How the Inverted Retina Enhances Vision Acuity

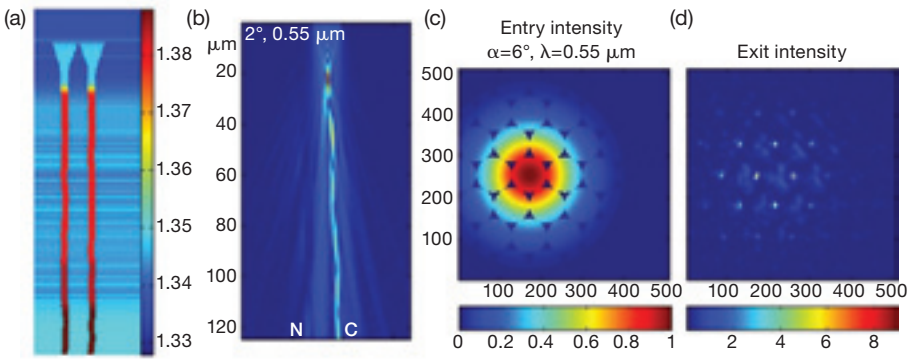
Amichai M. Labin and Erez N. Ribak

The visual system is one of the most complex and important biological systems of the human body. Our eye forms an image on the retina, which converts it into an electrical signal. Detection is performed by the photoreceptors, which divide into low-light-level sensitive rods and color-sensitive cones. They are located at the bottom of the retina, behind layers of transparent nuclei and neurons, which process and transmit the image to the brain. This backwards structure posed a major problem in understanding human and vertebrate vision.

Across the neural layers run the glial cells (also called Mueller cells). They span the entire thickness of the retina and open up as a funnel towards the pupil. On the other side, they are each connected to one cone and a few rods. Until recently, the main functions attributed to Mueller cells were metabolism and mechanical support for the neuron layers. Measurements of refractive indices of retinal tissue and recently of glial cells show evidence of waveguide properties of the latter.[1] Considering these facts, it is intriguing to investigate the effect of the array of glial cells on human vision acuity.

An analytical description of light propagation along waveguide structures,[2] such as an irregular array of biological cells, is very difficult to apply and unlikely to be accurate. Thus, we chose a direct three-dimensional numerical solution of the Helmholtz equation, known as the split-step beam propagation method.[3]

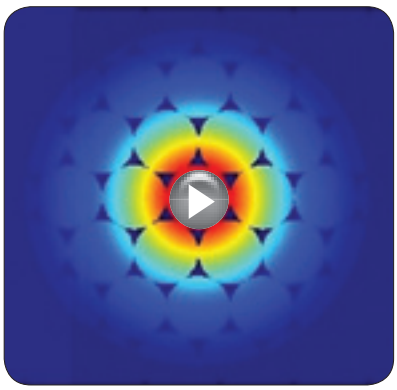
To study the glial cells array, images of human cells were digitized to define their width as a function of depth. These were inserted in a data cube with their corresponding refractive indices. A Gaussian beam was propagated across this volumetric description of the retina. The output light intensity at the bottom of the retinal structure was calculated throughout the visible regime at various incidence angles. The latter are associated with increasingly eccentric entry positions within the pupil.[4]



(a) and (b) A cut across the retina model. (a) Refractive index profiles of two cells and the cross layers. (b) Tilting the cells by 2°, we illuminate with green light the right cell (C), but the field amplitude does not leak to its neighbor (N). (c) Taken from above, now we illuminate a number of cell funnels with a Gaussian beam at 6°. (d) After propagation, the intensity is concentrated by a factor of nine at the cones, and the rest of the light is scattered onto the surrounding rods.

The results presented a surprising picture: For small incidence angles (up to 5°) corresponding to a smaller pupil as in daytime (photopic) vision, the amount of electromagnetic field coupling into a neighbor glial cell is low, less than 3 percent. More significant coupling occurred for higher incidence angles, when the pupil is wider—in other words, at night, when we use scotopic vision. Thus, light is concentrated into the cones during the daytime. However, more of it is scattered into the surrounding rods after dark. Another significant result obtained was that in the center of the visible spectrum (0.5 to 0.6 μm), a lower coupling loss was calculated, even for higher arrival angles, thus conserving an optimal image resolution and reducing chromatic aberrations.[5]

These results provide evidence for a natural parallel waveguide array, which almost perfectly preserves images obtained under the constraints of the pupil diameter, eye size and refractive index. We revealed the seemingly illogical inverted structure of the retina, long taken as a contradiction to its optical purpose, to be an optimal configuration for improving the sharpness of images.



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Sparsity-Based Reconstruction of Subwavelength Images from their Optical Far-Field

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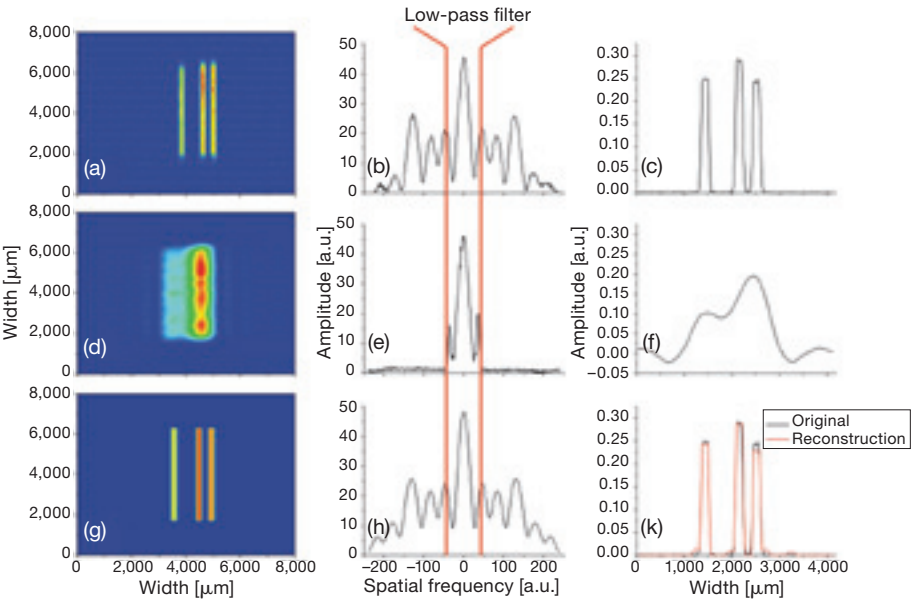
A fundamental restriction of optical imaging is given by the diffraction limit, stating that the maximal resolution is half of the optical wavelength λ. This is a result of the evanescent nature of waves associated with spatial frequencies exceeding 1/λ.[1] Reaching beyond the diffraction limit is a subject of intense research, culminating in various approaches. However, none captures images in real time: They either require point-by-point scanning in the near-field or necessitate averaging over multiple experiments with florescent particles. Apart from these "hardware solutions," algorithmic attempts have been made to extrapolate the frequency content above the cut-off dictated by the diffraction limit. Such extrapolation methods were extremely sensitive to noise in the measured data and the assumptions made about the information. They all failed in recovering optical sub-λ information.[1]

In recent papers, we have shown that sub-λ information can be recovered from the far-field of an optical image.[2,3] The idea is based on compressed sensing (CS) techniques,[4] which are generically used for efficient data sampling, and are robust to noise in the measured data. Their only condition is that the information is sparse in a known basis (say, in real space). Sparse optical images are common, e.g., living cells, where the fraction of nonzero pixels is about 5 percent.

Subwavelength imaging can be represented as a bandwidth extrapolation problem, where propagation is equivalent to passing through a low-pass filter, with the diffraction limit as the cutoff frequency.[1] The question is how to identify the correct extrapolation, out of the infinite possible extrapolations. Here, sparsity comes into play: CS implies that, in the absence of noise, if the original information is sparse in a basis that is sufficiently uncorrelated with the measurement basis, then the sparsest solution is unique. For sub-λ imaging, this implies there is only one continuation of this truncated spectrum that corresponds to the sparsest image. Hence, if we know that our image is sparse in real-space, and only that, we just need to find the sparsest solution generating the observed far-field image. The uniqueness of the solution guarantees that this is the correct one. In the presence of noise, simulations reveal that the solutions, although not unique anymore, are very close to the original information when the noise is not exceedingly large. Hence, searching for the sparsest solution (that is consistent with the measured data), yields a reconstruction that is very close to ideal under typical experimental conditions. Finding the sparsest solution can be done through various algorithms. For EM fields, we proposed a new algorithm[2] reconstructing amplitude and phase.

We tested the ideas theoretically with sub-λ information and devised experimental proof-of-concept: a 4-f imaging system with a tunable spatial filter at the Fourier plane. The filter mimics the optical transfer function by eliminating all frequencies above its cutoff. The reconstructed images contain spatial frequencies far beyond the highest frequency passing the low-pass filter. The figure displays the reconstruction of an image of three stripes, whereas the low-pass filtered image was a single broad stripe within which fine features can't be resolved. Recently, we showed the recovery of true sub-λ images of sparse information, reconstructing 100-nm features borne on 532-nm light, at 30-nm resolution.[5]



(a,b,c) The original information consisting of three vertical stripes. (a) Its Fourier spectrum and (b) a horizontal cross-section, taken through the real-space image (c). (d,e,f) Using a slit, the signal is low-pass filtered at the vertical red lines (e), yielding a highly blurred image (d), where the three stripes merge into one (f). (g,h,k) Sparsity-based reconstruction yields a high-quality recovered image (g) and its Fourier spectrum (h). The strong correspondence between original and recovery is shown in the cross-section (k).

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Lensfree Fluorescent On-Chip Imaging Using Compressive Sampling

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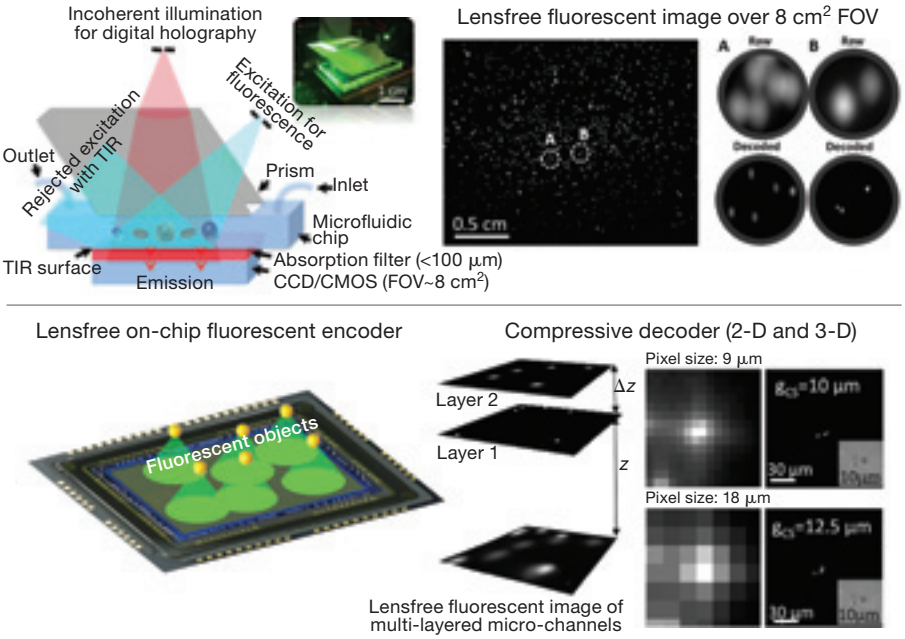
Optical imaging tools have found widespread use in medicine and biology. Specifically, fluorescent microscopy has lately experienced a fascinating renaissance, expanding our capabilities to probe various biological processes with much better resolution, field-of-view (FOV), speed, signal-to-noise ratio, etc. While these advanced imaging technologies add to our biophotonic toolset, there is still a mismatch in terms of, for example, throughput, compactness and cost-effectiveness between these sophisticated optical platforms and most high-throughput lab-on-a-chip devices. On the other hand, miniaturized and cost-effective formats of microfluidics and lab-on-a-chip analysis have already found several biomedical applications, particularly in point-of-care and field diagnostics.

To provide a better match to this important need, lensfree on-chip imaging is becoming a powerful alternative to conventional techniques.[1-4] Today's digital sensor arrays have significantly improved space-bandwidth products, dynamic ranges and signal-to-noise ratios. When combined with new image reconstruction algorithms, they provide an opportunity to create imaging modalities that can make up for the lack of complexity of optical components.

Recently we have introduced an ultrahigh throughput on-chip fluorescent imaging platform that can achieve 10-µm resolution over an FOV of >8 cm^2 without the use of any lenses, thin-film filters or mechanical scanners.[2,3] This lensfree fluorescent imaging modality uses a prism-interface to pump the objects-of-interest (e.g., cells or biomarkers) located within a microfluidic chip, where the excitation light is rejected through total internal reflection occurring at the bottom facet of the substrate. Fluorescent emission from the objects is then collected using a dense fiber-optic faceplate and delivered to a large-format sensor array that has an active area of, for example, more than 8 cm^2.



Because the platform is lensless, the fluorescent emission from each source rapidly diverges, which creates a wide point-spread function (PSF) of about 40 µm in width. However, the limitations of such a wide PSF can be digitally removed by using compressive sampling algorithms,[3] which stem from a recently introduced theory aiming to recover a sparse signal from much fewer samples than it is required according to the Shannon's sampling theorem.[5] Based on such compressive decoding algorithms, the detected lensfree fluorescent image is then rapidly reconstructed to yield about 10-µm resolution over an ultra-wide FOV of more than 8 cm^2.[3]

To further increase the throughput, we also demonstrated simultaneous lensfree imaging of vertically stacked microchannels that are separated by 50-100 µm in depth. In such a multi-layered micro-fluidic device, two or three channels can be rapidly decoded to digitally focus to each microchannel's fluorescent image without the use of any mechanical scanners.

This platform would be useful for various lab-on-a-chip applications, including detecting and quantifying circulating tumor cells, monitoring HIV patients, and conducting high-throughput cytometry and microarray research.

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