Signals from 13 bipolar and 30 amacrine cell classes converge upon retinal ganglion cells, generating 15-20 filtered versions of the visual world. We will acquire the complete network (CN) map by fusing computational molecular phenotyping (CMP), transmission electron microscopy and advanced image processing. The critical strategy is the propagation of CMP maps into the dataset, creating classified descriptions of all cells, connections, and morphological parameters. This map will enable definition of network-derived response attributes, prediction of new neuronal features, discovery of new cell classes and restoration strategies for rebuilding networks corrupted by diseases such as age-related macular dystrophy. The workflow is: 1. Forming a physical 2-3 Tb CN map database, 2. Registering and mosaicking, 3. Segmenting ultrastructure, 4. Propagating CMP classifications into the segmented dataset with refinement, 5. Network descriptions.

Forming a physical CN map database. Serial TEM stacks are sandwiched between multiple CMP planes. Each stack is composed of mosaicked 5300x1201dpi TEM tiles, registered with tools from the Univ. of Utah Scientific Computing Institute (www.sci.utah.edu). Each plane can be re-probed and CMP reclassified after TEM to refine classifications as needed.

0.2 x 0.2 mm retinal patch x 0.025 mm IPL
230 images/plane @ 5300x = 63 Gb/16-bit plane
GCL = 48 CMP (optical) = 50 TEM sections, IPL = 277 TEM sections
INL = 48 CMP = 50 TEM sections, OPL = 50 TEM sections
Total = 427 TEM sections = 2.5 terabytes (98,210 TEM image tiles)

The CRM Project: Building micronetwork arrays

Generation of complete network diagrams: The expected basic architecture for a network with "directional selectivity", that is, the ability to discriminate optic field flow directionality and report it to the mid-brain for vestibular control. The essential concept is that light stimuli activate patches of cone cells (1.1.2.1.1C and 1.1.2.1.2C) that drive a target bipolar cell population (represented by a single element, 1.2.2.1.2BC). These cells then drive both a ganglion cell class (1.3.6.GC) and a special amacrine cell class (2.2.1.8AC) that has a displaced axonal field (2.2.1.8AC ax). Amacrine cells are inhibitory and the displacement generates a delay line. Stimuli arising from "above" in this case generate inhibition before excitation arrives. This creates a NULL response. Conversely, stimuli arising from below drive excitation first, followed by delayed inhibition, creating an ON response. There are likely more elements in this one network than have been discovered and the goal of the CN mapping project is generation of similar, but complete networks for all cells.

Image mosaicking based on intensity correlation. Left: initial positions of two images shown in magenta and green. Right: registered images. Grey pixels (magenta + green = gray) demonstrate good registration, whereas colored pixels are misregistered.

Image denoising preliminary results. Top row: A small portion of a TEM image (left), coherence enhancing PDE (right). Bottom row: Hessian PDE (left), ( ) UINTA filtering (right).