BIOGRAPHY

Professor Ralph Müller, Ph.D.
Institute for Biomechanics
ETH Zürich
Gloriastrasse 39
8092 Zürich, Switzerland

e-mail: ram@ethz.ch
web: http://www.bone.ethz.ch/

Dr. Ralph Müller is a Professor of Biomechanics in the Department of Health Sciences and Technology at ETH Zürich. He studied electrical engineering at ETH Zürich, where he also earned his doctoral degree in 1994. He then served as project manager for the micro-computed tomography initiative of the EU Concerted Action BIOMED 1 “Assessment of Bone Quality in Osteoporosis,” contributing to the development of a desktop micro-tomography system that has since been commercialized and is now used worldwide.

In 1996, Dr. Müller moved to Boston, where he became a tenure-track Assistant Professor of Orthopedic Surgery at Harvard Medical School and Associate Director of the Orthopedic Biomechanics Laboratory. From 2000 to 2011, he first held an SNF Professorship in Bioengineering in the Department of Information Technology and Electrical Engineering at ETH Zürich, before being appointed Associate and later Full Professor of Biomechanics in the Department of Mechanical and Process Engineering.

In 2012, he became one of the founding members of the newly established Department of Health Sciences and Technology, which he chaired from 2014 to 2016. His research combines state-of-the-art biomechanical testing, advanced computational simulation, and innovative bioimaging and visualization strategies for musculoskeletal tissues. These approaches enable quantitative assessment and monitoring of structure–function relationships in tissue regeneration, growth, and adaptation. They are now widely used for precise phenotypic characterization of tissue responses in mammalian genetics, mechanobiology, and regenerative medicine.

Dr. Müller has authored more than 1,400 scientific articles and abstracts. His work has been cited more than 52,000 times on Google Scholar, with an h-index of 119. He has received numerous distinctions, including the Mike Horton Award from the European Calcified Tissue Society (ECTS), the Huiskes Medal for Biomechanics from the European Society of Biomechanics (ESB), and the Muybridge Award from the International Society of Biomechanics (ISB). He is an Elected Member of the Swiss Academy of Engineering Sciences (SATW), an Honorary Member of the ESB, and a Fellow of the European Alliance for Medical and Biological Engineering and Science (EAMBES), the World Council of Biomechanics (WCB), and the American Society for Bone and Mineral Research (ASBMR). In 2017, he received a prestigious ERC Advanced Grant from the European Research Council.

He is active as an organizer of international symposia and workshops and serves on editorial boards and review panels for scientific journals and funding agencies. He is a former President of both the European Society of Biomechanics (ESB) and the Swiss Society for Biomedical Engineering (SSBE) and previously served as Secretary of the International Federation of Musculoskeletal Research Societies (IFMRS). He has held scientific and management roles on more than 80 research grants and currently receives funding from the Swiss National Science Foundation, the Australian Research Council, the Singapore National Research Foundation, and multiple ETH intramural programs.

Dr. Müller is a founder and co-organizer of the ETH graduate program in Biomedical Engineering. He teaches the courses “Imaging and Computing in Medicine,” “Orthopaedic Biomechanics,” and “Multiscale Bone Biomechanics” at ETH Zürich. He co-founded three spin-off companies: Pearl Technology AG, which develops and markets novel patient positioning systems for medical imaging; b-cube AG, now part of Scanco Medical; and compagOs, a diagnostics biotechnology company engineering personalized bone organoids and organotypic fracture models.

In Vivo Bone Imaging: From Mechanics to Mechanomics

Professor Ralph Müller, PhD
Institute for Biomechanics, ETH Zurich, Zurich, Switzerland

The rapid aging of populations worldwide is driving a marked increase in osteoporosis, frailty, and fracture susceptibility. These demographic changes highlight the need for a deeper mechanistic understanding of how bone senses and responds to mechanical forces, how it fails under reduced loading, and how it regenerates after injury. Traditionally, research in this area has been grounded in *mechanics* – focusing on whole-bone loading, structural properties, and tissue-level adaptation. However, recent technological advances now enable a shift toward *mechanomics* – the integrated study of how mechanical cues regulate biological processes across multiple scales, from organ-level mechanics to gene expression within individual cells.

Bone is a dynamic, hierarchical, and highly mechanosensitive tissue. Its adaptation relies on the coordinated actions of osteoblasts, osteoclasts, and particularly osteocytes, which act as mechanosensors embedded within the mineralized matrix. Age-related bone loss is closely associated with diminished mechanical usage, while even subtle cyclic loading can stimulate bone formation. Work over the past decades has demonstrated how strain, frequency, and local mechanical environments influence bone remodeling. Today, in vivo micro-computed tomography combined with micro-finite element modeling allows direct visualization and quantification of these adaptive responses in living animals. Time-lapsed imaging reveals where bone forms, remains quiescent, or resorbs, and how these processes respond to controlled loading or whole-body vibration therapy.

These imaging-based studies are increasingly integrated with mechanobiologically targeted interventions. Mechanical loading interacts strongly with anabolic agents such as parathyroid hormone and sclerostin antibody treatment, while showing more limited synergy with antiresorptives. Such combined approaches provide new opportunities for precision modulation of bone formation in osteoporotic conditions. Moreover, individualized mechanical loading paradigms have been shown to accelerate fracture healing, and in vivo micro-CT enables detailed assessment of mechanoregulation during the entire regeneration process.

The emerging shift toward *mechanomics* extends these concepts by integrating mechanical information with cellular and molecular profiling. Histology, immunohistochemistry, and high-resolution imaging provide unprecedented detail on the local cellular environment. Spatial transcriptomics now allows unbiased mapping of thousands of genes in their native spatial context, enabling direct links between local mechanical strain and gene expression signatures. Registering these molecular maps into the corresponding 3D micro-CT datasets situates biological activity within a fully characterized mechanical and structural environment. This integration creates a multiscale mechanomics platform capable of revealing how mechanical forces influence cell states, signaling pathways, and regenerative outcomes.

This presentation highlights the convergence of state-of-the-art in vivo imaging, computational modeling, mechanical loading paradigms, and spatial molecular profiling. Together, these developments mark a decisive shift from studying bone primarily as a mechanical structure toward understanding it as a mechano-responsive biological system. By embracing mechanomics, we gain a more comprehensive view of how mechanical cues orchestrate bone maintenance, how therapeutic strategies can be optimized through mechano-targeting, and how personalized interventions may reduce drug reliance while promoting healthier aging.

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