Using GeneLab for VESGEN Systems Analysis of Vascular Phenotypes from Stress and Other Signaling Pathways

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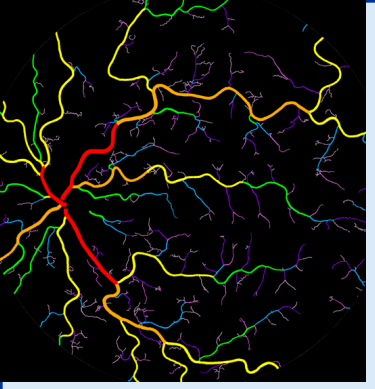
One fundamental requirement shared by humans with all higher terrestrial life forms, including other vertebrates, insects, and higher land plants, is a complex, fractally branching vascular system. NASA's VESsel GENeration Analysis (VESGEN) software maps and quantifies vascular trees, networks, and tree-network composites according to weighted physiological rules such as vessel connectivity, tapering and bifurcational branching. According to fluid dynamics, successful vascular transport requires a complex distributed system of highly regulated laminar flow. Microvascular branching rules within vertebrates, dicot leaves and the other organisms therefore display many similarities. A unifying perspective is that vascular patterning offers a useful readout of molecular signaling that necessarily integrates these complex pathways. VESGEN has elucidated changes in vascular pattern resulting from inflammatory, developmental and other signaling within numerous tissues and major model organisms studied for Space Biology.

For a new VESGEN systems approach, we analyzed differential gene expression in leaves of Arabidopsis thaliana reported by GeneLab (GLDS-7) for spaceflight. Vascular-related changes in leaf gene expression were identified that can potentially be phenocopied by mutants in ground-based experiments. To link transcriptional, protein and other molecular change with phenotype, alterations in the spatial and dynamic dimensions of vascular patterns for *Arabidopsis* leaves and other model species are being co-localized with signaling patterns of single molecular expression analyzed as information dimensions. Previously, *Drosophila* microarray data returned from space suggested significant changes in genes related to wing venation development that include EGF, Notch, Hedghog, Wingless and Dpp signaling. Phenotypes of increasingly abnormal ectopic wing venation in the (non-spaceflight) *Drosophila* wing generated by overexpression of a Notch antagonist were analyzed by VESGEN. Other VESGEN research applications include the mouse retina, GI and coronary vessels, avian placental analogs and translational studies in the astronaut retina related to health challenges for long-duration missions.

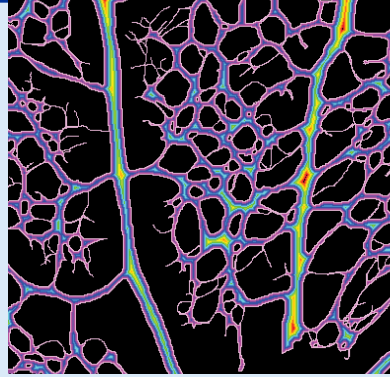
Research partially supported by Ames Center Innovation Award to PP-W.



Human Retina

NASA'S VESGEN Software

Research Discovery Tool
for Fundamental and Translational
Space Biology Research



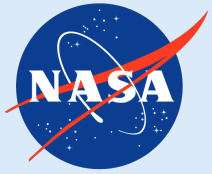
Mouse Retina

Using NASA's GeneLab for VESGEN Systems Analysis of Vascular Phenotypes from Stress and Other Signaling Pathways

Patricia Parsons-Wingerter
Space Biosciences Research Branch

Space Biosciences
NASA AMES RESEARCH CENTER

NASA



Collaborators

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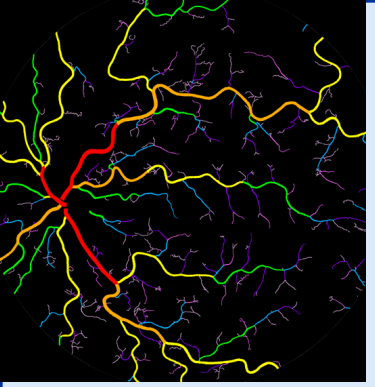
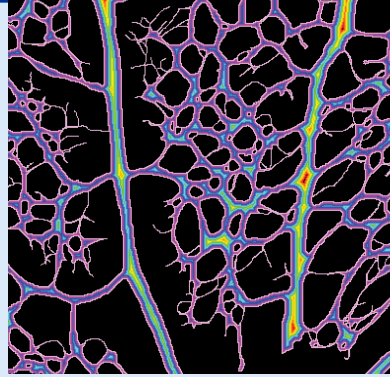
Sarah E. Wyatt, Environmental and Plant Biology, Ohio University, Athens OH



Human Retina

NASA'S VESsel GENeration Analysis [VESGEN] Software

Mapping and Quantification of Branching Vascular Patterns from Physiological Branching Rules



Mouse Retina

- Vascular trees, networks, and tree-network composites from set of weighted parameters for vessel connectivity, tapering and bifurcational branching

- *Requirements of fluid dynamics for laminar flow*
  Aqueous vascular transport by complex distributed system of fractal-based bifurcational branching

- Microvascular rules for fractal-based branching within humans, vertebrates, insects and dicot leaves therefore display many similarities

VESGEN Patents Pending

Space Biosciences
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Parsons


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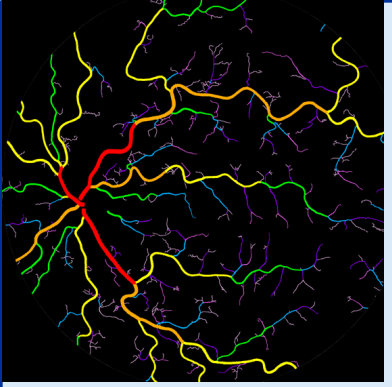
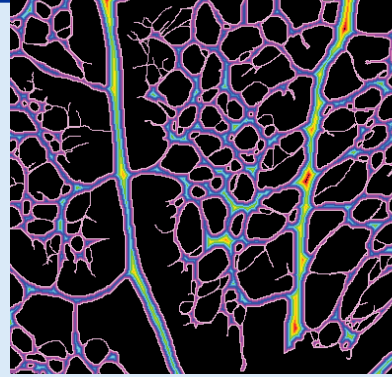


Human Retina

VESGEN Analysis for Fundamental Space Biology Research with Translational Applications to Astronaut Health and Countermeasures



Mouse Retina

Vascular Trees

Retinas of Astronauts and Human Bed Rest; Diabetic Retinopathy
Mouse/Avian Coronary Vessels, Chorioallantoic Membrane (CAM), Yolksac

Vascular Networks

Mouse Intestinal Inflammation, CAM Lymphatic Vessels, Abnormal Mouse Corneal Angiogenesis, ***Drosophila* (Fruitfly) Wing**

Vascular Tree-Network Composites

Mouse Postnatal Retina
Early Embryonic Coronary Vessels, ***Arabidopsis* Leaf Venation**

VESGEN Patent Pending

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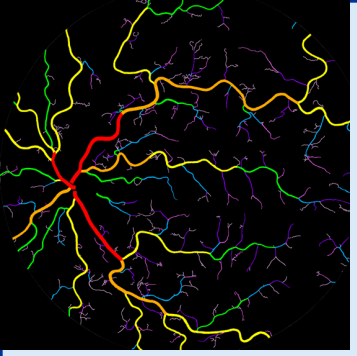
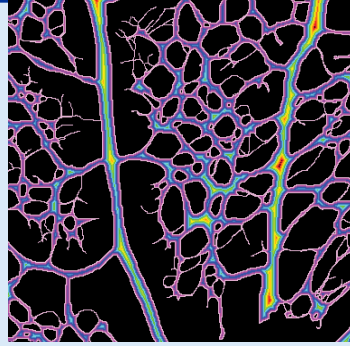


Human Retina

VESGEN
Analysis of Vascular Patterns



Mouse Retina

Research Hypothesis

Vascular patterning offers useful readout of molecular signaling that necessarily integrates crosstalk among complex signaling pathways

Fractal-Based Physiological Branching Rules

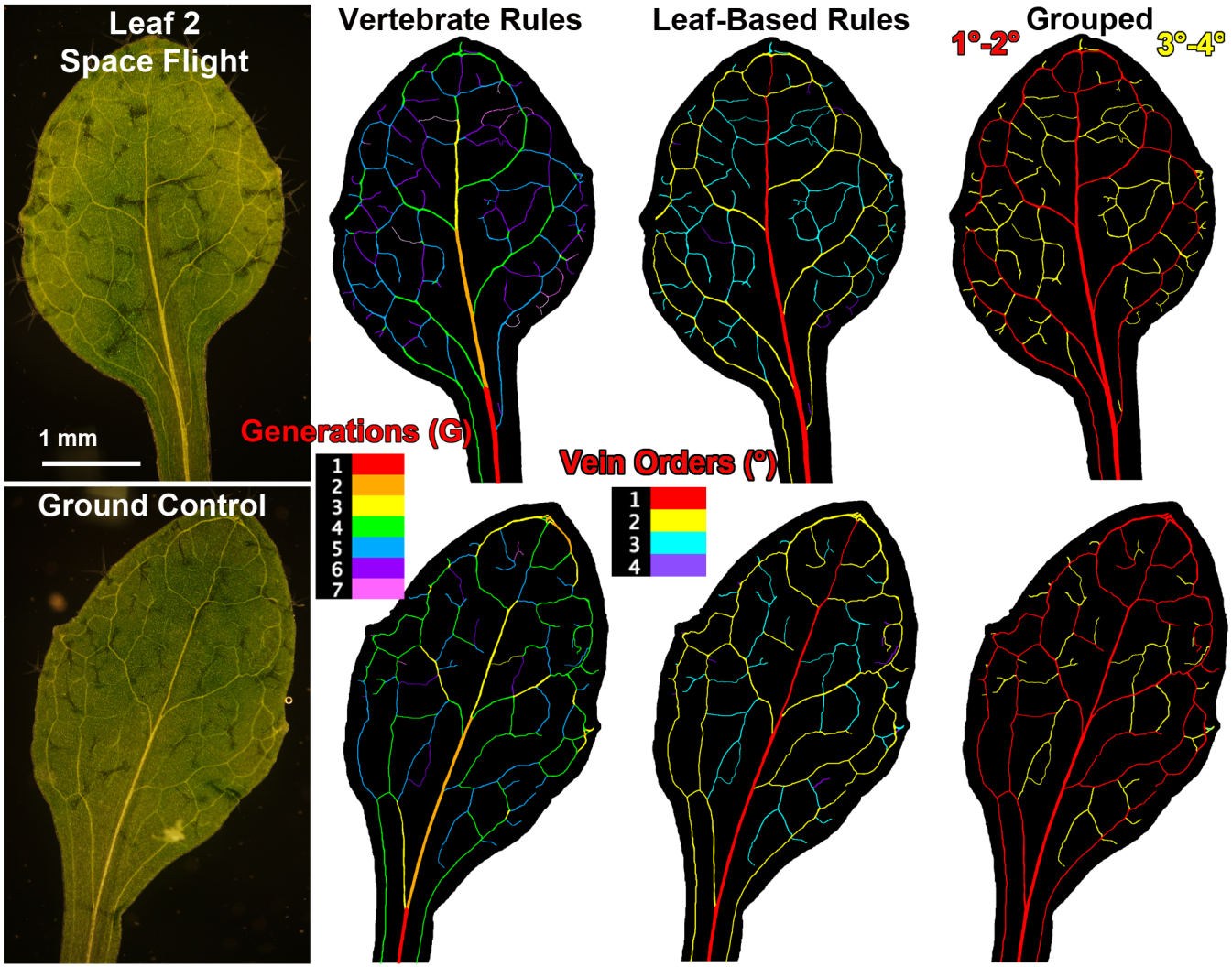
from fluid mechanics, anatomy, microscopic observations

Mapping and Quantification by Multiparametric Weighted Analysis

Fractal Dimension, D_f
Vessel Number Density, N_v
Vessel Length Density, L_v
Vessel Diameter, D_v
Branchpoint + Endpoint Densities, Br_v+E_v

VESGEN Patent Pending

Arabidopsis leaves from ISS: STS-130

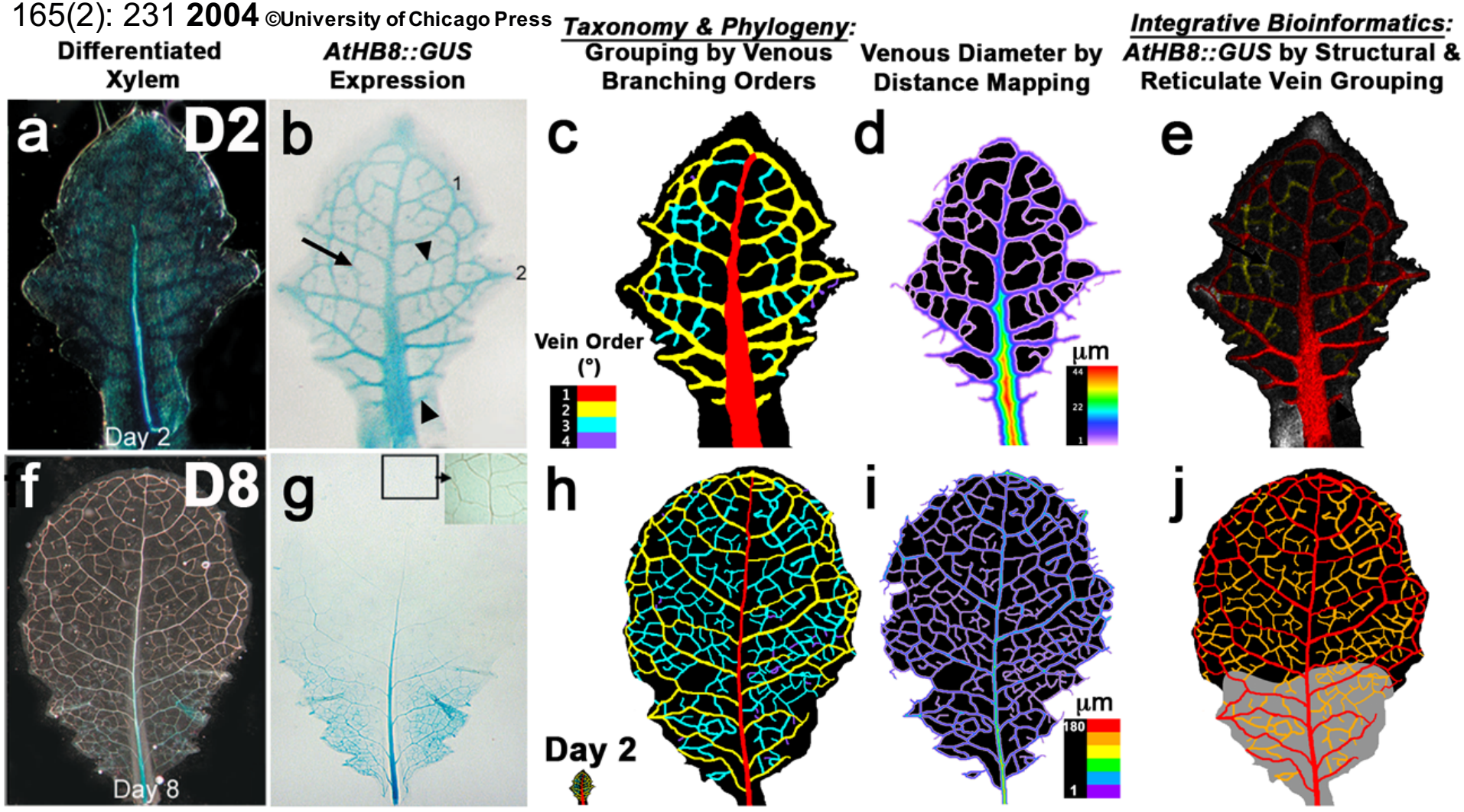


ARF19 GUS

Images of STS-130 leaves provided by A-L Paul & RJ Ferl, analyzed by P Parsons & M Vickerman
P Parsons, M Vickerman, A-L Paul, R Ferl, ASGSR 2012 *Grav and Space Research* 2(1) 2014

VESGEN mapping of Arabidopsis leaf venation with bioinformatic analysis

Kang & Dengler, *Int J Plant Sci*
165(2): 231 **2004** ©University of Chicago Press



P Parsons, M Vickerman, A-L Paul, R Ferl, ASGSR 2012 *Grav and Space Research* 2(1) 2014

GeneLab

Open Science
for Exploration

Home Repository Data Data Mining Tools Submit Data Contact Us Search Data

The Arabidopsis spaceflight transcriptome: a comparison of whole plants to discrete root, hypocotyl and shoot responses to the orbital environment

2 datasets available for download here:

ISA-TAB Metadata file
Raw Data File

GeneLab Accession Number	GLDS-7
Source Accession Number	E-MTAB-1264

Contacts

Name	Role	Organization	Email
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Anna-Lisa Paul	Investigator	University of Florida	alp@ufl.edu
Agata Zupanska	Submitter	University of Florida	zupanska@ufl.edu

Space Grown *Arabidopsis* with Microarray Data from GeneLab: Identification of Genes Important in Vascular Patterning

(A Weitzel, P Parsons, S Wyatt; ASGSR 2016)

- Analysis of transcriptomic data from space flight and ground control leaves identified differential expression of 22 genes, of which seven may be related to plant vasculature

- Two gene clusters suggest there may be phenotypic changes in leaf venation resulting from development in microgravity

  KISS **M**E **D**EADLY [KMD] coding F-box genes

  NAM, **A**TAF1/2, and **C**UC2 [NAC] related genes

- Vascular-related changes in leaf gene expression can potentially be phenocopied by mutants in ground-based experiments and corroborated by VESGEN analysis

- Genetic, transcriptional and other molecular changes reported by GeneLab can be mapped to vascular phenotypes by VESGEN by bioinformatic co-localization of single molecular expression

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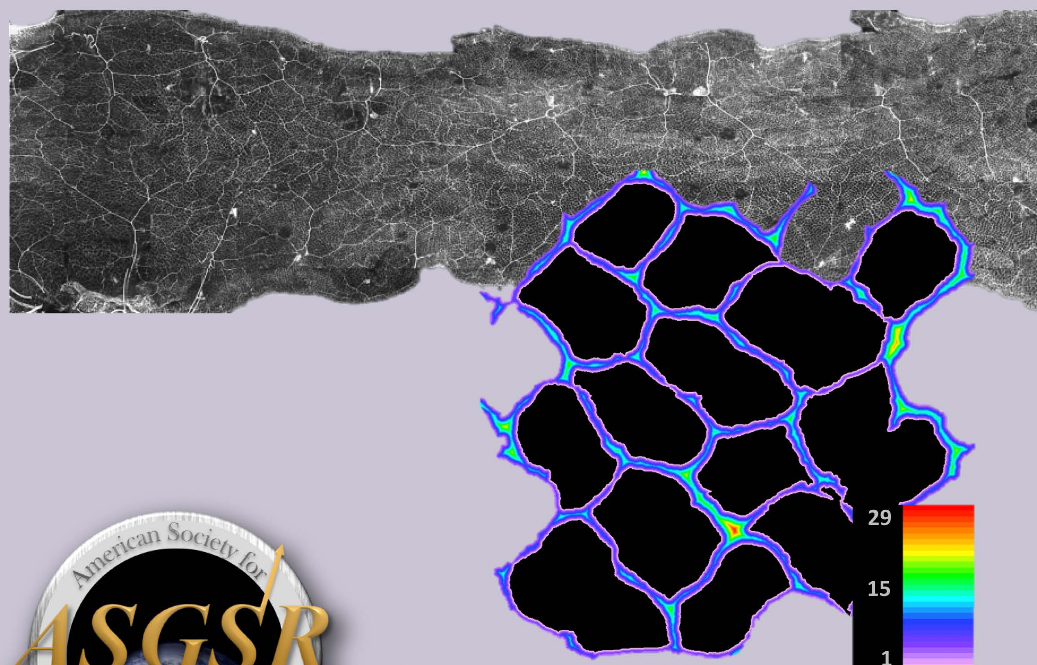
Volume 26, Number 2 October 2012

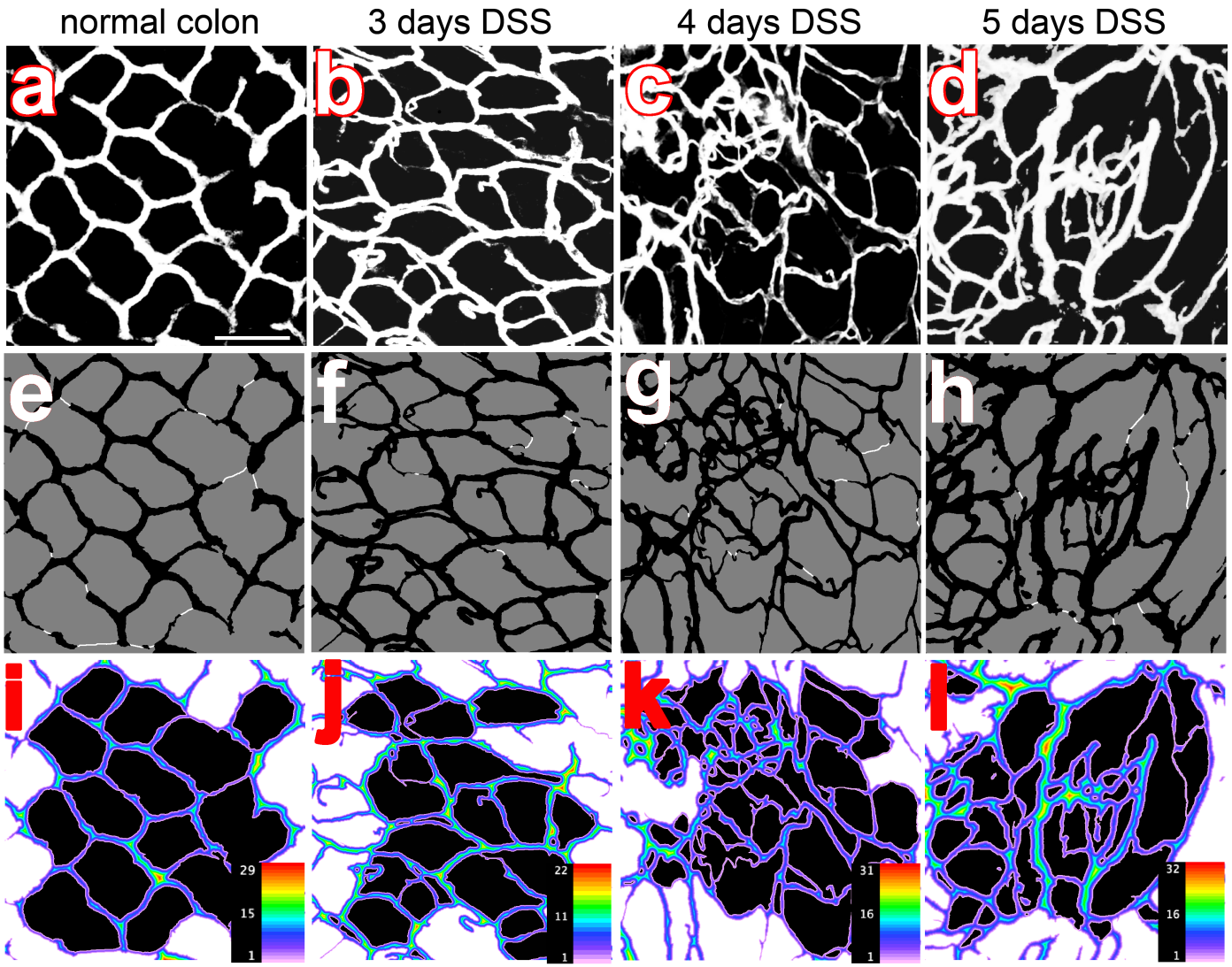
Gravitational and Space Biology

Publication of the American Society for Gravitational and Space Research



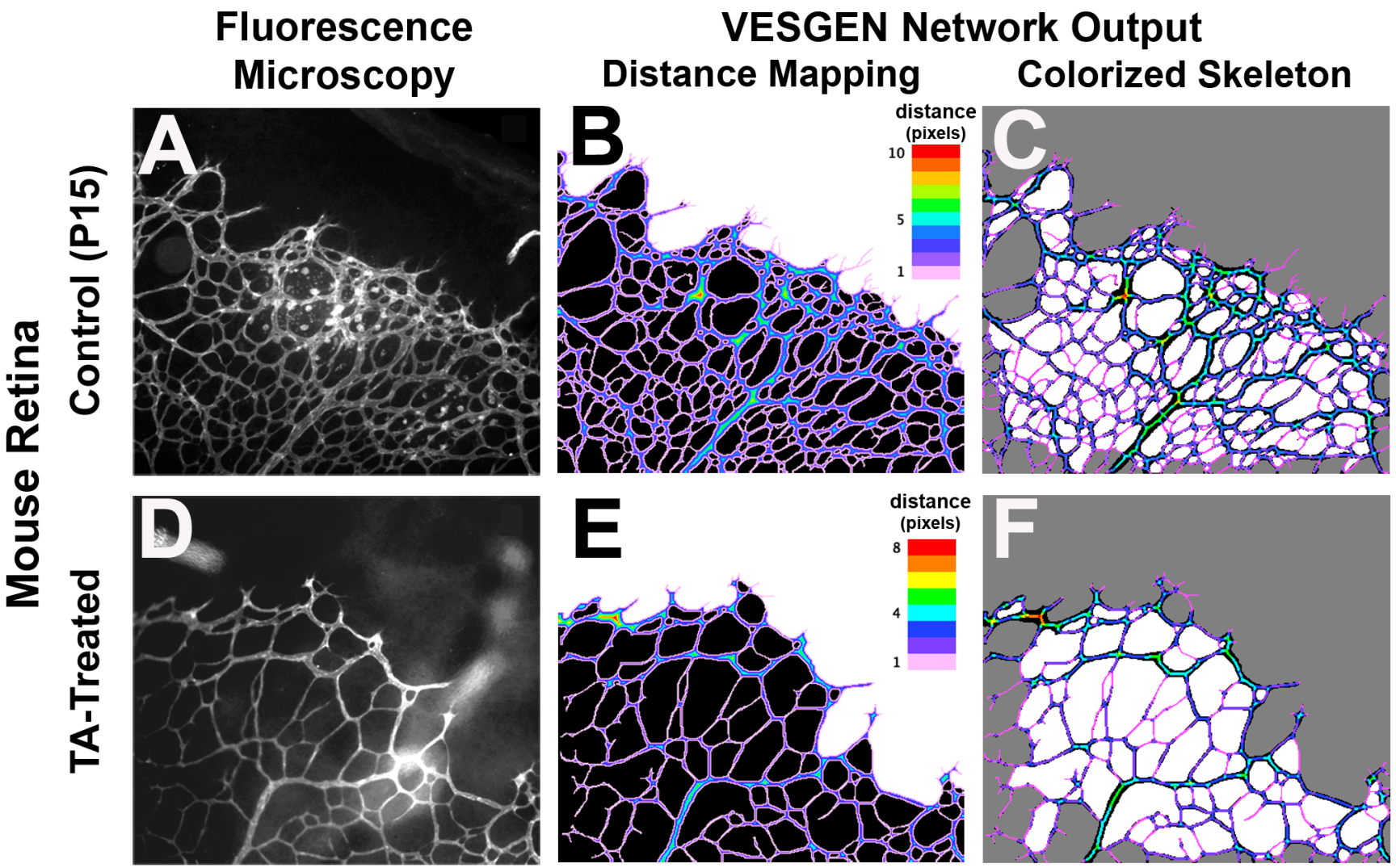
American Society for Gravitational and Space Research
ASGSR

VESGEN mapping of vascular networks for progressive GI inflammation progression with mouse model



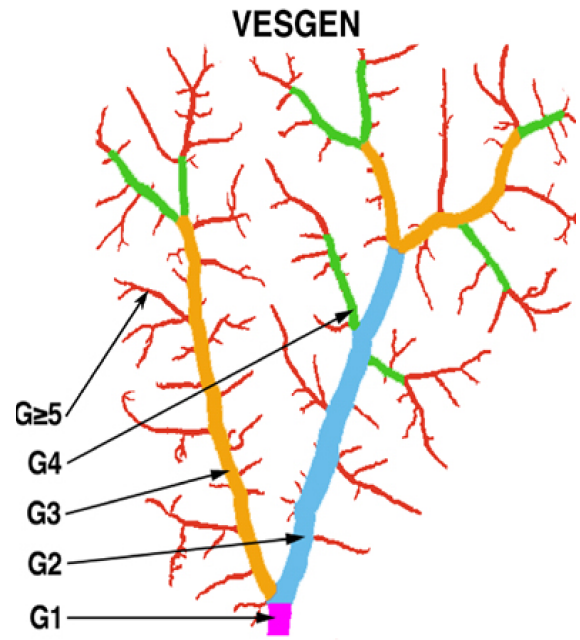
Parsons, Reinecker, Chen et al *Gravitational Space Biology* 25(1):69 2012; PlosONE 2013

Vascular Networks in Transgenic Mouse Retina



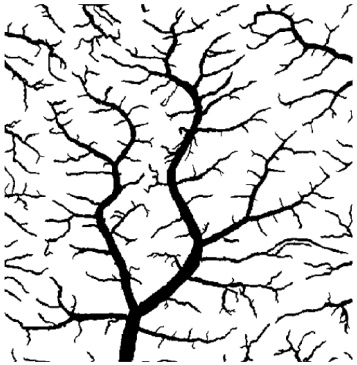
with J Sears & Q Ebrahem (Cole Eye Institute), from Vickerman et al, *Anat Rec* 292(3), 2009

VESGEN Hypothesis *'Fingerprint'* or '*Signature*' Vascular Pattern as Useful Integrative Readout of Complex Molecular Signaling Pathways



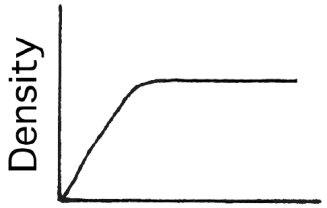
'he form of an object is a 'diagram of forces'

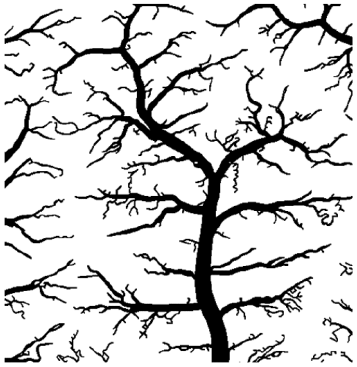
D' Arcy Thompson



bFGF as Simple Stimulator

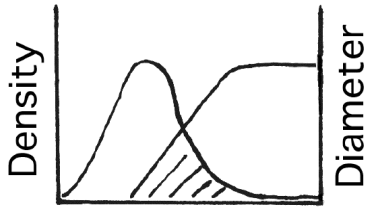
Arterio Thromb Vasc Biol 20 (2000)

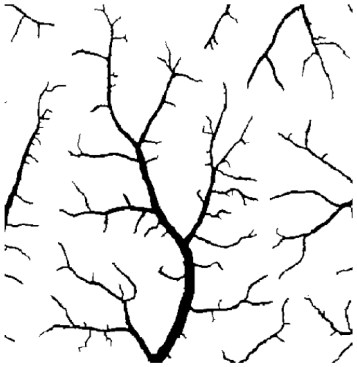




VEGF as Vascular Complexity Factor: Phenotypic Readout with eNOS Signaling

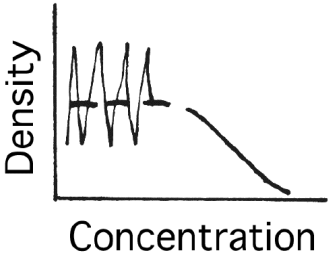
Microvascular Research 72 (2006)



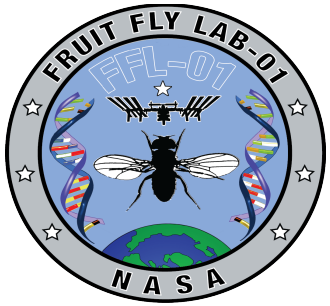


TGF-β1 as Simple Inhibitor but Complex Potentiator

Microvascular Research 59 (2000)



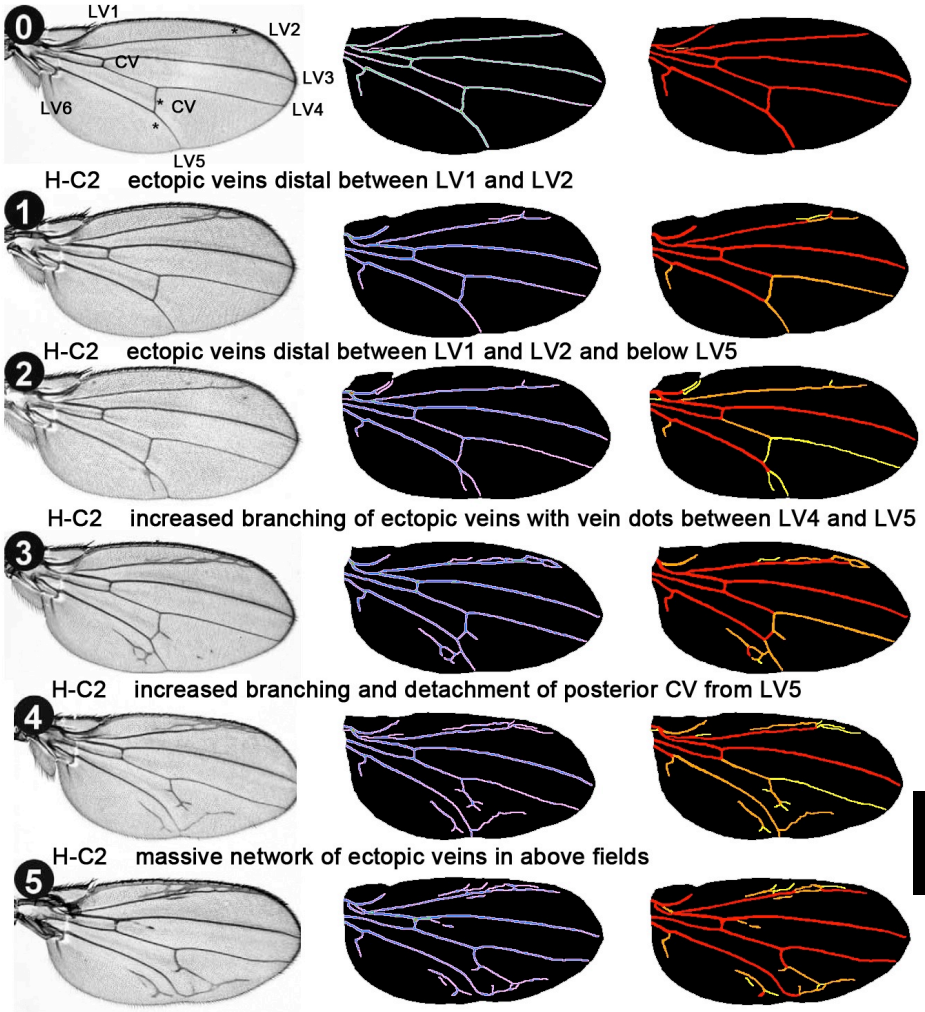
Fruitfly (*Drosophila melanogaster*): Major Genetic Model Organism



Mapping by VESGEN: Hairless (H-C2) overexpression induces phenotypic series of increasing ectopic wing venation

6 Longitudinal Veins (LV) with anterior and posterior Cross Veins (CV)

Wildtype, no heat shock * where veinlets may arise after heat shock in wt or H-C2



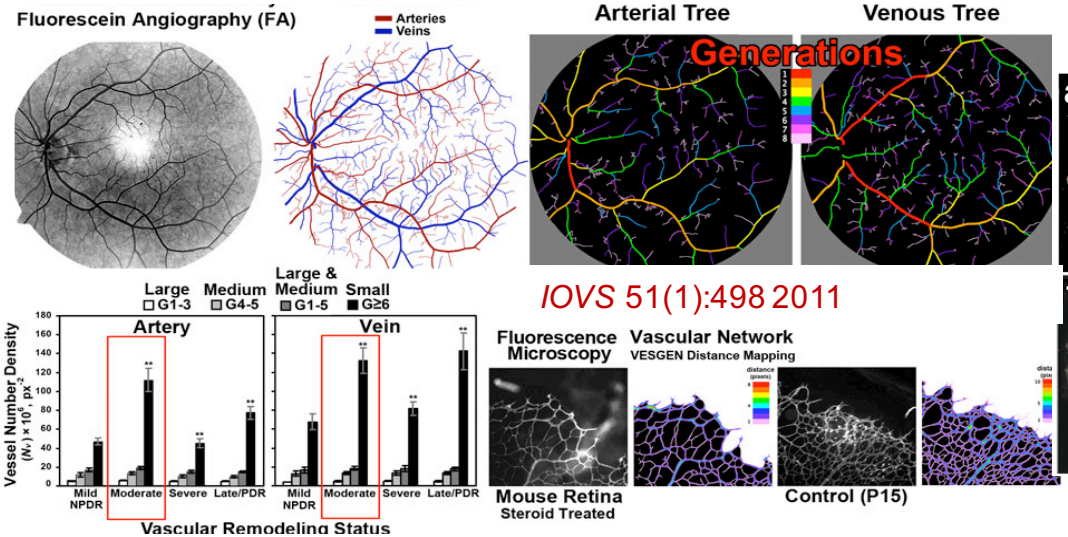
Johannes B, Preiss A. Wing vein formation in Drosophila melanogaster: hairless is involved in the cross-talk between Notch and EGF signaling pathways. Mechanisms of development 2002; 115(1-2): 3-14

Expression of Genes Involved in Drosophila Wing Morphogenesis and Vein Patterning Are Altered by Spaceflight

Parsons, Hosamani, Vickerman, Bhattacharya
Grav Space Res 3(2):54-64 2015, ASGSR 2012

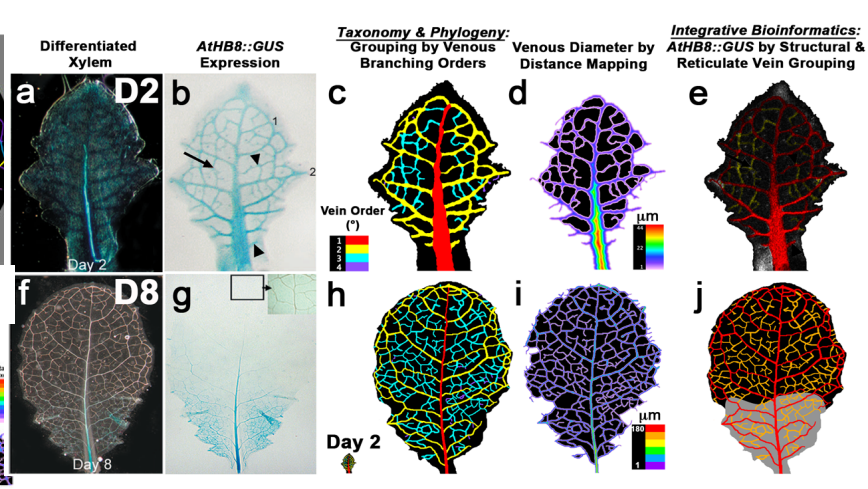
VESGEN Analysis of Vascular Patterning for Fundamental Space Biology with Translational Applications to Astronaut and Terrestrial Health

Insights into progression of visually impairing disease

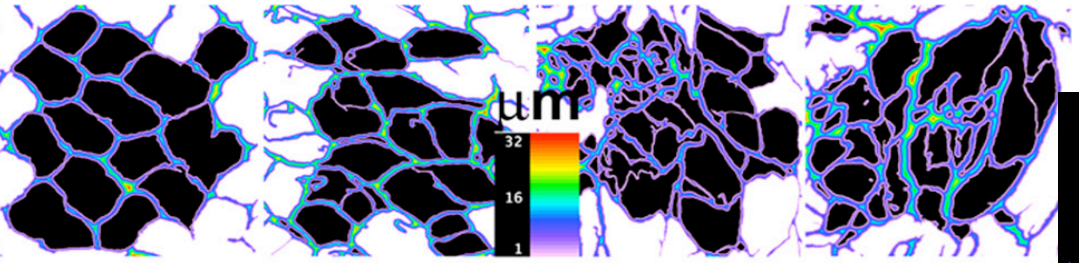


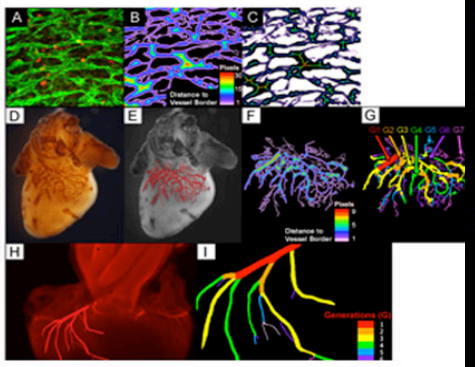
GSR 2(1):68 2014

IOVS 51(1):498 2011



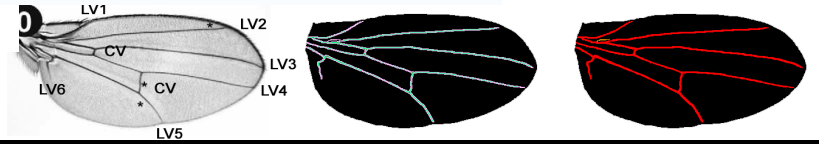
GSB 26(2):2 2012 , *PloS One* 8(5):e64227 2013

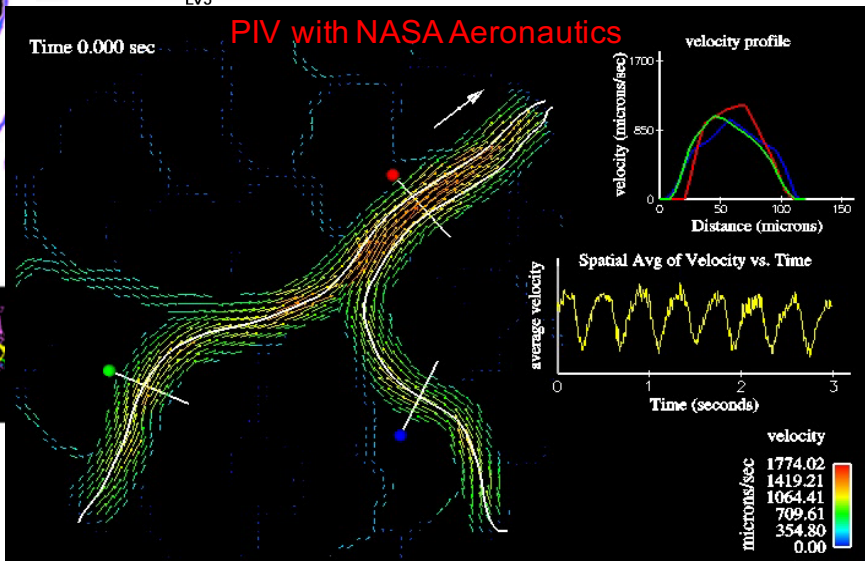




Wildtype *where veinlets may arise in H-C2 mutant

GSR 3(2):54-64 2015





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