Musculoskeletal System:
Stem Cells  Development  Regeneration  Disease  Evolution

Gabrielle Kardon
Department of Human Genetics
Musculoskeletal System

Muscle

Muscle connective tissue

Cartilage/Bone

Tendon
Interactions between muscle and connective tissue are critical for multiple processes:

- Development
- Regeneration, homeostasis, aging
- Evolution
- Disease, birth defects
Atlas of Limb Development
What is the normal sequence of muscle, tendon, bone, and nerve development that results in a functional limb?
Atlas of Limb Development
A Practical Workflow for Making Anatomical Atlases for Biological Research

Yong Wan, A. Kelsey Lewis, Mary Colasanto, Mark van Langewtie, Gabrielle Kardon, and Charles Hansen • University of Utah

A
n anatomical atlas provides a detailed map for medical and biological studies of anatomy. These atlases are important for understanding normal anatomy and the development and function of structures, and for determining the etiology of congenital abnormalities. Unfortunately, for biologists, generating such atlases is difficult, especially ones with the informative content and aesthetic quality that characterize human anatomy atlases. Building such atlases requires knowledge of the species being studied and experience with an art form that can faithfully record and present this knowledge, both of which require extensive training in considerably different fields.

With the latest innovations in data acquisition and computing techniques, atlas building has changed dramatically. We can now create atlases from 3D images of biological specimens, allowing for high-quality, faithful representations. Labeling of structures using fluorescently tagged antibodies, confocal 3D scanning of these labeled structures, volume rendering, segmentation, and surface reconstruction techniques all promise solutions to the problem of building atlases.

However, biology researchers still ask, "Is there a set of tools we can use or a practical workflow we can follow so that we can easily build models from our biological data?" To help answer this question, computer scientists have developed many algorithms, tools, and program codes. Unfortunately, most of these researchers have tackled only one aspect of the problem or provided solutions to special cases. So, the general question of how to build anatomical atlases remains unanswered.

For a satisfactory answer, biologists need a practical workflow they can easily adapt for different applications. In addition, reliable tools that can fit into the workflow must be readily available. Finally, examples using the workflow and tools to build anatomical atlases would demonstrate these resources' utility for biological research.

To build a mouse limb atlas for studying the development of the limb musculoskeletal system, University of Utah biologists, artists, and computer scientists have designed a generalized workflow for generating anatomical atlases. We adapted it from a CG artist's workflow of building 3D models for animated films and video games. The tools we used to build the atlas were mostly commercial, industry-standard software packages. Having been developed, tested, and employed for industrial use for decades, CG artists' workflow and tools, with certain adaptations, are the most suitable for making high-quality anatomical atlases, especially under strict budgetary and time limits. Biological researchers have been largely unaware of this technique.

FASEB BioArt 2012 Winner

Nikon Small World 2012 Image of Distinction

A. Kelsey Lewis, Yong Wan & Gabrielle Kardon
What developmental defects lead to limb malformation in Ulnar Mammary Syndrome?
Discovery on new musculoskeletal defects in UMS
Diaphragm Development

How is the development of muscle, connective tissue, tendon, bone, and nerves coordinated to make a functional diaphragm?
How do defects in development cause congenital diaphragmatic hernias (CDH)?

- Occurs in 1:3000 births
- 50% mortality rate
- $250 million/year in medical costs

Intestine protruding through hole in diaphragm
2 Photon imaging of live diaphragm explants
Tracking of cell migration during diaphragm development
Muscle connective tissue controls development of the diaphragm and is a source of congenital diaphragmatic hernias

Allison J Merrell¹, Benjamin J Ellis²–⁴, Zachary D Fox¹,⁴, Jennifer A Lawson¹, Jeffrey A Weiss²,³ & Gabrielle Kardon¹
How do muscle stem cell migrate and fuse to make the diaphragm muscle?
Thanks!

Eric Bogenschutz  Allyson Merrell  Zac Fox  Mary Colasanto

Jennifer Lawson  Alex Keefe

Department of Bioengineering, University of Utah
Benjamin Ellis  Jeffrey Weiss
Scientific and Computing Institute, University of Utah
Yong Wan  Charles Hansen

US-Israel Binational Science Foundation
National Institute of Child Health and Development
March of Dimes
Wheeler Foundation
Cherubs

Columbia University Medical Center
Wendy Chung