Yuan-Cheng Fung

September 15, 1919–December 15, 2019
Elected to the NAS, 1992

A Biographical Memoir by Shu Chien

Photo credit: University of California, San Diego

Yuan-Cheng Fung, also known as YC or Bert, made superb contributions to science, engineering, and humanity through his research and its applications, as well as through his words and deeds. By setting the highest standards of rigor and excellence, training many outstanding students and their students, and providing his exemplary leadership, YC Fung had a tremendous impact that spans the globe and transcends time. He established the foundations of biomechanics in many living tissues, including the lung, heart, blood vessels, blood cells, ureter, intestine, skin, as well as other organs and tissues. With his vision of using the power of modeling to explain and predict biological phenomena, Fung opened new horizons for bioengineering, from organs and systems to molecules and genes. He fostered research in many institutions in the United States and elsewhere in the world. He made outstanding contributions to education in bioengineering and contributed service to professional organizations and translation to industry and clinical medicine. He is widely recognized as the "Father of Biomechanics" and the leading bioengineer in the world. His extraordinary accomplishments in and command of science, engineering, and the arts made him a Renaissance Man whom the world was most fortunate to have. At his centennial celebration, his friends, colleagues, students, and admirers held symposia, wrote papers, organized parties, and sent greetings to express their warmest feelings for this marvelous man. Additionally, the *Journal of Biomechanical Engineering* published a special issue in his honor.[1] This memoriam for the NAS is based on my tribute to Dr. Fung in that celebration.[2] Most of Dr. Fung's publications have been collected in a two-volume treatise entitled *Selected Works on Biomechanics and Aeroelasticity*, which provides a very valuable reference resource.[3]

Early Education & Contributions to Aeronautics

Fung was born on September 15, 1919, in Yuhong, Wuxi, Kiangsu, China. He received a bachelor of science in 1941 and a master of science in 1943 in aeronautics from the Central University in Chongqing, graduating at the top of his classes. After working as a research fellow at the Bureau of Aeronautical Research in Chengdu from 1943 to 1945, Fung traveled to the United States to pursue a Ph.D. in aeronautics and mathematics at the California Institute of Technology (CalTech). He completed his doctoral study in less than three years and received his Ph.D. in 1948, graduating *summa cum laude*. Fung stayed on at CalTech as a research fellow in aeronautics and then was hired as a faculty member. He was promoted to full professor in 1959. At CalTech, Fung conducted outstanding research on airplane dynamics in turbulent weather and safety, as well as on the performance and design of aircraft and spaceships. In 1955, he published the definitive textbook *An Introduction to the Theory of Aeroelasticity*, which is still used broadly.[4]

Biomechanics

In the late 1950s, Fung became interested in the mechanics of the eye because his mother was afflicted with glaucoma, and later also considered the application of mechanics to other biological systems. He conceived that if the structure and mechanical properties of a living organ can be determined, then the functions of that organ can be predicted by the principles of physics. He organized a landmark symposium on biomechanics in 1966.[5] That same year, Fung and Benjamin Zweifach were recruited to the University of California, San Diego (UCSD) to start a new Bioengineering Program in the Department of Aeronautical and Mechanical Engineering Science (AMES), with biomechanics and microcirculation as the central themes. In the 1980s, Fung created a new direction for bioengineering by using engineering principles and techniques to repair, regenerate, and replace tissues. Tissue engineering has become the focus of bioengineering efforts in many programs in the world and has given rise to the field of regenerative medicine. Thus, Fung played a major role in two important disciplines—biomechanics and tissue engineering—that have been major foci in bioengineering.

Fung's contributions to biomechanics were immense. He created the field by combining his superb expertise in engineering mechanics with path-setting work in biomedical sciences for applications to important clinical problems. He integrated biology and mechanics at different scales, from organs/systems to molecules/genes. He correlated structure and function in terms of growth, geometry, and remodeling, with emphases on temporal and spatial features, as well as active vs. passive responses. He combined experiments (performed with innovative technology and rigorous execution) and theory (formulated with creative thoughts and elegant analysis), with effective iteration and feedback. He established the foundation of biomechanics in the lungs, heart, blood vessels, skin, as well as other organs and tissues. He is recognized as the Father of Biomechanics.

Blood Cells, Endothelial Cells, and Microcirulcation

Fung investigated the mechanics and geometry of human red blood cells (RBCs) by using elegant engineering analyses and innovative experimental approaches. These included stress analysis in RBC swelling, determination of RBC 3D geometry through interference microscopy, and the use of the extreme theorem to analyze the extreme value statistics of RBC geometry.[6,7,8]

Fung also studied the behavior of blood cells in blood vessels, especially at the branch points. He used experimental studies and engineering analyses to elucidate the mechanism of the stochastic nature of flow in capillaries. He showed that a small difference in flow at a bifurcation can cause a dramatic nonlinear effect on the distribution of blood cells between two daughter branches.[9] With the use of a lab model system, he demonstrated the important role of RBCs in modulating the interaction of white blood cells (WBCs) with the vascular endothelial cells (ECs).[10] He showed how a high RBC concentration can push the WBCs toward the vessel wall to enhance WBC-EC interactions. These findings have important implications for the hemodynamic modulation of WBC behavior in the microcirculation in health and disease, including inflammation.

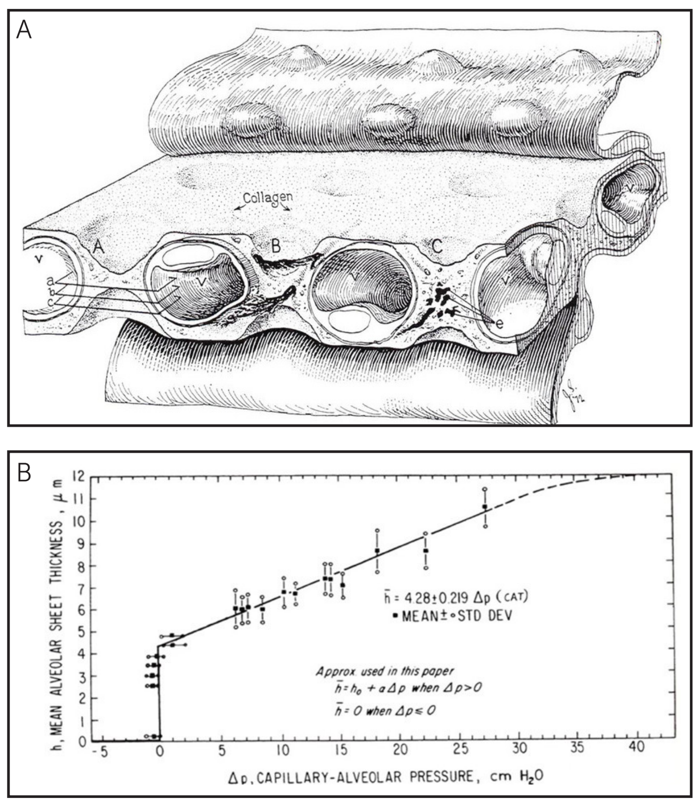

Figure 1 A. Schematic drawing of a pulmonary alveolar microvascular sheet. B. Mean alveolar sheet thickness as a function of capillary–alveolar pressure difference. From ref. [12].

Fung computed the blood-flow pattern in vessels beyond local constriction and demonstrated that the complex flow behavior in such regions, including flow reversal, reattachment, and stagnation, has major effects on the structure and function of vascular endothelial cells and may thus play a significant role in atherogenesis.

Fung made outstanding contributions on the interplay of circulatory and respiratory systems at the microcirculatory level. In his pioneering work with Sidney Sobin and other colleagues, involving rigorous experiments and elegant analyses, Fung formulated the innovative concept of sheet flow through the pulmonary capillaries between the posts that span sheets of the alveolar wall.[11] This sheet-flow theory was applied to compute alveolar sheet thickness and alveolar sheet flow as functions of the pressure differential between the capillary and alveolus.[12] The application of this theory to experimental data provides a quantitative understanding of the interplay among many factors, including alveolar blood flow and blood volume, their regional differences, and transit time distributions, thus allowing the computation of the effects of blood flow on arterial, alveolar, and venous pressures; alveolar area; mean A-V path length; and alveolar membrane tension.[13] These innovative findings opened a new frontier for research on pulmonary microcirculation in health and disease. Fung also applied the morphometric technique to study the topographical arrangements of arterioles and venules in the cat lung and generated novel findings on the difference in distribution patterns between them. He discovered that each terminal precapillary arteriole supplies an average of 24.5 alveoli and each terminal postcapillary venule drains an average of 17.8 alveoli.

Fung applied morphometric analysis to determine the geometric features of coronary artery circulation in the right ventricle of the pig under normal and hypertensive states. These results have generated important information on coronary artery remodeling in cardiac hypertrophy.

Residual Stress and Vascular Remodeling

One of Fung's very fundamental and innovative contributions was his research on residual stress, which is the stress that remains after the removal of external forces. He developed the ingenious approach of cutting open a biological structure in two different directions and then using the opening angle to determine the residual stress. An aorta was removed to be devoid of pressure load. After slicing it crosswise to obtain a ring, it was cut open in the radial direction to result in a zero-stress state.[14] The opening angle provides a measure of the residual stress in the vessel wall resulting from the geometry and wall constituents (Fig. 2). It is truly amazing that an extremely important biomechanical parameter

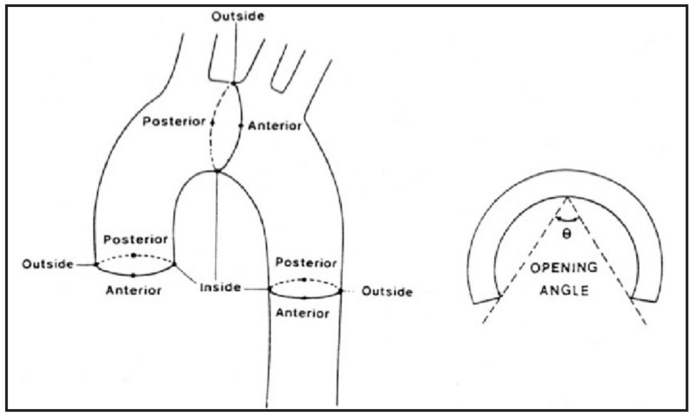

Figure 2 Diagrammatic illustration that the remodeling of a blood vessel is best described by the change of its zero-stress state, which results from changes in cellular and extracellular mass and configurations, as depicted in these drawings. From ref. [14].

can be measured with such a simple experimental procedure, requiring only a pair of scissors!

Fung demonstrated the strikingly different residual stress between ileal artery and ileal vein as indicated by their opening angles.[15] This opening angle measurement can also be applied to determine residual stress in the heart ventricles, trachea, and other organs and tissues.

Fung's pioneering work on residual stress led him to formulate the concepts that the remodeling of a blood vessel is best described by changes in its zero-stress state and that vascular growth results from changes in cellular and extracellular mass and configuration.[16] These concepts led to the design of specific ways to test the biomechanical properties of tissue-engineered vascular grafts in order to match the hemodynamic conditions encountered *in vivo*.

Through a combination of experimental and theoretical approaches, Fung determined the 3-D stress distribution in an artery and also the stress-strain relations of collagen and elastin, two important interstitial constituents of the vessel wall.[17] These results led to the elucidation of the relationship of the biomechanical behavior of a blood vessel to its molecular constituents, thus contributing to the role of chemical composition in tissue remodeling. Fung established the "Fung exponential strain energy function," which is still widely used.

Fung conducted a systematic study on the time course of the remodeling of pulmonary arteries in normal and hypertensive rats in response to hypoxia.[18] By using DNA microarray technology to investigate changes in gene expression under hypoxia-induced pulmonary hypertension, he was able to match the time course of changes in the expression of a number of genes with the alterations of specific structures and functions in the pulmonary artery.[19] This pacesetting study provides a genetic correlate of the functional abnormalities in pulmonary hypertension. Based on these and other findings, Fung proposed that:

> "DNA replication and transcription involve molecular motion through a viscous medium to reach the appropriate site, and the lengthening takes place through the balance between the chemical energy of binding and the kinetic energy of molecular motion. Therefore, these processes involve accelerations, strains and strain rates with directions. They need to be treated as force vectors and stress tensor."

Translation of Biomechanics to Technology, Industry, and Clinical Medicine

Fung's outstanding research was aided by the sophisticated instrumentation he developed to meet the experimental needs. Examples include the innovative "Biodyne" device for testing the mechanical properties of a variety of biological materials as well as instrumentation to study skin biomechanics,[20,21,22] peristaltic transport,[23] and peeling force in a biological graft.[24] Fung's research formed the foundation of industrial applications in a variety of bioengineering fields, including the tissue engineering of cardiovascular, urinary, musculoskeletal, and cutaneous systems. His studies on the biomechanics of the skin played a significant role in the development of skin substitutes to treat burn patients. He contributed to the development of tissue-engineered vascular grafts with mechanical matching to the existing vessels. Fung's research has led to the advancement of diagnosis and treatment of a variety of important diseases, including pulmonary hypertension and emphysema, myocardial infarction, heart failure, atherosclerosis, systematic hypertension, musculoskeletal disorders, dysmotility of the digestive and urinary systems, and many others. His important translational contributions led to his winning of the prestigious Fritz J. and Dolores H. Russ Prize from the National Academy of Engineering for "advancing science and engineering, ultimately improving the human condition," and specifically "for the characterization and modeling of human tissue mechanics and function, leading to prevention and mitigation of trauma."

Teaching

In addition to his groundbreaking research, Fung also made outstanding contributions to bioengineering education. At UCSD, he built the superb graduate and undergraduate programs that have educated bioengineers who have made important contributions to bioengineering endeavors in universities, medical schools, hospitals, and industries. Many of his students and postdoctoral fellows hold key faculty positions in universities and industries in the United States and abroad, and many are heads of departments of bioengineering. In the most recent National Research Council survey of graduate education, published in 2010, UCSD Bioengineering was ranked number 1 in biomedical engineering. Fung's vision and leadership played a significant role in this accomplishment.

Fung's educational influence extended beyond his excellent teaching in the classrooms and laboratories at UCSD. He defined the pedagogy of biomechanics by writing authoritative books that are widely used in the United States and abroad and are read by virtually everyone in the field.[25,26] These books have been translated into many languages and updated in several editions, setting the standard for all textbooks in bioengineering. He made important contributions to education and training in many countries, especially his homeland of China. He played a major role in the birth of biomechanics and biomedical engineering in China by training the leaders, giving lectures, and organizing meetings there (such as the China-Japan-U.S.A. Conference on Biomechanics that he initiated).

Fung was strongly devoted to the education and support of the younger generation. This was clearly illustrated by my personal experience when I attended the Microcirculatory Society (MCS) meeting in Atlantic City in 1965 as an assistant professor at Columbia University. While at a restaurant with my wife and two daughters for dinner, I saw YC Fung at a neighboring table with members of the MCS council and went over to say hello to him. Then, he came over to our table and sat down to chat with us for nearly an hour until the MCS council members and we all left. At that time, I had met him only once very briefly. His kindness to spend time with the young people was extremely impressive and greatly appreciated. I still remember vividly that wonderful experience more than fifty years later.

Service to Professional Organizations

Fung was strongly dedicated to the advancement of bioengineering, and he served in many key positions in professional organizations. He was president of the American Academy of Mechanics and the Biomedical Engineering Society (BMES) and vice president of the International Society of Biorheology. He was chair of the Third International Congress of Biorheology, the Second World Congress of Microcirculation, and the First China-Japan-U.S.A. Conference on Biomechanics. He was also chair of the Applied Mechanics Division in the American Society of Mechanical Engineers (ASME), the U.S. National Committee for Biomechanics (later an honorary chair), and the World Council for

Biomechanics (also later an honorary chair). Fung was a member of the Microcirculatory Society Council, the American Physiological Society Council of Circulation, the American Heart Association Council on Basic Science, and the World Congress of Biomechanics Steering Committee.

Figure 3 Professor Fung receiving the U.S. National Medal of Science from President Bill Clinton in 2001. From left: President Clinton, Mrs. Fung, Professor Fung. From ref. [2].

Awards and Honors

Fung received many awards and honors for his remarkable body of work. He was a member of the National Academy of Sciences, the National Academy of Engineering, and the National Academy of Medicine in the United States and was a Foreign Member of the Chinese Academy of Sciences and Academia Sinica (Taiwan), and he was an honorary member of several scientific organizations. Fung was a fellow of the American Academy of Mechanics, the American Institute of Aeronautics and Astronautics, ASME, the American Institute of Medical and Biological Engineering, and the Cardiovascular Section of the American Physiological Society. He also received numerous honorary doctoral degrees and professorships from many universities and gave many named and plenary lectures.

Fung received all the major awards in his fields of endeavor, including the Eugene Landis Award from Microcirculatory Society (1975), Theodore von Kármán Medal from American Society of Civil Engineers (1976), Lissner Award for Bioengineering from ASME (1978), Centennial Medal from ASME (1981), Worcester Reed Warner Medal from ASME (1984), Poiseuille Medal from International Society of Biorheology (1986), Excellence in Research Award from UCSD (1987), ALZA Award from BMES (1989), Timonshenko Medal from ASME (1991), Borelli Award from American Society of Biomechanics (1992), Lifetime Achievement Award from the Association of Chinese Scientists and Engineers of California (1992), Distinguished Alumnus Award from California Institute of Technology (1994), Melville Medal from ASME (1994), and Bioengineering Award from the Japan Society of Mechanical Engineering (1995). He notably received the NAE's Founders Award (1988) for "outstanding engineering accomplishments by an engineer over a long period of time and of benefit to the people of the United States." In 2001, Fung was awarded the U.S. National Medal of Science, the highest honor for scientists and engineers in the United States, from Pres. Bill Clinton for his "outstanding contributions to knowledge in the physical, biological, mathematical or engineering sciences." (Fig. 3)

In 1986, ASME established the "Y.C. Fung Young Investigator Award" in his honor. The Chinese Association of Biorheology, Chinese Society of Biophysics, International Society of Biorheology and International Society of Clinical Hematology established the Chien-Fung Young Investigators Award. UCSD established the Y.C. Fung Professor of Bioengineering endowed chair in 2006.

Family Life

Fung and his wife Luna Hsien-Shih Yu married on December 22, 1949, in Pasadena, California. Luna was an excellent mathematician with a bachelor of science from Central University in China and a master's degree from CalTech. They had two wonderful children, Conrad and Brenda. After sixty-eight marvelous years of marriage, Luna passed away on April 14, 2017.

Conrad has two sons Anthony (Tony) and Michael, and Brenda has a son Nicholas Manos (Fig. 4). Tony will soon complete his Ph.D. in bioengineering at UCSD, the program started by his grandfather. Michael is pursuing an MBA degree and is an excellent opera singer. Nick graduated from the

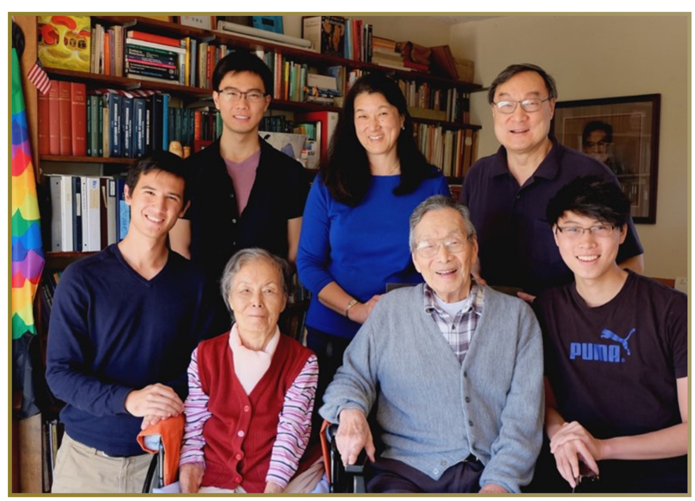

Figure 4 The Fung family in their La Jolla home in November 2014. Seated from left: Nick Manos, Luna and Y.C. Fung, Michael Fung. Standing from left: Tony Fung, Brenda Fung Manos and Conrad Fung. From ref. [2].

University of Southern California majoring in marketing and is an implementation specialist; his wife Claire is a pediatric occupational therapist. They live in Portland, Oregon.

A Renaissance Man

Fung was not only a superb scientist and engineer, but also a wonderful artist. He excelled in Chinese calligraphy and poetry. He had marvelous talents in making Chinese chops (or seals, usually for people's names); the imprints of these can be found in the front pages of many of his books. Thus, he excelled in science, engineering, and art. He was a renaissance man, a peer of Leonardo DaVinci.

Acknowledgments

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References

1 Han, H. C., X. E. Guo, and S. Q. Liu, eds. 2019. Special issue: A tribute to Dr. Y. C. Fung. *J. Biomech. Eng.* 141.

2 Chien, S. 2019. Dr. Y.C. Fung's contributions to biomechanics, bioengineering and humanity: Warmest celebration for a magnificent centenarian. *J. Biomech. Eng.* 141(9):091001.

3 Fung, Y. C. 1997. *Selected Works on Biomechanics & Aeroelasticity.* Two vols. Singapore: World Scientific.

4 Fung, Y. C. 1955. *An Introduction to the Theory of Aeroelasticity.* New York: John Wiley and Sons.

5 Fung, Y. C. 1966. *Biomechanics; Proceedings of a symposium sponsored by the Applied Mechanics Division of the ASME, at the annual meeting, November 30, 1966, New York, N.Y.* New York: American Society of Mechanical Engineers, United Engineering Center.

6 Fung, Y. C., and P. Tong. 1968. Theory of the sphering of red blood cells. *Biophys. J.* 8:175–198.

7 Evans, E., and Y. C. Fung. 1972. Improved measurements of the erythrocyte geometry. *Microvasc. Res.* 4:335–347.

8 Chen, P. C. Y., and Y. C. Fung. 1973. Extreme value statistics of human red blood cells. *Microvasc. Res.* 6:32–43.

9 Fung, Y. C. 1973. Stochastic flow in capillary blood vessels. *Microvasc. Res.* 5:34–49.

10 Schmid-Schoenbein, G. W., Y. C. Fung, and B. W. Zweifach. 1975. Vascular endothelium- leukocyte interaction: Sticking shear force in venules. *Circ. Res.* 36:173–184.

11 Fung, Y. C., and S. S. Sobin. 1969. Theory of sheet flow in the lung alveoli. *J. Appl. Physiol.* 26:472–488.

12 Rosenquist, T. H., S. Bernick, S. S. Sobin, and Y. C. Fung. 1973. The structure of the pulmonary interalveolar microvascular sheet. *Microvasc. Res.* 5:199–212.

13 Fung, Y. C., and S. S. Sobin. 1972. Elasticity of the pulmonary alveolar sheet. *Circ. Res.* 30:451–469.

14 Fung, Y. C. 1991. What are the residual stresses doing in our blood vessels? Annals of Biomedical Engineering 50th Anniversary Collection. *Ann. Biomed. Eng.* 19(3):237–249.

15 Fung, Y. C., and S. Q. Liu. 1992. Strain distribution in small blood vessels with zero-stress state taken into consideration. *Am. J. Physiol.* 262(2):H544–H552.

16 Chuong, C. J., and Y. C. Fung. 1983. Three-dimensional stress distribution in arteries. *J. Biomech. Eng.* 105:268–274.

17 Sobin, S. S., Y. C. Fung, and H. M. Tremer. 1988. Collagen and elastin fibers in human pulmonary alveolar walls. *J. Appl. Physiol.* 64 (4):1659–1675.

18 Liu, S. Q., and Y. C. Fung. 1989. Relationship between hypertension, hypertrophy, and opening angle of zero-stress state of arteries following aortic constriction. *J. Biomech. Eng.* 111:325–335.

19 Huang, W., Y. P. Sher, K. Peck, and Y. C. Fung. 2002. Matching gene activity with physiological functions. *Proc. Nat. Acad. Sci. U.S.A.* 99:2603–2608.

20 Pinto, J. G., J. M. Price, Y. C. Fung, and E. H. Mead. 1975. A device for testing mechanical properties of biological materials—the "Biodyne." *J. Appl. Physiol.* 39:863–867.

21 Lanir, Y., and Y. C. Fung. 1974. Two-dimensional mechanical properties of rabbit skin—I. Experimental system. *J. Biomech.* 7:29–34.

22 Lanir, Y., and Y. C. Fung. 1974. Two-dimensional mechanical properties of rabbit skin—II. Experimental results. *J. Biomech.* 7:171–182.

23 Yin, F. C. P., and Y. C. Fung. 1971. Mechanical properties of isolated mammalian ureteral segments. *Am. J. Physiol.* 221:1484–1493.

24 Dong, C., et al. 1993. Development of a device for measuring adherence of skin grafts to the wound surface. *Ann. Biomed. Eng.* 21:51–55.

25 Fung, Y. C. 1990. *Biomechanics: Motion, Flow, Stress, and Growth.* New York: Springer.

26 Fung, Y. C. 1993. *Biomechanics: Mechanical Properties of Living Tissues.* New York: Springer.