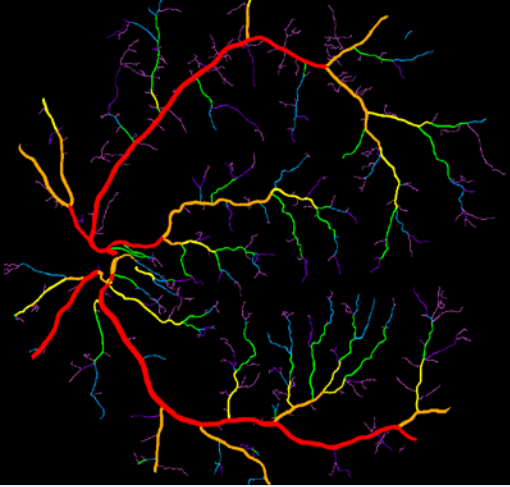


Mapping and Quantification of Vascular Branching in Plants, Animals and Humans by VESGEN Software

Humans face daunting challenges in the successful exploration and colonization of space, including adverse alterations in gravity and radiation. The Earth-determined biology of humans, animals and plants is significantly modified in such extraterrestrial environments. One physiological requirement shared by humans with larger plants and animals is a complex, highly branching vascular system that is dynamically responsive to cellular metabolism, immunological protection and specialized cellular/tissue function.

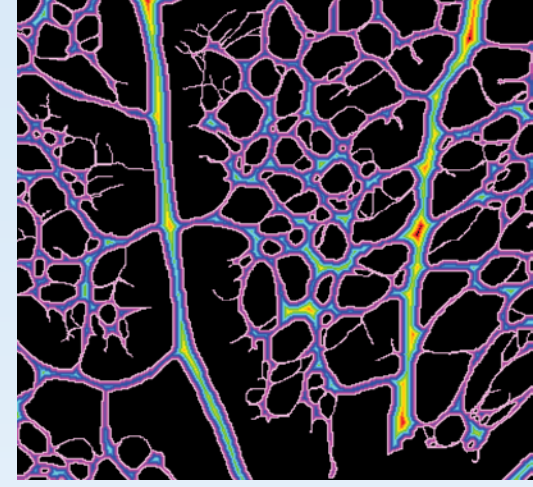
The VESsel GENeration (VESGEN) Analysis has been developed as a mature beta version, pre-release research software for mapping and quantification of the fractal-based complexity of vascular branching. Alterations in vascular branching pattern can provide informative read-outs of altered vascular regulation. Originally developed for biomedical applications in angiogenesis, VESGEN 2D has provided novel insights into the cytokine, transgenic and therapeutic regulation of angiogenesis, lymphangiogenesis and other microvascular remodeling phenomena. Vascular trees, networks and tree-network composites are mapped and quantified. Applications include disease progression from clinical ophthalmic images of the human retina; experimental regulation of vascular remodeling in the mouse retina; avian and mouse coronary vasculature, and other experimental models *in vivo*. We envision that altered branching in the leaves of plants studied on ISS such as *Arabidopsis thaliana* can also be analyzed.

(Supported by NASA GRC IR&D04-54 and 2010 TTP Fund, NIH EY-01759 & NSF Center of Excellence, University of Washington Engineered Biomaterials)



VESGEN

Innovative
Research Discovery Tool



Mapping and Quantification of Vascular Branching in Plants, Animals and Humans by VESGEN Software

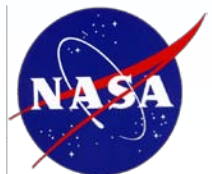
Patricia A. Parsons-Wingerter, Mary B. Vickerman and Patricia A. Keith


Point of Contact: Patricia Parsons-Wingerter PhD
Biomedical Research Engineer, patricia.a.parsons-wingerter@nasa.gov
216-433-8796

Glenn Research Center

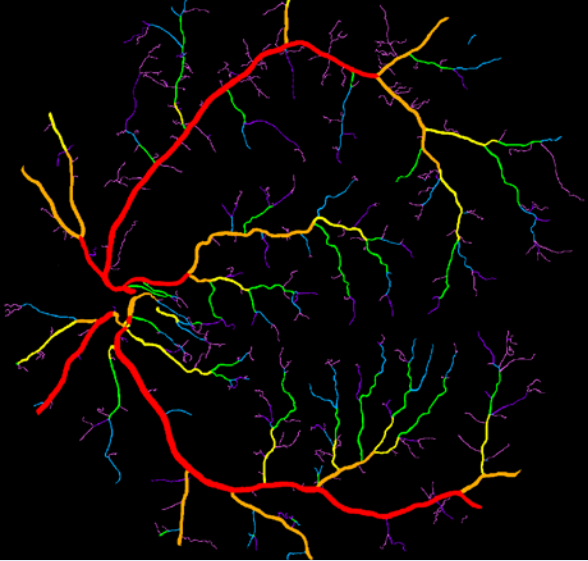
VESGEN Patent Pending

at Lewis Field



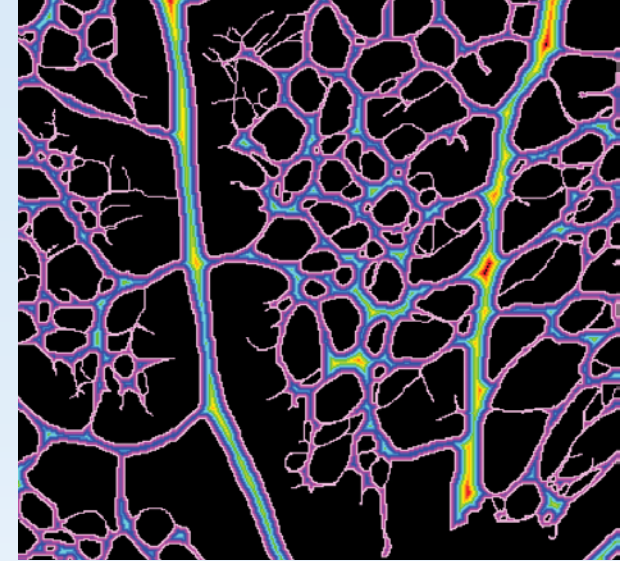
A photograph of an astronaut in a white space suit floating in space. The astronaut is holding a white document with a triangular warning symbol. The Earth's blue and white horizon is visible in the background, along with a bright sun creating a starburst effect. The astronaut's helmet has a small light on the side.

Vascular Alterations, Immunosuppression & Bone Loss:
NASA-defined risk categories for human space exploration



VESGEN 2D

APPLICATIONS



Vascular Trees
Human Retina

Avian CAM, Yolksac and Murine/Avian Coronary Vessels
Plant Leaf Venation such as in Arabidopsis thaliana?

Vascular Networks

Mouse Postnatal Retina and Intestinal Inflammation
CAM Lymphatic Vessels

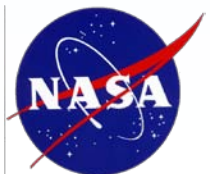
Vascular Tree-Network Composites

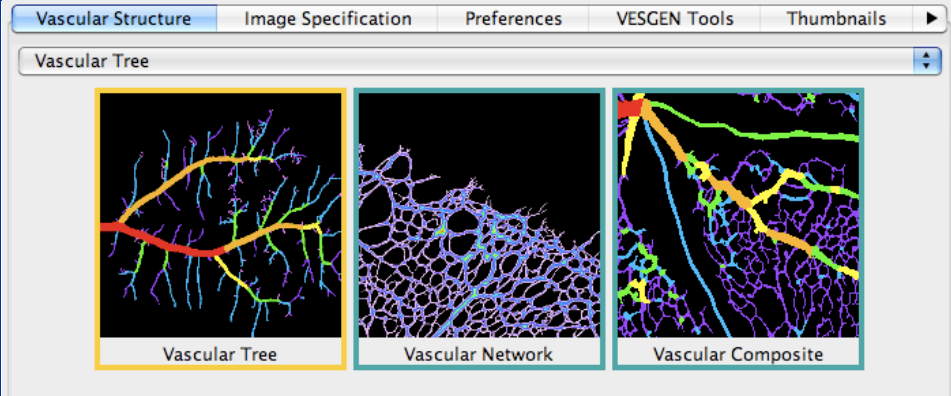
Normal and Abnormal Embryonic Coronary Vessels

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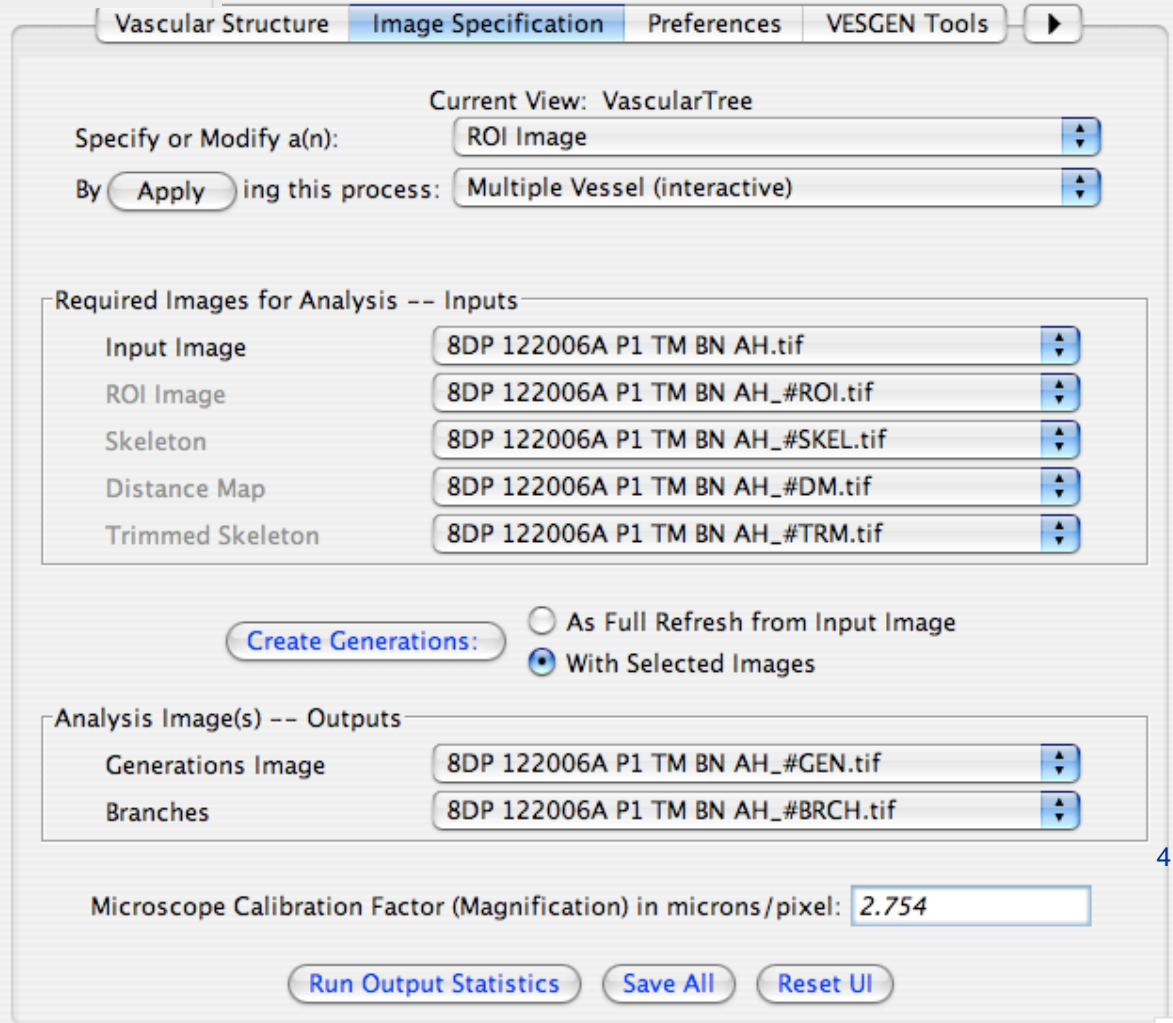


Panel to specify vessel type



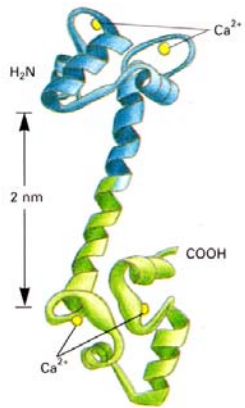
Main panel →

- Image specification
- Algorithm selection
- Process initiation

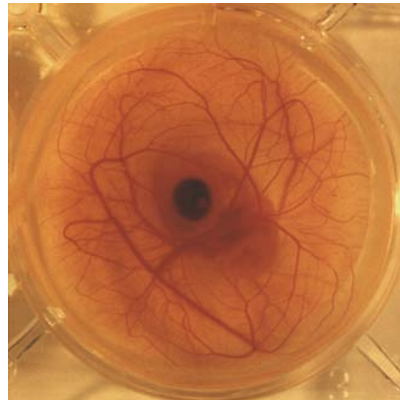


Mapping and Quantification of Microvascular Remodeling and Angiogenesis by **VESGEN**

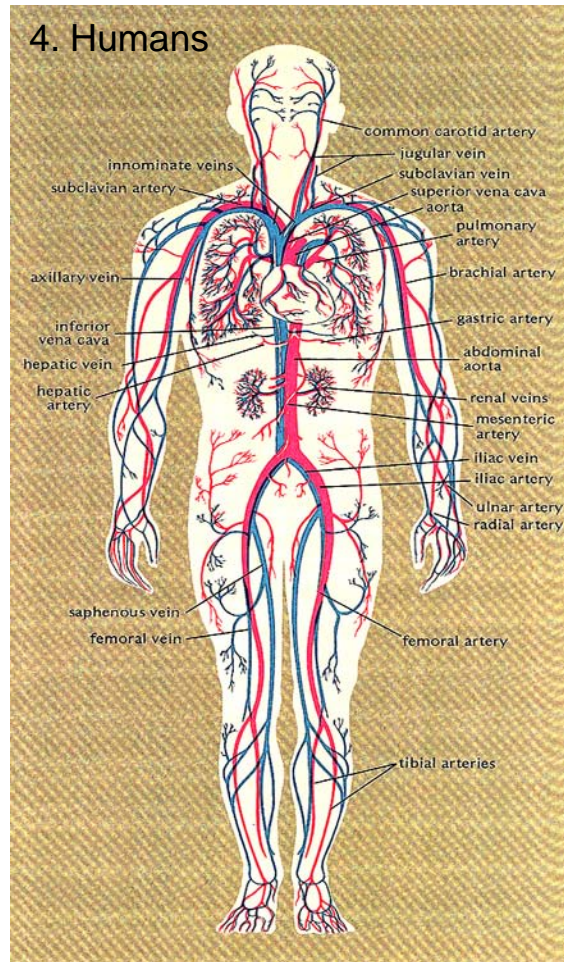
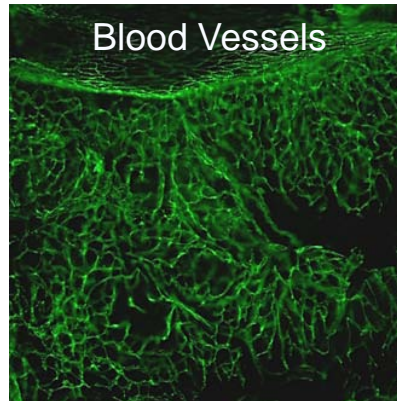
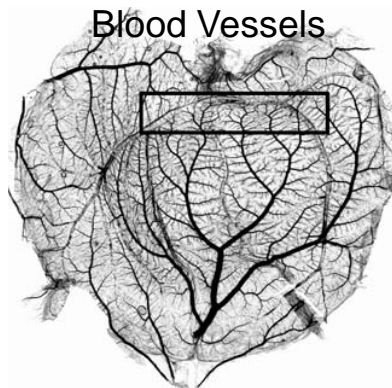
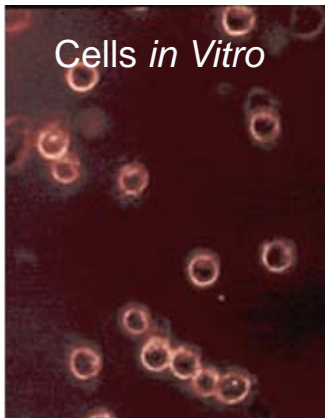
Molecular Regulation



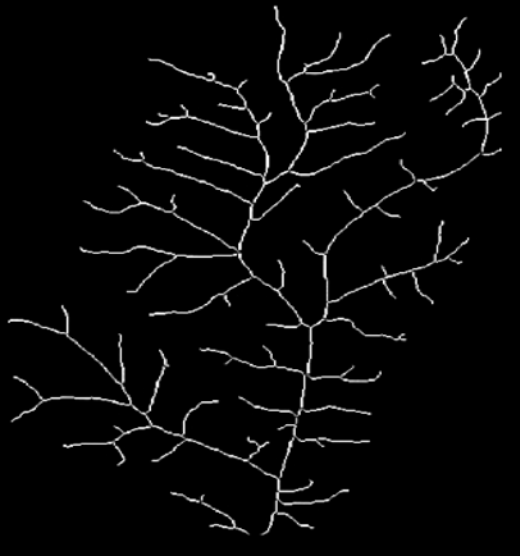
Avian CAM



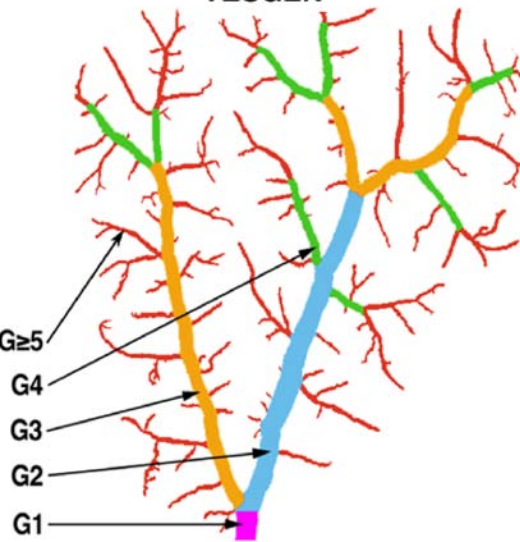
Transgenic Mouse



FRACTAL



VESGEN



The **form** of an object is a 'diagram of **forces**'
 - D'Arcy Thompson

VEGEN Hypothesis: 'Signature' Vascular Patterns



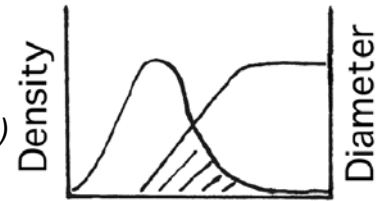
FGF-2 as a Simple Stimulator
 (Fibroblast Growth Factor-2)



Arterio Scler Thromb Vasc Biol 20 2000



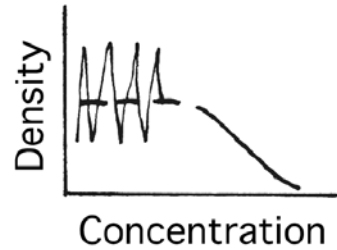
VEGF as a Complexity Factor
 (Vascular Endothelial Growth Factor-2)



Microvascular Research 72(3) 2006



TGF-β1 as a Simple Inhibitor
 But Complex Potentiator
 (Transforming Growth Factor-β1)



Microvascular Research 59(2) 2000

Long-Term Hypothesis

Vascular pattern provides an integrative read-out of dominant molecular regulators in complex signaling pathways of angiogenesis and microvascular remodeling

VESsel GENeration (VESGEN) Analysis Software

Vessel Number Density, N_v

Vessel Length Density, L_v

Vessel Diameter, D_v

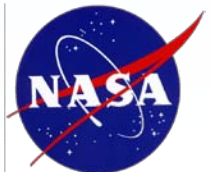
Fractal Dimension, D_f

Branchpoint + Endpoint Densities, $Br_v + E_v$

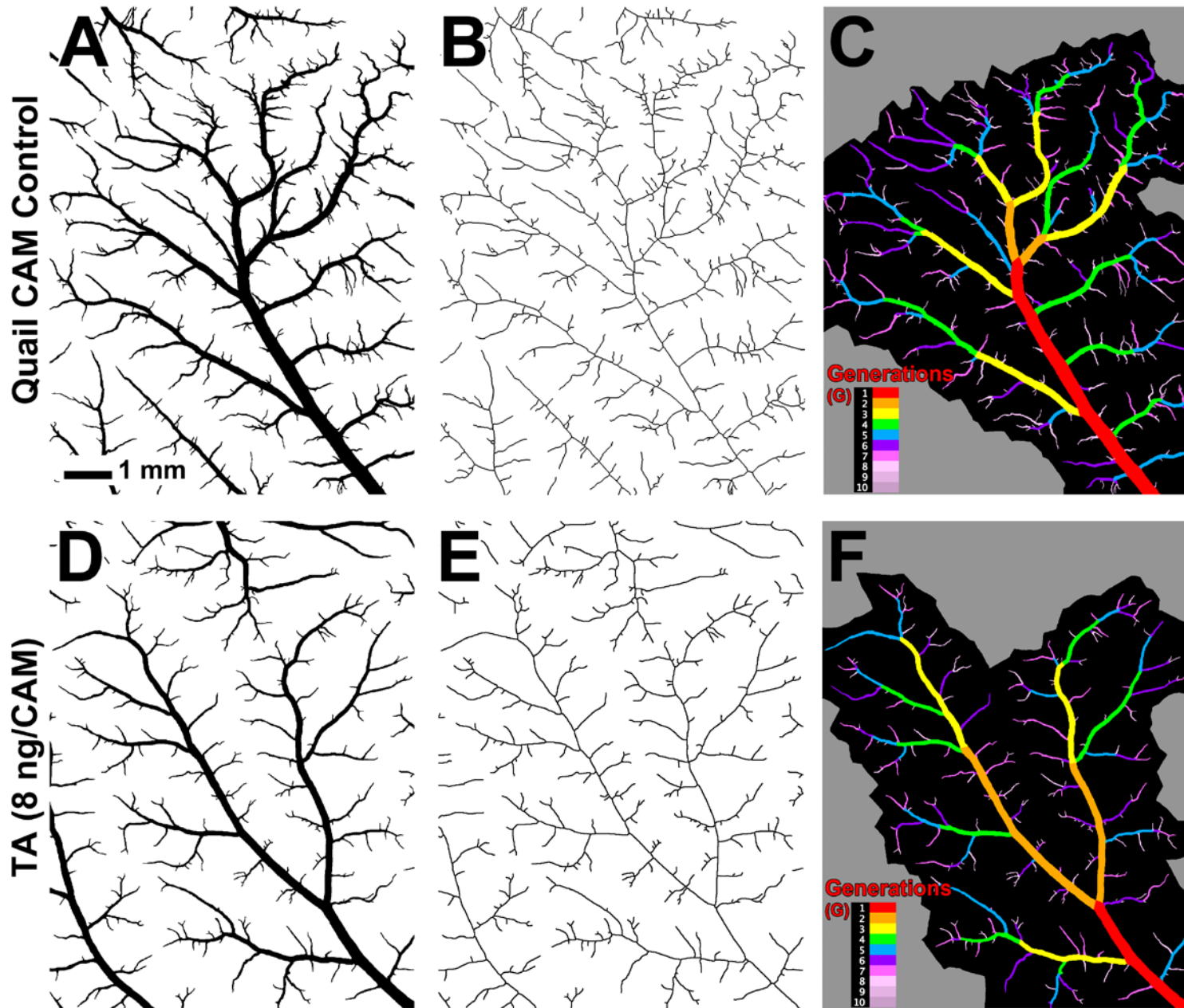
Glenn Research Center

VESGEN Patent Pending

at Lewis Field



Clinical Steroid (TA) Treatment in CAM Vascular Tree



Reviewed in *Anatomical Record* 2009; *Investigative Ophthalmology & Visual Science* 2008



On Rarity And Richness

Two researchers take a stab at explaining why oceans have far fewer species than terrestrial habitats



IF BIODIVERSITY WERE AN OLYMPIC SPORT, life on land would take home the gold and the sea might not even enter a team. Given the vastness of the oceans and the length of time life has thrived there, you might expect marine species to outnumber terrestrial ones. Yet, microbes aside, upward of nine in 10 species crowd into the 30% of Earth's surface that's dry.

It wasn't always that way, say Richard Grosberg and Geerat Vermeij. These researchers from the University of California (UC), Davis, have been studying land and ocean features to understand how evolution proceeds in these two realms. At a recent meeting,* they argued that the difference in diversity is a recent phenomenon.

Back in the Devonian period, 400 million years ago, the seas were home to an abundance of species, perhaps even more than on land. But about 110 million years ago, land plants went through a burst of speciation; so did the pollinators, fungi, and herbivores associated with them. These relationships made "rare" species possible, as plants acquired help in dispersing their pollen and seeds, resulting in relatively low population densities for individual species. Quickly, their numbers left marine biodiversity behind. The trigger for this terrestrial explosion, Grosberg and Vermeij say, was the evolution of a more efficient way in which land plants use water.

"This is an excellent and thoughtful paper addressing an issue in biodiversity that has rarely been tackled," says Michael Benton, a paleontologist at the University of Bristol in the United Kingdom. Jeremy Jackson, a marine ecologist at the Scripps Institution of Oceanography in San Diego, California, calls it "a very big-picture paper. ... It's the kind of paper that you think about forever."

A physical phenomenon?

Grosberg started thinking about these issues when he was preparing a series of talks for the 200th anniversary of Charles Darwin's birth. "To me, the interesting question is why are there so many fewer species in the sea than on the land," says Grosberg.

The difference is striking. In 1994, Robert May of the University of Oxford in the United Kingdom concluded that 85% of the world's macroscopic species lived on land, based on the existing record of species across the globe. A 2009 study by Benton found landlubbers to be even more common, accounting for 95% to 98% of the world's multicelled species. "Both recognized that the estimates were ballparks, simply because we don't actually know how

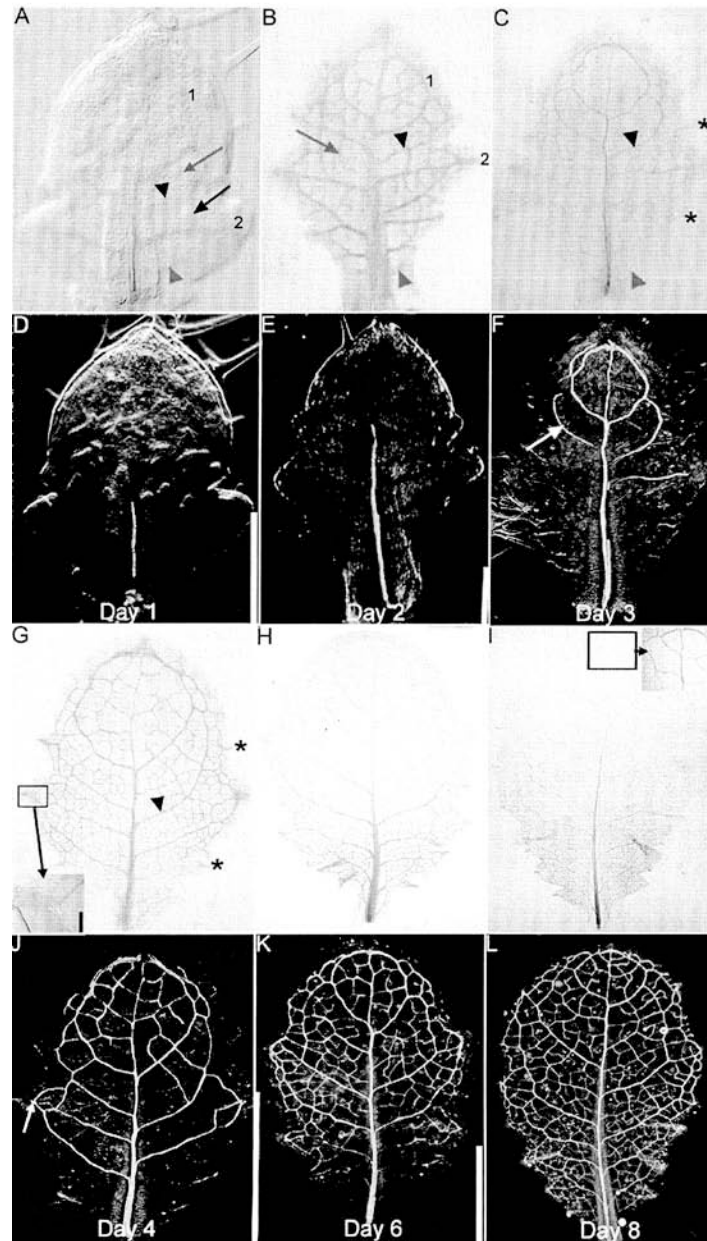
*The Society for Integrative and Comparative Biology meeting was held 3 to 7 January in Seattle, Washington.



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CREDIT: M. TWOHAY/SCIENCE

Vein pattern development in adult leaves
of *Arabidopsis thaliana*



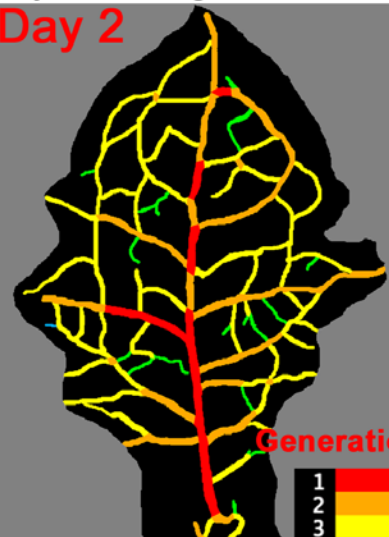
Kang J & Dengler N, Int J Plant Sci 165:231(2004)

See also Candela H et al, 'Venation Pattern Formation in *Arabidopsis thaliana* Vegetative Leaves', Developmental Biology 205:205(1999)

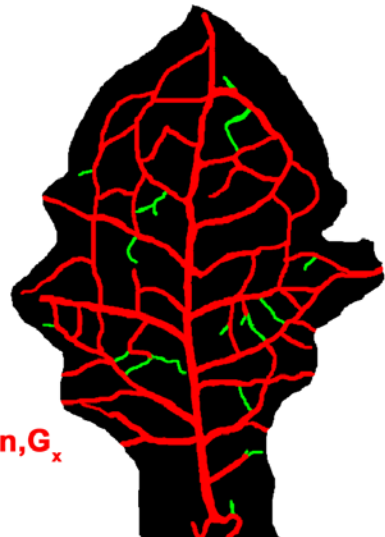
VESGEN

Research Tool for Mapping and Quantification of Vascular Branching Pattern in Genetically Engineered *A. thalia* on ISS

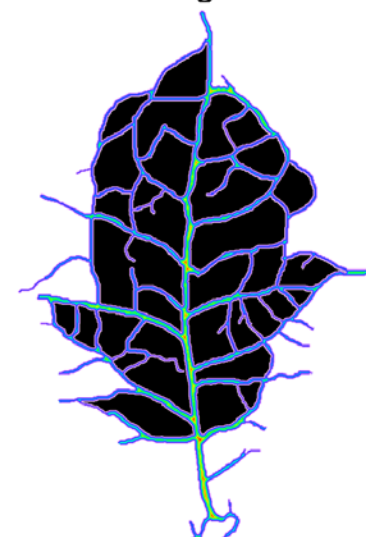
Vascular Pattern by Branching Generation



Grouping of Generations: **LARGE** and **SMALL**



Avascular Spaces of Branching Networks



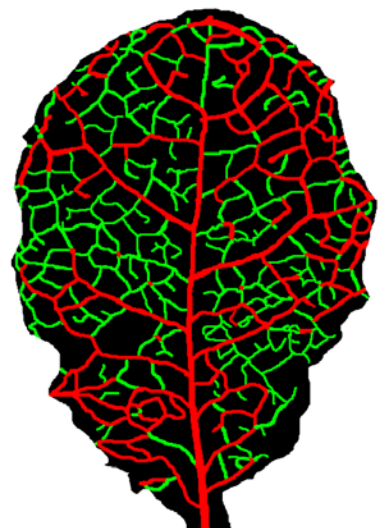
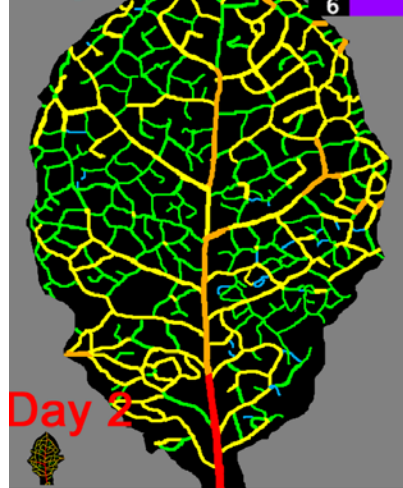
Results

Fractal Dimension
 $D_f = 1.32$
 Area, Length,
 Branchpoint Densities
 $A_V(\text{LARGE}) = 0.195$
 $A_V(\text{SMALL}) = 0.013$
 Average Vessel
 Diameter (μm)
 $D_V(\text{LARGE}) = 11.8 \mu\text{m}$
 $D_V(\text{SMALL}) = 7.0 \mu\text{m}$

Conclusions

Less mature branching

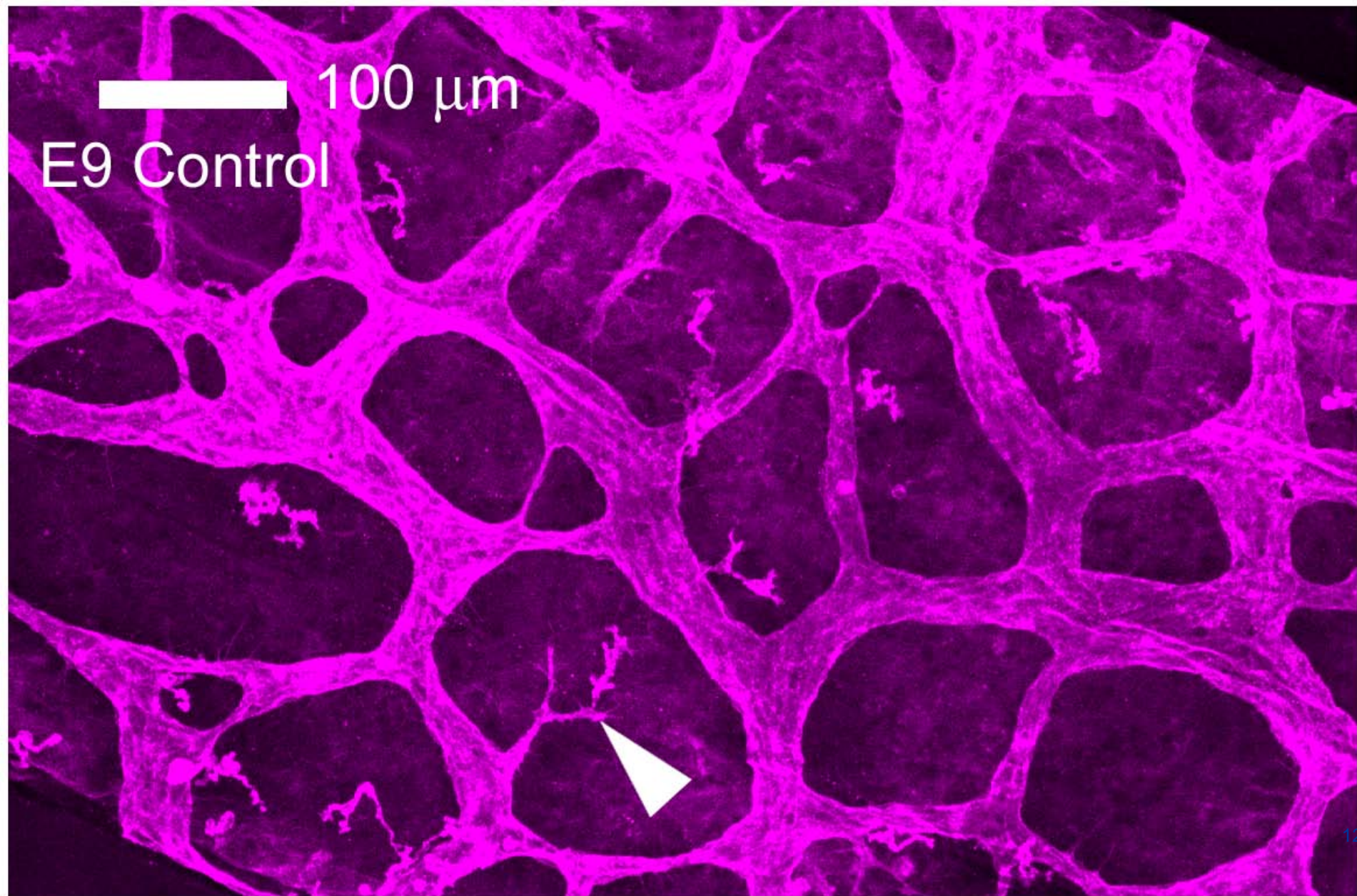
Day 8

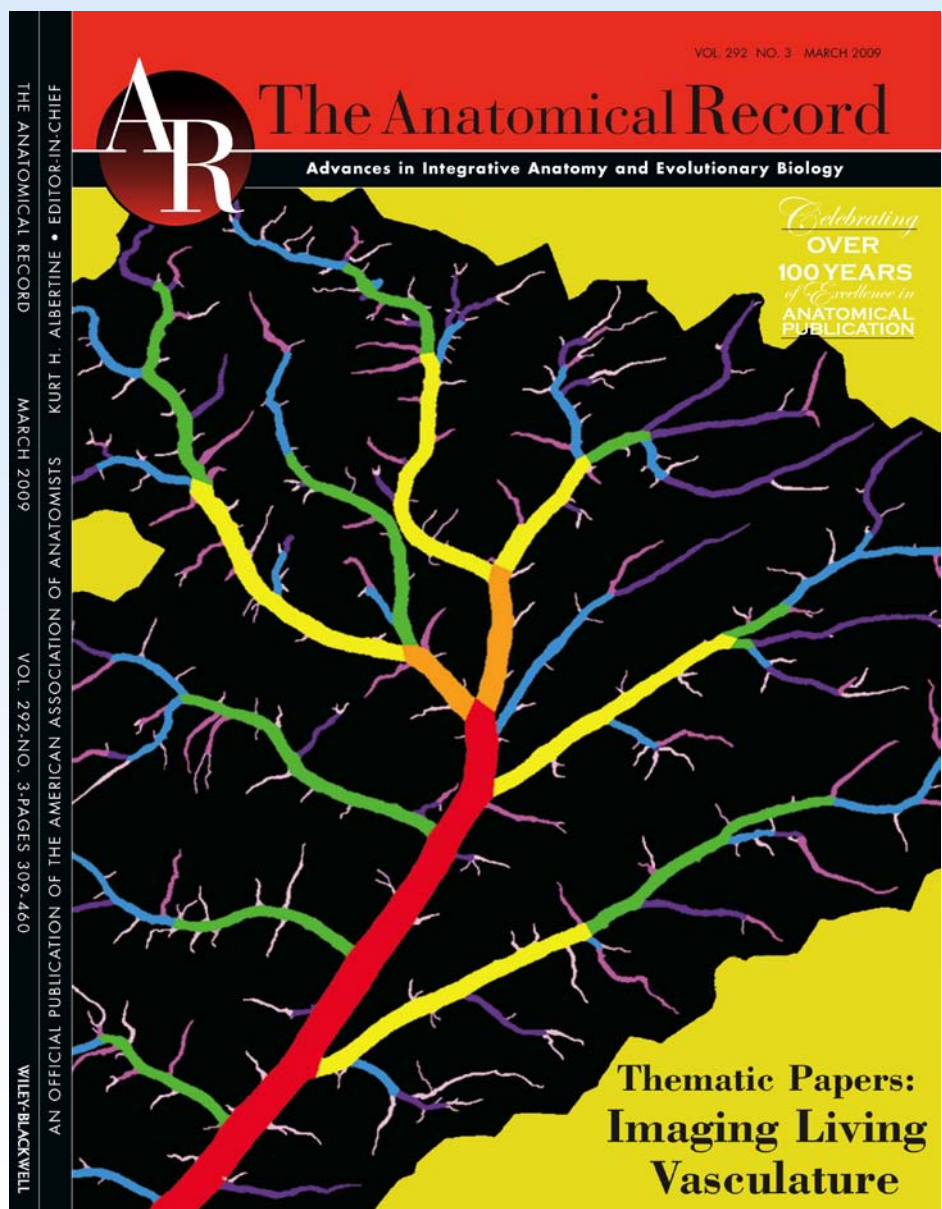
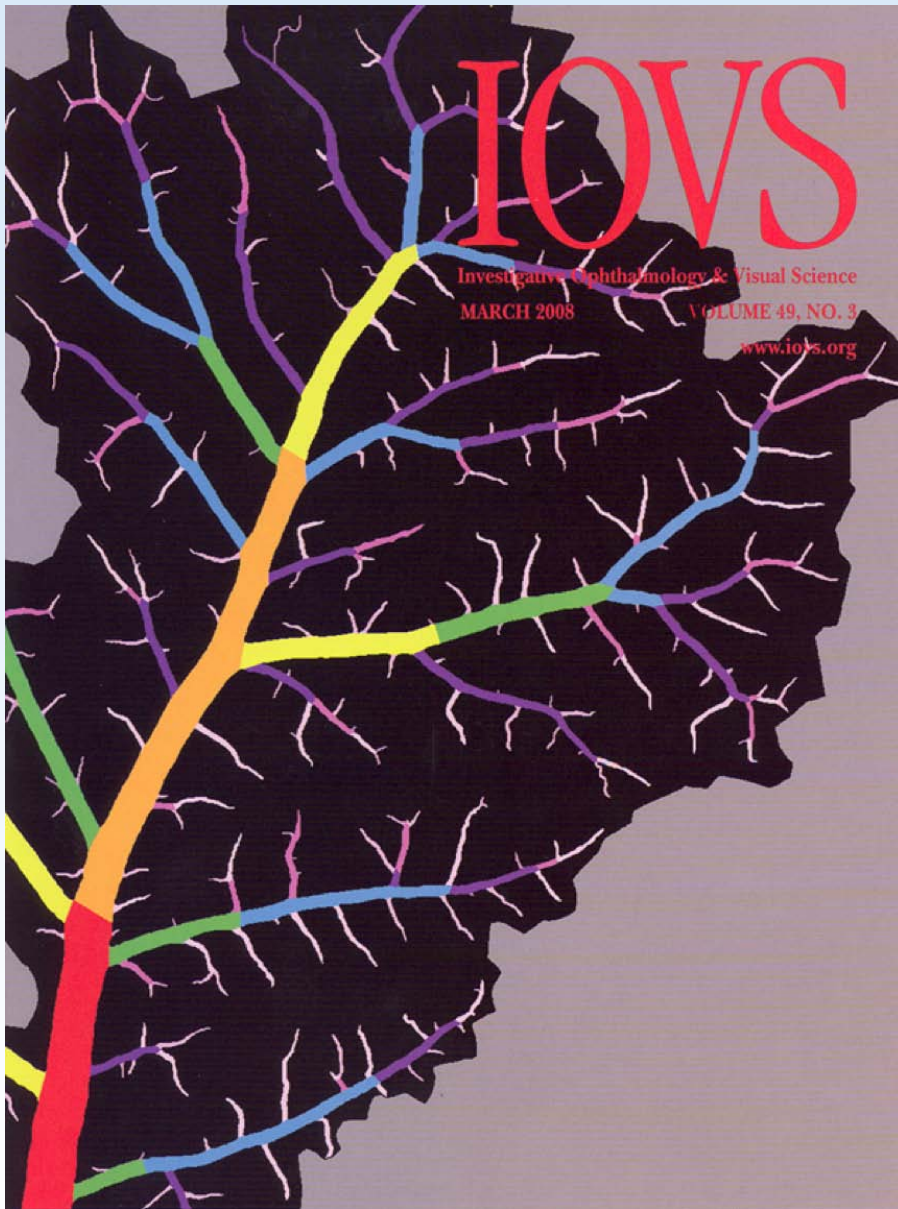


$D_f = 1.47$
 $A_V(\text{LARGE}) = 0.159$
 $A_V(\text{SMALL}) = 0.276$
 $D_V(\text{LARGE}) = 93.1 \mu\text{m}$
 $D_V(\text{SMALL}) = 66.8 \mu\text{m}$

Increased vascular complexity—

especially density of smaller vessels

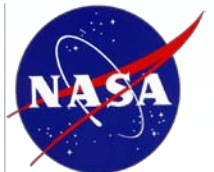




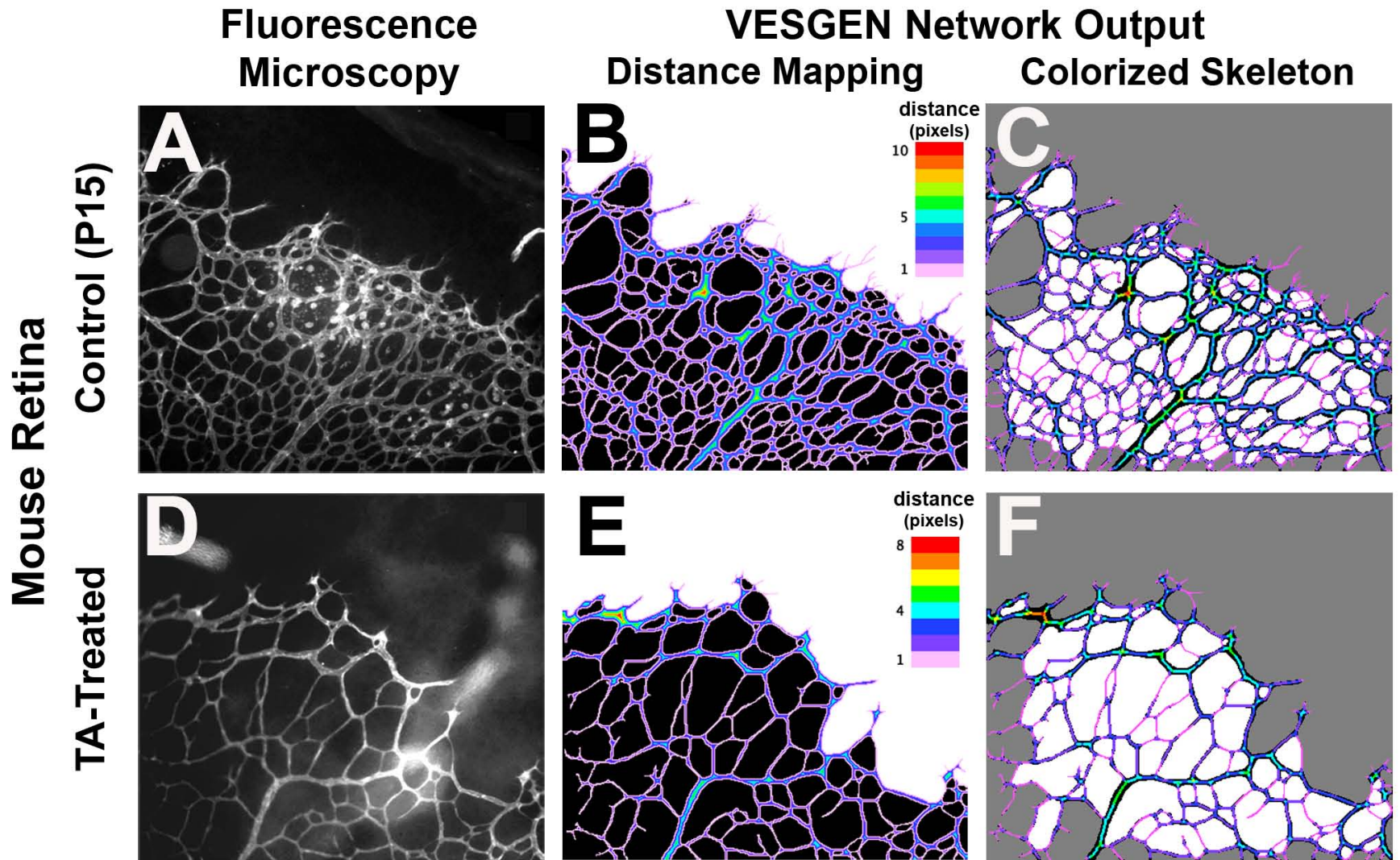
Glenn Research Center

VESGEN Patent Pending

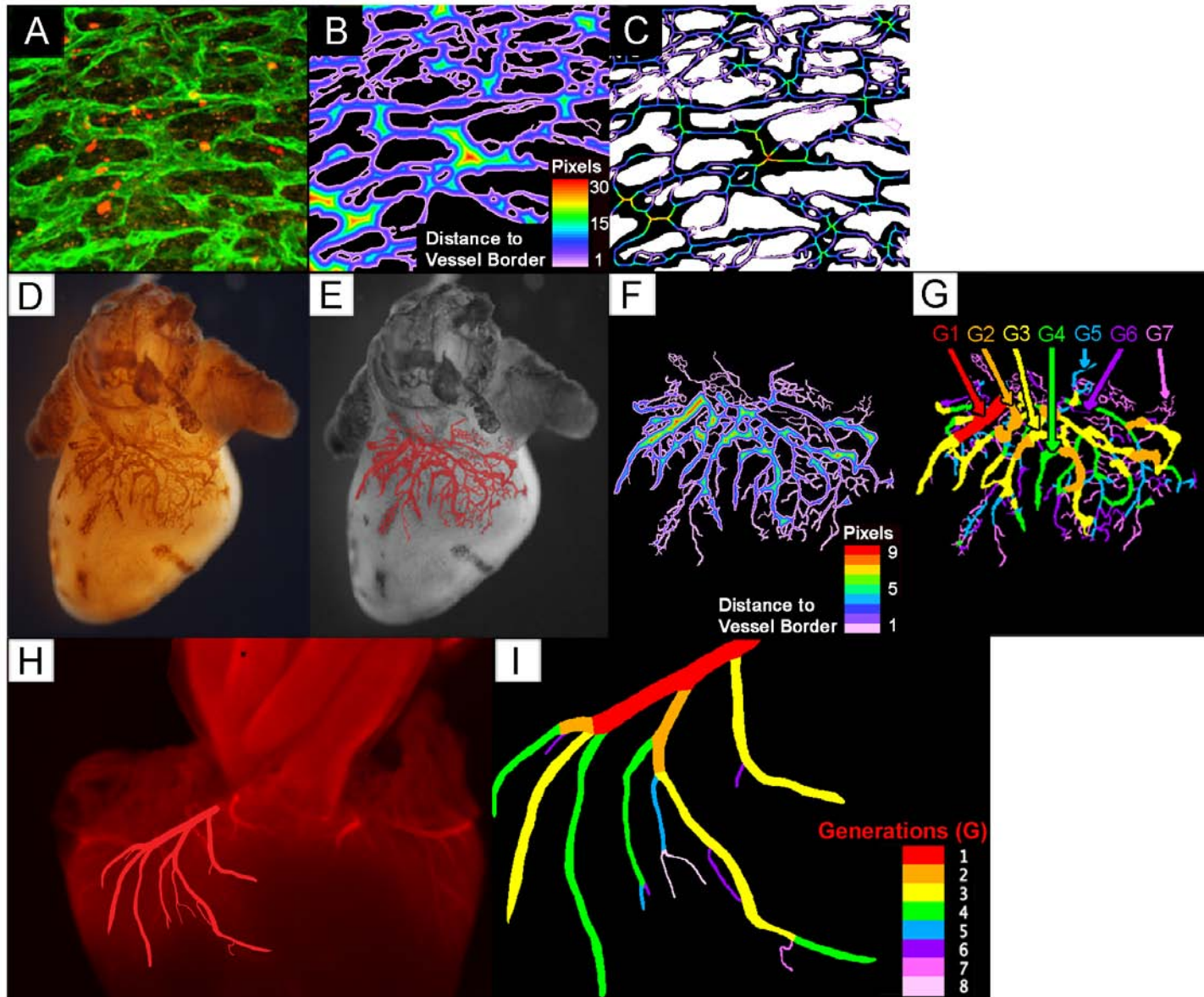
at Lewis Field



VASCULAR NETWORKS IN TRANSGENIC MOUSE RETINA



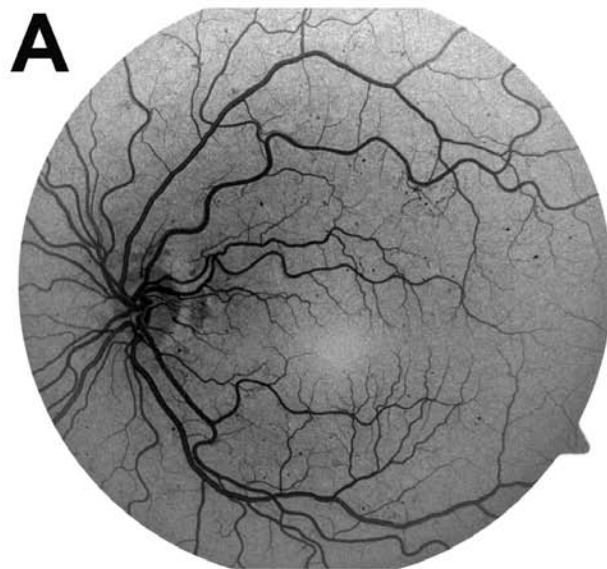
CORONARY VESSEL NETWORK-TO-TREE TRANSITIONS



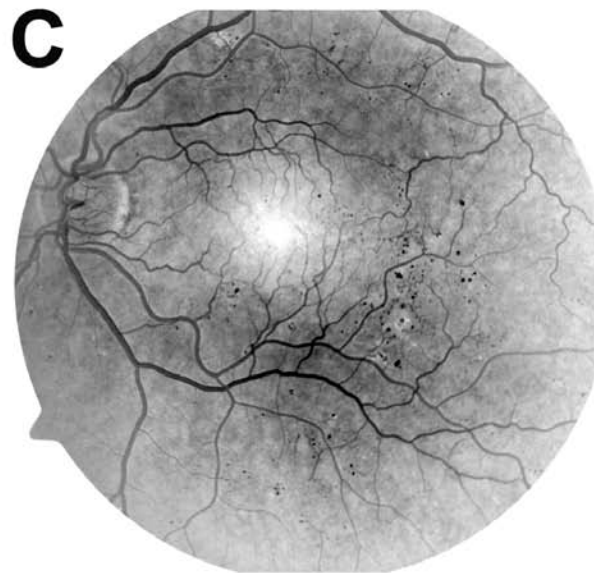
Vickerman et al, VESGEN Review, *Anatomical Record A* 292(3), 2009

Clinical Fluorescein Angiography of Human Retina

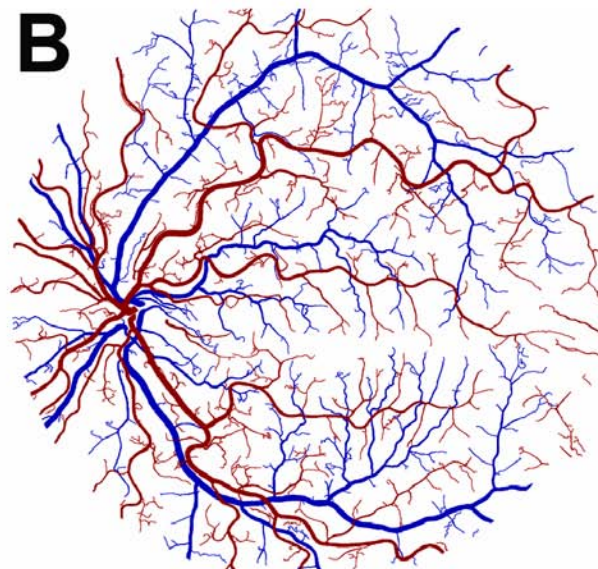
Mild/Moderate NPDR



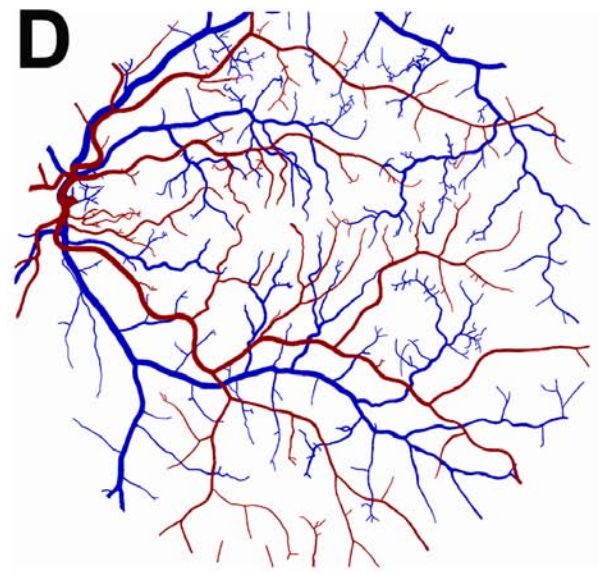
Severe NPDR



Vascular Trees



— Arteries
— Veins



Mapping of Progressive Diabetic Retinopathy by VESGEN

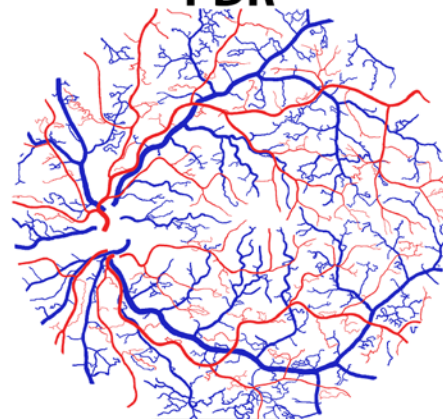
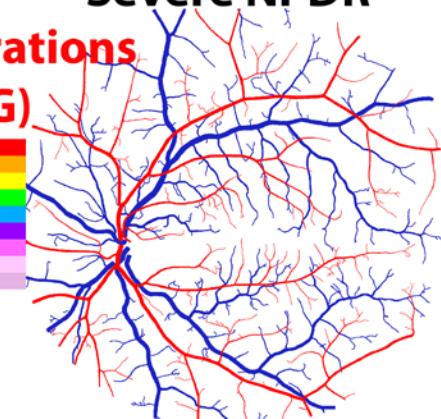
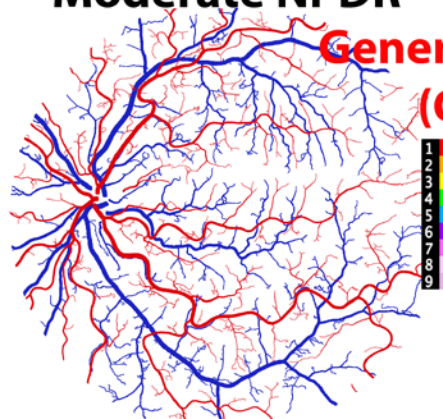
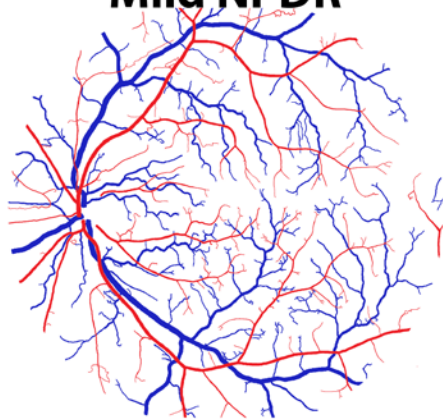
Mild NPDR

Moderate NPDR

Severe NPDR

PDR

Vascular Trees

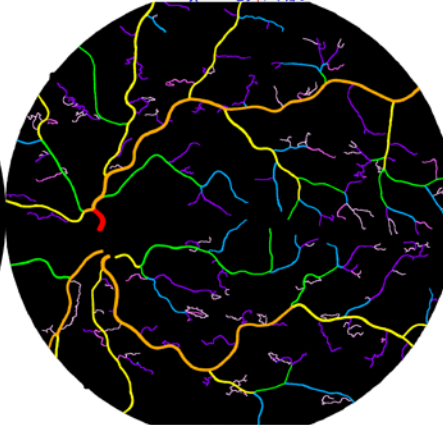
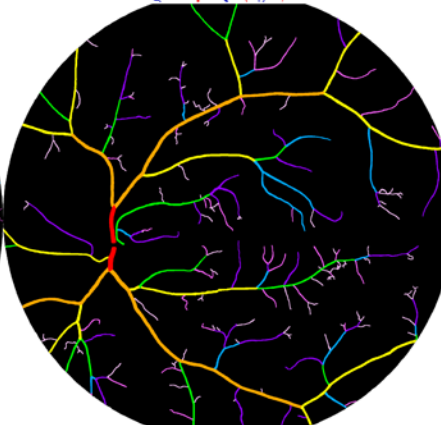
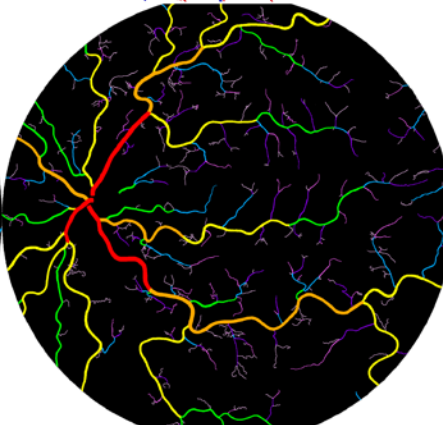
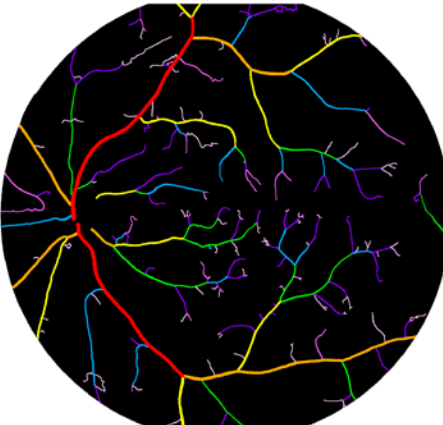


Generations

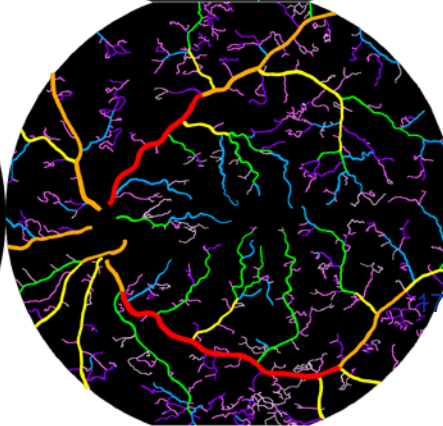
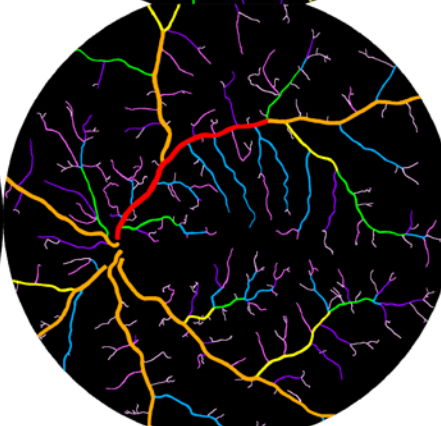
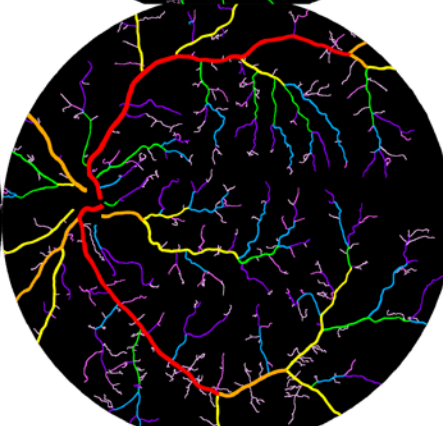
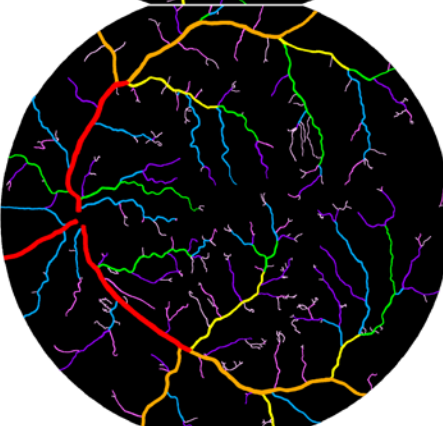
(G)



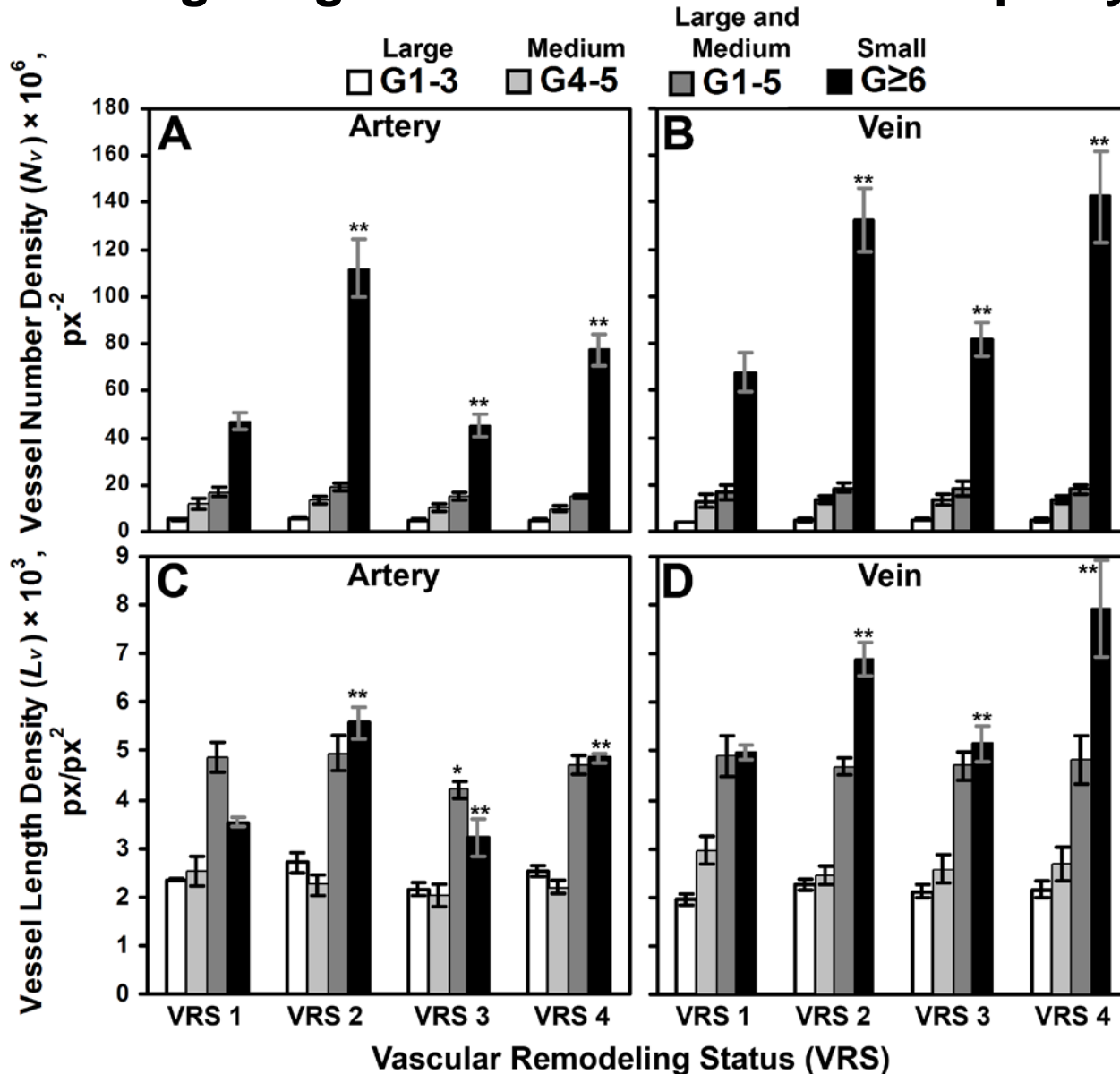
Arteries

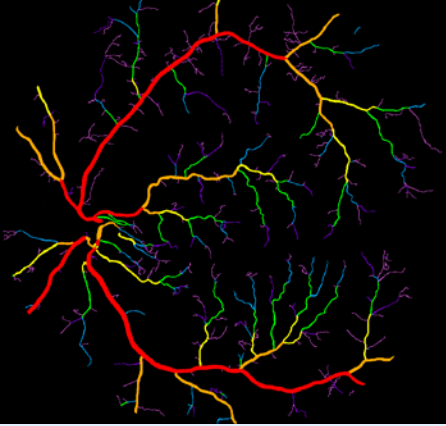


Veins



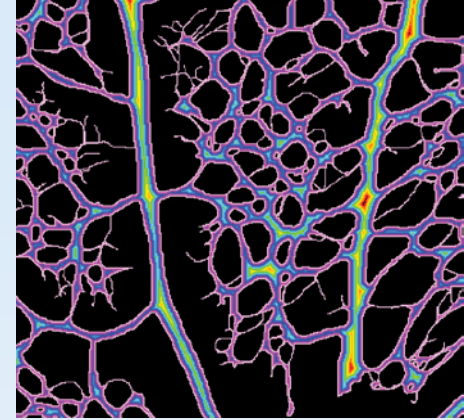
Surprising Oscillation of Angiogenesis with Vascular Dropout during Progression of Diabetic Retinopathy





VESGEN

**as Collaborative
Research Discovery Tool
with Biologists and Physicians**



Integrative Systems Biology:

**‘Fingerprint’ or ‘Signature’ Mapping of Dominant Vascular Patterns
Induced by VEGF and Other Angiogenesis Regulators**

Fractal-Based VESGEN for Multi-Parametric Pattern Analysis according to
Branching Generation

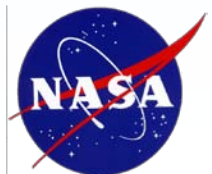
Research Discovery Tool for

Variety of plant, animal and human applications on ISS?

Glenn Research Center

VESGEN Patent Pending

at Lewis Field



Acknowledgements

NASA Glenn Research Center

Mary Vickerman MS, Patricia Keith MS, Mark Wernet PhD, Terri McKay BS, Dan Gedeon, Alan Hylton MS, Daniela Ribita BS, Harry Olar BS, Camille Everhart, Dedra Whitfield

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Cole Eye Institute

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Lerner Research Institute

Paul DiCorleto PhD, Unni Chandrasekharan PhD, Ron Midura PhD

University of New Mexico School of Medicine/Ohio Aerospace Institute

Krishnan Radhakrishnan MD PhD

University Hospitals, Case Western Reserve University

Steven Fisher MD, Hong-Bin Liu PhD

Michiko Watanabe PhD, Ganga Karunamuni BS, Monica Montano PhD

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