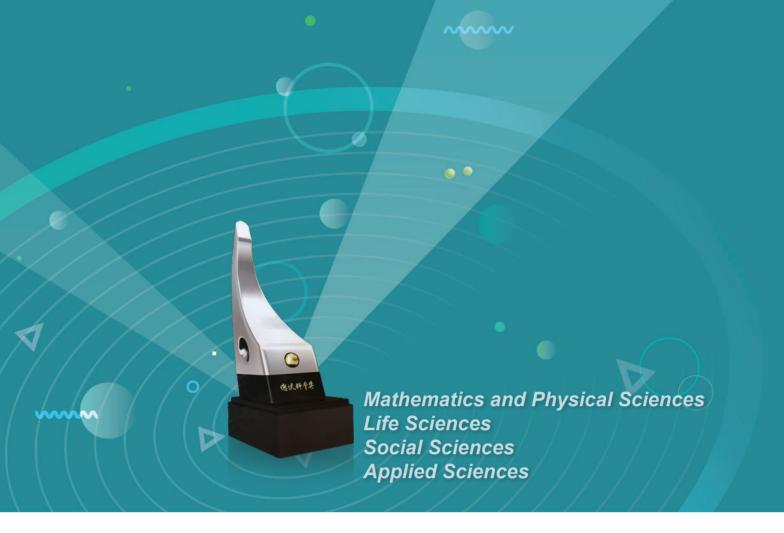
## 2021 總統科學獎表揚實錄 PRESIDENTIAL SCIENCE PRIZE

愧诀科ギ栗

Award Ceremony Program



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Established in 2001 and presented every two years, this is the 11th Presidential Science Prize. This prize symbolizes in the highest academic honor to pay respect to the most outstanding scientists in the Republic of China (ROC).

To promote Taiwan's position in the international science community, the Office of the President has established the Presidential Science Prize to recognize innovative researchers who have made monumental contributions to international research in the fields of Mathematics and Physical Sciences, Life Sciences, Social Sciences, Applied Sciences, especially those scholars whose works have had major impact on the development and applications of these fields in Taiwan.

To implement the selection and award of this prize, the President of Academia Sinica has convened a steering committee of fifteen distinguished scientists and related cabinet ministers. Nominees for the Presidential Science Prize are only taken into consideration when

(1) they are nominated by academicians of Academia Sinica and/or Presidential Science Prize awardees;

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(2) they are nominated by academic and research institutions and associations and leaders of the community invited by the Presidential Science Prize Steering Committee.

After nomination, four selection committees in the abovementioned fields perform nominee screening tasks. This year, through a careful nomination and selection process, the three awardees of this prestigious honor have been chosen as: Mathematics and Physical Sciences Category-Dr. Sunney I. Chan.

Conferred by the head of state, the Presidential Science Prize gives recognition to those scientists for their long-term efforts at conducting scientific research and cultivating young researchers. This prize also aims to pay respect to outstanding scholars who have made top-notch academic achievements and to have scientific R&D fully benefit people's livelihood.





## 26 A Track Record of Achievements

### Mathematics and Physical Science Category — Sunney I. Chan Cracking the Mystery of Methane Oxidation in a Membrane Protein and Inventing a Molecular Catalyst

#### Sunney Chan Has Inspired Countless Talented Minds for the Love of Science and Humanity

In the 60 years of his scientific research career, Sunney I. Chan has navigated the fields of physical chemistry, chemical physics and biophysics. His research achievements are as broad as they are essential, cracking one black box after another in basic science. Every 20 years, he would come up with a ground-breaking discovery that takes the study of biological systems to a new epoch.

Sunney Chan is best known for developing and applying innovative spectroscopic and biophysical methods to solve fundamental problems on the structure and dynamics of membranes, nucleic acids and proteins, especially membrane proteins and metalloproteins of biological importance. To the general public, these terms may appear abstruse and unfamiliar, but his findings are like torches illuminating the dark, unknown territories, and paving the way to many more important discoveries in basic and applied science.

#### Ended Scientific Debate by Discovering 'Vertical Interactions' between Nucleic Acid Bases

In the early 1960s, Sunney Chan used nuclear magnetic resonance (NMR) spectroscopy to study the stacking of nucleic acid bases in aqueous solution. At that time, scientists around the world were still debating whether or not 'horizontal' interactions of hydrogen bonds in nucleic acid were sufficient to account for the stability of the structure of the DNA double helix at room temperature. In pioneering NMR experiments undertaken during 1962-64, Sunney Chan established that in a water solution, there exist strong 'vertical' interactions between the nucleic acid bases in DNA, and the nucleic acid bases stack in water in order to minimize the disruption of the hydrogenbonded network structure of the water, now commonly referred to as the 'hydrophobic effect'. Consequently, this discovery of his brought to an end the scientific debate on why and how the Watson-Crick A-T and G-C base pairs can be formed in water.





#### Cracking the Myth of Cytochrome *c* Oxidase: A Redox-Linked Proton Pump

One of Sunney Chan's most significant scientific researches is his probing of membrane proteins, particularly membrane-bound metalloenzymes, using novel biophysical methods to unravel the structures, functions, and kinetic behavior of these important molecular machines. His work on cytochrome *c* oxidase from bovine heart mitochondria was pioneering and elegant. In the late 1970s, Sunney Chan became the world authority in this field and his laboratory was particularly well known for the many original and insightful contributions elucidating the structure and function of this complex and important enzyme system.

Cytochrome c oxidase is an electron-driven proton pump, important for establishing the protomotive force obligatory for ATP synthesis in the mitochondrion. However, cytochrome c oxidase was a 'black box' for scientists at that time. Sunney Chan's laboratory carried out decisive experiments during the early 1980s to delineate the ligand structures of the metal cofactors. With this structural information, Sunney Chan and his students established the rules on how the electrons and protons must be gated by redox linkage between the metal cofactors and the protein scaffold during proton pumping in order to kinetically control the flow of electrons and the coupled movement of the protons uphill against the protomotive force across the inner membrane of the mitochondrion.

#### How pMMO Converts Methane into Methanol: A Tripcopper Cluster at the Catalytic Center

In the early 1990s, Sunney Chan initiated a new venture directed toward understanding how methane is converted into methanol with high efficiency by the particulate monooxygenase (pMMO). Before moving to Academia Sinica in Taiwan, his laboratory at Caltech had succeeded in isolating and purifying the pMMO to homogeneity. He continued this research in Taiwan. During the 2000s, Sunney Chan's Taiwan team developed novel methods to characterize the enzyme in depth and established the nature and identity of the copper cofactors in the protein, and discovered that a tricopper cluster is the critical element in the catalytic mechanism. This discovery is regarded one of the holy grails in organic chemistry. In recent years, Sunney

Chan's team at Academia Sinica and National Taiwan University has successfully developed the first molecular catalyst capable of efficient conversion of methane into methanol by  $O_2$  at room temperature. This marks a breakthrough milestone in methane oxidation. Today, with net zero carbon and decarbonization becoming the world's most urgent mission, reducing methane emissions will help slow down global warming, and Sunney Chan's discovery is more significant than ever.

As further evidence of his broad interests and research activities, Sunney Chan also devoted several years to understanding protein folding, an essential process in biosystems that creates muscles, hormones, enzymes, etc. It was one of biology's biggest mysteries to be solved. Sunney Chan developed the use of caged compounds to study the very early events in protein folding initiated in the absence of denaturants. This work has demonstrated the importance of kinetic channeling in protein folding.

On top of his academic brilliance, Sunney Chan's career is also marked by his love of humanity. As a teenager, he once vowed to join the priesthood. After gaining world-class recognition as a scientist, he stepped out of American science from one of the world's most prestigious research institution-Caltech, and came to Taiwan to devote himself to building paradigms and infrastructures of advanced research for the then still-developing Academia Sinica. He was like a missionary spreading his faith. During his tenure as Vice President of Academia Sinica, he formulated a roadmap for the Genomics Research Center; he also worked with the National Science Council of Taiwan in creating the National Research Program in Genomics Medicine. Both have laid solid foundation for the booming of Taiwan's applied medicine and biotechnology industry.

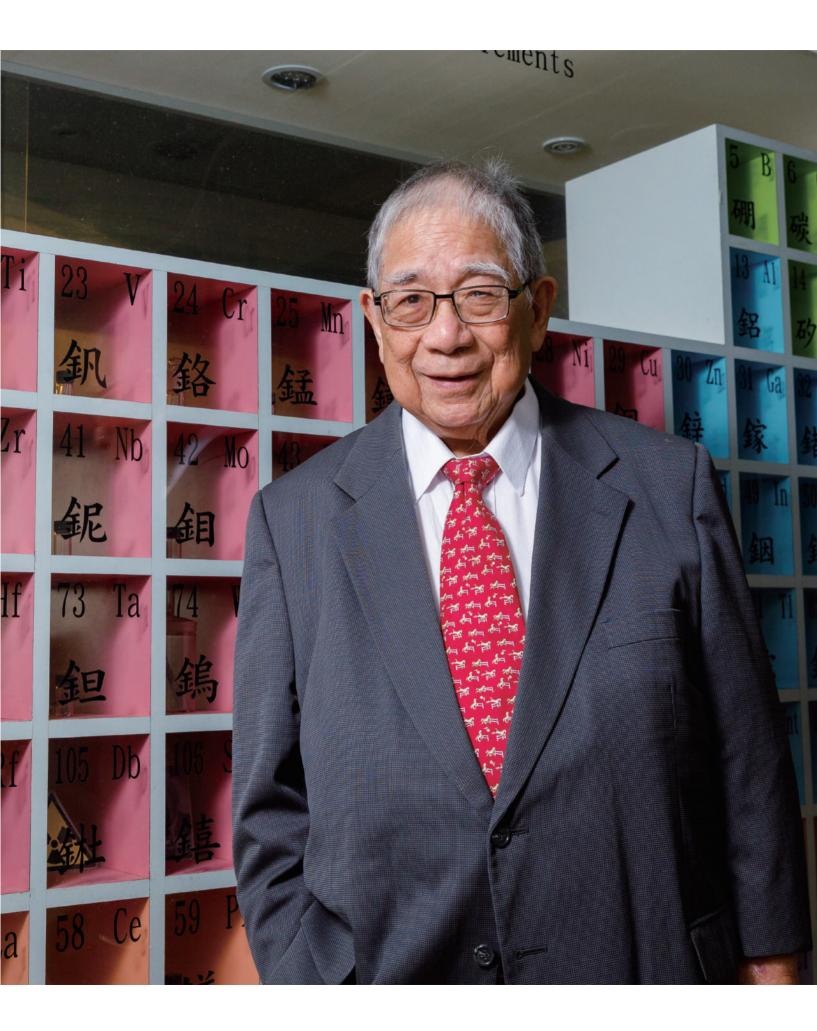
The TIGP (Taiwan International Graduate Program) in Academia Sinica was founded by Sunney Chan with an aim to attract global talents to undertake their graduate training in Taiwan. TIGP was established 20 years ago and it remains one of the most successful programs in Academia Sinica for the diversity and enrichment it has brought.

Leveraging his academic connections, Sunney Chan invited internationally-recognized researchers to lecture in Taiwan, significantly elevating Taiwan's worldwide visibility and academic strengths. Over

the years, he has organized many international symposia on cutting edge research in the frontiers of many fields, including chemical biology, biocatalysis and chemical catalysis, and energy, fuels, and sustainability. He is a visionary scientist with a keen sense of the directions that science is moving toward.

Sunney Chan was applauded by his fellow academicians for his selfless devotion in training young talents. He moved his research projects to Taiwan two decades ago and have since mentored hundreds of students: postdocs, graduate and undergraduate students. Among them, at least 25 from Taiwan are currently working in academic and research institutions, such as Ohio State University in the US and Max Planck Institute of Molecular Biology in Freiburg, Germany. Sunney Chan retired 10 years ago and still carries on his mission as a scientist and an educator. To this date, he continues to inspire many young minds in Taiwan and abroad, passing on his inheritance as valuable assets for generations to come.

# <u>30</u> The Story of a Champion





### A Scientist, an Educator and an Adventurer, Planting Seeds without Asking for Harvest

## Sunney Chan Turned Academia Sinica into a World-class Institution

Coming from a humble background, Sunney Chan invented his own legend with curiosity, passion and intellectual giftedness in science. Vowed to become the first Asian Pope as a teenager, he dived into scientific research instead, finding more joy and fulfillment and reaching groundbreaking accomplishments in biological physics and biological chemistry. As a world-renowned scholar, he doesn't like the limelight . He didn't pursue science for personal or financial gains. He enjoyed the journey of discovery with fellow researchers and guiding the way forward for young talented minds. He has taught different generations of his students one valuable thing: how to do science.

Sunney Chan engineered the establishment of the Genomics Research Center for Academia Sinica without taking credits. His contribution in introducing solid paradigms and system architecture for Taiwan's advanced research is pivotal to the transformation of Academia Sinica into a premier research institute today, outshining its peer institutions in Asia. He plants seeds of hope like a missionary. It is simply Taiwan's privilege to have such a world-class scholar dedicating his best years in this land.

Sunney Chan was brought up in the US. His parents were firstgeneration immigrants from southern China to California. Both of them didn't have any formal education and worked long hours as 'sweatshop laborer' in a denim factory for Levi Strauss & Co. Sunney Chan grew up in the Chinatown ghetto, a socially and culturally disadvantaged environment.

As a teenager, he had no family members to emulate as role models, scholars or scientists. He became the first in his family to attend university and obtain a PhD degree. "How I ever got to where I ended up makes for an interesting saga. It was not by design or program," Chan said.



### The Boy in the Ghetto Wanted to Become the First Asian Pope

By the time he finished sixth-grade, Sunney Chan was a typical "banana", an Asian American who is yellow outside and white inside. His father decided that he needed to understand his Chinese heritage and sent him to a Chinese-speaking middle school in Hong Kong. He had just turned 12 and didn't understand a single word of Chinese, not even what was taught in the "English" class. Not surprisingly, he flunked out at the end of the term. "It was a socially humiliating experience, if not a psychological trauma that took many years to shake off," Sunney Chan recalled.

Chan was then transferred to an English-speaking school run by the Irish Jesuits, where his interests in academics were kindled by a number of excellent math and science teachers.

In the fall of 1953, he returned to California and entered the University of San Francisco with the intention of joining the priesthood and becoming a science teacher. "My career aspiration at the time was to be the first Asian Pope." This ambition did not take shape since the rigid lifestyle of a Jesuit priest was too much for a 16-year-old who was set to explore the world and curious about everything in his surroundings, and fortunately so or the world would have one less outstanding scientist and passionate educator. His parents have different expectations to him, too. "My mother wanted me to be a medical doctor. I did try and dropped out. Dissecting a frog in pre-med class was an experience I didn't enjoy. My father wanted me to be an engineer and return to China to rebuild the country out of poverty."

Sunney Chan transferred to U.C. Berkeley to study chemical engineering for a bachelor degree. "U.C. Berkeley was a difficult school for me," he said. The rigorous curriculum was intimidating for a transfer student; it also took some efforts for Sunney to build up confidence in the new environment. Luckily, two professors at Berkeley were inspirational to him: Professor George Pimentel's lucid lectures on chemical equilibrium stimulated his interest of learning; Professor Andrew Acrivos taught him applied mathematics and kinetics as well as introducing him to the process of self-study and independent research. By the senior year, he was prepared to learn from sources outside the classroom and auditing courses not on the formal curriculum.

Sunney Chan stayed at Berkeley for a PhD in physical chemistry. His PhD thesis was on the microwave spectrum of oxetane and its molecular structure. In less than three years, he obtained the PhD degree with lucrative job offers awaiting him. "By the early spring of 1960, I had lined up attractive positions at MIT Lincoln Laboratories, Lockheed, General Electric and IBM."

### Giving up High-paying Positions for a Post - doc at Harvard

Sunney's PhD mentor, however, had a different plan for him. "He insisted that I apply for an NSF Postdoctoral Fellowship to work with Professor Norman Ramsey (1989 Nobel laureate in Physics) in the department of physics at Harvard University," Chan said. High-resolution solution NMR was developing at the time; he was suggested to enter the field leveraging his background in microwave spectroscopy of gases to study the NMR of small molecules in molecular beams.

Just to keep peace with his professor, Sunney Chan filed an application for a National Science Foundation postdoctoral fellowship. When the word came that he had won the fellowship, he was taken aback. Ultimately, he accepted to go to Harvard; the professor was pleased but his father was disappointed that he rather took the \$4500 fellowship instead of the much-higher-paying positions at General Electric and IBM. "My father said to me, 'Son, I don't have a PhD, but I make much more money than you do'," Sunney Chan remembered.

In September 1960, Sunney arrived at Harvard and began his postdoc research. While deeply engrossed in research, he was fascinated by the intellectual power of savvy scholars at Harvard. One day, he had made a significant discovery in the lab, and J. H. van Vleck (1977 Nobel laureate in physics) happened to be there. The next morning, Dr. van Vleck reappeared in the lab and explained the observation using "perturbation theory" on the chalk board. To a novice scientist, it was an impressive demonstration of real intellectual power. It left a deep and lasting impression on Sunney Chan; he was reinforced that he had made the right decision to do his postdoctoral study at Harvard.

In 1961, he was offered a position as an assistant professor at the University of California at Riverside (UCR), his first teaching job. The graduate program in chemistry at UCR had just started, "I thought I could contribute to building a high-quality program," he said. It was here that Sunney Chan's original interest in science teaching began to take shape.

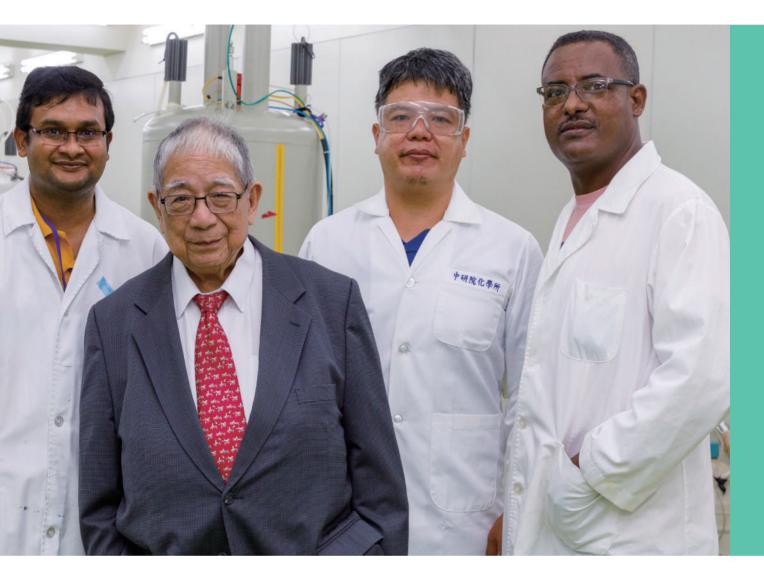
"My graduate training at Berkeley and postdoctoral experience at Harvard had convinced me that research training was a great way to encourage young people to develop their potentials to become



original and independent research scientists." Sunney Chan decided to become an academic scholar as well as a teacher who can stimulate students in learning. He was about to turn 25.

His career goal was settled, but his research plans at UCR was far from crystallized. Sunney Chan didn't want to continue in NMR of molecular beams which, like microwave spectroscopy, was maturing and becoming less likely to generate new concepts or breakthroughs.

"To train students, I felt that the research they worked on had to be 'discovery' driven," Chan said. With curiosity as an impetus, young people could learn to define the science question, develop the research plan, formulate the hypotheses to be tested, and design the experiments to test them. To him, this solid set of system was the way to do science. So he decided to try a number of research areas that were new to him, including the structure of transition metal complexes in solution by NMR,



NMR of purine and pyrimidine bases, and EPR of concentrated alkali metal ammonia solutions.

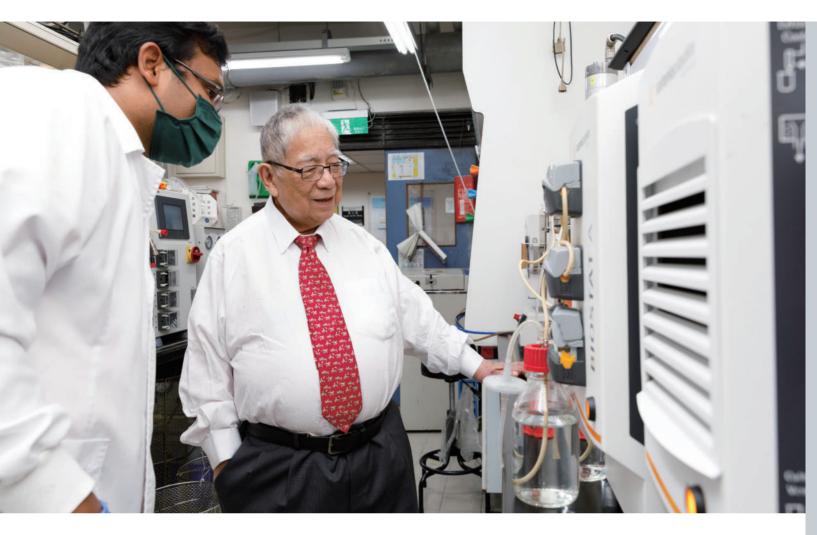
Sunney Chan's stay at UCR was very brief. He was invited to present at a seminar at Caltech shortly after he arrived UCR. "To my surprise, I was offered to join the Caltech chemistry faculty the following week." He turned down the offer immediately, mainly because his research program at UCR was about to gel. "Caltech was such a high-power place. I wasn't sure that I was up to the challenge," he added.

Caltech asked him to reconsider. At the same time, a similar offer was extended to him from the chemistry department at Yale. "Perhaps it was telling me that I should consider the long-term impact of a stimulating environment and high-quality graduate students on the development of my research career." Caltech has world-class scholars, its graduate students are firstrate, all the way around, there is quality. So Sunney Chan moved across town from UCR to Caltech and stayed there for 40 years.

### Early Years in Caltech: From Physical Chemistry to Biophysics

In Caltech, Sunney Chan embarked on his first research in biophysics: base-stacking of nucleic acids in aqueous solution. He focused on the application of NMR to address the structure of biological molecules and their interactions in solutions. The base-stacking interaction is now commonly known by scientists but at that time, while molecular biology was centered on the structures of the Watson-Crick A-T and G-C base pairs, there was a debate as to whether or not these 'horizontal' interactions were in fact sufficient to account for the stability of the structure of the DNA double helix in water at room temperature.

"As I began to embark on the new field of biophysics, little did I know that my background in chemical physics would serve me well in my future endeavors," Sunney Chan said. "It seemed a major handicap to have no formal training in biochemistry



or biology, but it turned out to be quite the opposite. Molecular biophysics was a relatively virgin field, and not knowing too much was a blessing in disguise."

"To me the more serious hurdle was finding out what was known and what was unknown, as well as identifying the scientific questions that needed to be solved and the tools that would get me to the heart of the matter." Sunney Chan's background in physics gave him the insights to formulate and analyze complex problems rigorously from the outset.

In pioneering NMR experiments undertaken during 1962-64, Sunney Chan's laboratory showed that in water solution, there exist strong "vertical" interactions between the nucleic acid bases in DNA (and RNA), and the nucleic acid bases stack in water in order to minimize the disruption of the hydrogen-bonded network structure of the water, now commonly referred to as the "hydrophobic effect." Consequently, this discovery brought to an end the scientific debate on why and how the Watson-Crick A-T and G-C base pairs can be formed in water. In 1968, his lab began to probe the phospholipid bilayer membrane with NMR and discovered that the membrane is neither a solid nor a liquid and could undergo only restricted molecular motions with a hierarchy of timescales from picoseconds to nanoseconds to microseconds and to milliseconds. This uncovered the picture of the dynamic structure of the biological membrane that we have come to know today.

Following this seminal work, Sunney Chan moved on to study the effects of cholesterol, amphipathic peptides and membrane proteins on the structure of the fluid bilayer membrane. These molecules affect the cooperative domain size of the bilayer membrane, the correlation length of the collective motions, the surface curvature, the elasticity, lateral diffusion of the phospholipid molecules within each leaflet of the bilayer, the exchange of the lipid molecules between the two leaflets, and the phase behavior of mixtures of phospholipids in the membrane. He also studied on lipid-protein interactions and lipid-mediated protein-protein forces.

#### Cracking the Mystery of Cytochrome *c* Oxidase and the Holy Grail of Organic Chemistry

With so many membrane proteins in cells and so many discoveries made in research on membrane proteins, Sunney Chan turned his attention to unraveling the structure and function of molecular machines within living cells in the late 1970s. Many of these molecular machines are membrane proteins, which are extremely difficult to isolate and purify for in-depth study. His group was able to purify the cytochrome c oxidase, the terminal enzyme in the mitochondrial respiratory chain, which is crucial to generate energy for cells to complete their activities.

However, cytochrome c oxidase was a black box at that time. Under Sunney Chan's leadership, his student and postdocs systematically worked out the structure of the metal cofactors that mediate the electron transfer, the sequence of electron flow between metal cofactors, and details of how the dioxygen molecule is cleaved to form the high potential redox intermediates required to drive the proton translocation (cytochrome c oxidase is a proton pump!). These studies allowed them to predict the chemical structures of the various metal cofactors and their possible role in the overall function of the enzyme. Sunney Chan became the world authority in this field, and his early papers on the mammalian cytochrome c oxidase were among the first to place the understanding of this important enzyme on the molecular level, well before the X-ray structures of the cytochrome c oxidase became available in the early 1990s.

In 1992, Chan initiated a new venture toward understanding how methane is converted into methanol with high efficiency by the particulate methane monooxygenase (pMMO). Before moving to Academia Sinica in Taiwan, Sunney Chan's laboratory at Caltech had succeeded in isolating and purifying the pMMO to homogeneity. During the 2000s, his Taiwan team elucidated the catalytic mechanism of biological methane oxidation. The mechanism is based on the deployment of a tricopper cluster to harness a singlet oxene from molecular oxygen ( $O_2$ ) for facile direct O-atom insertion across the C-H bond. This chemistry is novel, and beautifully illustrates how nature exploits metal clusters to catalyze difficult chemistry with a powerful oxidant without self-



destruction of the catalyst itself. The conversion of methane into methanol, a gas-to-liquid process, is extremely difficult chemistry because the C-H bond in methane has the highest bond energy among organic substrates. For this reason, the process has been one of the "holy grails" in the field of organic chemistry. Recently, Sunney Chan and coworkers in the Institute of Chemistry at Academia Sinica and the Department of Chemistry at National Taiwan University, have developed the first molecular catalyst capable of efficient conversion of methane into methanol by  $O_2$  at room temperature. This is yet another ground-breaking invention in the field of methane oxidation.

During the 40 years at Caltech, Sunney Chan became world-renown because of his groundbreaking discoveries in two benchmark systems: "bovine cytochrome c oxidase" and "pMMO in methane oxidation."

#### House Master for 800 Students, Confronting Drug Dealers

What brings fulfillment to Sunney Chan is not just scientific adventure, but also his interaction with

students. "I was the Master of Student Houses at Caltech. It was quite an experience." There were 800 students in the school's dormitories, or Houses. The term of office of the previous master was about to expire, and students were not very fond of the candidate suggested as successor by the Caltech Administration. Sunney Chan taught freshman chemistry at the time and was loved by students. One morning in May 1980, a group of students approached Sunney Chan after class and asked if he was willing to take the job. "I had no idea what a house master is and what the master does or needs to do." Sunney Chan sought advice from a fellow colleague on campus, an elder Chinese and academician of Taiwan, who noted that "if I take the job, I'll be the first Chinese American to assume an administrative role at Caltech. It will be a milestone." With this subtle pressure, Sunney Chan decided to consider the position and the unforeseen challenges that came with it.

For this concurrent position, Chan and family moved to the neighborhood of the student houses. He organized extracurricular activities every weekend and cooked dinners for students. He became a caretaker/counselor for these brilliant young people. As the students' "gang lord", Sunney Chan undertook the responsibility of making sure they were out of harm's way and standing with them in the face of knotty problems. It was the end of the Hippie era, but narcotics abuse was still rampant in the school campus. One day, a drug dealer was peddling drugs on the campus and spotted by Sunney Chan. Sunney stopped the drug dealer and asked him to leave. The drug dealer refused to go and took out a gun to intimidate Chan. "In the face of such a menace, I could only say to him, 'please go away or I will call the police.' Luckily, the drug dealer backed down, ending this daunting episode without any mishap."

During the four years of the House Master's tenure, Sunney Chan helped many students: those with depression and were suicidal because of pressure from schoolwork, those who had relationship and gender identity issues or family problems. "We all encounter problems when we are growing up. These students were willing to come to me and I was able to provide them with a helping hand. That was the most rewarding thing."

Over the years in the US, Sunney Chan has also been active in community and public service. He



TASCO award ceremony with President Wu on Dec 2018

was a founding member of the Chinese-American Faculty Association (CAFA), a service organization devoted to the welfare of academics of Chinese descent working within the Southern California community. He served two terms as the CAFA President. He has also chaired the Caltech Y Board of Directors (1992-1993) and the Board of the Chinese-American Chemical Society (1988-98). Chan has been a regular consultant of the National Institute of Health (NIH) in Bethesda since 1970, and has served on many NIH Advisory Committees, including the Biophysics and Biophysical Chemistry Study Section (1970-74), the Physical Biochemistry Study Section (1989-93; chair, 92-93), the National Cancer Institute Review Board (1996-97), and Study section on Small Business Innovation Research (1992-2002). In addition, he is a member of many scientific advisory committees in the US and abroad.

In 1988, Sunney Chan was elected as the Academician by Academia Sinica in Taiwan. In 1997, he was invited by Lee Yuan Tseh, the then President of Academia Sinica, to move to Taiwan and help modernize the institution. "This was certainly a big news at that time. Sunney's decision



to retire from Caltech and move to Taiwan made quite a splash in the academic circle," Shie-ming Peng, Academia Sinica Academician and Honorary Professor at the Department of Chemistry, National Taiwan University recalled. Peng said that Sunney Chan was already a top scientist in the world and willing to give up the fame and resources at Caltech for an entirely new beginning, "I think it has a lot to do with his father. He always wanted Sunney to contribute more to humanity."

Sunney Chan's father had great expectation for him, more than making big money or achievements. He always told Chan to cherish what he has and contribute to the global Chinese community. That is why Chan was sent to Hong Kong for middle school education—to not forget his cultural origins.

In 1997, Sunney Chan accepted the invitation of Lee Yuan Tseh, then President of Academia Sinica in Taiwan, and came to Taiwan with a goal: to transform the Institute of Chemistry and the entire Academia Sinica into a modern, world-class research center.

In Academia Sinica, he began with the position as Director of the Institute of Chemistry. In the Christmas party that year, Sunney Chan put on a Santa Claus costume to entertain the faculty. Professor Peng recalled, "his figure and temperament are exactly like Santa, always willing to help and always kind and nice. We'd use to call him "s-orbital", the most stable orbital in atomic physics."

Chan is as much a gastronome as a scientist, and he is well known for his hospitality. When he first came to Taiwan as acting director of the Institute of



Sunney was promoted to become Vice President of Research, Academia Sinica on July 1997

Molecular Biology at Academia Sinica in 1989, he roasted a turkey to celebrate Thanksgiving with his colleagues. In 1997, he relocated to Taiwan; within two years, he had visited all the gourmet restaurants in Taipei. The Dragon Restaurant, the must-go place for authentic roast duck and exquisite dim-sum. The ChianTangTsuen, named after a scenic river in the east coast of China and offered Shanghai delicacy, and several other restaurants he visited regularly, still have "Sunney Chan's menu" today. In his 85th birthday this year, he will host a banquet at The Dragon Restaurant, Neihu for friends and colleagues. Harry Gray, Professor of Chemistry at Caltech would on occasions fly to Taipei just to attend Chan's birthday parties.

### TIGP Elevated Taiwan's International Visibility

Chan was appointed the Academic Vice President of Academia Sinica, steering the direction of research development and academic standards for the entire institution. Over the four years in this capacity, he led the effort to establish the Taiwan International Graduate Program (TIGP) at Academia Sinica, an English-speaking program to attract international graduate students to participate in Academia

Sinica's research projects. Sunney Chan leveraged his connection in the global academic circle and invited world-class scientists to give lectures in Taiwan, which significantly elevated Taiwan's international visibility, and therefore attracting more young talents, creating a mechanism for Academia Sinica to strengthen its human resources and establish its global reputation.

During the tenure as Academic Vice President of Academia Sinica, Sunney Chan has another epochmaking contribution for Taiwan. He formulated a roadmap for the Genomics Research Center; he also worked with the National Science Council of Taiwan in creating the National Research Program in Genomics Medicine. Both have laid solid foundation for the booming of Taiwan's applied medicine and biotechnology industry.

#### A Scientist and an Educator, Generations of Young Talents Are Nurtured

"What I really admire him is his selflessness in mentoring generations of young talents. He is a scientist and an educator." Professor Peng said, Sunney Chan systematically trained his students and research team members to do science properly. Sometimes he also helped them with the literature of the thesis; with English being Chan's native language, a slight modification of a word or two will turn the academic expression neat and elegant.

Over the years, more than 200 graduate students, postdocs and visitors have the privilege to take part in Chan'sresearch ventures. This number is quite rare in the basic sciences. During the last ten years at Caltech, Chan made breakthroughs in the role of pMMO in methane oxidation into methanol. He then moved this project to Taiwan, and in recent years has made major discoveries and inventions. What is most important to Sunney Chan is that these discoveries and inventions have been made by students and postdocs working in Taiwan. Thanks to that, a number of young Taiwanese scholars in his team have now stepped onto the international stage, ready to fly higher with Sunney Chan as the wind beneath their wings.

Among his students, at least 25 from Taiwan are currently working in academic and research institutions, including Ohio State University in the US and Max Planck Institute of Molecular Biology in Freiburg, Germany, and almost 10 hold academic



and research positions at Academia Sinica and the National Universities in Taiwan. Many of his students and postdocs trained at Caltech have also taken on academic positions in major universities throughout the world. Some of his students have achieved success in industry. For example, Ming-Chu Hsu, founder of Taigen Biotechnology was in Chan's lab at Caltech for postdoctoral training during the early 1970s. She's among the first generation of successful biotech entrepreneurs in Taiwan after the local biotech industry took off 20 years ago. Sunney Chan retired from Academia Sinica 10 years ago and still carries on his mission as a scientist and an educator. To this date, he continues to inspire many young minds in Taiwan and abroad, passing on his inheritance as valuable assets for generations to come.



Sunney Chan's zeal for scientific research did not wane after his retirement from Caltech. He devoted himself in yet another unrevealed frontier: protein folding. In his own words, "To close out my scientific career, I decided to return to a simpler issue." Protein folding is an important mechanism in living science since with this process, muscles, hormones and enzymes are formed. However, how it works was still a mystery some 20 years ago. Sunney Chan developed the use of "caged" compounds to study the very early events in protein folding initiated in the absence of denaturants. In this work, Chan has demonstrated the importance of kinetic channeling in protein folding.

In retrospect, Sunney Chan said, "I have had an exciting career. The journey that ultimately led me to the world of membrane proteins was hardly programmed. It evolved serendipitously (although

 15th Taiwan International Graduate Program (TIGP) certificate conferral ceremony

logically) from the chemical physics of simpler systems, from the dynamic structure of the lipid bilayer to lipid-protein interactions, to membrane biophysics of ion transport, and culminated in the structure and function of several membrane protein systems."

As the systems he studied became more complex, Chan said, he learned how to manage the research undertaking, how to define a myriad of complex biological problems from scratch without knowing much about them, and how to formulate research strategies to approach the various issues. "A problem like pMMO is so complex that it transcends generations of coworkers, with the next generation of experiments building on the outcome of earlier ones." He noted that in academia, with



limited research resources, it's not possible to build a large team and solve problems in a short amount of time as is done in industry. "However, with a more deliberate pace, it is possible to take advantage of emerging technologies as they develop," Chan said.

#### Shaping an Open Environment for Taiwan's Academia

While at Caltech, the bulk of Chan's membrane research was supported by the National Institute of General Medical Sciences of NIH and he was able to sustain NIH funding for more than 30 years. He said that the level of support was adequate to cover most research expenditures, with the exception of upgrades of research instrumentation or the purchases of major pieces of equipment. In contrast, after he moved to Taiwan, his research program was funded by Academia Sinica. Although the level of support was not as high, Academia Sinica did provide funds for upgrade of research facilities and the acquisition of state-of-the-art instrumentation as justified by the research. This capability greatly accelerated the progress of his work in Taiwan.

"In Taiwan, resources (funding and research facilities) are not too bad, but the research

 William A. Rose Award from the American Society of Biochemistry and Molecular Biology in 2004

environment could be more open." Chan believed that along the long, exhausting journey of pursuing scientific truth, young people need to be motivated by passion and intellectual inquiry. "It is intellectual curiosity that fosters creativity. Not just learning textbook or journal science."

In Chan's opinion, developing one's "scientific judgement" is also important in science, but that requires experience. He categorized science into three different kinds: (1) discovery science (or exploratory science); (2) mainstream science (popular areas actively pursued such as materials chemistry, water splitting, new drug development, machine learning or quantum computing); and (3) mature science (issues largely defined but need fine-tuning). Among them, discovery science is most fascinating to Chan. "This is an area that nobody knows anything or much about it, so you need to ask questions and find the answers from scratch. It was like Christopher Columbus embarking on his journey to the west. He had a hunch. He didn't know he would discover the new continent. He simply asked himself: what is out there?"

To Chan, discovery science is about stretching one's imagination, groping in the dark and probing the unknown. "When you hit the road, you have nothing but a black box in hand, without any clues about what is in the box. This doesn't mean nobody has never asked the question before. But nobody has found the answer yet. Or the nut was too hard to crack."

In this manner, discovery science is a high-risk and long-term investment, with high intellectual content but low productivity, at least at the beginning, Chan said. "I was fortunate enough to have randomwalked into scientific issues that later became mainstream."

Act of fortune, however, does not explain his accomplishment. To him, science is not about research grants, research publications or awards; it's all about intellectual curiosity. "I have always wanted to understand my surroundings, about nature and human behavior." He doesn't like the limelight. He doesn't enjoy competing with others nor into oneups-man-ship. "After all, I am just an educator, or a scientist, a thinker or an intellectual at best," Chan said.

### Loves Intellectual Discovery More than its Commercial Value

If Chan chose a different career, he supposed he could have succeeded, too. "My mother wanted me to be a medical doctor. My father wanted me to be an engineer. But I discovered that I was more interested in ideas than applications." Chan said that he could have ended up like many of his cousins as a teller in the bank, a post office clerk, a grocery checker or a butcher, and be happy about it. This was the typical career path for a young Chinese Americans of his generation grown up in San Francisco Chinatown. "I could have been a high school science teacher and enjoyed it, however."

When Chan turned 50, already an established scholar, his father wanted him to take over the family business. "That would have been a nightmare for me. I do not like wheeling and dealing. I would have been bored my entire life."

Professor Shie-Ming Peng, a good friend of Chan's, agreed. "Some scholars dedicate in research to find a marketable solution or product, such as new drugs or vaccines. Sunney is not like that. He loves basic science. He enjoys discovering the unknown in a stimulating environment with his teams. That is why he spares no efforts in teaching and training young people. He is not commercial-minded at all."

Chan is often invited to give lectures. In earlier days, he spoke mostly about the profound topics of his scientific researches. In recent years, he started to share his scientific career in school campuses, hoping to inspire more students. His advice to young people who are passionate about academic studies: "Research is about searching and searching until you are intellectually satisfied with the answer; it takes hard work, discipline, patience and a degree of stubbornness. Therefore, it's not for everyone."

Although basic science research is definitely for him, Chan has broader perspective. Citing the science of chemistry as an example, he said, "we train chemists not only for industry and academia, but a multitude of other professions: public policy, risk analysis, chemical safety, environment protection, environmental law, patent law, etc."

In his article titled "Opportunities for Innovation in Chemical Science" published in the Chemical Education Journal, Chan talked about the breakthroughs in chemistry over the past one hundred years: discovery of the elements, how molecules are formed, how molecules react to form new molecules and how to synthesize molecules in the laboratory.

The field of chemistry is moving on but it's also experiencing some sort of an identity crisis. The contribution of chemistry to human life and industry is no longer mentioned, mainly because a series a tragic incidents caused by serious pollution such as



Sunney discussing the structure and mechanism of enzymes mediating methane oxidation with British microbiologist Sir Howard Dalton at C1 Meeting, Magdalen College, Oxford in August 2006.

the impacts of DDT and dioxin on ecology and human health, the use of tetraethyl lead in gasoline causing neurotoxicity, the methyl isocyanate leak resulting in serious casualties in India, and the contribution of freons to the depletion of ozone. These tragic events have tarnished the image of chemistry as a science.

Today, when the news media discuss sequencing of genomes, vaccines, cholesterol-lowering statins, a new drug for type II diabetes, chemistry is never mentioned. But the truth is, these breakthroughs all involve chemistry. "In other words, we need to make the general public more related to chemistry. The basic research of chemistry is still very vibrant and contributive to human life," Chan said.

The world needs diversified talents, and Sunney Chan is cultivating them for the world. "Many of my students have gone into new territories. I think it's only natural. And I'm proud of them." But for Chan himself, cracking the mystery of nature is still the most charming task. "No matter how complicated biological problems may appear to be, there is a simple answer to the outcome when all is said and done. In my view, nature is intrinsically simple, and it is fun to discover how the behavior of a complex biological system is explicable in terms of the law and physics and chemistry as we now understand them to be."

Sunney Chan is more than a world-class scientific researcher or a selfless educator. For Taiwan, he's like the Santa he dressed up to be in his first year in Academia Sinica, bringing to this island the gift of system reform and academic leap. But ultimately, he is just an adventurer who took to the untrodden route with insight, navigated the path to truth with strategy and patience, and inspired bright young gangs to march ahead together. And that has made all the difference.

Sunney became a permanent resident of Taiwan in April 24.2015



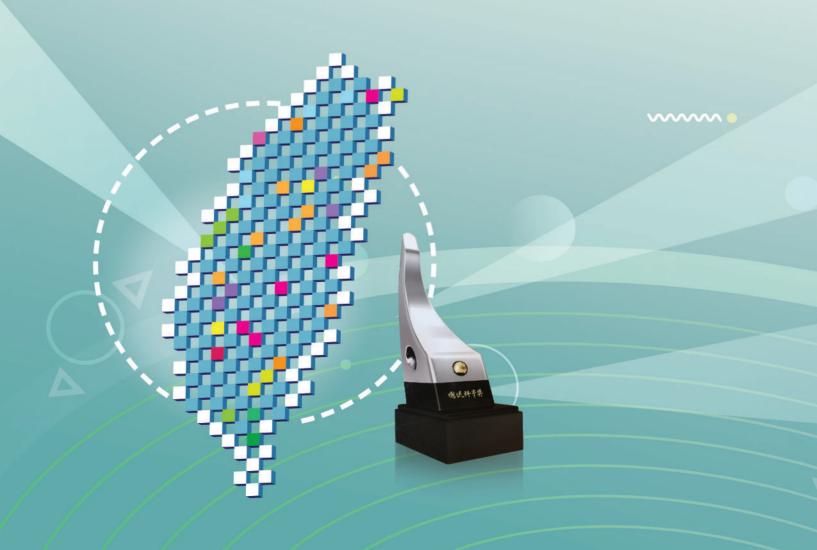
#### **List of Selected Publication**

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- 8. "Proton pumping in cytochrome c oxidase: The coupling between proton and electron gating", Sunney I. Chan\*, Proc. Nat. Acad. Sci. USA 107, 8505-8506 (2010).
- "Efficient oxidation of methane to methanol by dioxygen mediated by tricopper clusters", Sunney I. Chan\*, Yu-Jhang Lu, Penumaka Nagababu, Suman Maji, Mu-Cheng Hung, Marianne M. Lee, I-Jui Hsu, Pham Dinh Minh, Jeff C.-H. Lai, Kok Yoah Ng, Sridevi Ramalingam, Steve S.-F. Yu,\* and Michael K. Chan\*, Angew. Chem. Int. Ed. 52, 3731–3735 (2013).
- "Copper centers in the cryo-EM structure of particulate methane monooxygenase reveal the catalytic machinery of methane oxidation", Wei-Hau Chang\*, Hsin-Hung Lin, I-Kuen Tsai, Shih-Hsin Huang, Szu-Chi Chung, I-Ping Tu, Steve S.-F, Yu\*, and Sunney I. Chan\*, J. Am. Chem. Soc. 143, 9922-9932 (2021).

Chosen from a number of excellent candidates, the three awardees of the 2020-2021 Presidential Science Prize - Dr. Sunney I. Chan of the Mathematics and Physical Sciences Category is the most outstanding and internationally-recognized scholars who has achieved great contributions in scientific R&D.

Indeed, for decades, they have distinguished themselves in various fields of research with selfless attitude and a sincere spirit of inquiry. Thanks to their dedicated endeavors, Taiwan now can stand side-by-side with advanced countries in various fields of scientific research. Moreover, their research achievements have not only benefited people in this country but also had far-reaching influence on the prosperity of all mankind.

Looking toward the future, scientific development still requires persistent efforts of all scientists around the world. Working hand-in-hand, we will be able to make even greater breakthroughs in science and usher in a new era of international scientific cooperation.



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(2020 - 2021)

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