Microscopy Focus

Multilayer Tissue-Like Optical Phantom; a Model for Skin in Optical Coherence Tomography Imaging

Optical coherence tomography (OCT) is an advanced high-resolution non-invasive imaging tool, which delivers three-dimensional (3D) images from the microstructure compartments within the skin tissue. Using OCT one can extract optical properties (scattering coefficient and anisotropy factor) of normal or diseased skin to generate an optical model for skin, which can be used for diagnosis. To verify and validate the optical properties extraction algorithm a tissue-like optical phantom is needed. If the phantom can be multilayer, it can model the skin more accurately.

> ***"Multilayer phantoms can be a good way of evaluation of optical coherence tomography and its related algorithms."***

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WHAT IS PHANTOM AND WHY IS IT NEEDED?

Phantom is a virtual tissue with well-controlled optical properties (refractive index, scattering coefficient, anisotropy factor and absorption coefficient) and can be constructed in solid or liquid states depending on its application. Phantoms are being used for testing the design of the system, system optimisation, and performance evaluation of the system. In optical imaging modalities in particular, phantoms are used for measurement/evaluation of the system parameters such as longitudinal and transversal resolutions, image contrast, point spread function (PSF), system sensitivity, system differentiability between two types of tissues, and system detectability of a certain concentration. In this study, we used phantoms to evaluate the accuracy and precision of the optical properties extraction algorithm in calculating the values of scattering coefficient and anisotropy factor.

HOW CAN WE EXTRACT OPTICAL PROPERTIES FROM OCT IMAGES?

The optical properties (scattering coefficient and anisotropy factor) can be extracted from the OCT images by fitting the OCT signal which is obtained based on extended Huygens-Fresnel (EHF) principle, onto the averaged A-line vector in a specific region. The fitting procedure and corresponding curves are shown in *Figure 1* and *Figure 2*, respectively. One can generate an optical model for skin by specifying the range of variation of the optical properties for the healthy skin. Then the values out of this range can be used for the diagnosis of diseased skins.

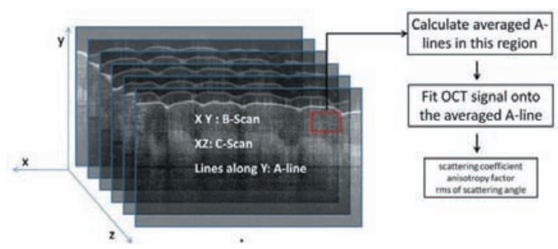

Figure 1: Stages of the optical properties extraction algorithm

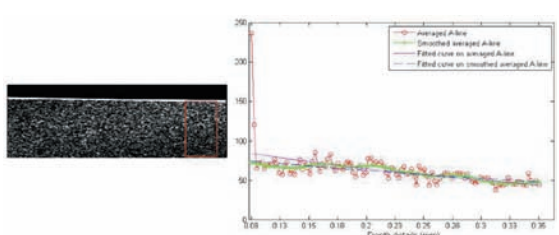

Figure 2. Left: OCT image of polystyrene microsphere embedded in epoxy-resin.

HOW IS A PHANTOM DESIGNED?

To design a phantom one would need to know the interaction of particles within the phantom with the incident light, which can be simply described by Mie theory. Mie theory is a common approach to model the scattering in tissue, which treats scatterers as isolated spheres with given size and refractive index relative to the surrounding medium. For this reason we need to understand the structure of the skin and size of the compartments in different depths within the skin. In each layer of skin, we use scatterer, absorber and hardener with determined concentrations. Different combinations of scaterrer and absorber can be used to construct the phantom according to the application. We have experimented phantoms composed of one of TiO_2, Iron, super white polystyrene microsphere, white and black polystyrene microspheres and gold microsphere embedded in epoxy-resin or Agarose. Among them, we used polystyrene microsphere with combination of Agarose to construct a multilayer solid phantom.

HOW IS THE STRUCTURE OF SKIN?

Skin is composed of four layers; Stratum Corneum (SC), Epidermis (ED), Dermis (D), and hypodermis (HD) (*Figure 3*). The layers are with different structures and compartment sizes. Looking at the literature, we extracted the information of the structure of the layers; viscosity and concentration. The amount of hardener, Agarose, and the scatterer were then computed accordingly. The conclusion was as follows. Multilayer phantoms can be a good way of evaluation of optical coherence tomography and its related algorithms. This means higher than normal (1 portion Agarose, 100 portion of water). Also as there is no melanin in the SC, there is no absorber needed in this layer. The largest size of our microspheres was used in this layer. Higher concentration of the hardener also resembles the diffusivity of this layer, which is the major feature of this layer. Epidermis is about 0.1mm thick; it however varies in different sites throughout the body. Epidermis consists of mainly connective tissue and cells so called melanosomes that produce pigment melanin. The major property of this layer is the fact that this layer is highly absorbing due to melanin. The melanin was modelled in the phantom by using Proj90N that is molecular nano-size absorber. To model the epidermis, we used smaller size of microspheres with less concentration and higher absorption than those have been used in SC. Dermis is composed of two sub layers; papillary dermis and reticular dermis. However in this study we considered dermis as only one layer. Papillary dermis composed of dense collagen tissue, which reflects most of the incident light reflected from this layer. Reticular dermis consists of dense irregular connective tissue, which is made up of mainly loose connective tissue. Blood vessels and the nerve endings are in this layer. To model the dermis, the concentration of Microspheres considered to be higher and the size of the scatterers smaller than those of the two top layers. We modelled the blood vessels in dermis using very narrow fibres. The summary of the material selection is given in *Table 1*.

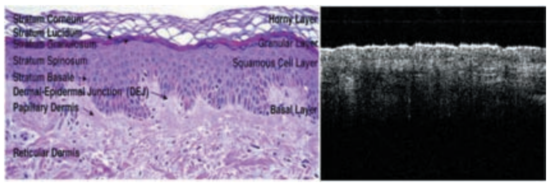

Figure 3. Left: Skin layers including sub-layers in epidermis and dermis, right: OCT B-scan of dorsal skin of hand from a 25-years old girl

Table 1. Relative concentration of scaterrer, absorber and hardener used to model the skin layers

Skin layer	Agarose concentration	Microsphere concentration	Microsphere size	Absorber
Stratum Corneum	high	highest	largest	None
epidermis	lowest	low	large	Highest
dermis	highest	lowest	smallest	low

WHAT MATERIAL DID WE USE?

Based on the relative concentration of the scatterer and absorber in the skin layers and taking into account the scattering and absorption coefficients of the skin extracted from the literature, we computed the amount of each of the constitutions using Mie calculator. *Table 2*, shows the amount of the scatterer, absorber, and the hardener required to resemble the scattering and absorption coefficients of the skin layers.

Table 2. Concentration of scatterer, absorber and hardener in modeling the skin layers calculated by Mie theory. C, stands for concentration

Skin layer	Thickness	Polystyrene microspheres	Absorber	Absorption coefficient	scattering coefficient	Agarose concentration
Stratum Corneum	50 µm	1.58mg (5µm sphere) C=0.0028	7.68µg	$0.3mm^{-1}$	$102.83\ mm^{-1}$	10mg Agarose+ 10ml water
Epidermis	1mm	4.8ml (1µm sphere) C=0.04	15.37µg	$0.6mm^{-1}$	$42.366\ mm^{-1}$	10mg Agarose+ 10ml water
Dermis	1.5mm	9ml (820nm spheres) C=0.06	7.68µg	$0.3mm^{-1}$	$29.418\ mm^{-1}$	10mg Agarose+ 10ml water

WHAT IS DF-OCT?

We used time domain dynamic focus OCT (DF-OCT) for imaging the phantoms. With dynamic focus scheme, which is added to the time domain OCT, a wide imaging range With a high lateral resolution throughout the depth is obtained.

The confocal gate of the presented system was measured 180 µm. Using the features described in *Table 1* and *Table 2*, we constructed the multilayer phantom. The DF-OCT and the images taken of the phantom are given in *Figure 4*.

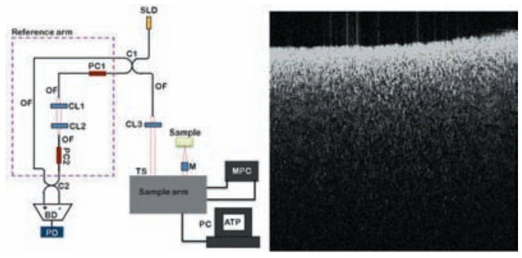

Figure 4. Left: Dynamic focus time domain OCT optical setup. SLD: super luminescent laser diode, PD: photodiode, C1: 2 2 coupler, PC: personal computer, BD: balance detection, CL: Collimator lens, MPC: Mirror positioning controller, MC: Motion controller, PC: polarisation controller. Right: OCT image of the multilayer phantom obtained from the DF-OCT.

CONCLUSION

- We modelled human skin using Agarose, different sizes of polystyrene microsphere and molecular absorber.
- The preliminary results showed that the constructed phantoms could be used for evaluation of the optical properties extraction algorithm.
- A more comprehensive study is required to model the compartments of skin in each layer particularly in epidermis where it has five sub layers. Such a model can then be used for differentiating cancerous and healthy skins.

REFERENCES

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Winners of Carl Zeiss Nano Image Contest Announced

After an exciting finish the winners of the first Carl Zeiss Nano Image Contest have now been selected. The winners of the four categories will each receive a pair of cinemizer Plus video glasses from Carl Zeiss.

The winners are Heinrich Badenhorst from the University of Pretoria, South Africa category Scanning Electron Microscopy (SEM), Norman Hauke and Arne Laucht of the Walter Schottky Institute of Munich Technical University, Germany category CrossBeam (FIB-SEM), Dr. Emile van Veldhoven of the TNO Research Institute in Delft, Netherlands, category Helium Ion Microscopy (HIM) and Dr. Andrey Burov of the Russian Academy of Sciences in Saratov in the category Transmission Electron Microscopy (TEM).

The Managing Director of Carl Zeiss NTS, Dr. Frank Stietz, is very pleased at the excellent response to the contest with over 120 entries: "The broad spectrum of application topics, the technical quality and the artistic composition of the nano images are fascinating. We would like to thank all participants for their entries and extend our congratulations to the winners."

First prize in the SEM category was awarded to Heinrich Badenhorst with his image of a bizarre landscape made of graphite, captured with an ULTRA REM. With a total of 7000 points, his image received the most votes of all categories. "Our ZEISS ULTRA has allowed me to make massive progress in my research in the past year. ZEISS SEM technology helped me to uncover aspects of graphite oxidation which I have never seen before," stresses Badenhorst, a scientist working in the field of graphite technology.

The winning image of Norman Hauke and Arne Laucht in the FIB-SEM category shows a photonic crystal, produced and captured with an NVision 40 CrossBeam Workstation. The two PhD students are delighted at their unexpected victory: "It is an honour for us to be the winners of the 2010 Carl Zeiss Nano Image Contest. This innovative and high-quality research has only been made possible by the state-of-the-art equipment at Schottky Institute, such as the nano-lithography and nano-imaging systems from Carl Zeiss. This constantly provides us with stunning views of nano worlds."

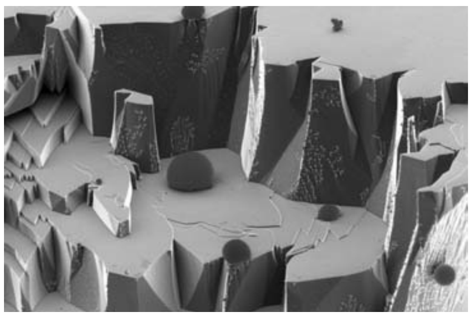
The logos of Delft Technical University, the TNO Institute and Carl Zeiss on a surface of only 2x2 micrometers are shown in the image of Dr. Emile van Veldhoven, with which he won first prize in the HIM category." Our ORION helium ion microscope is the tool which enables me to create and image with extreme nanometer precision," van Veldhoven explains.

Dr. Andrey Burov came in top in the TEM category with an artistic image of golden nanoparticles, generated with a LIBRA 120 TEM. He finds the link between technology and art in nano microscoping totally remarkable: "It is great when work brings not only results, but also esthetic pleasure. I thank Carl Zeiss for the possibility to realize my talent as an artist."

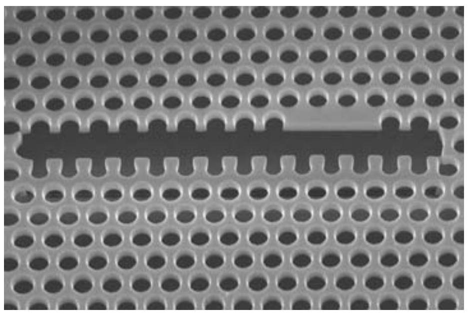
Competition

A total of 123 microscopy images were submitted for the contest that ran from the middle of May to the end of August. After the end of the submission period, both the participants and all the visitors to the website were given the opportunity to vote for their favourite images and therefore selected the winners.

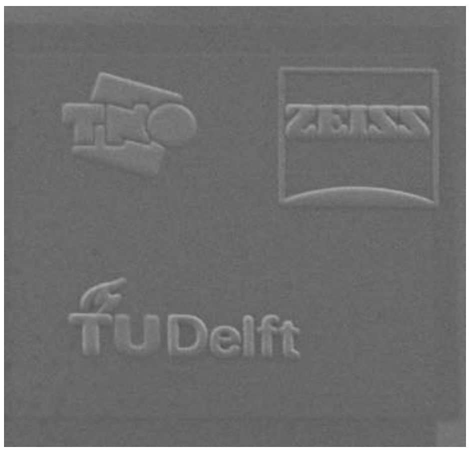
Heinrich Badenhorst



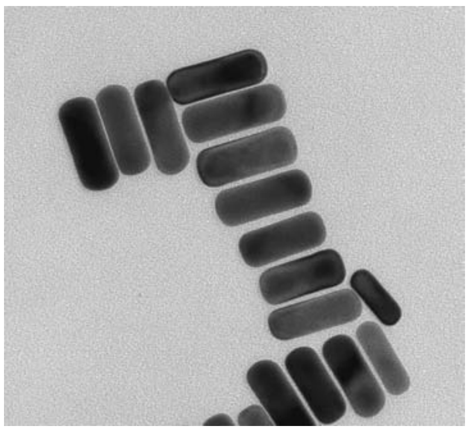
Graphite structure- H. Badenhorst (SEM)



Photonic crystal – N.Hauke/A.Laucht (FIB-SEM)



Logos – Dr E.van Veldhoven (HIM)



Golden nanoparticles - Dr A. Burov (TEM)

Mosquito Heart Captures First Place in Small World Competition

What looks like the familiar green lines of a heart monitor printout in a textured navy blue sea is actually a close-up of a mosquito heart, and the winner of the 2010 Nikon Small World Photomicrography Competition. Jonas King, from Nashville, Tennessee, USA, took the photo of Anopheles gambiae (mosquito heart) magnified 100 times and using fluorescence technology. The image is both beautiful and scientifically significant, as it is used in King's research on how mosquitoes carry and transmit pathogens including malaria.

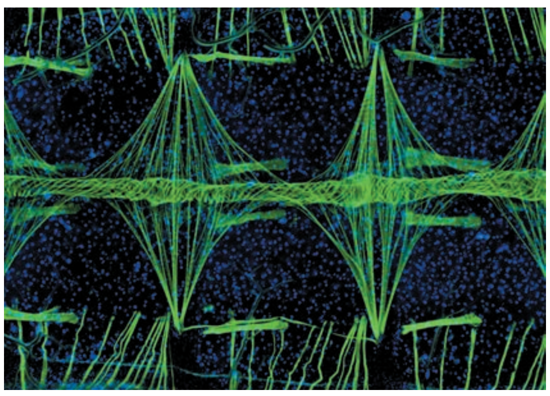
Nikon Small World recognizes King's image, along with the other winners from this year, for showing the duality of how photomicrographs can carry both scientific and artistic qualities. Celebrating its 36th year, the competition received more than 2,200 entries in 2010 – a new record – from scientists and artists across the world.

"Mosquitoes remain one of the greatest scourges of mankind and this image of the mosquito heart helps us understand how they transport nutrients, hormones, and even pathogens such as malaria throughout their bodies," said King, a researcher at Vanderbilt University. "I'm happy that such an important and aesthetically pleasing image was selected as the winner of the Nikon Small World competition, which in my mind is the most respected competition devoted entirely to microscopy."

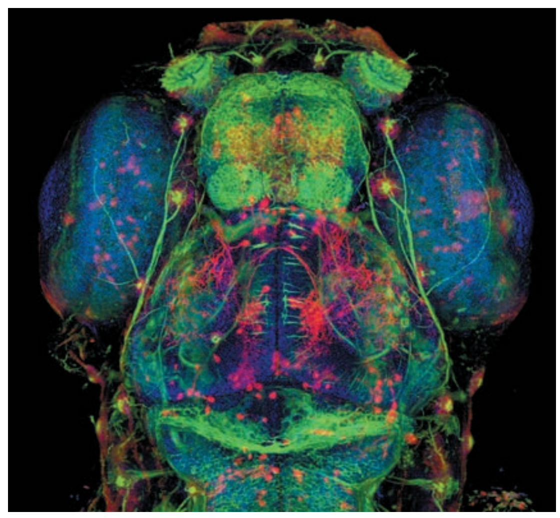
"It is a privilege to honour some of the world's foremost researchers and photomicrographers for their amazing work with Nikon Small World," said Eric Flem, Communications Manager, Nikon Instruments. "We are thrilled that we continue to receive images that awe and surprise us every year – ranging from everyday household items to microscopic specimens used for science's most pressing research. This competition truly demonstrates the fun of science as well as the importance of the many microscopic techniques and processes in use today."

The Nikon Small World Photomicrography Competition is open to anyone with an interest in photography.

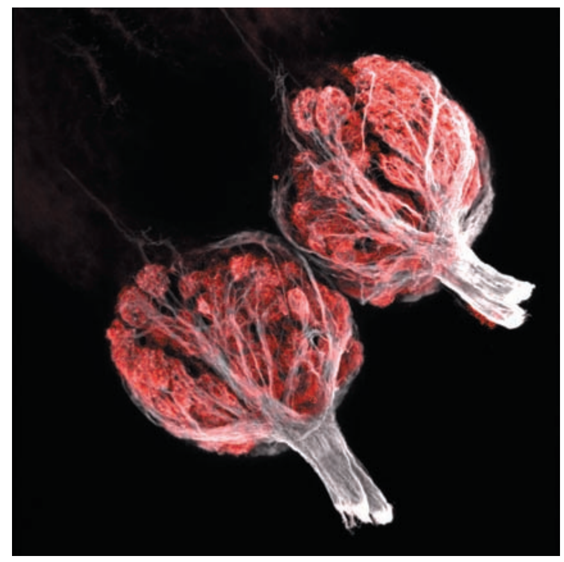
For additional information, please visit www.nikonsmallworld.com, or follow the conversation on Facebook and Twitter @NikonSmallWorld



1st Place
Jonas King
Vanderbilt University, Department of Biological Sciences
Nashville, Tennessee, USA
Anopheles gambiae (mosquito) heart (100X)
Fluorescence



2nd Place
Dr. Hideo Otsuna
University of Utah Medical Center, Department of Neurobiology and Anatomy
Salt Lake City, Utah, USA
5-day old zebrafish head (20X)
Confocal



3rd Place
Oliver Braubach
Department of Physiology & Biophysics, Dalhousie University
Halifax, Nova Scotia, Canada
Zebrafish olfactory bulbs (250X)
Confocal

Popular vote winner.

A female black bean aphid (apetrous aphid fabae) with its offspring still inside inspired the public and received the distinction of being the Popular Vote winner for the 2010 Nikon Small World Photomicrography Competition.

The image, taken by Dr. Tomas Cabello of the Universidad of Almería in Roquetas de Mar, Spain, was the public's favorite from among the 120 finalists featured at **www.nikonsmallworld.com**

Dr. Cabello's winning image was also chosen as an Image of Distinction in this year's competition by Small World's panel of expert judges.

Dr. Cabello teaches and conducts research in agricultural entomology, specializing in greenhouse crop pest species such as the black bean aphid, which is unique in that it demonstrates live birth instead of laying eggs like most insects.