Program: Scientific Contributions by the Current Nobel Prize Winners in Physics, Chemistry, and Medicine
Speakers: Dick Carter, Alan Schmidt, Tom Lauer, Scientech Club members
Introduced by: Jim Willson
Attendance: 124
Guests: Steve Conger, Teresa Hatfield, Bob Hooker, Ann Manders
Scribe: Hank Wolfla
Editor: Carl Warner

Dick Carter provided the Royal Swedish Academy of Sciences 2018 Nobel Prize winner in physics review. The 2018 prize winners were Arthur Ashkin (Bell Labs), Gerard Mourou (Ecole Polytechnique – France), and Donna Strickland (University of Waterloo – Canada) for groundbreaking inventions in the field of laser physics. Half the prize goes to Ashkin for a device called "optical tweezers" for grabbing and manipulating objects in biological systems. The other half was jointly awarded to Mourou and Strickland for their method of generating high intensity ultra-short optical pulses. These inventions were a breakthrough in the use of laser beams for practical purposes. The recognition of Strickland's contributions was made as she was a graduate student. Strickland was the third female physicist to receive the Nobel Prize award and the first to do this since 1962. Ashkin received his prize for work at Bell Labs between the 1960's and 1980's. He invented optical tweezers that use laser light to trap microscopic objects such as particles, atoms, and viruses. They are capable of manipulating nanometer and micron size dielectric particles by exerting small forces via a highly focused laser beam. They are now used to capture living bacteria.

Donna Strickland and Gerard Mourou developed chirped pulse amplification (CPA), a method of generating high-intensity, ultra-short pulses. CPA is now a universally used laser technology and has paved the way for high-intensity, ultra-sharp laser beams now used in millions of corrective eye surgeries. The CPA laser pulse is stretched out in time prior to introducing it to the gain medium using a pair of gratings that are arranged so that the low-frequency component of the laser pulse travels a shorter path that the high frequency component does. CPA has allowed ultra-high-power laser systems that are small. These high peak energy CPA systems have been used in many areas of medicine. One that most have heard of is the LAZIK eye surgery to correct vision issues. Also, this very short burst of laser light has totally changed photography. It has allowed extremely high-speed motion pictures and has given us the ability to view the atom and its parts.

Alan Schmidt gave a review of the 2018 Nobel Prize in Chemistry. One half of the prize was given to Frances Arnold (California Institute of Technology), and the other half was split between George P. Smith (University of Missouri) and Sir Gregory Winter (Laboratory of Molecular Biology – Cambridge, UK). The prize was awarded for the way they have taken control of evolution and used it for the greatest benefit to humankind. Enzymes developed through directed evolution are now used to produce biofuels and pharmaceuticals among other things. Antibodies evolved using a method called phage display that can combat autoimmune diseases and, in some cases, cure metastatic cancer. The process of random mutations is introduced in the gene for the enzyme that will be changed. The genes are inserted in bacteria, which use them as templates and produce randomly mutated enzymes. The changed enzymes are tested. Those that are most efficient at catalyzing the desired chemical reaction are selected. The new random mutations are introduced in the genes for the selected enzymes. Then the cycle is repeated. Random changes-mutation happens in the genetic code for the enzyme. These mutated genes in the bacteria produce enzyme variants. The best enzyme at breaking down casein was in a solution with DMF 45% dimethylformamide. The 3rd generation found a variant that worked 256 times better in DMF than the original enzyme. The

enzyme variant had a combination of ten different mutations. These genes could be inserted in a bacterium to produce a protein. This process is called gene cloning; the use of phages' simple

construction to find an unknown gene for a known protein. Smith introduced a gene into the existing gene in the DNA for a protein in the phages capsule. The phage DNA was then inserted into bacteria that produced phages. The peptide part of the protein from the introduced gene ended up as part of the capsule protein on the surface of the phage. Smith was able to fish out the phage using an antibody designed to attach to the peptide. The genetic information for the antibody's binding site is inserted into the phage's DNA. This creates a library with a huge variety of antibodies. The phages' strong attachment to a specific target is ideal for pharmaceuticals. Before another selection is conducted, random mutations are introduced into the antibodies that attached to the target. With each subsequent generation, the antibodies attach more strongly to the target protein. These antibodies can attach to cancer cells with a high level of specificity. The antibodies can neutralize a protein, TNF alpha, that drives many autoimmune diseases and are used in many of today's drugs to treat inflammatory diseases such as lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, etc.

Tom Lauer gave the 2018 Nobel Prize in Physiology or Medicine review. James P. Allison and Tasuku Honjo won this prize for their discovery of cancer therapy by inhibition of negative immune regulation. James P. Allison studied a known protein that functions as a brake on the immune system. He realized the potential of releasing the "brake" and thereby unleashing our immune cells to attack tumors. In parallel, Tasuku Honjo discovered a protein on immune cells and, after careful exploration of its function, eventually revealed that it also operates as a brake, but with a different mechanism of action. The fundamental property of our immune system is the ability to discriminate "self" from "non-self" so that invading bacteria, viruses and other dangers can be attacked or eliminated. In the 1990's Allison studied the T-cell protein CTLA-4. He found that CTLA-4 functions as a brake on T cells. He then developed an antibody that could bind to the CTLA-4 and block its function. In 1992 before Allison's discovery, Tasuku discovered PD-1, another protein expressed on the surface of T-cells. He found that PD-1, like CTLA-4, functions as a T-cell brake but operates by a different mechanism. After clinical studies showing the effects of CTLA-4 and PD-1 blockade, the clinical development has been dramatic. This is now called "immune checkpoint therapy" that has fundamentally changed the outcome of certain types of cancer (melanoma, non-small cell lung, bladder, non-Hodgkin's lymphoma, head and neck).