

BioMedical Optics Applications with FRED

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Applications in the fields of biophotonics and medical optics usually entail the illumination of a biological sample from an illumination system and then collection of signal light from the sample and delivery of this signal light to an analytical detector. The illumination system typically consists of a coherent or incoherent light source. The energy from the light source must be captured with some sort of condenser optical system and then typically spatially homogenized to uniformly illuminate the biological sample. The biological sample when illuminated with energy from the illumination source will generate a signal from one or more of the optical methods of – diffraction, reflection, absorption, transmission, scatter, or fluorescence. The illumination may be monochromatic or across a broad spectrum and the signal may be collected in a narrow spectral band or over a large spectral width. One of the high value benefits of using FRED is that one can create a virtual prototype of the biophotonic instrument and evaluate all of the opto-mechanical ideas and issues prior to committing to hardware.

In this white paper we will investigate several biophotonic and medical optics systems to get an applied understanding of the capabilities of the software. The applications we will look at include:

- Gonioscopy Lens for Illumination and Imaging of the Anterior Chamber of the human eye.
- Laser Induced Fluorescence in a Capillary for the Analysis of Biological Fluids

These biophotonic and medical optics applications require a broad set of capabilities from an optical engineering software program such as FRED. These capabilities include:

Light Source and Illumination System Modeling and Analysis

- Light Source Model Creation – Surface and Volume Emitters
- Source File Model Interpretation and Use (Radiant Source Models)
- Source Collection
- Illumination Source Spatial Homogenization
- Illumination System Modeling
- Illumination System Radiometry and Efficiency
- Illumination Plane Irradiance Analysis
- System Dosimetry

Signal Capture Path Modeling and Analysis

- Surface Scatter using various standard scatter models
- Volume Scatter – Coming Summer 2004?
- Volume Source to simulate volume scatter
- Scatter Importance Modeling for Efficient Modeling
- Scatter/Source Collection Modeling
- Sequential and Non-Sequential Raytracing

- Image/Illumination Plane Analysis – Spot Diagrams, Polarization Analysis, Irradiance Distribution, Energy Density, Coating Characteristics.
- Graphic Visualization of Illumination and Signal Capture Paths

For a complete list of the capabilities of FRED please see the current FRED Technical Description at: www.photonengineering.com/software.htm#Brochure

FRED Medical Optics Example 1: Gonioscopy Lens

A gonioscopy lens is used for the purpose of measuring the angle between the iris and the internal surface of the cornea in the human eye. The measurement of this angle between the two surfaces, is a critical diagnostic tool in glaucoma patients, and can tell an ophthalmologist about the pressure inside the eye. To measure this angle one must illuminate the intersection of these two surfaces through the front of the eye. The optical system must then collect and focus the scattered light from the intersection onto an image sensor in order to measure the angle of the two surfaces.

Let's take a look at how this optical system can be modeled in FRED. The first thing we need is an optical model of the human eye. This eye model is created from a reference model of the eye^{1,2}. The eye surface model is input sequentially as a normal lens assembly and is graphically shown below. The graphical display capabilities, features, and ability to customize the visual attributes of rays and surfaces in FRED are truly outstanding. The aspheric surfaces parameters of the eye surfaces are input using the surface geometry input window in FRED, this is also where the optical properties of the surface are added such as index, dispersion, reflectivity, coatings, scatter model and properties, and surface visualization parameters.

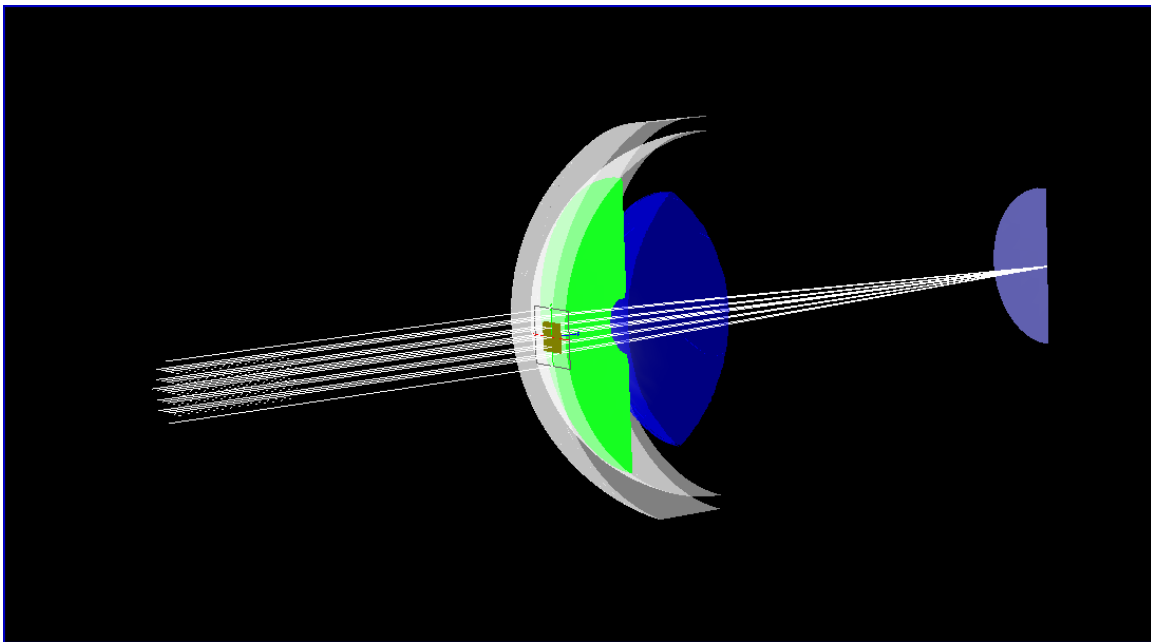


Figure 1. Cross section view of the human eye

In this model of the eye one can see the front and rear surfaces of the cornea, the iris, the eye lens, and the retinal surface where the rays come to a focus. All of the appropriate optical materials have been input to properly model the refractive index and dispersion, including the aqueous fluid and vitreous humor materials.

Now that we have a properly working model of the eye we can add the gonioscopy lens to the front surface of the cornea. We also need to illuminate the anterior chamber of the eye (between the inside of the cornea and the iris) with a slit of light. We will need to place the proper scattering properties onto the second surface of the cornea and also onto the front of the iris. As these two surfaces are illuminated they will become a new scattering sources and the signal for the detection system to collect and deliver to the analysis detector plane.

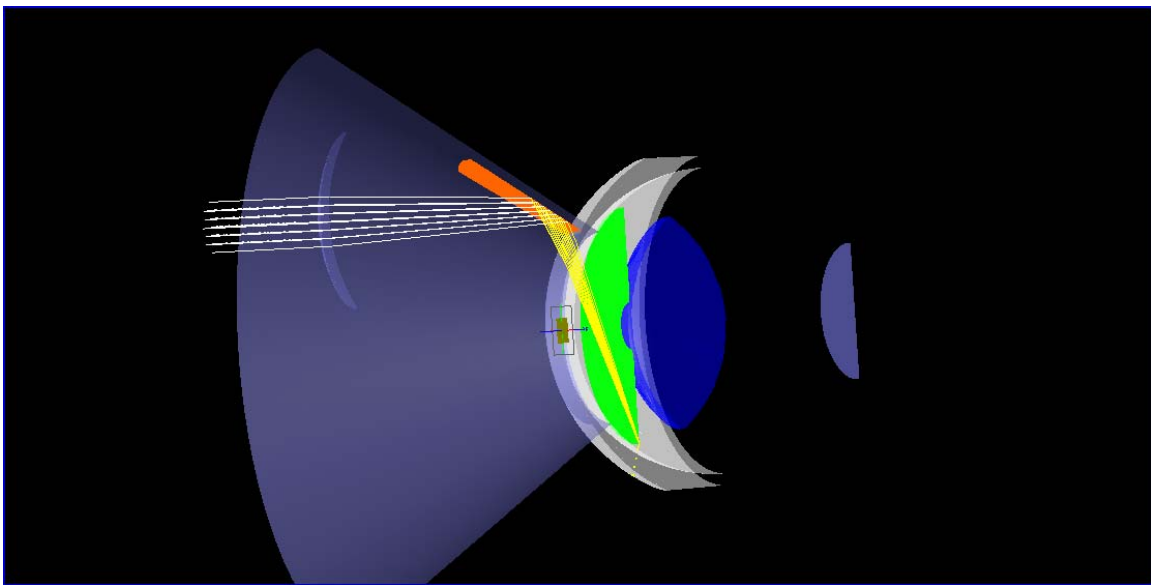


Figure 2. Collimated input beam focusing at the target intersection

Here we can see the collimated beam of rays entering the gonioscopy lens (single mirror Goldman lens) and being refracted by the entrance surface lens, and then being reflected by the flat mirror on the conical part of the Goldman lens. This converging beam is then refracted through the exit surface of the gonioscopic lens through a coupling fluid called goniogel and finally into the corneal surfaces and into the anterior chamber of the eye. If FRED we can tell the program what is the optical material on each side of the optical surfaces such as air:glass; glass:glass; glass:goniogel; goniogel:cornea; cornea:aqueous humor and so forth. Properly defining the properties of the optical materials in the system enables FRED to accurately model different optical effects in the system such as refraction, reflection, scatter, diffraction, and transmission.

The light source is now given the real one-degree half-angle rectangular divergence and we find that the target location in the anterior chamber of the eye is illuminated with a rectangular slit of light as specified in the instrument design specification. Now that we can properly illuminate the target location we need to set the scattered light properties of the illuminated surfaces in the eye, namely the second surface of the cornea and the front

surface of the iris. The scattered light from these two illuminated surfaces is the signal that we want to capture for diagnostic purposes of determining the angle.

Let's take a look at how to make surfaces scatter in FRED. The illumination source illuminates the front surface of the iris and the iris is an absorbing surface that also scatters light. If we edit the front surface of the iris we can set the scatter properties to be a Lambertian scattering surface with 96% diffuse reflectivity.

If we did not control the scatter direction, in this model, the scattered light would scatter into the whole hemisphere in front of the iris. This would be a great waste of scattered rays and consume unnecessary computing resources. It would also make for a visually confusing modeling illustration to show others. Fortunately FRED has an efficient method to only scatter rays towards directions that are important to us or to surfaces that we specify in the optical system. The particular method we use here is called importance sampling and we tell the front surface of the iris to scatter light only in the direction of the mirror on the gonioscopy lens, this mirror then reflects the light back toward the incoming source, based upon the law of reflection, and finally towards the imaging lens and the analytical detector (not shown yet).

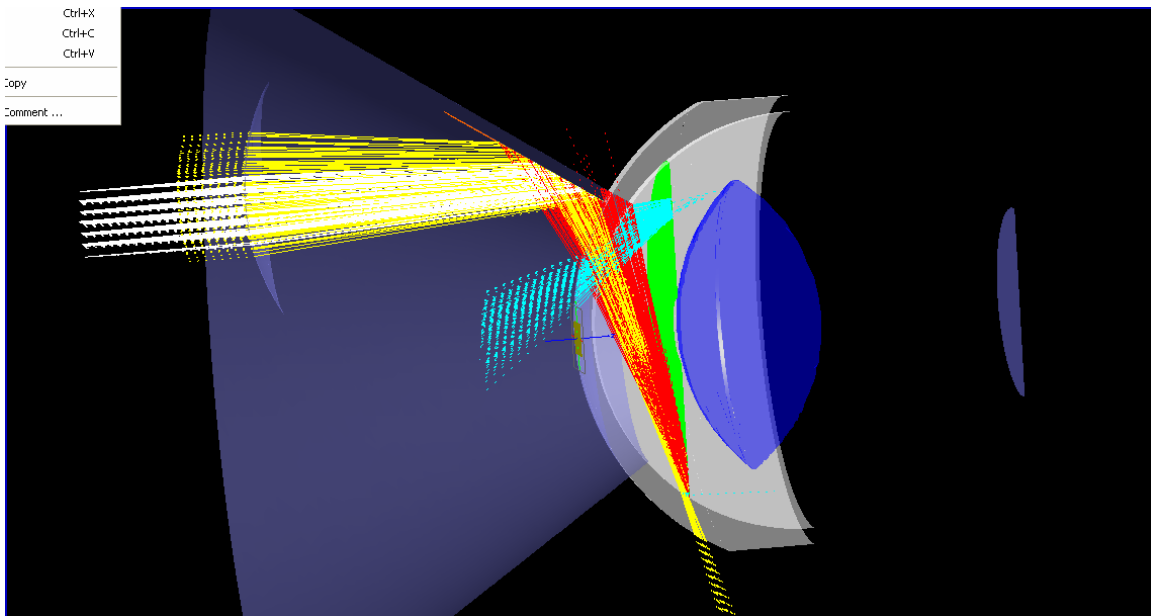


Figure 3. Scattered light from the iris

In Figure 3 cross-section view we can see the incoming white rays from the source and they turn yellow upon reflection from the mirror and are incident upon the front surface of the iris and the second surface of the cornea. The light is scattered from the front surface of the iris, and we have asked FRED to turn the scattered rays from the iris red. This ray coloring based upon optical property of transmission, reflection, scatter, and diffraction is a very powerful graphical visualization aid in FRED. We have asked FRED to turn the rays reflected from the second surface of the cornea light blue. The red rays scattered from the iris are only scattered towards the importance surface, the mirror, and after reflection from the mirror are turned yellow on their way to the analysis detector.

We can also see the rays that are reflected from the second surface of the cornea are turned light blue. These reflections are from the scattered rays off of the iris as they are propagating back towards the second surface of the cornea towards the mirror or importance surface. As the scattered ray encounters the second surface of the cornea part of the energy is reflected and converges to form a ghost image spot on the iris (light blue) and the rest is refracted through the cornea, into the gonioscopic lens and off the mirror towards the analysis detector. The diverging light blue rays are reflection from the incident illumination rays and reflect off of the second surface of the cornea on the way into the iris.

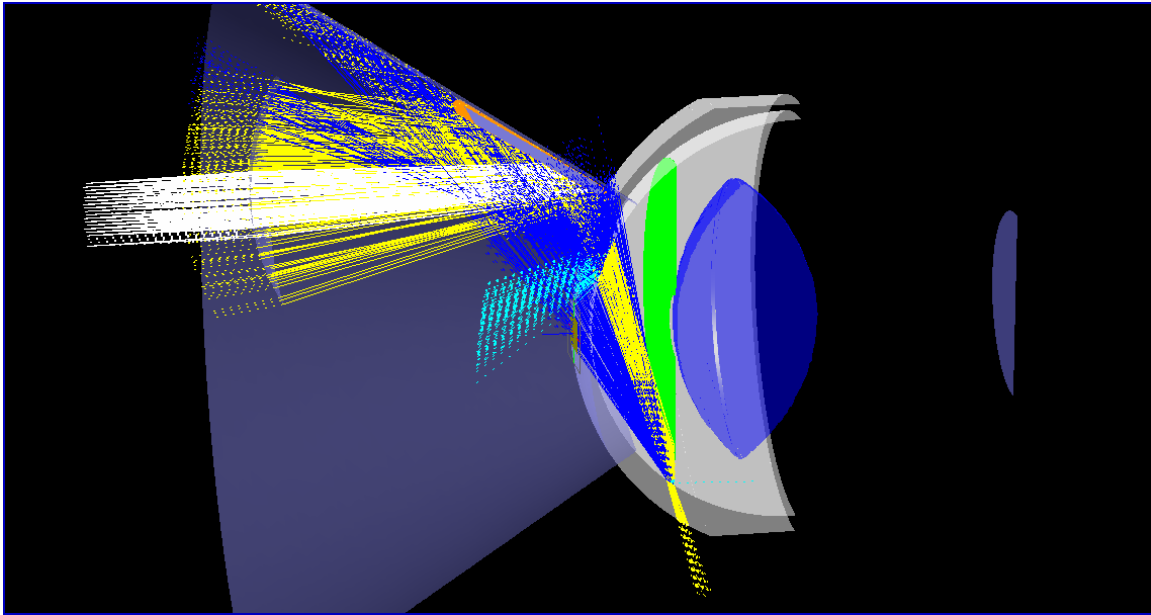


Figure 4. Scattered light from the cornea

To aid in the visualization of illumination, scattered light, stray light, ghost reflection, imaging and signal analysis FRED has the capability to turn on and off the various combinations of reflections, diffraction, scattered light, and transmission at each surface in the system. To illustrate this powerful capability in FRED we have turned off the scatter from the iris and are now only showing the scattered light from the second surface of the cornea. We have asked the program to turn the yellow illumination light rays, blue when the light is scattered from this second surface of the cornea. Again for ray tracing and analysis efficiency we have asked FRED to only scatter light from the second surface of the cornea toward the importance surface which has been designated as the fold mirror. We can see the blue scattered rays turn yellow upon reflection from the fold mirror, as discussed previously, on the way to the analysis detector.

In Figure 5 below we can see the combination of the scattered light from both the iris and the cornea shown in red and blue scattered light respectively.

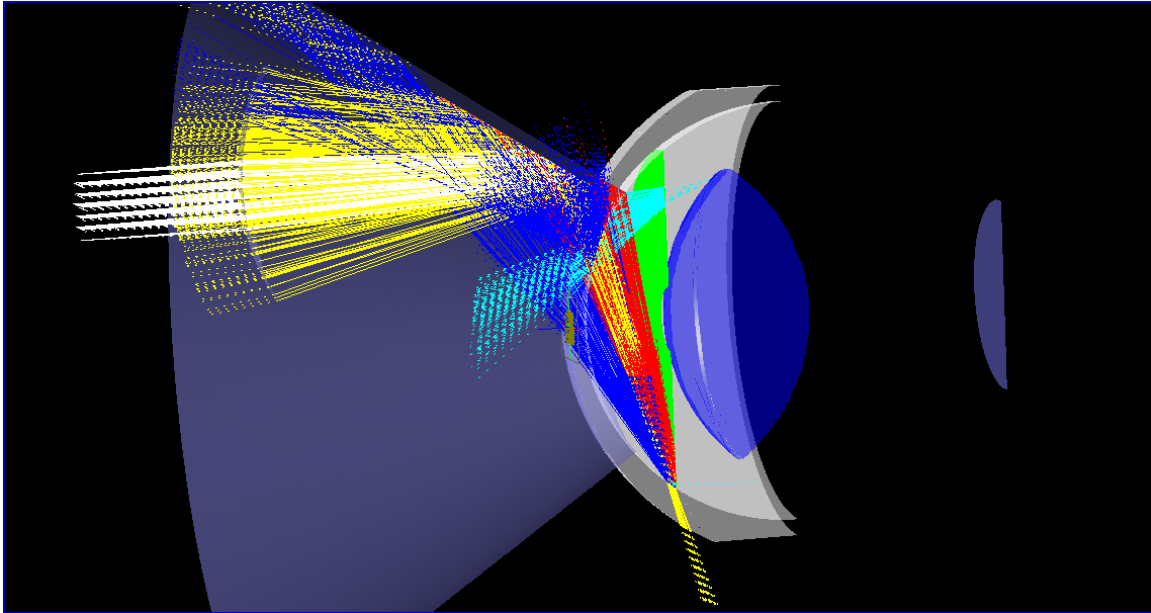


Figure 5. Illuminated target surface and scattered light from both surfaces

Here we have turned the scattering on both of the surfaces at one time and show how the real application will scatter light from both the iris and the second surface of the cornea back to the analysis detector. In order to capture and focus the scattered light from the measurement surfaces we need to insert an imaging lens to collect the light and focus it onto the analysis detector. A simple catalog lens from one of the vendor catalogs that is inherent to FRED was inserted and moved to the proper location in space and an analysis detector was added and moved into location at the focus of the lens.

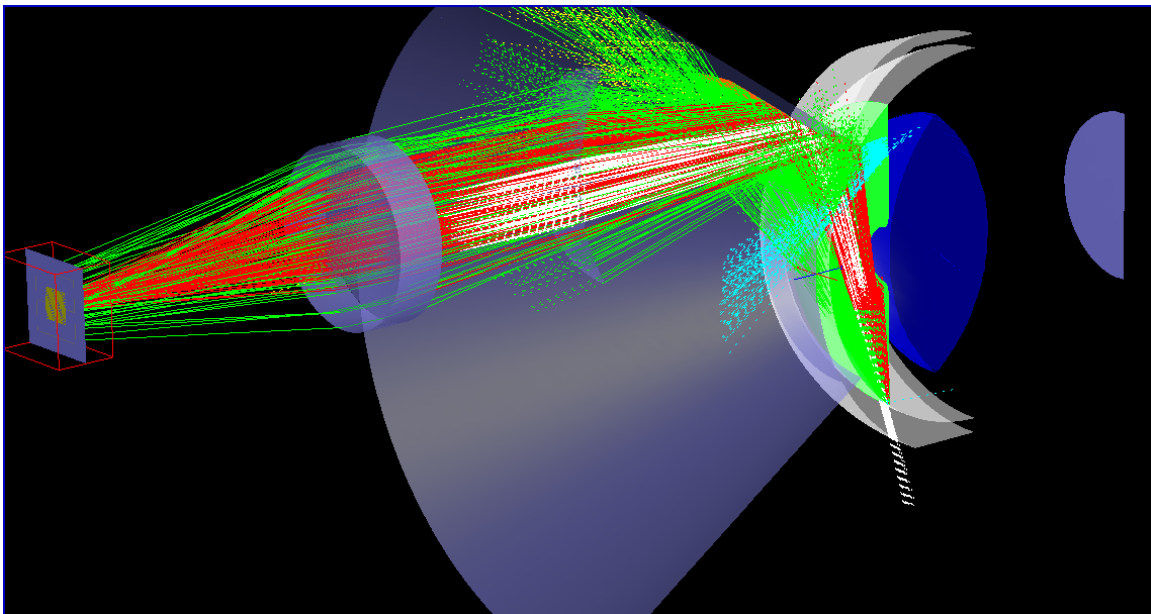


Figure 6. Scattered light capture and imaging onto the analysis detector

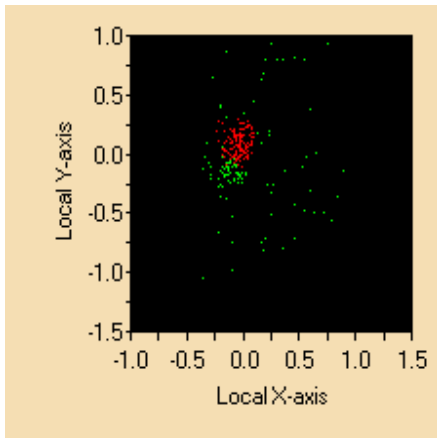


Figure 7. Plano Iris, Detector

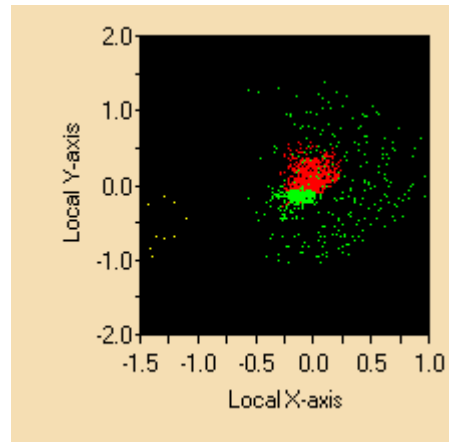


Figure 8. Curved Iris, Detector

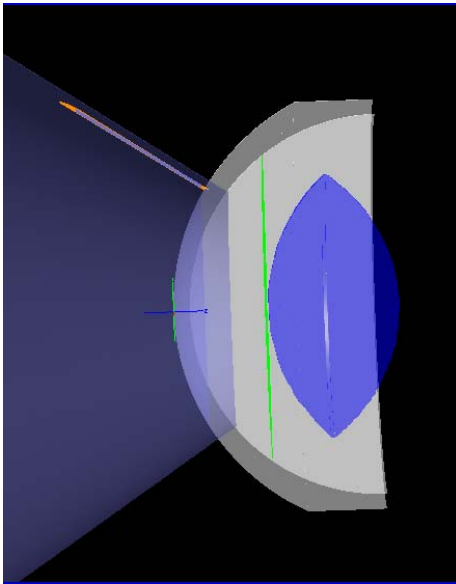


Figure 9. Plano Iris Cross Section

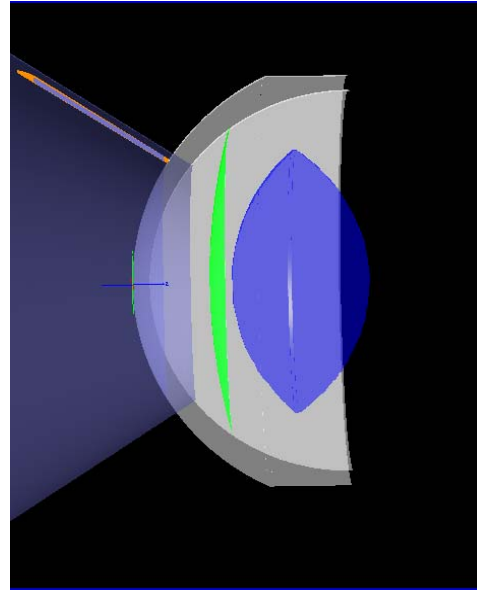


Figure 10. Curved Iris Cross Section

We can see the illumination spot diagrams from the scattered light off of the iris and inside of the cornea on the analysis detectors in Figures 7 and 8. These two spot diagrams in FRED show the two different cases with different gonioscopic angles between the iris and cornea. Case one shown in Figure 9 has a plano iris and case two shown in Figure 10 has a curved iris and therefore a smaller angle between the iris and cornea. As expected we can see the image shearing with the smaller or closed angle in Figure 8. One of the powerful abilities of optical engineering modeling tools like FRED is that one can model different physical scenarios and determine what the analysis image should look like prior to building an instrument.

1. The Eye and Visual Optical Instruments, G. Smith & D. Atchison, Cambridge University Press, 1997
2. Visual Optics Course Notes, Jim Schwierling, Optical Sciences Center, University of Arizona, 2000.

Laser Induced Fluorescence – Capillary Electrophoresis

In this medical optics application we have a collimated laser beam being focused into the center of a glass capillary column. The glass capillary tube has an inside diameter of 0.250 mm and an outside diameter of 0.400 mm. The biconvex objective lens focuses the laser beam into the center of the glass capillary tube. The liquid to be analyzed is flowed through the capillary in the presence of a high voltage. The high voltage accelerates particles with more mass faster through the capillary column. When certain particles or compounds pass through the laser illumination beam they fluoresce at a longer wavelength. There is an optical system that is oriented at 90 degrees to the laser illumination beam that collects the fluorescent light from the particles and focuses this fluorescent light onto an analysis detector. Lets take a look at how we can set up this medical optics instrument in FRED.

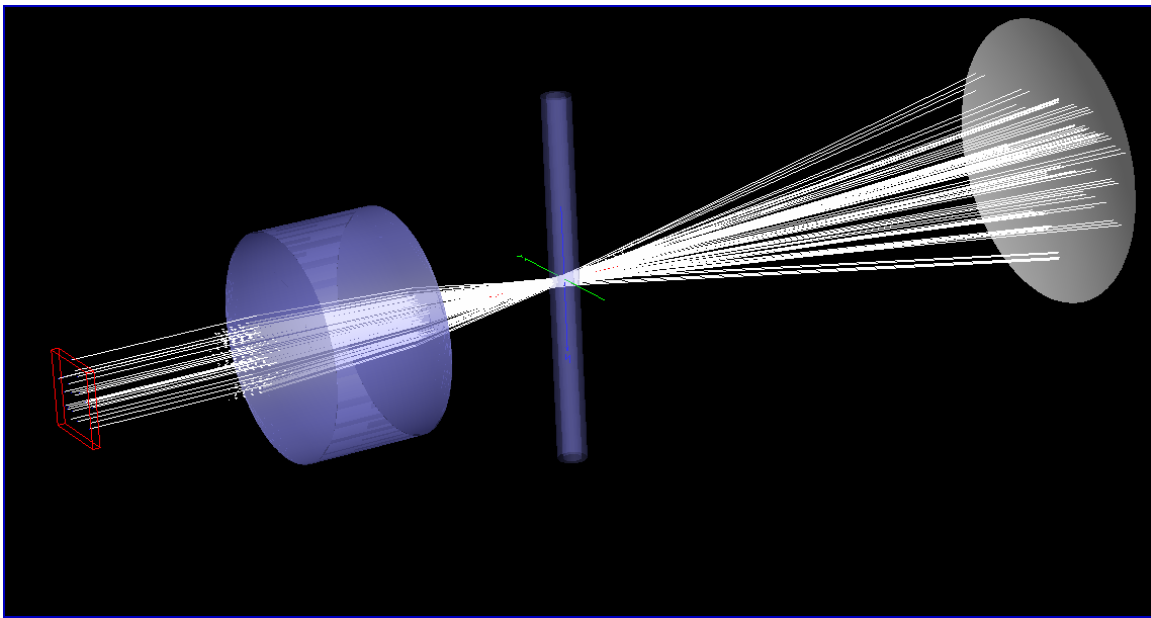


Figure 11. Laser Illumination System with Capillary and Retromirror

In Figure 11 we can see the collimated laser beam is focused by the catalog biconvex objective lens into the center of the glass capillary. The laser beam transmits through all four surfaces of the glass capillary and hits the retro mirror. The retro mirror has a slight tilt to it so that it retroreflects the light back to the center of the capillary, but slightly off set from the original beam. This creates a focused strip of laser illumination. This larger strip of illumination will increase the illumination volume and that increases the fluorescent signal that we are trying to collect. The initial laser illumination rays are white and after reflection from the retro mirror they are turned yellow for visual distinction.

In Figure 12 below we can see the strip of light used to illumination the fluid that is being sent down the center of the capillary tube. We can also see the particle that is about to flow through the laser illumination path in the center of the capillary and when illuminated with become a fluorescent surface emitter at the longer fluorescent

wavelength. It will be the function of the light collection channel to capture this fluorescent light and get it imaged onto the analysis detector.

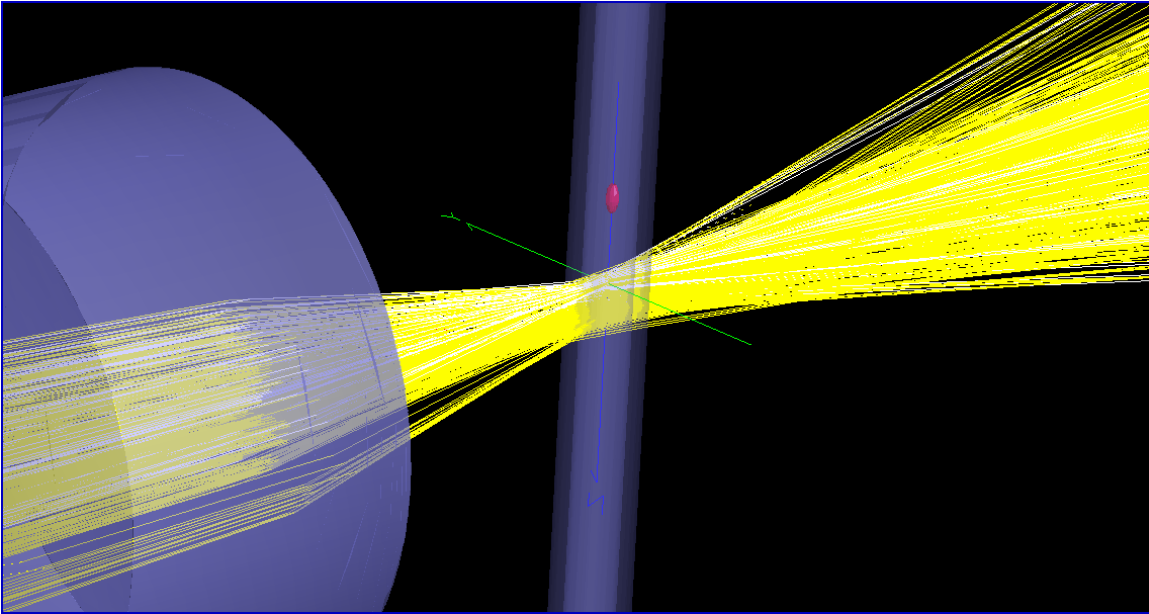


Figure 12 Close Up of Capillary illumination and retro reflection from mirror

As the particle enters the laser illumination path the particle absorbs the light from the illumination source and re-emits this light at a longer wavelength or fluoresces. The fluorescent particle becomes a volume emitter inside the capillary. We need to capture this fluorescent emission and optically steer it to an analysis detector.

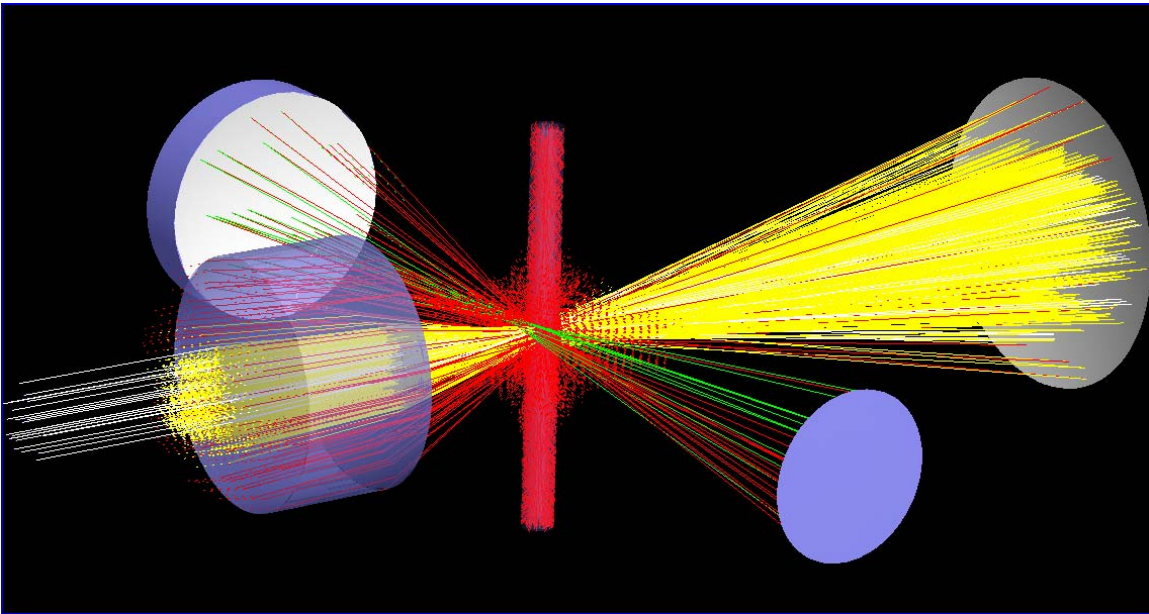


Figure 13. Shows the particle fluorescing in red light

The fluorescent emission is red in the center of the capillary. You can see some of the fluorescent light being emitted toward the fluorescent retro mirror with the white surface in Figure 13. This light is reflected from this slightly off set mirror and after reflection the rays are turned green. These green rays can be seen passing by the side of the capillary column and hitting the large detector.

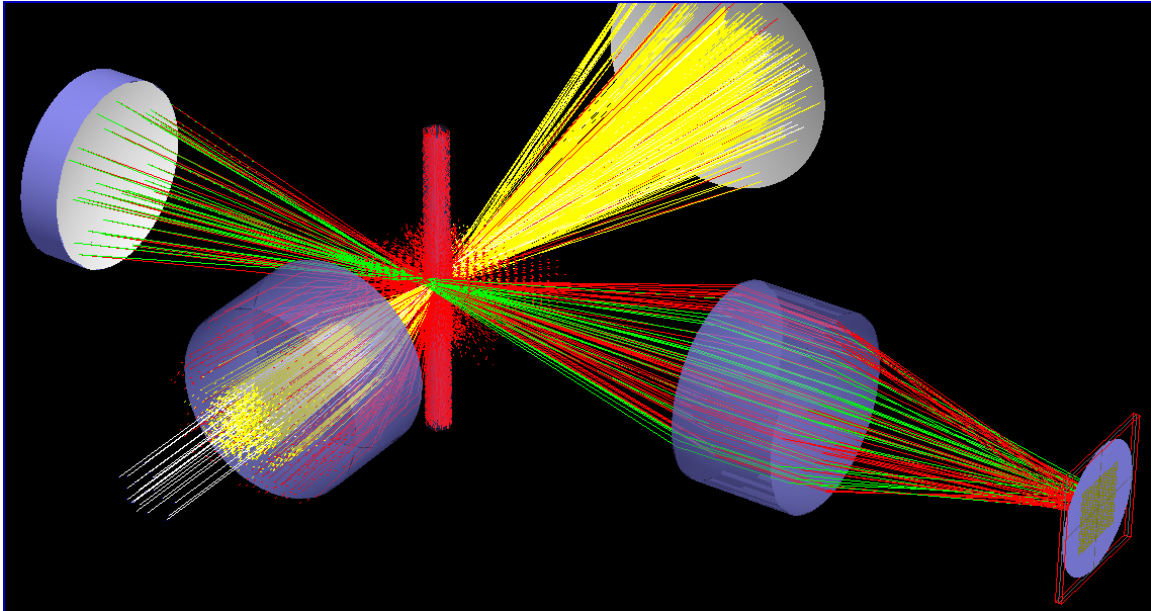


Figure 14. Laser Induced Fluorescence Capillary Electrophoresis System

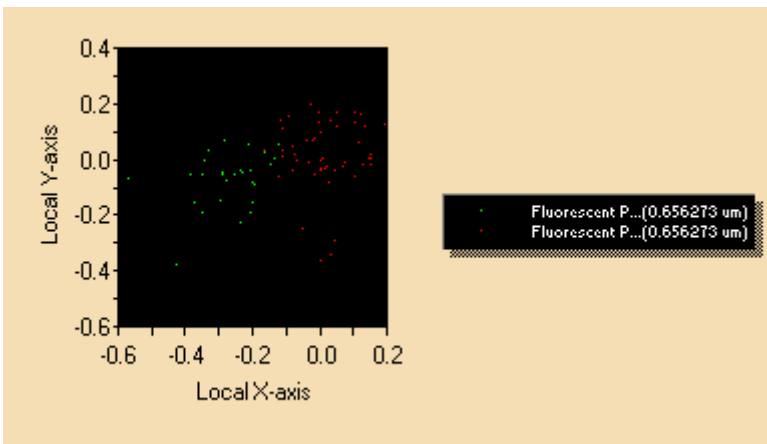


Figure 15. Analytical Detector with Fluorescent Energy

In Figure 14, we can see that the collection lens has been put into the fluorescence channel and it is focusing the fluorescent rays onto the analysis detector. In Figure 15 we can see the two groups of fluorescent rays on the detector, the green batch are from the retro-reflection mirror that pass by the side of the capillary. The red rays are the fluorescent rays that are collected by the imaging lens.

In Figure 15 we can see that the two retro mirrors have reflective surfaces, which optically is the important surface. If we are concerned about the opto-mechanics,

packaging, weight, and other instrument design and integration issues we might want to have the full mirror substrate in the design. The full mirror substrate is very easy to enter in FRED we can put all of the information in on one input menu, such as radius, mirror shape and dimensions, mirror thickness, coatings, and substrate material. The fluorescent channel mirror was inserted into the design using this method. The retro mirror in the laser illumination path was inserted as just the optical surface.

BioMedical Optics with FRED Summary

In biomedical optical system and instrument design and analysis it is important to have certain capabilities such as:

- Light Source Model Creation – Surface, Volume Emitters, Laser Beams
- Source File Model Interpretation and Use (Radiant Source Models)
- Source Collection for Efficient Transfer of Illumination
- Illumination Source Spatial Homogenization of Illumination Targets
- Illumination System Modeling and Analysis
- Illumination System Radiometry and Throughput Efficiency
- Illumination Plane Irradiance Analysis
- System Dosimetry
- Surface Scatter using various standard scatter models
- Volume Scatter – Coming Summer 2004?
- Volume Source to simulate volume scatter
- Scatter Importance Modeling for Efficient Modeling and Ray Tracing
- Scatter/Source Collection Modeling for Throughput Efficiency
- Sequential and Non-Sequential Raytracing to Analyze Scatter and Ghosts
- Image/Illumination Plane Analysis – Spot Diagrams, Polarization Analysis, Irradiance Distribution, Energy Density, Coating Characteristics.

As you have seen in these two biomedical optics examples FRED has the some very important and visually dynamic modeling, analysis, and graphical display capability. If you have any questions regarding FRED's capability to model and analysis your biomedical optical system please call us at 520-733-9557 or email us at info@photonengr.com.