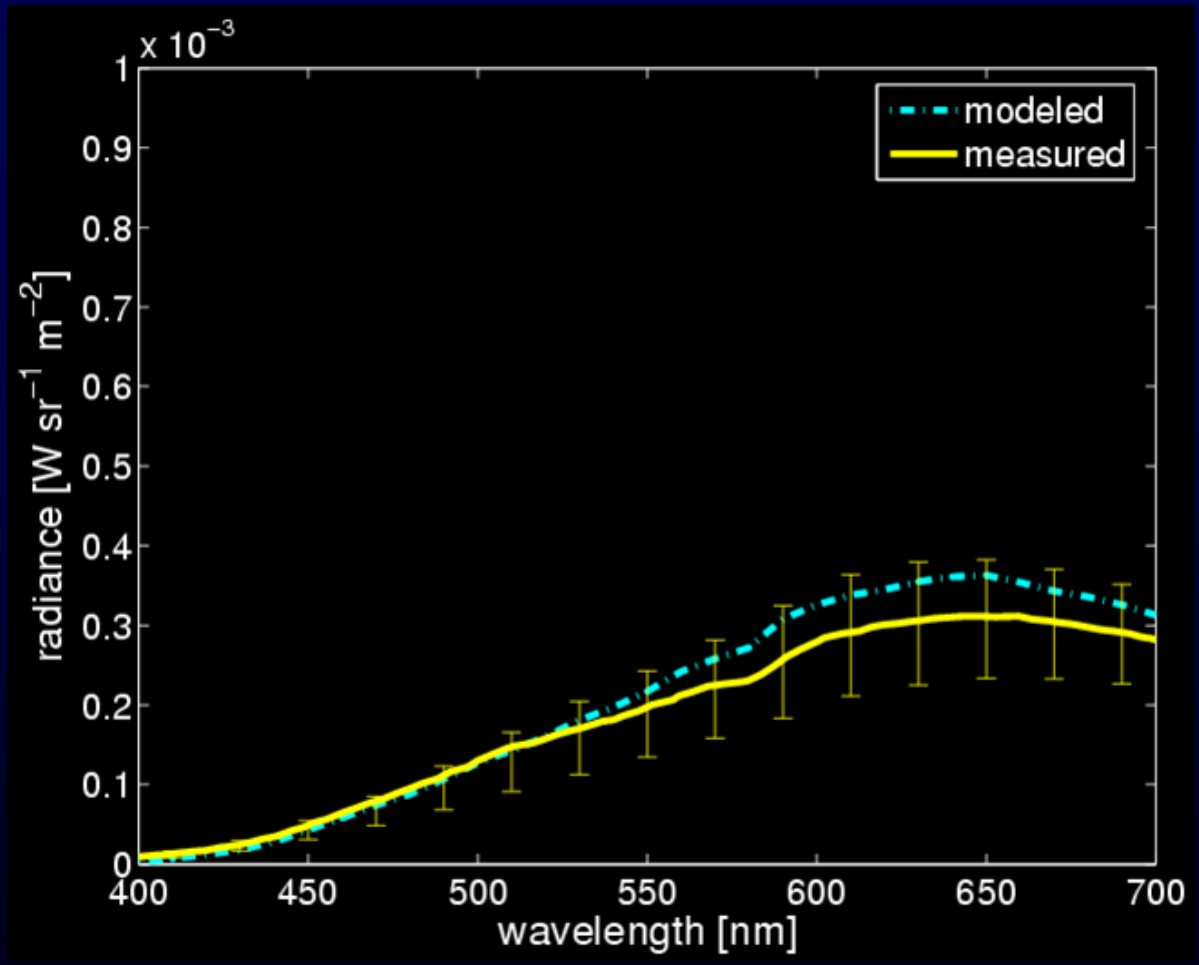
ILIT Model Control Flow



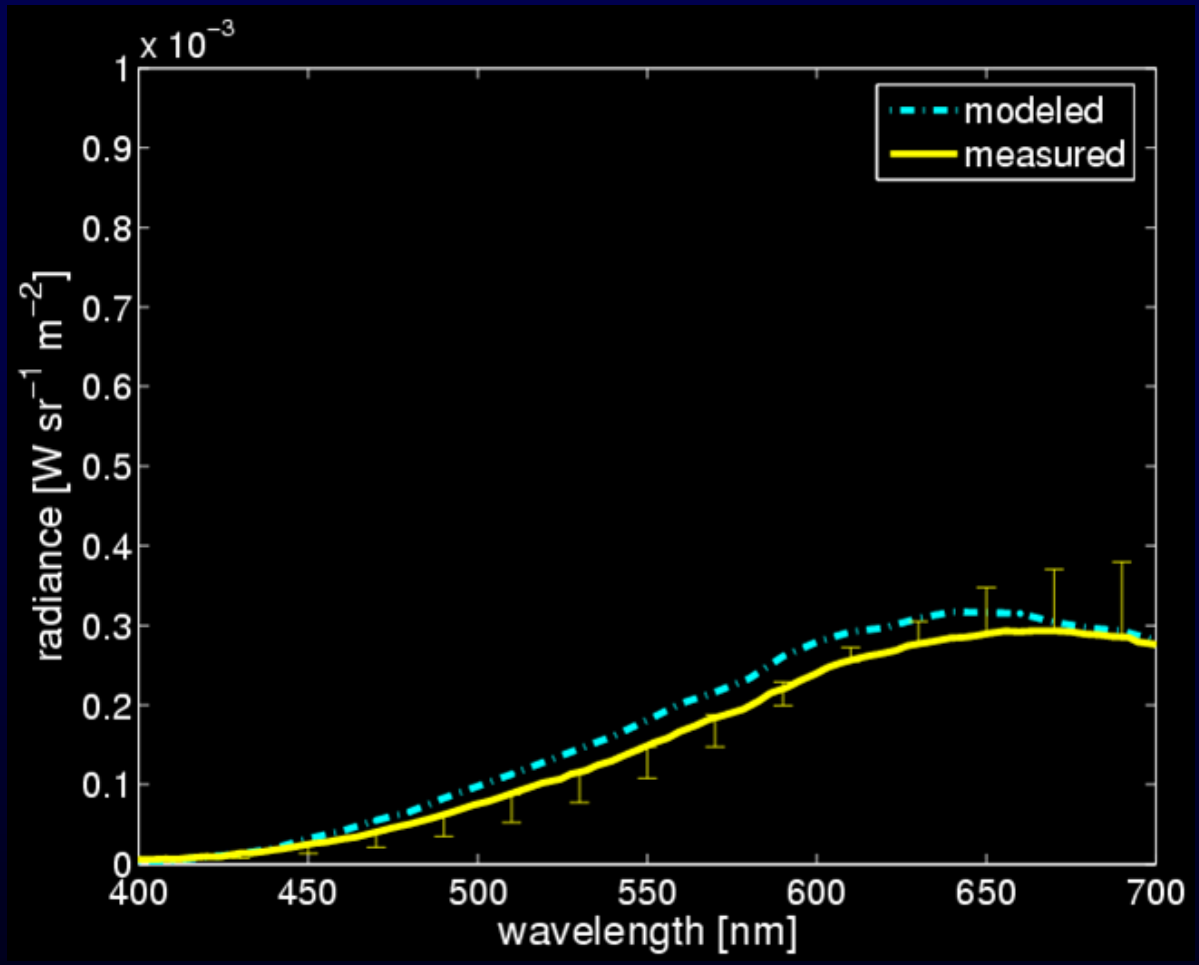
Lightly Pigmented Iris



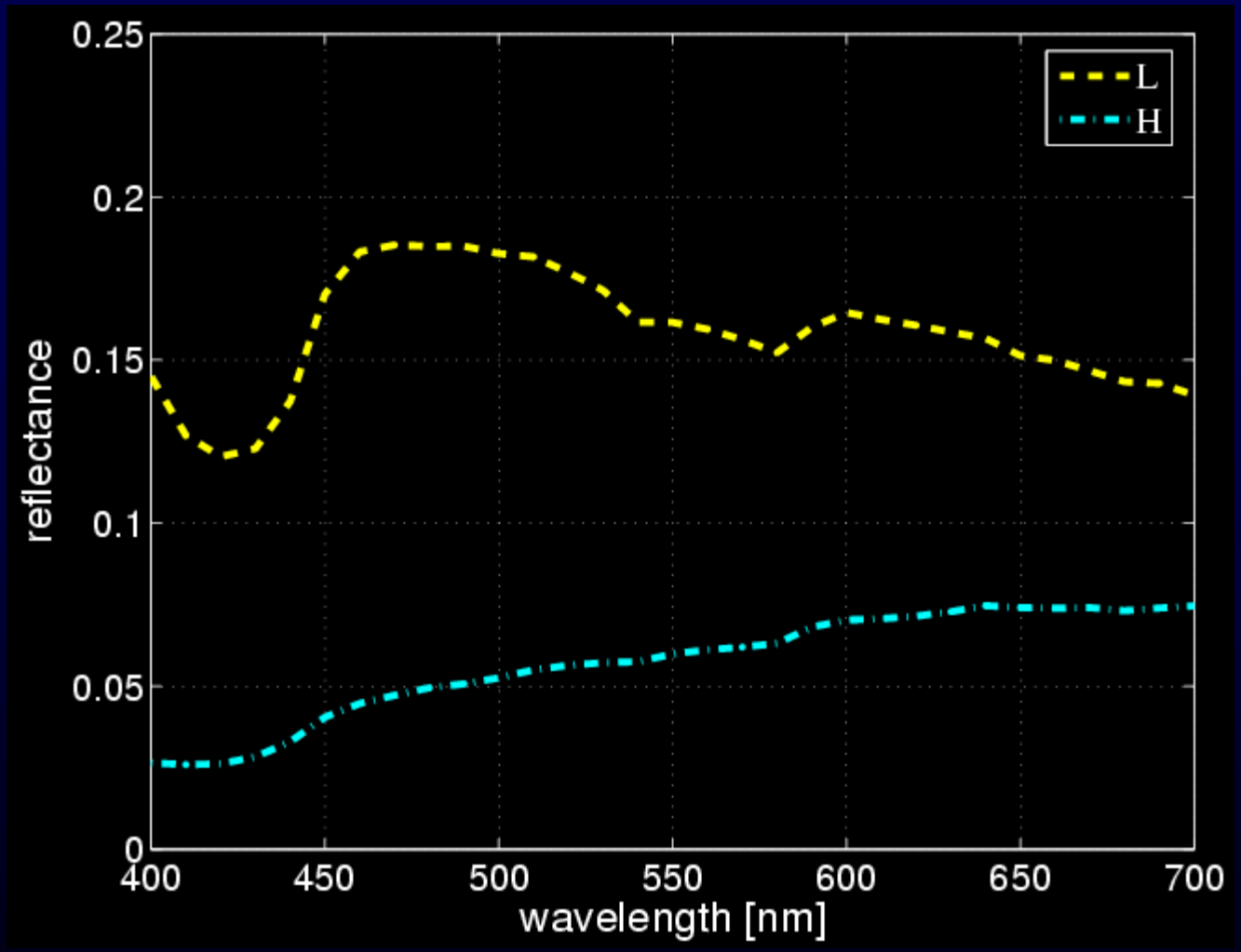
Moderately Pigmented Iris



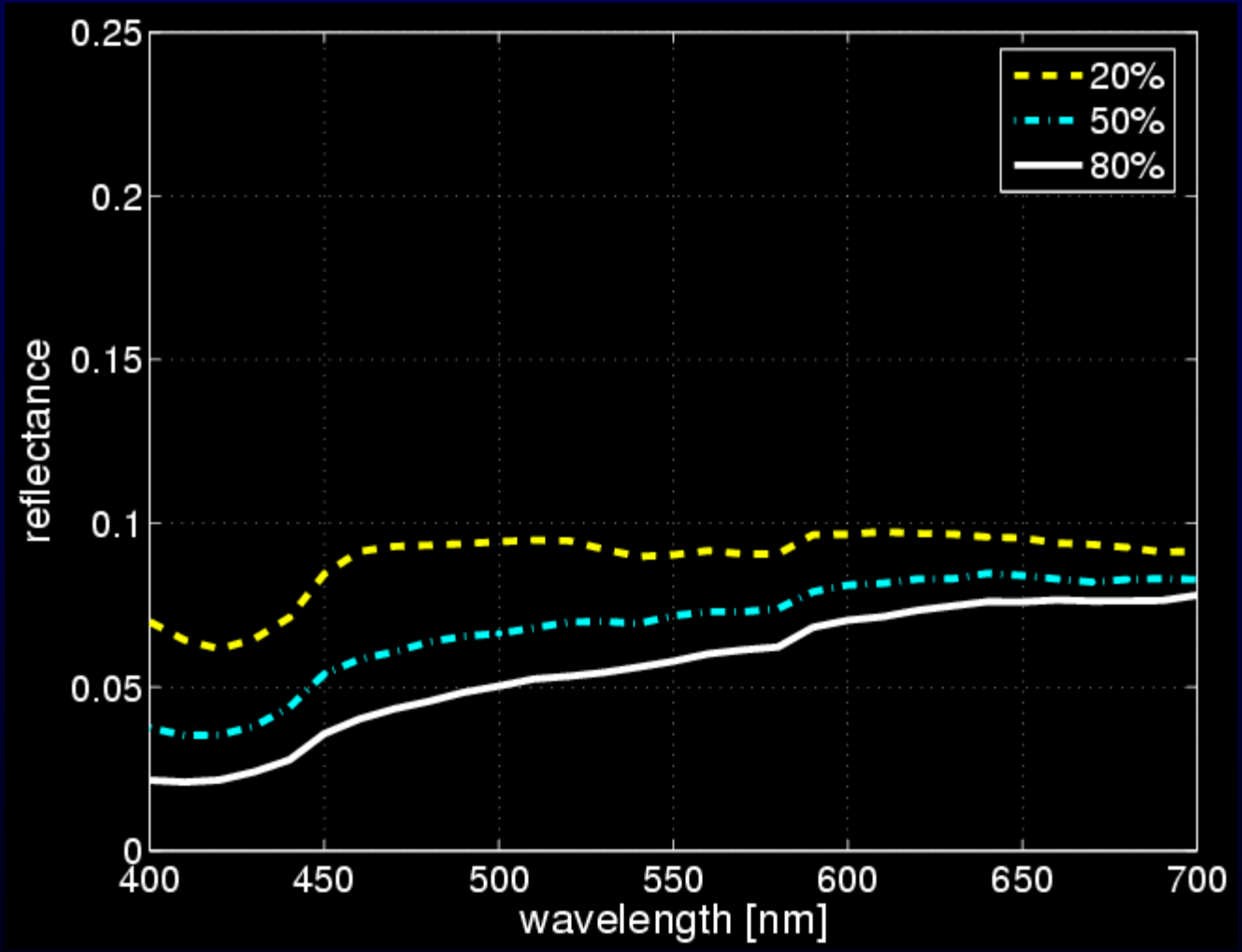
Heavily Pigmented Iris



Low *vs.* High Melanin Concentration in the ABL



Different Melanin Distributions in the ABL




Distribution (High ⟶ Low)
Concentration (High ⟶ Low)

- In summary: different distributions of melanin in the ABL can result in a darker appearance for moderately pigmented irides

- In summary: different distributions of melanin in the ABL can result in a darker appearance for moderately pigmented irides

- *In silico* hypothesis formulation:

  - Similarly, the darker appearance of lightly pigmented irides with low melanin content may result from different distributions of this pigment in the stromal layer

- In summary: different distributions of melanin in the ABL can result in a darker appearance for moderately pigmented irides

- *In silico* hypothesis formulation:

  - Similarly, the darker appearance of lightly pigmented irides with low melanin content may result from different distributions of this pigment in the stromal layer

    - "Qualitative assessment of undetectable melanin distribution in lightly pigmented irides" (Journal of Biomedical Optics 2007)

➢ Simulation guidelines:

- Employ the ILIT model to perform controlled *in silico* experiments in which the distribution of melanin is changed incrementally in the stromal layer of lightly pigmented irides

➢ Simulation guidelines:

- Employ the ILIT model to perform controlled *in silico* experiments in which the distribution of melanin is changed incrementally in the stromal layer of lightly pigmented irides

- Repeat the *in silico* experiments for different wavelength and PMSL (percentage of melanin in the stromal layer) values

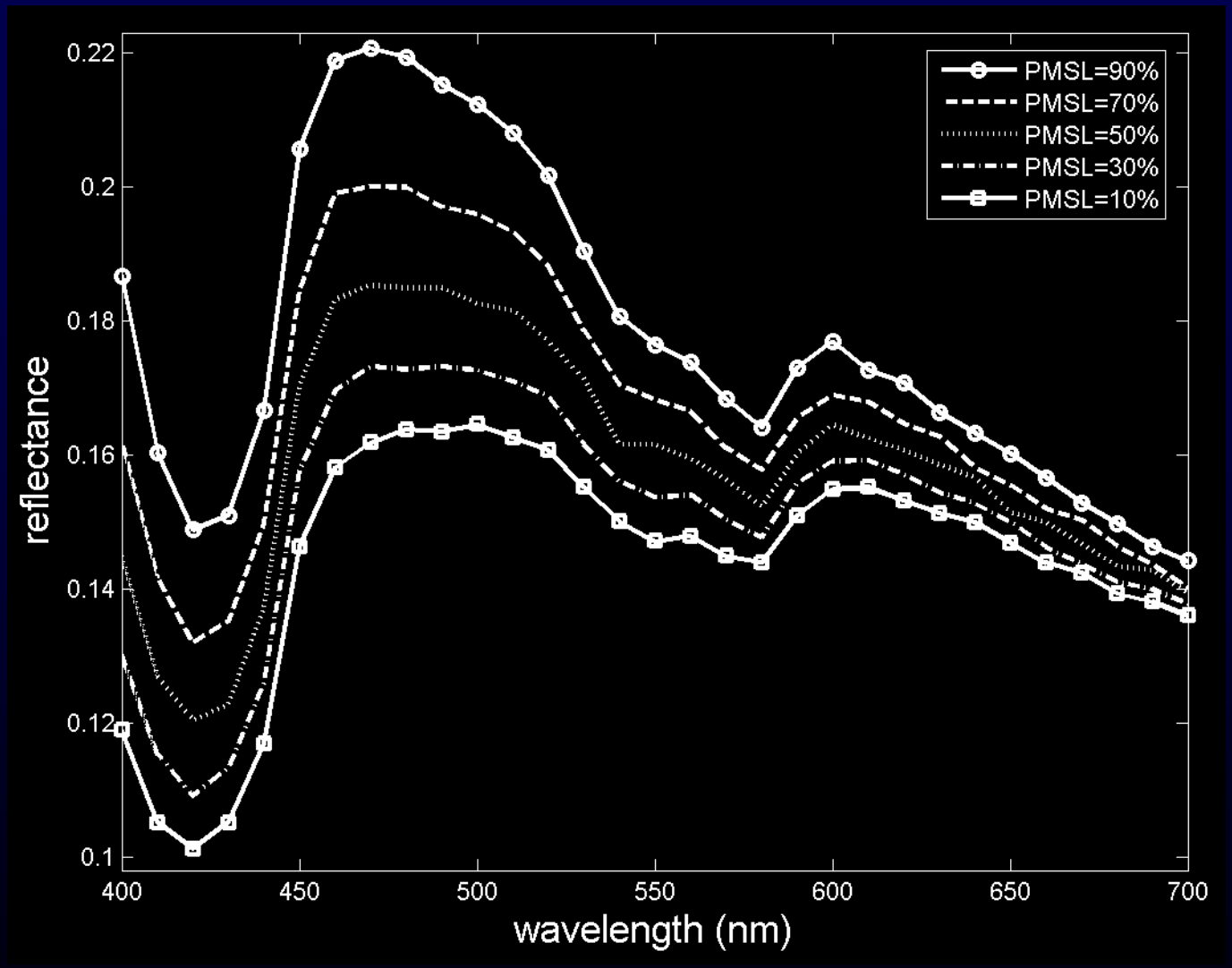
➢ Simulation guidelines:

- Employ the ILIT model to perform controlled *in silico* experiments in which the distribution of melanin is changed incrementally in the stromal layer of lightly pigmented irides

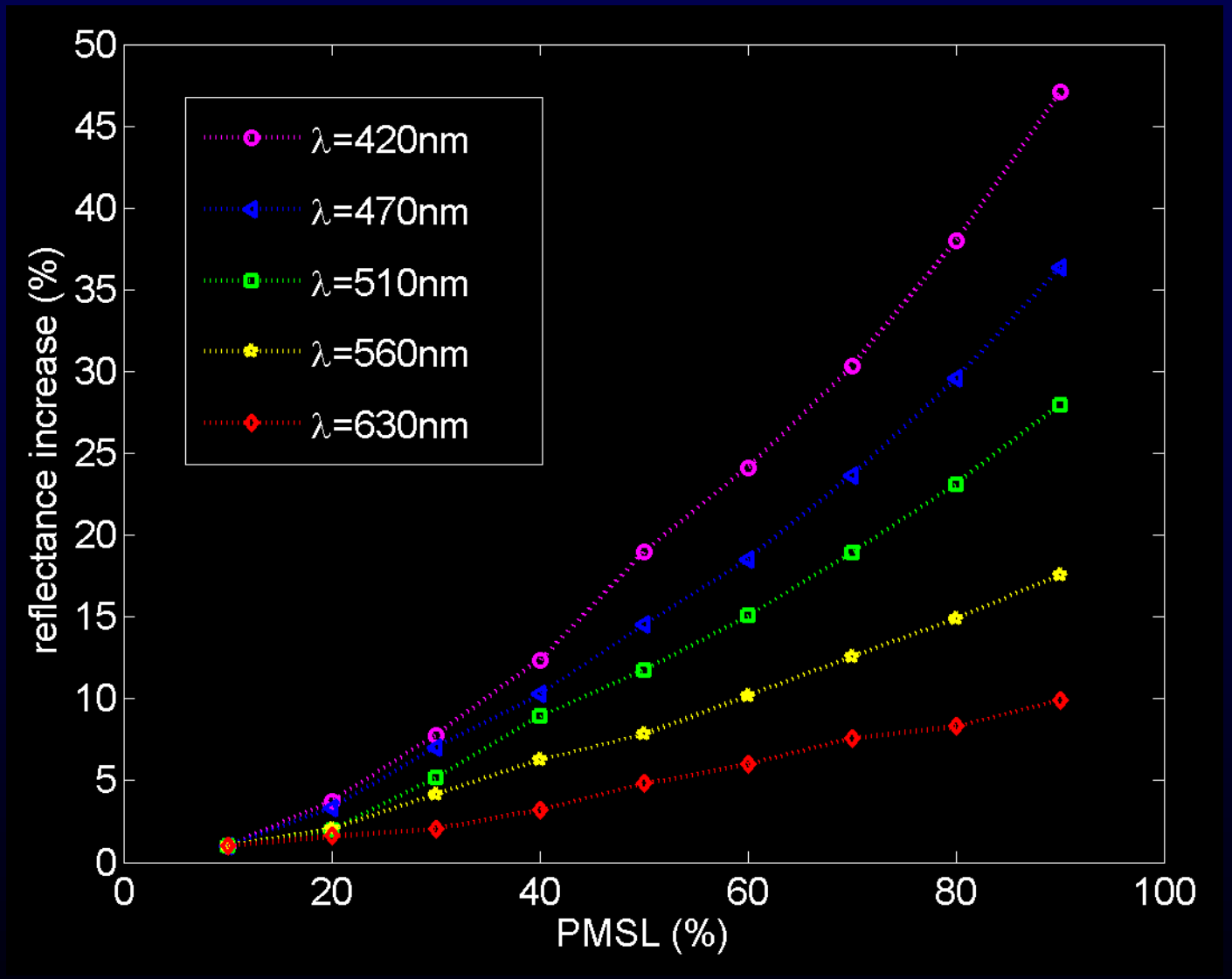
- Repeat the *in silico* experiments for different wavelength and PMSL (percentage of melanin in the stromal layer) values

- Employ the ILIT model to qualitatively reproduce the experimental observations made by Wielgus and Sarna (Pig. Cell Res. 2005)

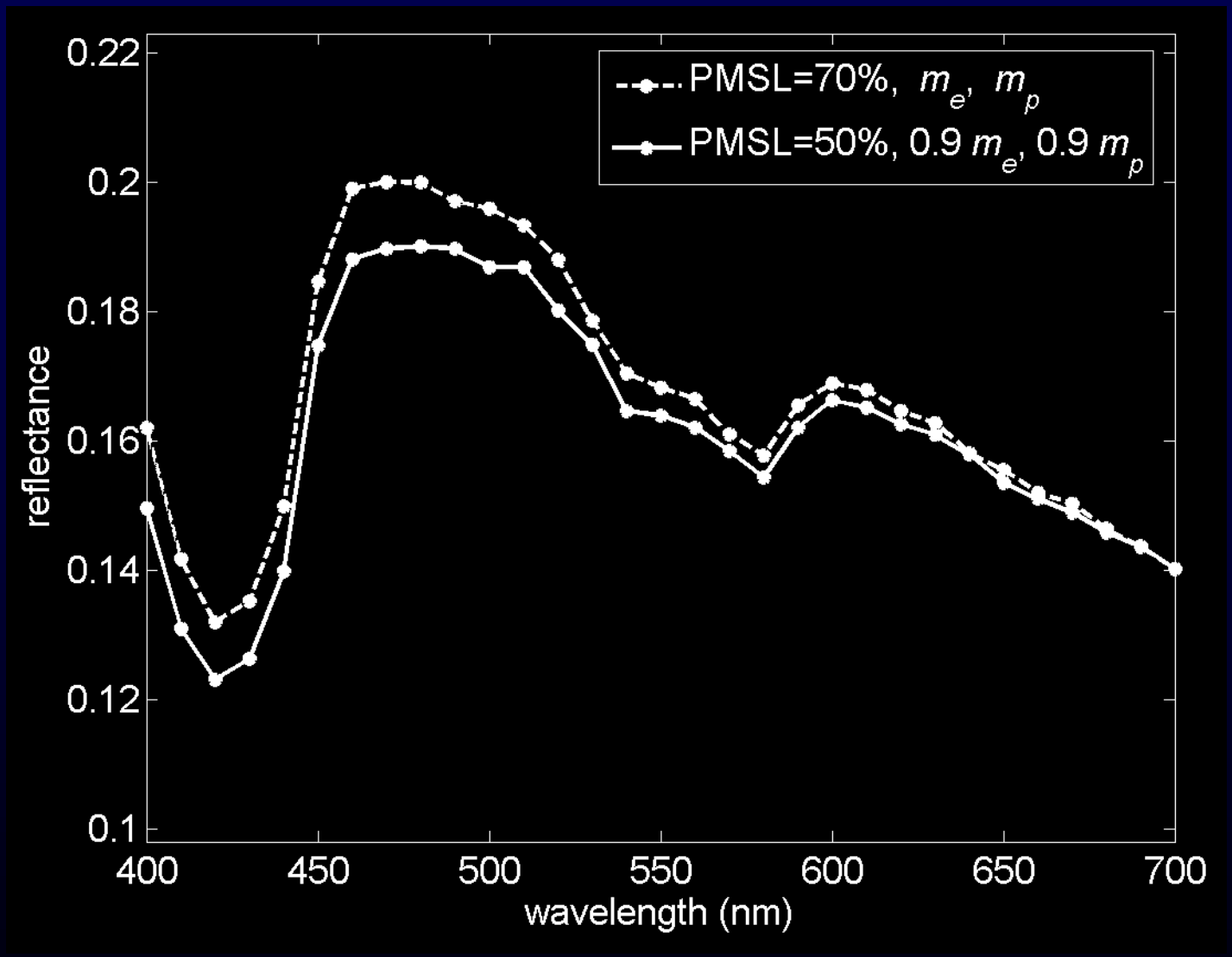
Spectral Signature Changes in Response to Different Percentages of Melanin in the Stromal Layer (PMSL)



Reflectance Increase Rates



Light Blue Iris *vs.* Medium Blue Iris



Outline

- ✓ Scope of Applications
- ✓ Case 1: Iridal Pigmentation
- ❑ Case 2: Relocation of Chloroplasts
- ❑ Case 3: Dysfunctional Hemoglobins
- ❑ Theoretical and Practical Perspectives

Case 2: Relocation of Chloroplasts

- Science question:

  - Apparently conflicting spectral responses measured for corn leaves under *in vitro* and *in vivo* water reduction procedures

Case 2: Relocation of Chloroplasts

- Science question:

  - Apparently conflicting spectral responses measured for corn leaves under *in vitro* and *in vivo* water reduction procedures

  - Measurements performed by Thomas *et al.* 1971 show an increase in the reflectance (visible spectral domain) of corn leaves subjected to *in vitro* moderate (~25%) water reduction procedures

- Thomas *et al.* (1971) also observed that leaves of plants under moderate *in vivo* water stress may appear darker than fresh (control) leaves

- Thomas *et al.* (1971) also observed that leaves of plants under moderate *in vivo* water stress may appear darker than fresh (control) leaves
  - Water stress may decrease reflectance under certain conditions

- Thomas *et al.* (1971) also observed that leaves of plants under moderate *in vivo* water stress may appear darker than fresh (control) leaves
  - Water stress may decrease reflectance under certain conditions

- Experiments by Maracci *et al.* (1991) show a reflectance decrease for corn leaves under moderate (*in vivo*) water stress (pigment content remained constant)

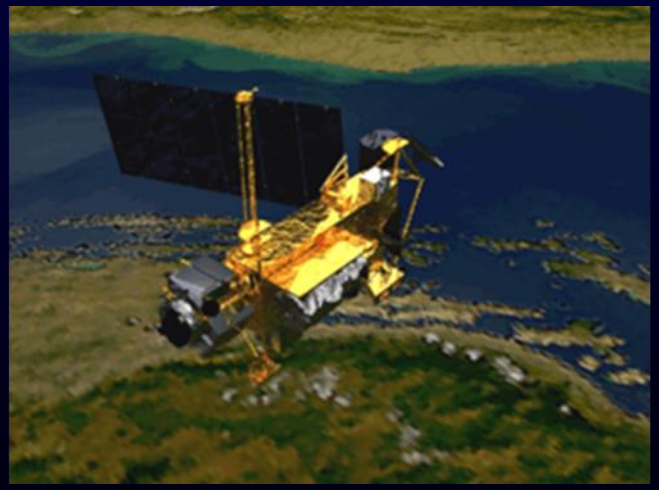
- Thomas *et al.* (1971) also observed that leaves of plants under moderate *in vivo* water stress may appear darker than fresh (control) leaves
  - Water stress may decrease reflectance under certain conditions
- Experiments by Maracci *et al.* (1991) show a reflectance decrease for corn leaves under moderate (*in vivo*) water stress (pigment content remained constant)
  - Need of further experiments to study this tendency

- Importance:
  - Increasing global demand of C4 plants (*e.g.*, corn)

- Importance:
  - Increasing global demand of C4 plants (*e.g.*, corn)
  - Limited understanding about their adaptive mechanisms

➢ Importance:

- Increasing global demand of C4 plants (*e.g.*, corn)
- Limited understanding about their adaptive mechanisms
- Need to develop more effective tools for the detection and monitoring of moderate water stress conditions



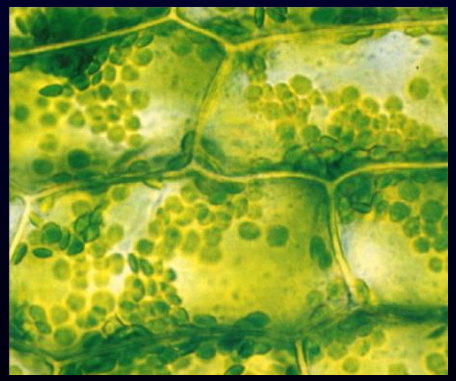
➢ Challenges:

- Difficulties to perform controlled experiments involving the same specimen under *in vitro* and *in silico* moderate water reduction procedures

➢ Challenges:

- Difficulties to perform controlled experiments involving the same specimen under *in vitro* and *in silico* moderate water reduction procedures

- *In situ* investigations of adaptive responses of C_4 plants, such as the relocation of chloroplasts due to an external stimulus, may affect the outcome of these responses with respect to other stimuli



➢ Possible explanation:

- Distinct spectral responses caused by intrinsic differences between *in vivo* and *in vitro* water reduction procedures

- Possible explanation:

  - Distinct spectral responses caused by intrinsic differences between *in vivo* and *in vitro* water reduction procedures

- *In silico* hypothesis formulation:

  - Intensification of detour effects due to a more homogeneous distribution of chloroplasts triggered by water deficit signals

- Possible explanation:

  - Distinct spectral responses caused by intrinsic differences between *in vivo* and *in vitro* water reduction procedures

- *In silico* hypothesis formulation:

  - Intensification of detour effects due to a more homogeneous distribution of chloroplasts triggered by water deficit signals

    - "*In silico* assessment of environmental factors affecting the spectral signature of C4 plants in the visible domain" (International Journal of Remote Sensing 2012)

➢ Simulation guidelines

- Use the same characterization parameters for the *in vivo* and *in vitro* water reduced specimens

➢ Simulation guidelines

- Use the same characterization parameters for the *in vivo* and *in vitro* water reduced specimens

- ABM-U model incorporates a bound for angular light (ray) deviations caused by the heterogeneous distribution of chloroplasts

➢ Simulation guidelines

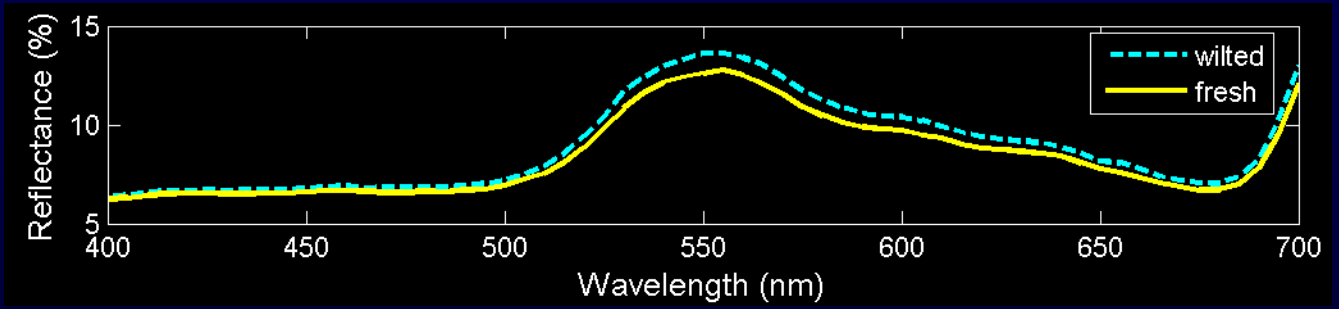
- Use the same characterization parameters for the *in vivo* and *in vitro* water reduced specimens

- ABM-U model incorporates a bound for angular light (ray) deviations caused by the heterogeneous distribution of chloroplasts

- Remove the bound for angular deviations in the case of *in vivo* water stressed specimens

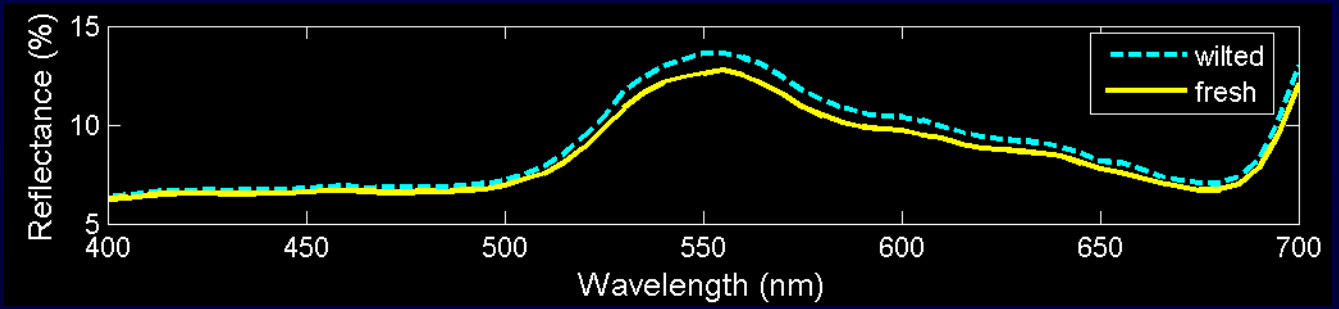
- Qualitative agreement with measured data for *in vitro* water wilted (25%) leaves (Thomas *et al.*, 1971)

Modeled (ABM-U) Reflectance Curves



- Qualitative agreement with measured data for *in vitro* water wilted (25%) leaves (Thomas *et al.*, 1971)

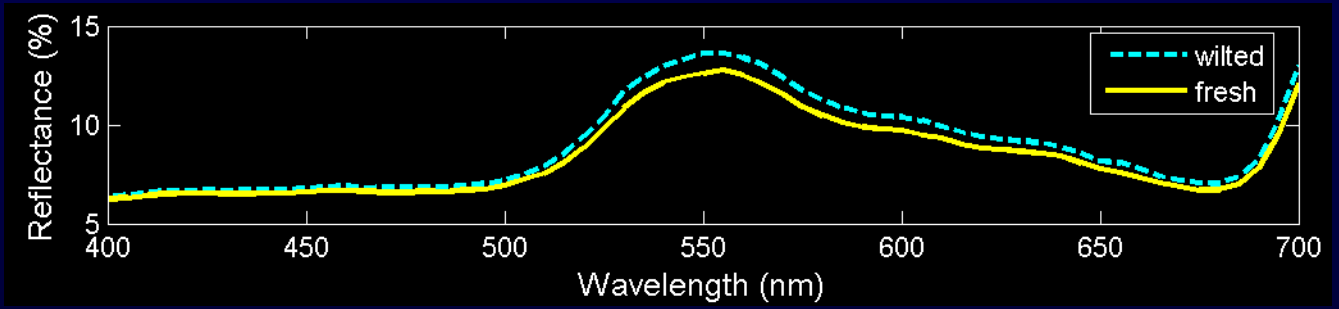
Modeled (ABM-U) Reflectance Curves



- Higher reflectance for the water wilted specimen

- Qualitative agreement with measured data for *in vitro* water wilted (25%) leaves (Thomas *et al.*, 1971)

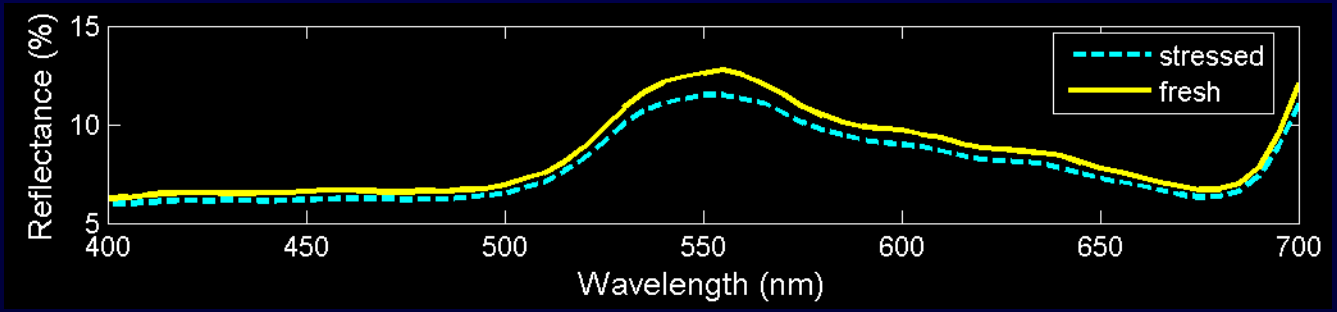
Modeled (ABM-U) Reflectance Curves



- Higher reflectance for the water wilted specimen
- More pronounce reflectance increase around 550nm

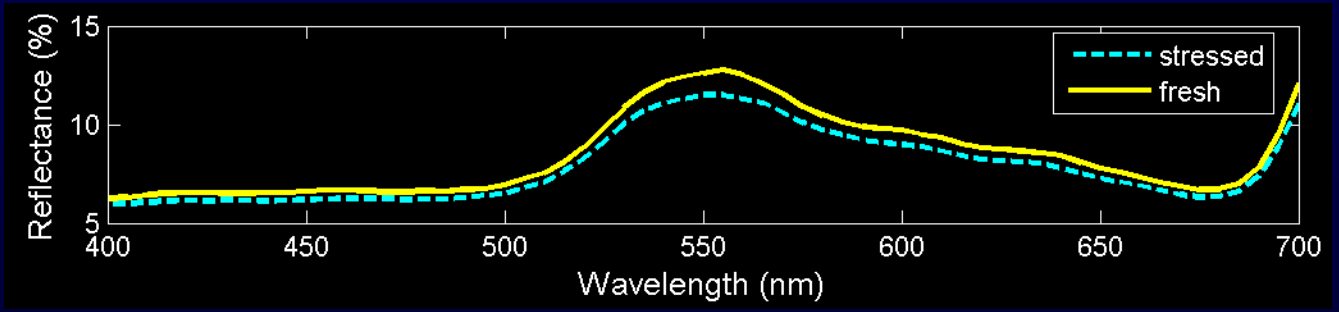
- Qualitative agreement with measured data for *in vivo* water stressed (25%) leaves (Maracci *et al.*, 1991)

Modeled (ABM-U) Reflectance Curves



- Qualitative agreement with measured data for *in vivo* water stressed (25%) leaves (Maracci *et al.*, 1991)

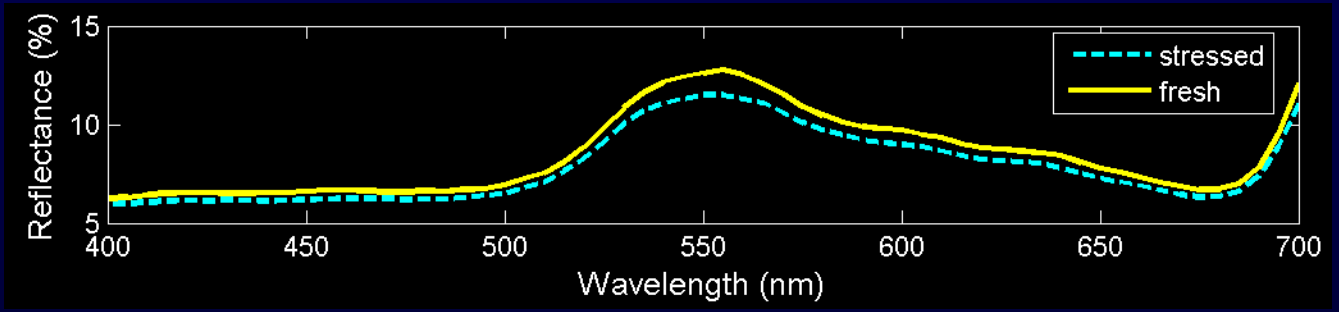
Modeled (ABM-U) Reflectance Curves



- Lower reflectance for the water stressed specimen

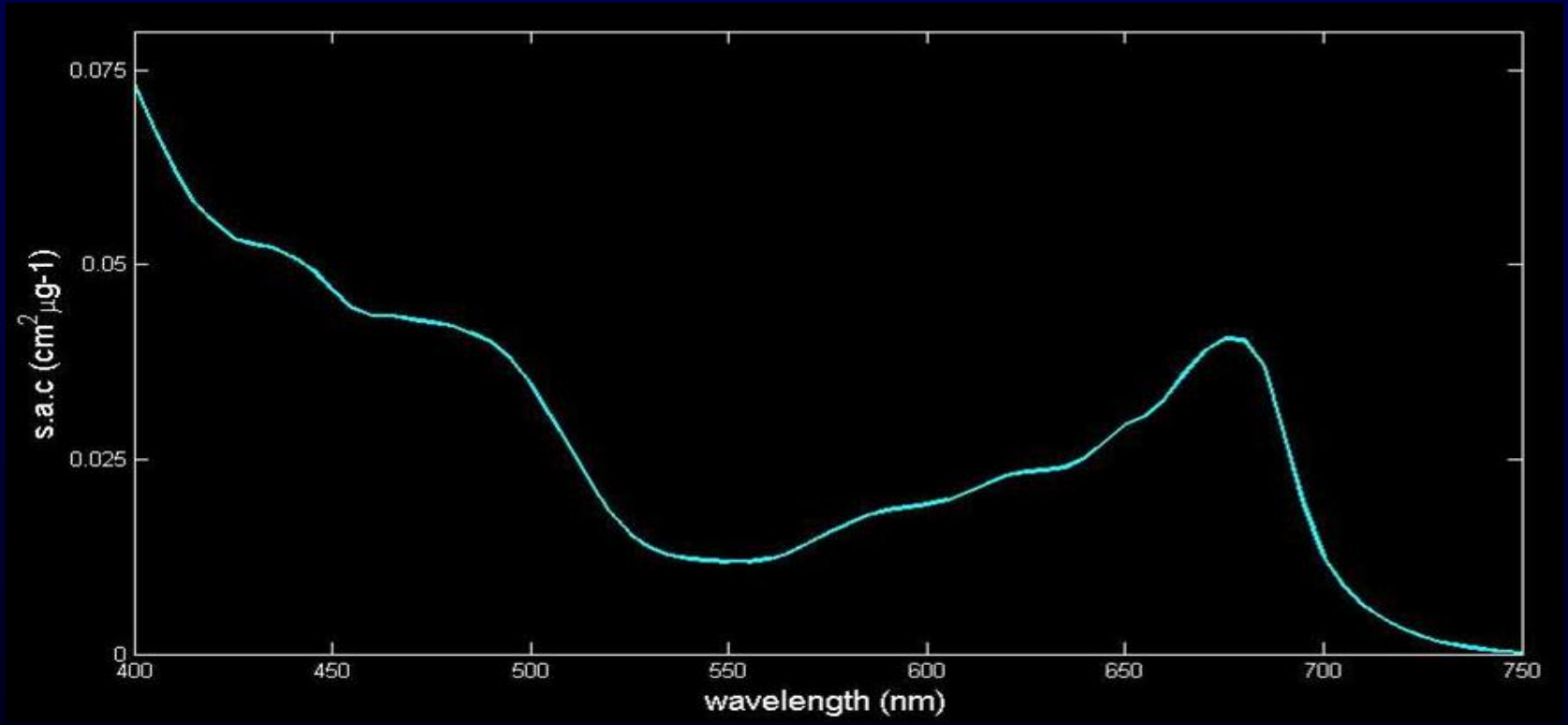
- Qualitative agreement with measured data for *in vivo* water stressed (25%) leaves (Maracci *et al.*, 1991)

Modeled (ABM-U) Reflectance Curves



- Lower reflectance for the water stressed specimen
- More pronounce reflectance decrease around 550nm

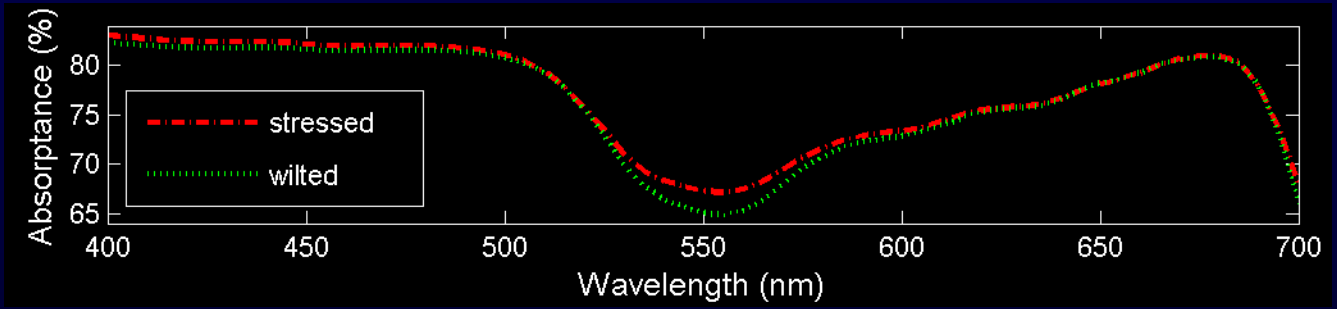
- Recall that detour effect decreases absorption, and the increase is more pronounced in bands of absorption minima (around 550nm for chlorophyll)



Absorption Spectra for chlorophyll *a*+*b*
(Jacquemoud *et al.* 1996)

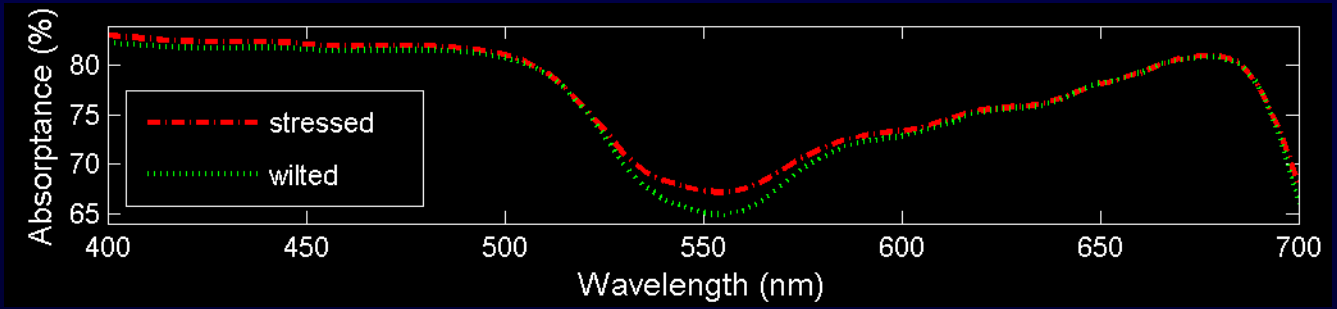
- Qualitative comparison of modeled bihemispherical absorptance values for wilted (*in vitro* water reduction) and stressed (*in vivo* water reduction) specimens

Modeled (ABM-U) Absorptance Curves



- Qualitative comparison of modeled bihemispherical absorptance values for wilted (*in vitro* water reduction) and stressed (*in vivo* water reduction) specimens

Modeled (ABM-U) Absorptance Curves



- Higher absorptance for the *in vivo* water stressed specimen in the photosynthetic region around 550nm

Outline

- ✓ Scope of Applications
- ✓ Case 1: Iridal Pigmentation
- ✓ Case 2: Relocation of Chloroplasts
- ❑ Case 3: Dysfunctional Hemoglobins
- ❑ Theoretical and Practical Perspectives

Case 3: Dysfunctional Hemoglobins

- Science question:
  - Differentiation of life-threatening blood related pathologies: methemoglobinenia and sulfhemoglobinemia

Case 3: Dysfunctional Hemoglobins

- Science question:
  - Differentiation of life-threatening blood related pathologies: methemoglobinenia and sulfhemoglobinemia
  - Under abnormal conditions, human blood may contain excessive amounts dysfunctional hemoglobins that do not bind with oxygen: carboxyhemoglobin, methemoglobin and sulfhemoglobin

➢ Challenges:

- Similar physiological symptoms in the early stages

➢ Challenges:

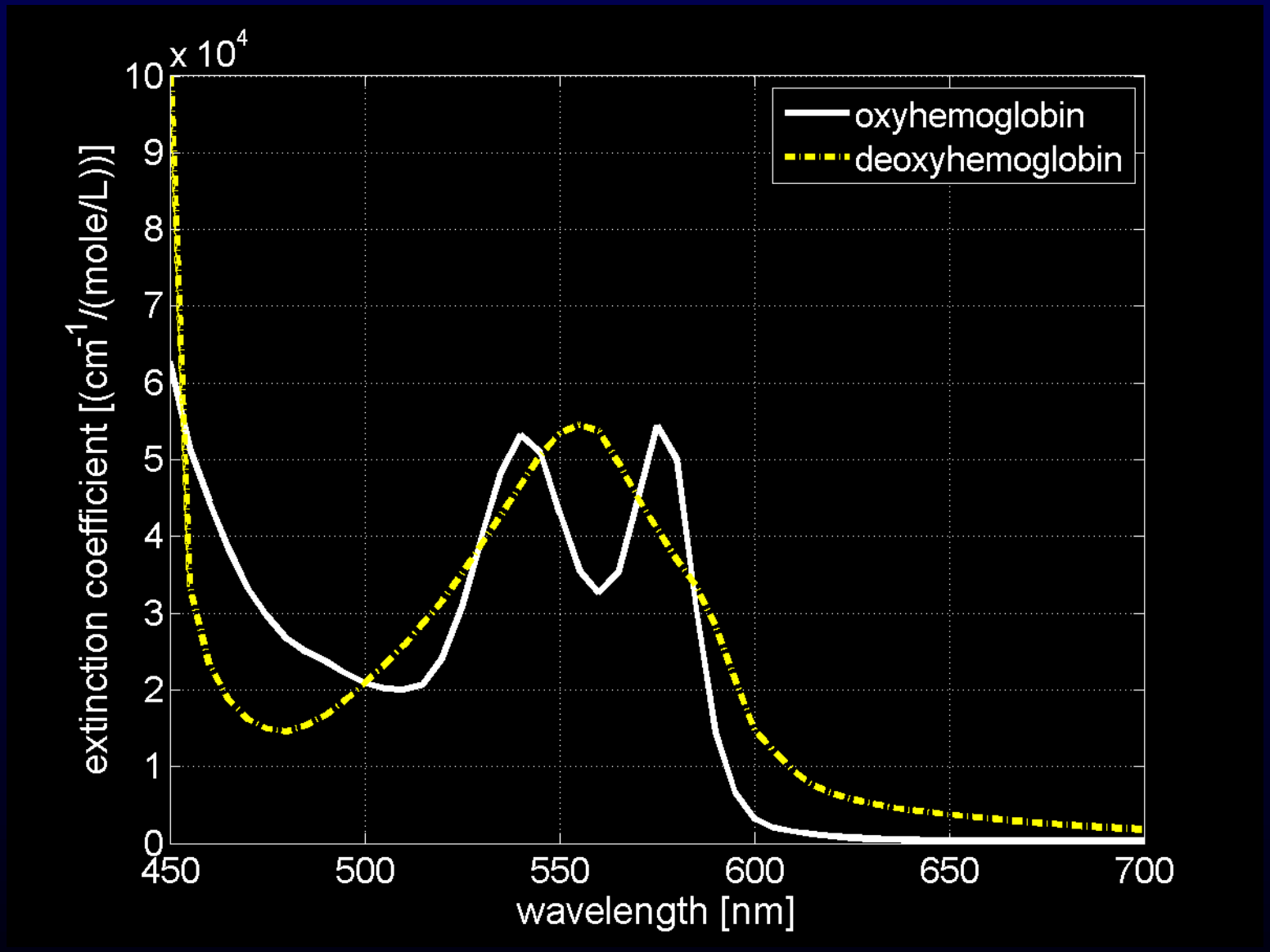
- Similar physiological symptoms in the early stages
- Scarcity of reliable biophysical data (*e.g.*, refractive indices and extinction coefficients)

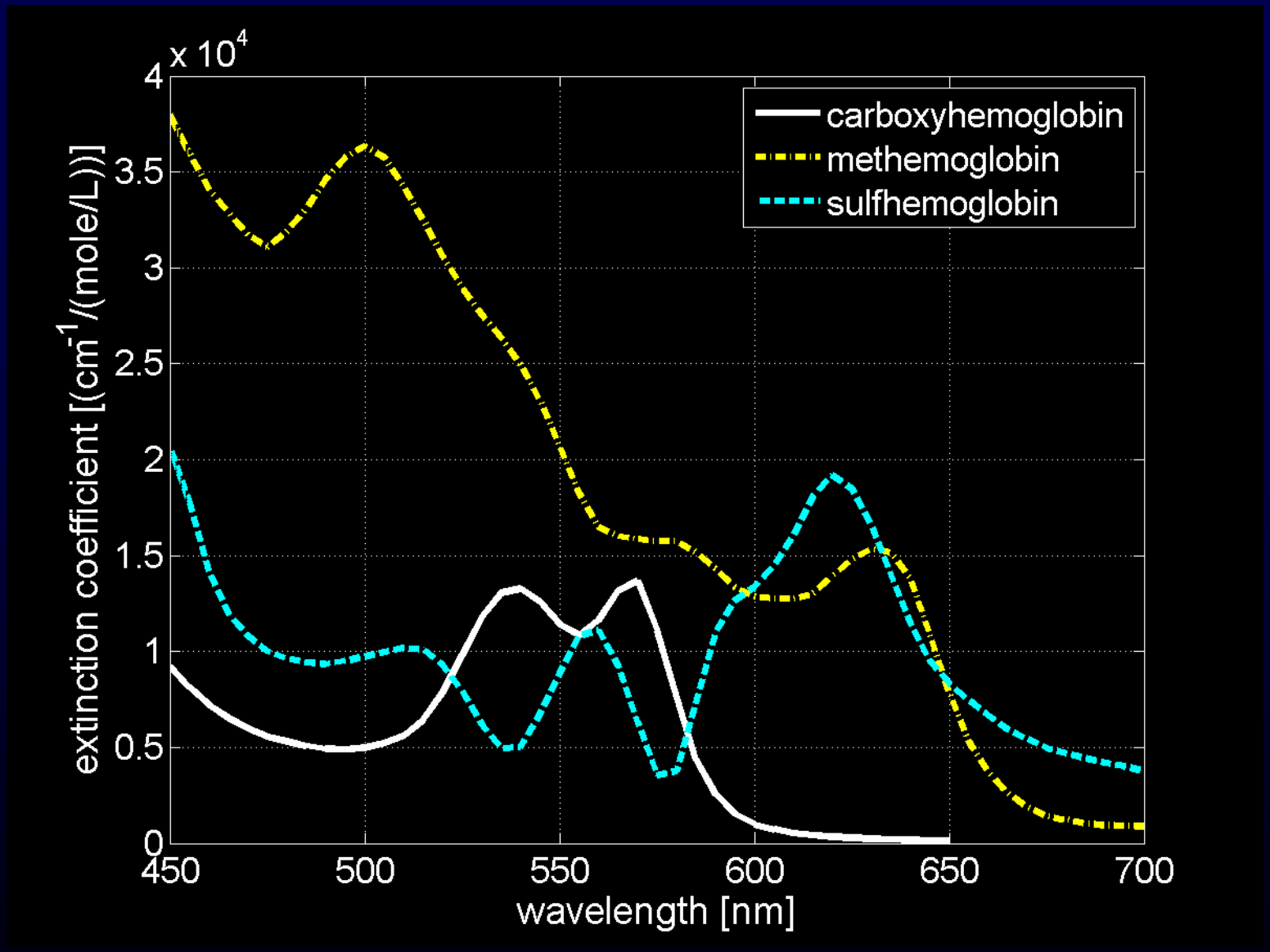
➢ Challenges:

- Similar physiological symptoms in the early stages
- Scarcity of reliable biophysical data (*e.g.*, refractive indices and extinction coefficients)
- Small number of cases reported in the biomedical literature (scarcity of specimen's characterization data)

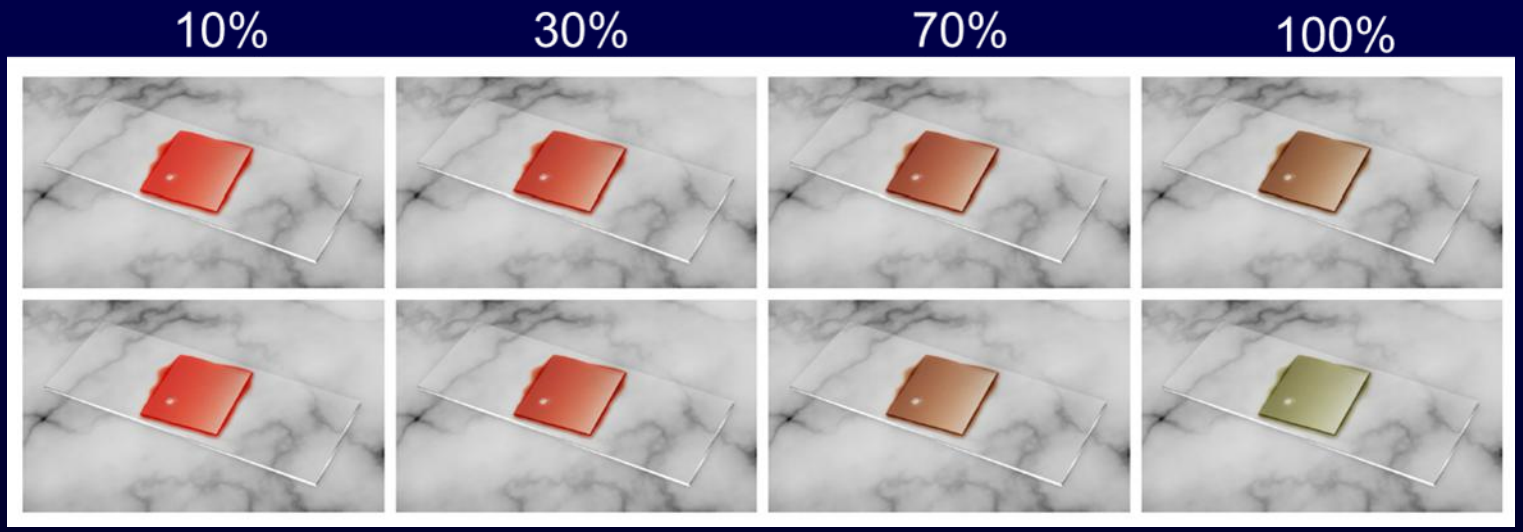
➢ Challenges:

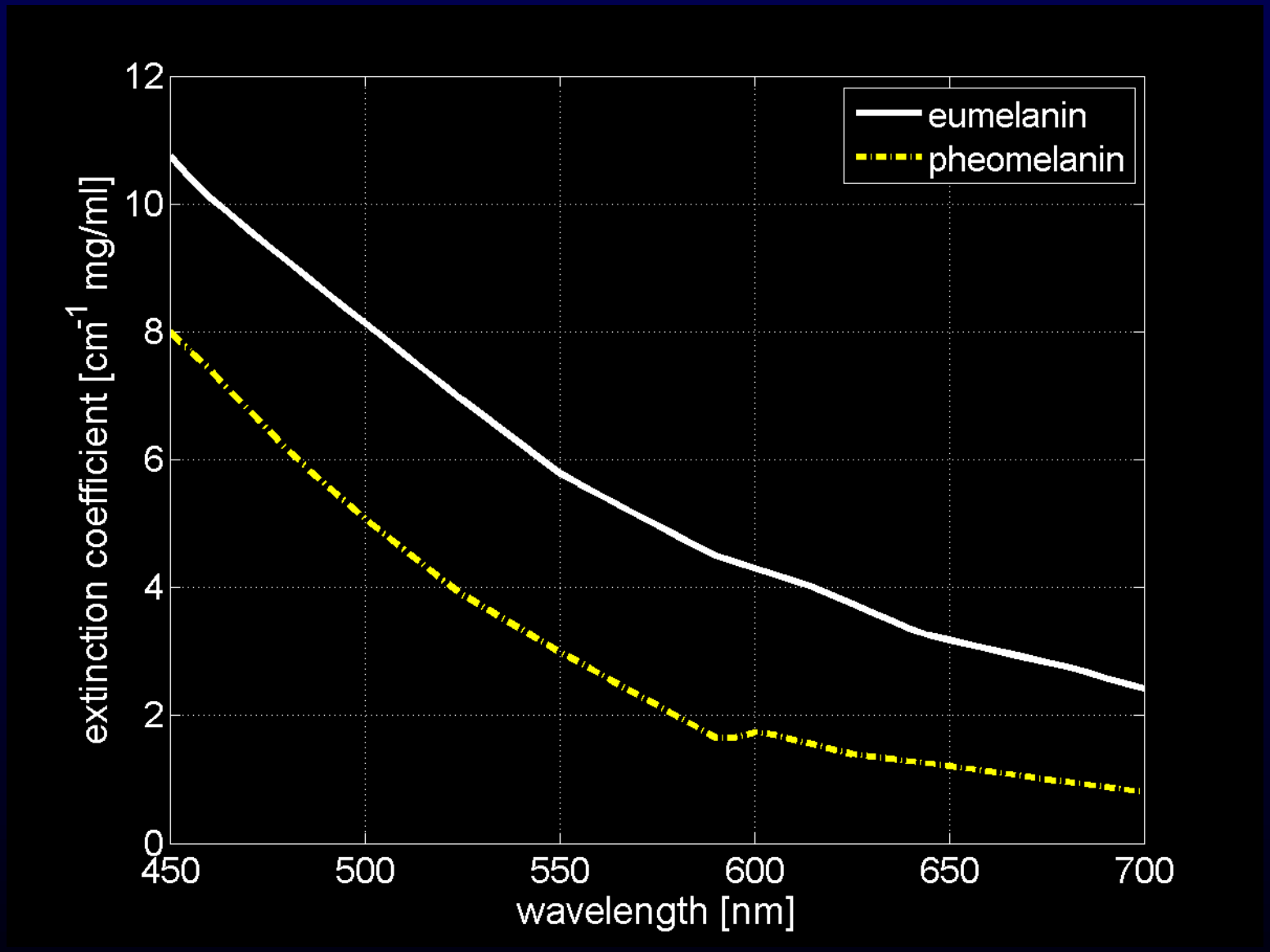
- Similar physiological symptoms in the early stages
- Scarcity of reliable biophysical data (*e.g.*, refractive indices and extinction coefficients)
- Small number of cases reported in the biomedical literature (scarcity of specimen's characterization data)
- Similar spectral appearance of subjects with abnormal amounts of dysfunctional hemoglobins due to the masking effects of skin pigmentation

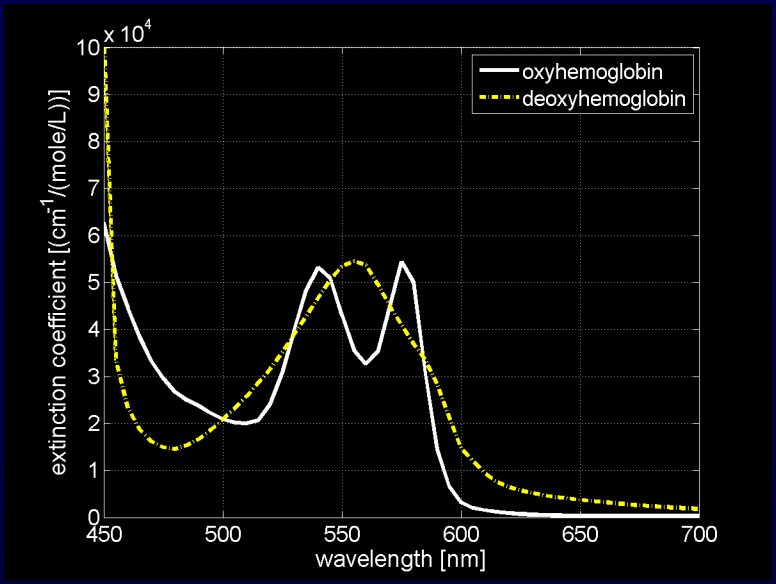

x 10^4
10
9
8
7
6
5
4
3
2
1
0
extinction coefficient [(cm^-1/(mole/L))]
oxyhemoglobin
deoxyhemoglobin
450
500
550
600
650
700
wavelength [nm]

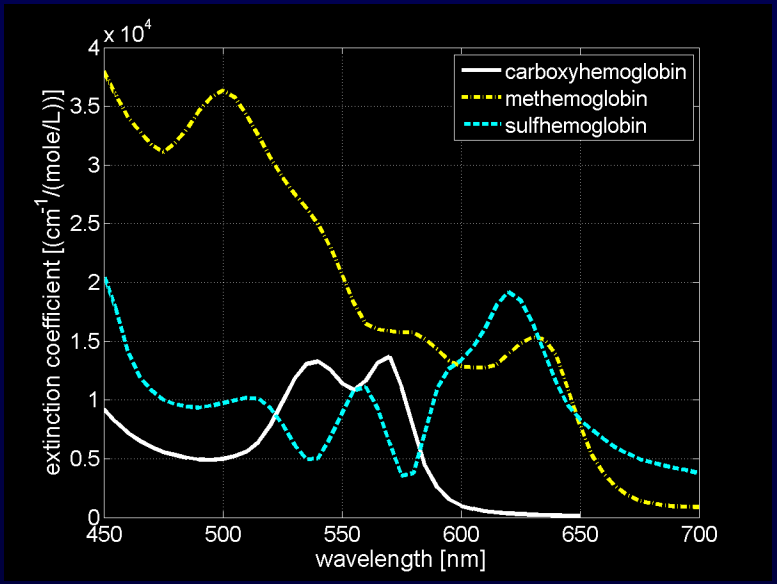

x 10^4
4
3.5
3
2.5
2
1.5
1
0.5
0
extinction coefficient [(cm^-1/(mole/L))]
450
500
550
600
650
700
wavelength [nm]
carboxyhemoglobin
methemoglobin
sulfhemoglobin

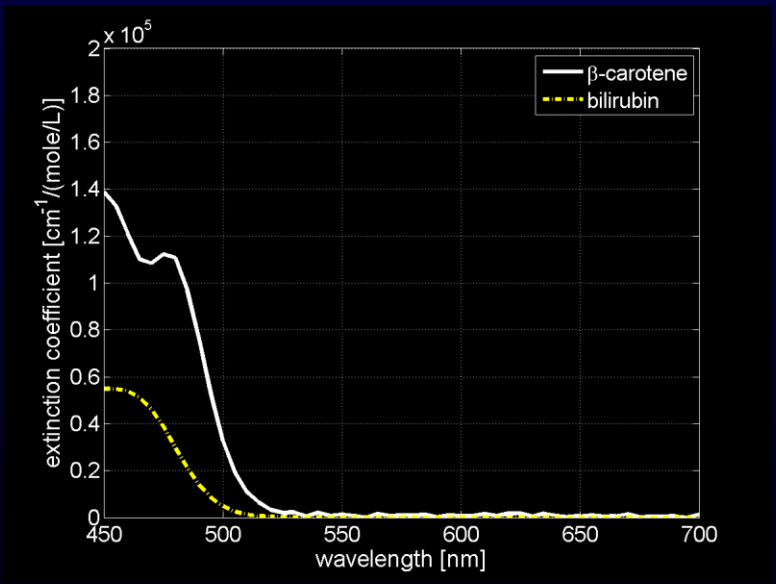
Modeled (CLBlood) Appearance Changes due to the Occurrence of two Dysfunctional Hemoglobins: Methemoglobin and Sulfhemoglobin

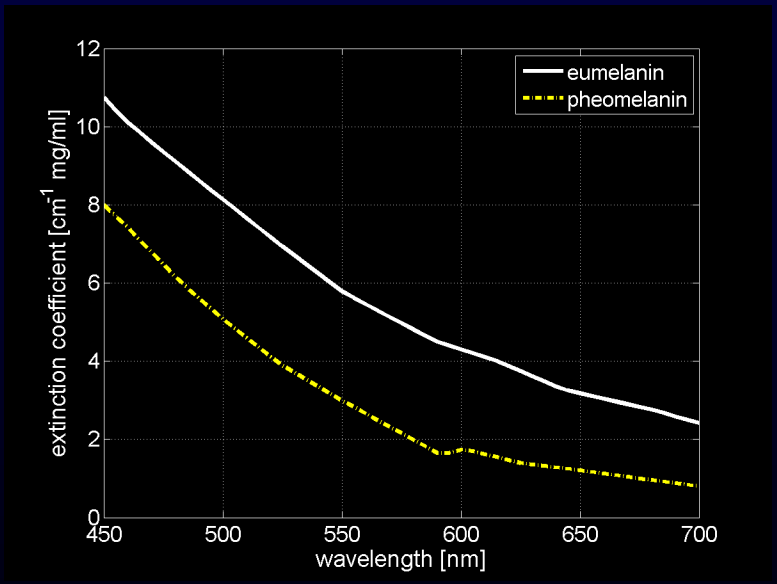


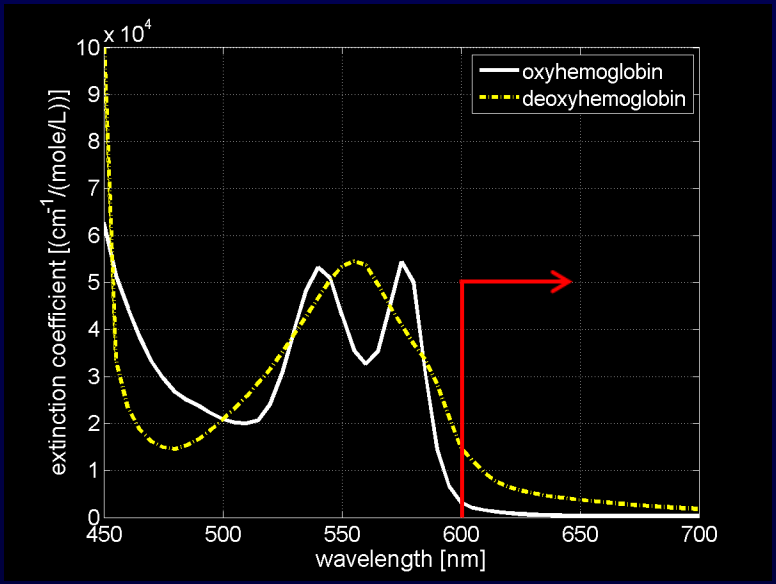

eumelanin
pheomelanin
extinction coefficient [cm-1 mg/ml]
wavelength [nm]
0
2
4
6
8
10
12
450
500
550
600
650
700

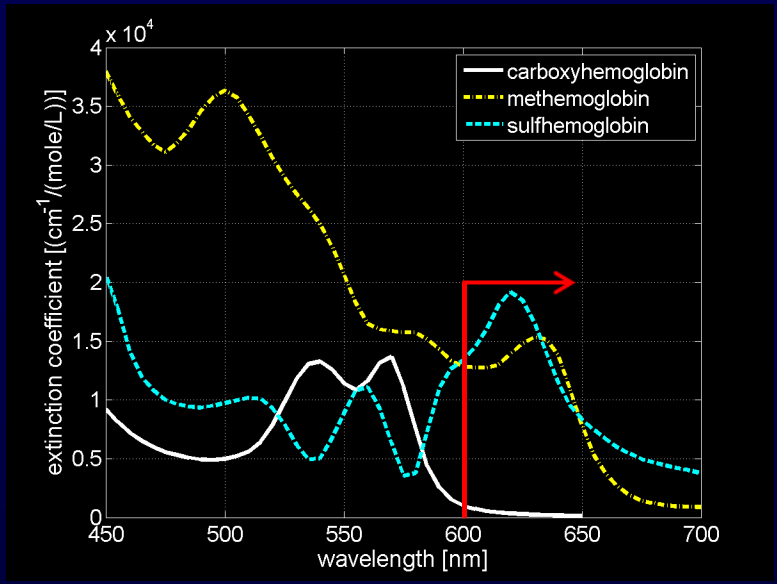

x 10^4
oxyhemoglobin
deoxyhemoglobin
extinction coefficient [(cm^-1/(mole/L))]
wavelength [nm]

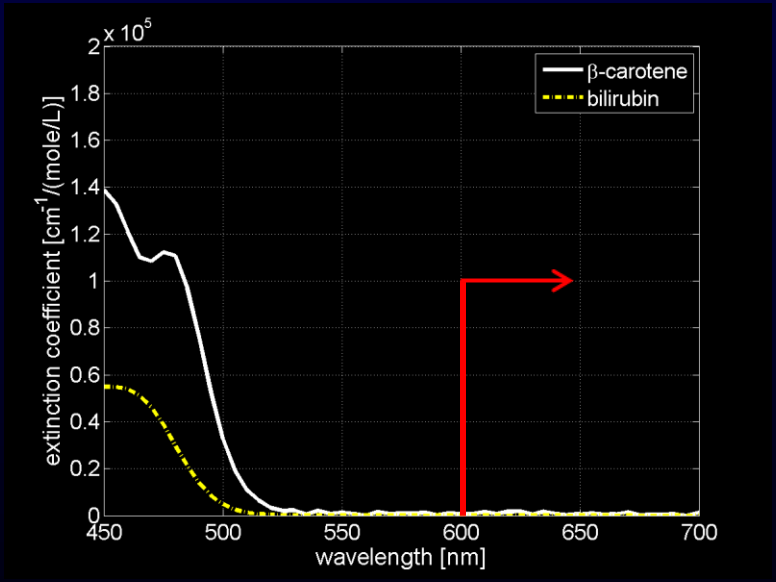

x 10^4
carboxyhemoglobin
methemoglobin
sulfhemoglobin
extinction coefficient [(cm^-1/(mole/L))]
wavelength [nm]

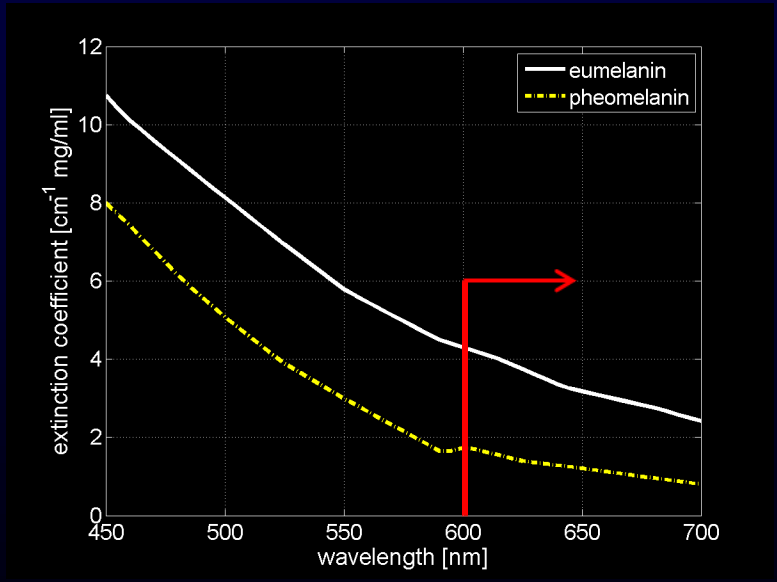

x 10^5
β-carotene
bilirubin
extinction coefficient [cm^-1/(mole/L)]
wavelength [nm]


eumelanin
pheomelanin
extinction coefficient [cm^-1 mg/ml]
wavelength [nm]


x 10^4
oxyhemoglobin
deoxyhemoglobin
extinction coefficient [(cm^-1/(mole/L))]
wavelength [nm]


x 10^4
carboxyhemoglobin
methemoglobin
sulfhemoglobin
extinction coefficient [(cm^-1/(mole/L))]
wavelength [nm]


x 10^5
β-carotene
bilirubin
extinction coefficient [cm^-1/(mole/L)]
wavelength [nm]


eumelanin
pheomelanin
extinction coefficient [cm^-1 mg/ml]
wavelength [nm]

➢ Importance:

- Methemoglobinemia and sulfhemoglobinemia are potentially fatal pathologies that require distinct treatments

- Importance:

  - Methemoglobinemia and sulfhemoglobinemia are potentially fatal pathologies that require distinct treatments

- *In silico* investigation of noninvasive monitoring and differentiation procedures:

  - Analysis of modeled (BioSpec) spectral signatures of skin specimens with abnormal amounts of MetHb and SHb

- Importance:

  - Methemoglobinemia and sulfhemoglobinemia are potentially fatal pathologies that require distinct treatments

- *In silico* investigation of noninvasive monitoring and differentiation procedures:

  - Analysis of modeled (BioSpec) spectral signatures of skin specimens with abnormal amounts of MetHb and SHb

    - "On the noninvasive optical monitoring and differentiation of methemoglobinemia and sulfhemoglobinemia" (Journal of Biomedical Optics 2012)

➢ Simulation guidelines:

- Perform controlled experiments in which the amounts of dysfunctional hemoglobins are increased incrementally

➢ Simulation guidelines:

- Perform controlled experiments in which the amounts of dysfunctional hemoglobins are increased incrementally

- Repeat the experiments for different illumination geometries and different pigmentation levels

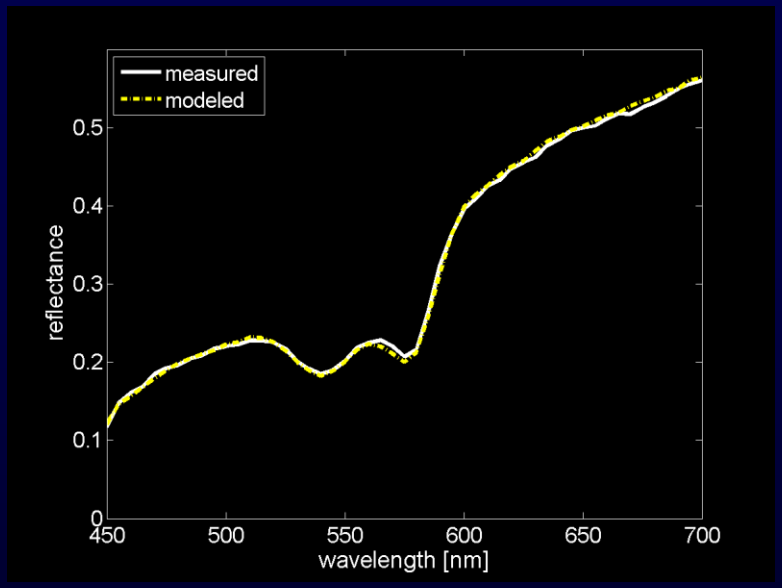
➢ Simulation guidelines:

- Perform controlled experiments in which the amounts of dysfunctional hemoglobins are increased incrementally

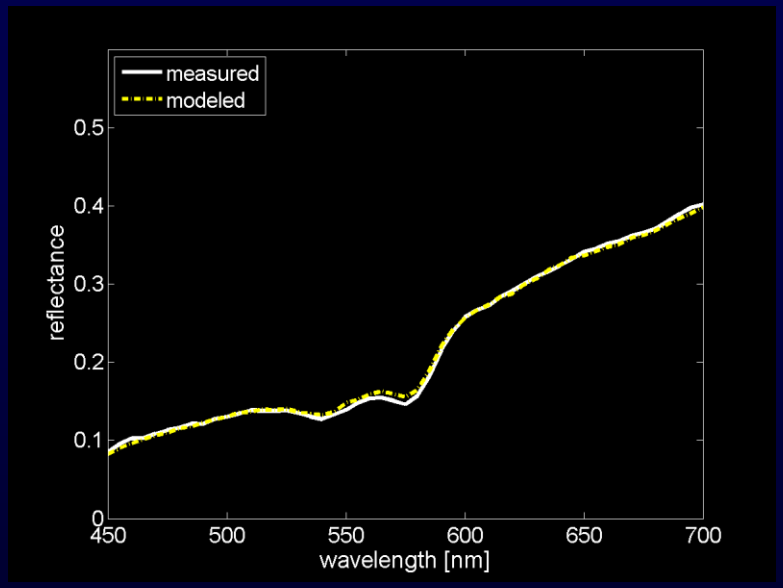
- Repeat the experiments for different illumination geometries and different pigmentation levels

- Use as baseline cases modeled data (BioSpec model) that have been compared with measured data (Vrhel *et al.* 1994) and showed good quantitative and qualitative agreement

Comparison of Modeled (Biospec) and Measured (Verhel *et al.* 1994) Skin Reflectance Curves



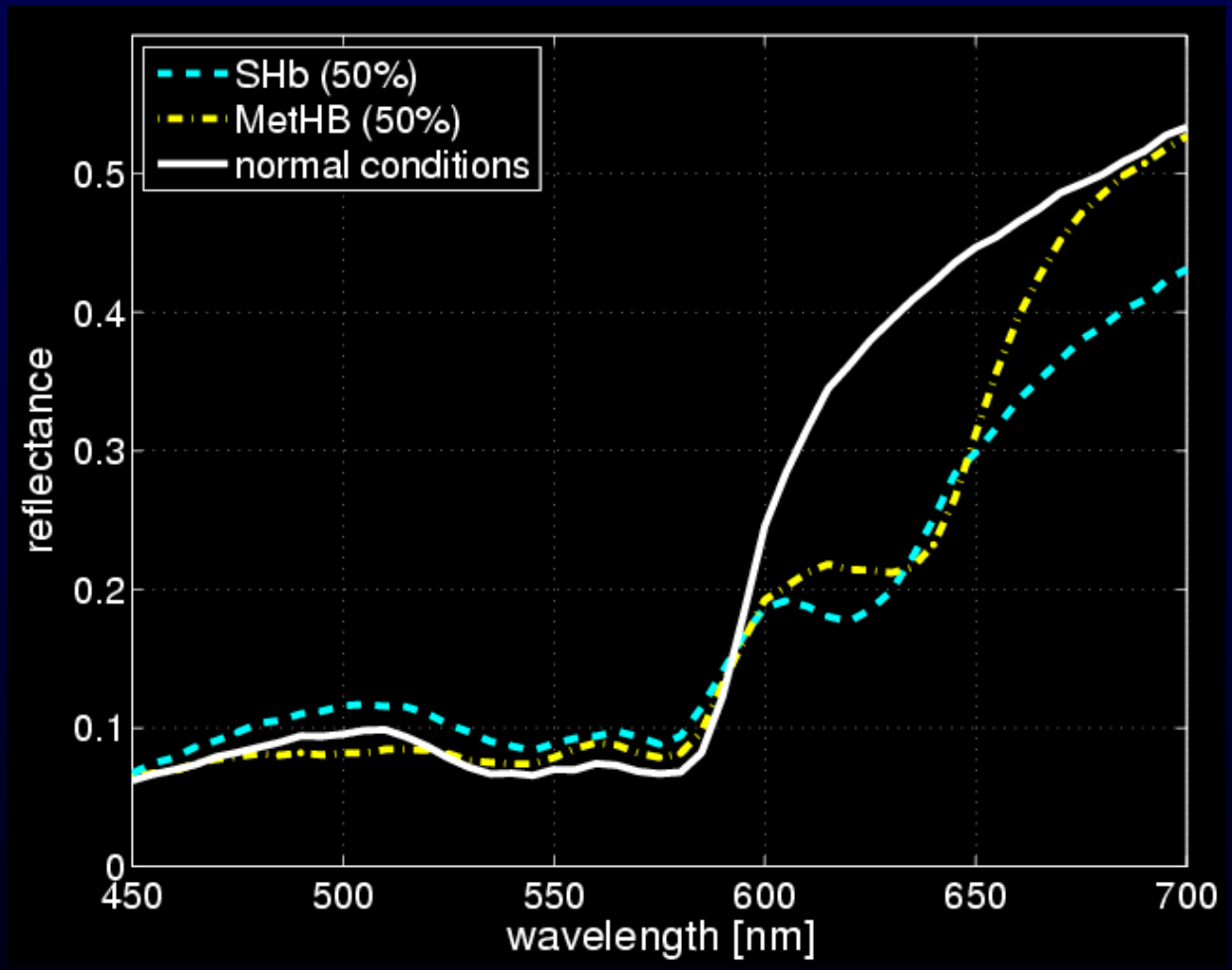
Lightly Pigmented (LP)



Moderately Pigmented (MP)

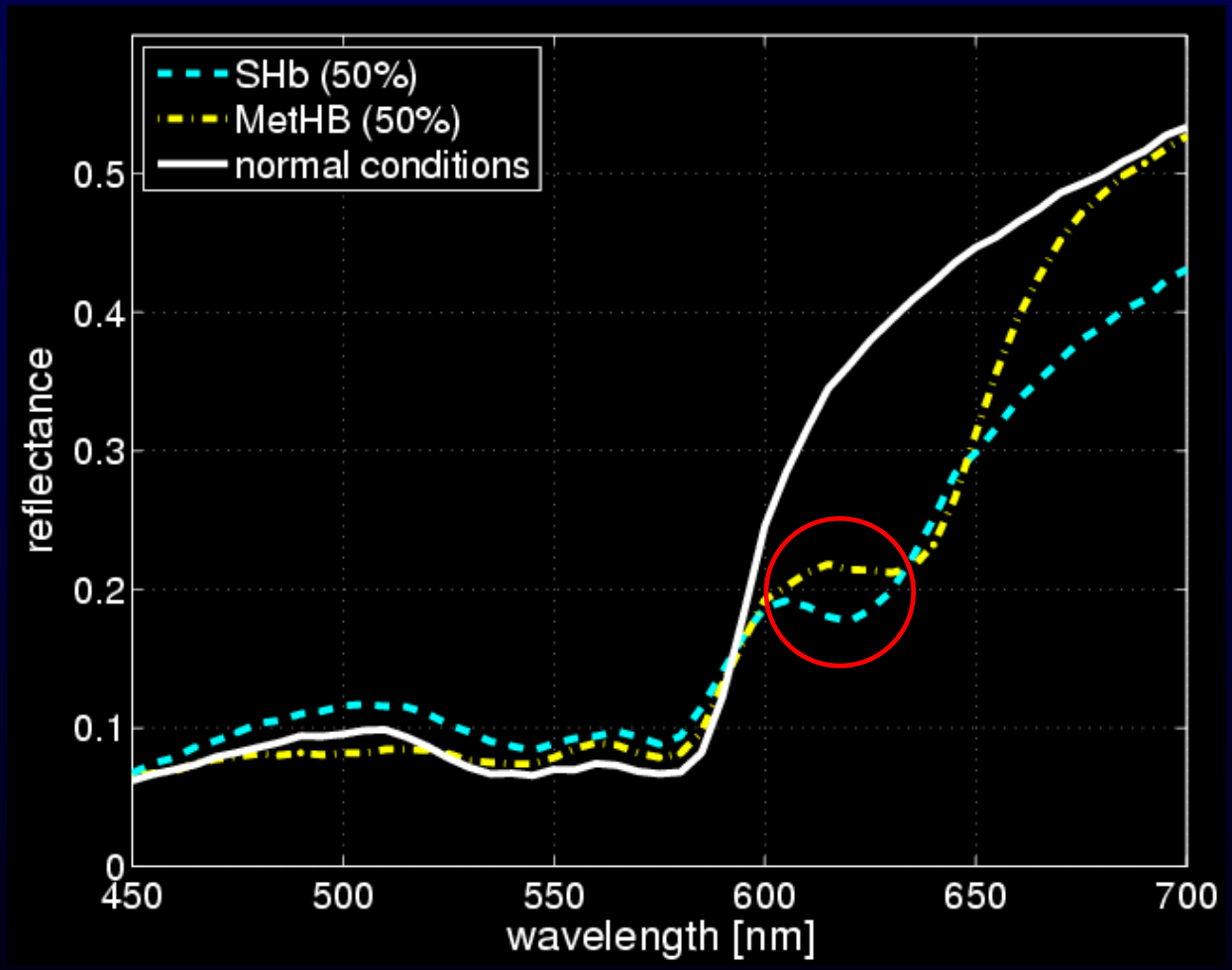
- Example of an experiment instance:

Modeled (BioSpec) Skin Reflectance Curves



- Example of an experiment instance:

Modeled (BioSpec) Skin Reflectance Curves



- Putative differentiation of methemoglobinemia and sulfhemoglobinemia for levels above 10%

Second Derivative Signs (at 615nm)

	MetHb				SHb			
	LP		MP		LP		MP	
	45°	0°	45°	0°	45°	0°	45°	0°
10%	–	–	–	–	–	–	–	–
20%	–	–	–	–	+	+	+	+
30%	–	–	–	–	+	+	+	+
40%	–	–	–	–	+	+	+	+
50%	–	–	–	–	+	+	+	+
60%	–	–	–	–	+	+	+	+
70%	–	–	–	–	+	+	+	+

LP MP

Outline

- ✓ Scope of Applications
- ✓ Case 1: Iridal Pigmentation
- ✓ Case 2: Relocation of Chloroplasts
- ✓ Case 3: Dysfunctional Hemoglobins
- ❑ Theoretical and Practical Perspectives

Theoretical and Practical Perspectives

- Is the rationale behind the *in silico* investigation of biophysical phenomena something new?

Theoretical and Practical Perspectives

- Is the rationale behind the *in silico* investigation of biophysical phenomena something new?

"We have to find a new view of the world that has to agree with everything that is known, but disagree in its predictions somewhere, otherwise it is not interesting."

R.P. Feynman
The Character of Physical Law, 1964

Theoretical and Practical Perspectives

- Is the rationale behind the *in silico* investigation of biophysical phenomena something new?

"We have to find a new view of the world that has to agree with everything that is known, but disagree in its predictions somewhere, otherwise it is not interesting."

"Science is only useful if it tells you about some experiment that has not been done; it is no good if it only tells you what just went on."

R.P. Feynman
The Character of Physical Law, 1964

- Viewed in this context, a predictive *in silico* experimental framework can also be used to:

  - Simulate the behavior of a system under various conditions, including those that are still open scientific questions

- Viewed in this context, a predictive *in silico* experimental framework can also be used to:

  - Simulate the behavior of a system under various conditions, including those that are still open scientific questions

  - Drive new investigations (*e.g.*, the study of physiological perturbations caused by abiotic stress factors)

- Viewed in this context, a predictive *in silico* experimental framework can also be used to:
  - Simulate the behavior of a system under various conditions, including those that are still open scientific questions
  - Drive new investigations (*e.g.*, the study of physiological perturbations caused by abiotic stress factors)
- Hence, it can truly be an instrument for productive interdisciplinary research

- Is interdisciplinary research really attainable?

- Is interdisciplinary research really attainable?

  - It requires a substantial amount of professional and personal effort to overcome technical barriers such as:

- Is interdisciplinary research really attainable?

  - It requires a substantial amount of professional and personal effort to overcome technical barriers such as:

    - Data scarcity
    - Terminology issues
    - Unsound generalizations, …

➢ Is interdisciplinary research really attainable?

- It requires a substantial amount of professional and personal effort to overcome technical barriers such as:
  - Data scarcity
  - Terminology issues
  - Unsound generalizations, …
- … and to acquire a comprehensive understanding about the target problem from a biophysical perspective

- How about political barriers?

- How about political barriers?

  - Intra-departmental

- How about political barriers?
  - Intra-departmental
  - Inter-departmental

- How about political barriers?
  - Intra-departmental
  - Inter-departmental
  - External
    - Conference and journal reviewing committees
    - Scholarship and grant selection committees

- Is it worth the effort?

- Is it worth the effort?

Depends!

- Is it worth the effort?

Depends!

- What kind of contributions do we want leave behind?

This concludes Lecture 5 and the Lecture Series!

Thanks!

Questions?

Credits: Images and Photos

- D. Yim
- M. Lam
- B. W. Kimmel
- A. Krishnaswamy
- T.F. Chen
- E. Miranda
- N. Y. Kiang
- J. Trobe
- NASA
- Wikipedia