THE VORTEX

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CALIFORNIA SECTION
NOVEMBER 2019

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ACS Chemistry for Life®

California Section

AI and Chemistry: Protein Engineering and East Bay Biotech

Tuesday – November 19, 2019 – 6:00 to 9:00 PM

Amyris
5885 Hollis St.
Suite 100
Emeryville, CA 94608

6:00 PM	Networking (Refreshments provided)
7:00 PM	Welcome, Panel, and Q&A
7:45 PM	Concluding Remarks
7:50 PM	Networking and Refreshments

Discussion on East Bay research - Come join us to learn more about the future of chemistry, protein engineering, and artificial intelligence within the biotech industry.

RSVP here!

Guests will sign a non-disclosure upon sign-in at the event. Event access is through the general access door facing Hollis Street.

Our Distinguished Panelists:

Yue Yang, PhD
Amyris
Director, Program Management

Loren Perelman, PhD
Riffyn
Vice President, Scientific Solutions

Louis Metzger, PhD
Tierra Biosciences
Chief Scientific Officer

The event is FREE and open to the community. More information at: calacs.org or email aliciaataylor@gmail.com

THE VORTEX

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Chair's Message

Holiday season is upon us and we have a full pallet of activities planned for our members and the general public this month.

On November 2nd, the California Section will have a booth at the Bay Area Science Festival taking place at Oracle Park. Stop by to say "hello" and participate in activities we have planned at our booth. On November 8th, the first annual "Bay Area Chemistry Symposium" will take place at the brand new Merck facility in South San Francisco. This event is unfortunately sold out but we plan to have another event next year. This event is organized in close collaboration with the Silicon Valley Section and made possible by amazing volunteers as well as generous sponsors. On November 19th, our third and final "AI & Chemistry" event in 2019 will occur at Amyris and our panelists will discuss "Protein Engineering and East Bay Biotech". This event is free but will require registration. If you are interested in attending any of our events, please e-mail RSVP@calacs.org to register.

We're in the process of filling out our 2020 Executive Committee and you can help by voting to fill the various positions up for election. We will announce the final position after the close of elections so stay tuned and make sure to vote!

Finally, our next executive committee meeting will take place at the Lafayette Library on November 5th. If you are interested in learning more about our section or would like to become more involved, please join us. For more information about this meeting or any of our upcoming meetings, please e-mail office@calacs.org.

Remember to follow us on @CaliforniaACS on twitter and we look forward to seeing you at our next event.

Sincerely,
Patrick S. Lee Ph.D.

Gifts & Donations

Thank you to all the members and organizations for their generous donations. They help support the programs noted in Chair's message and others. Donations to the California Section are tax deductible.

Lou Rigali, LR101898@aol.com

WCC Meeting Report MANYA: The Living History of Marie Curie

On Saturday, October 19, 2019, about 90 people gathered to watch Susan Marie Frontczak present her single-person performance on the life of Maria "Manya" Sklodowska Curie. The event was part of a celebration of the International Year of the Periodic Table and was hosted by the California Section, Women Chemists' Committee, the American Chemical Society, and the American Association of University Women. Laney College's Performing Arts Theater met all the requirements of Susan Marie Frontczak and was accessible by public transportation.

The show begins with a travel back in time to April 1915, as the actress impersonates Manya recalling her life up to that time, including numerous personal and professional challenges:

Her early life in Poland, including poverty and political repression;

Her coming to France for education and forming a professional partnership with fellow scientist Pierre Curie that bloomed into a romantic partnership;

The Curies' constant struggles for income and laboratory space while rearing two daughters;

The herculean task of extracting one tenth of a gram of radium from over a ton of pitchblende, using a converted shed as a laboratory;

The Curies' dismay at the disruptions in their lives after winning the Nobel Prize; and the irony of receiving the Curies' longed-for laboratory space only after Pierre's tragic death in a road accident.

The show ends with Manya coming out of her shell, overcoming her natural shyness to set up X-ray units at field hospitals so that soldiers wounded in World War I could be promptly diagnosed and treated.

Throughout, the actress used simple props and gestures to make her point. For example, the table on the right of the stage represented Marie's laboratory and the table on the left represented her life outside the lab. She uses shoveling motions while describing the difficulties of extracting radium from pitchblende. Most important, she explained the science in layman's terms, first explaining how she used tiny differences in the solubility of barium and radium salts to separate them, and introducing the formal scientific term "fractional crystallization" at the end. Overall, this was an entertaining performance that honors Curie's memory and makes her science accessible to the general public.

A shorter version of the Manya performance is available for use in schools. The California Section of ACS collaborated with the Korematsu Middle School in El Cerrito, CA to provide this shorter program for its

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It's Elementary (Part 3) by Bill Motzer

As part of the celebration of the 150th anniversary of the Russian chemist Dmitri Mendeleev's publishing of the modern periodic table, in Parts 1 and 2 (September and October 2019 Vortex), I discussed the known use of 10 elements by the ancients. In more modern times, Mendeleev's periodic table inspired and encouraged 19th century chemists to search for elements not yet discovered but predicted by his new periodic table. However, one Group – 18, was not added to the periodic table until 1902. These are the noble gases (aka, the inert gases or aerogens), which are odorless, colorless, monatomic gases having relatively low chemical reactivity.

The six naturally occurring noble gases are helium (He; Z=2), neon (Ne; Z=10), argon (Ar; Z=18), krypton (Kr; Z=36), xenon (Xe; Z=54), and the radioactive radon (Rn; Z=86). The most recently discovered (2006) element, Oganesson (Og; Z=118) has been predicted to be a noble gas or alternatively it may be a metal; however, its chemistry has not yet been investigated because only a few atoms have been made.

The discovery of the Group 18 elements may have begun in 1784, when the English chemist and physicist Henry Cavendish (1731-1810) discovered that the atmosphere contained a small quantity of a gas that was less reactive than nitrogen. Some scholars attribute that he had discovered helium (which occurs in the atmosphere at ~ 5 ppmv), but it was most likely argon, because he determined that the unknown air sample was about one percent of atmospheric air. On August 18, 1868, astronomers Pierre Janssen (1824-1907) and Joseph Norman Lockyer (1836-1920) independently and simultaneously discovered a new element in spectral lines observed in the solar chromosphere during a solar eclipse. Lockyer named this element helium (Greek for hḗlios for the Sun). At that time, chemical analysis was not possible, but helium was later determined to be a noble gas.

New discoveries and confirmation of earlier experiments of Group 18 elements had to wait for over a century. In 1895, English physicist John William Stratt (Lord Rayleigh) (1842-1919) discovered that atmospheric nitrogen samples had a different density than nitrogen derived from chemical reactions. Lord Rayleigh collaborated with Scottish scientist Sir William Ramsay (1852-1916). Rayleigh theorized atmospheric nitrogen was mixed with another gas and their experiments successfully isolated an element that they named argon (Greek for argós, meaning "idle" or "lazy" because of its nonreactive characteristics). They now realized that an entire group of gaseous elements was missing from the periodic table. Ramsay also isolated helium for the first time while treating with acid and heating the radioactive mineral cleveite (an impure form of uraninite or $UO_{2)}$ Cleveite became the first known terrestrial source of helium, occurring from the alpha decay of uranium to helium over time. Helium becomes trapped, accumulating within the mineral's crystal structure. Cleveite was named after Swedish chemist Per Teodor Cleve (1840-1905). In 1895, along with Nils Abraham Langlet (1868-1936), they succeeded in isolating helium from cleveite at about the same time as Ramsay's discovery.

Ramsay suspected that there were additional inert gases filling the corresponding spaces above and below argon in the periodic table. Using the fractional distillation of liquid air method, he continued searching for new noble gases by separating liquid air into several components. In 1898, he discovered and named krypton (Greek for kryptós or "hidden"), neon (néos or "new"), and xenon (ksénos for "stranger").

In 1899, Ernest Rutherford (1871-1937) and U.S. electrical engineer Robert B. Owens

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(1870-1940) and simultaneously Pierre (1859-1906) and Marie Curie (1859-1906) observed a radioactive gas emanating from radioactive elements. In 1900, German physicist Friedrich Ernst Dorm (1840-1915) while studying radium's decay chain identified a radioactive gas naming it 'radium emanation.' In 1909, Ramsay and English chemist Robert Whytlaw-Gray (1877-1958) determined radon's physical and chemical characteristics, including density and melting temperature, proposing that radon was the heaviest among all known gases. Radon was originally named niton (Latin for nitens, meaning "shining"). In 1923, The International Union of Pure and Applied Chemistry (IUPAC) named it as radon.

In 1902, Mendeleev (who's original 1869 periodic table had only seven groups) accepted evidence for the existence of helium and argon and included them as an eighth group (Group 0) in his periodic table. In 1904, Rayleigh and Ramsay went on to receive the 1904 Nobel Prizes in Physics and in Chemistry, respectively, for their noble gas discoveries; President of the Royal Swedish Academy of Sciences, J. E. Cederblom remarked that…: "the discovery of an entirely new group of elements, of which no single representative had been known with any certainty, is something utterly unique in the history of chemistry, being intrinsically an advance in science of peculiar significance".

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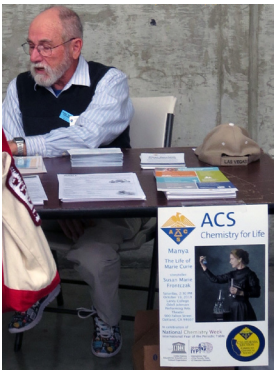
students free of charge. This West Contra Costa Unified School District school was chosen because of the very diverse nature of the 7th and 8th grade student body, and because it is the only school in El Cerrito named after an individual of Asian background — Presidential Medal of Freedom winner Fred T. Korematsu. Since much of Marie Curie's life history involves attempts to achieve freedom in accessing education, in speaking her native language (Polish), and in obtaining proper research facilities, this site was most suitable to mesh the natural school themes with the lessons of the show's main character. Over 700 students viewed the program in morning and afternoon assemblies held in their multipurpose room on October 17.

The importance of exposing young students to Curie's story was emphasized by a startling interaction before the performance at Laney: Elaine Yamaguchi talked to a male in his late thirties who had never heard of Marie Curie. He was curious about the event posters and what was going on at the theater, though he eventually decided on a walk around the lake instead. Although it was clear he was not a scientist, it seems strange indeed that anyone living on the same planet as the rest of us could not have heard of Marie Curie! No matter what these Korematsu middle schoolers become as adults, they will have learned the facts of Marie Curie's life and the obstacles she faced and overcame.

Nicki Davis, PhD



Natural GMOs" hype debunked
Details

Research has found (yet again) that horizontal gene transfer happens in nature – but it doesn't show GM is "natural" or safe, say scientists

"Many plants are naturally GMO, research finds", trumpets an article on the pro-GMO Cornell Alliance for Science website. It says, "Though much of the controversy around genetically modified crops is driven by the belief that the process of moving genes from one species to another is 'unnatural,' new research shows some 1 in 20 flowering plants are naturally transgenic.

"Dozens of plants, including bananas, peanuts, Surinam cherries, hops, cranberries, and tea, contain the Agrobacterium microbe — the very same bacterium that scientists typically use to create GM crops."But in reality, this research finding is neither new nor surprising. And contrary to the impression created by the article, the implications it has for GMO regulation are precisely zero.

The Cornell Alliance for Science article features a paper published in September in the journal Plant Molecular Biology. Researchers studied the genomes of some 356 dicot (flowering plants that have two seed leaves) species and found 15 naturally occurring transgenic species. “Thus, HGT [horizontal gene transfer] from Agrobacterium to dicots is remarkably widespread,” the authors stated. Horizontal gene transfer is the movement of genetic material between organisms, other than by the "vertical" transmission of DNA from parent to offspring.

The Cornell article suggests that the new finding should defuse much of the controversy around GM crops, on the basis that it shows that moving genes from one species to another is natural. The article goes on to mention a Danish scientist who has reportedly created a house plant using Agrobacterium, by an unspecified method, and believes that the plant should not be classified as a GMO.

New hype, old story. This is not the first time that GMO promoters have waxed lyrical about "natural" GMOs. A similar wave of hype was generated back in 2015, on the back of a research article announcing that the genome of a cultivated sweet potato contained gene sequences transferred from Agrobacterium through horizontal gene transfer.

The finding prompted a media article titled, “Genetically modified crops? Nature got there first: The sweet potato has been genetically engineered by bacteria”. The sweet potato finding is also cited by the new Cornell article.

In reality, however, the research finding regarding "natural" GMOs is, as we have said, neither new nor surprising, and there is nothing about it that would justify deregulating GMOs. We explained why in 2015 in the wake of the sweet potato finding.

But either GMO promoters’ memories are short, or they hope that if they repeat the same lies and half-truths often enough, people will come to believe them. So for their benefit, and that of anyone who is tempted to believe them this time round, here, once again, is the explanation.

Natural horizontal gene transfer consequences happen over evolutionary time

Scientists have known for years that horizontal gene transfer happens in nature as well as in GM. But the crucial difference is that in nature, HGT and its consequences are selected evolutionary timescales: that is, over hundreds, thousands, or even millions of years.

That's not to say that HGT in nature is "safe". Even in nature, HGT might cause potential negative consequences that are completely unknown to the scientists who wrote the recent study and to everyone else.

With this in mind, London-based molecular geneticist Dr Michael Antoniou commented on the new paper, "We don't know what effects these natural HGT events had on the plants themselves or on consumers of the plants. It could have been disastrous. What we are seeing are the survivors.

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"The authors say that this particular type of horizontal gene transfer (HGT) could play a role in plant evolution. But it could equally have played a part in plant devolution – such as an inherited decreased fitness.

However, the saving grace of such HGT events occurring over long co-evolution between plants and their human and animal consumers has been that any harms has been kept localised and limited. Humans and animals, as species, have had the time to learn which plants are safe to eat and which are toxic or otherwise dangerous.

But with GM, horizontal gene transfer is telescoped into an extremely short time period, and into a large global acreage of crops, without the benefit of co-evolution over long periods of time.

Irony

The irony of the latest PR messaging regarding the "naturalness" of genetic engineering is that originally, it was the critics of GM who originally flagged up the issue of HGT, pointing out that it meant genes deliberately introduced by genetic engineering into one organism might move into another by HGT. This concern was dismissed by GMO proponents, who, as Dr Michael Hansen, senior scientist at Consumers Union, noted below, either "denied that HGT happened or claimed it was unimportant".

Now the GMO proponents have adopted the reverse strategy and are hyping HGT as if it shows genetic engineering to be "natural" and safe i.e."Natural GMOs" and some how silenced the invading genes.

One crucial finding of the new paper has implications that have apparently gone unnoticed by the authors and the Cornell hypesters. This is that most of the so-called "naturally transgenic" plants that were found to contain Agrobacterium transgenes had actually inactivated those transgenes. As the authors state, "the majority have stop codons". A stop codon is a structure within messenger RNA that signals a termination of translation into proteins.

Dr Antoniou explained: "The transgenes were inserted as intact functional genes. But as the plant evolved, the genes picked up mutations (DNA damage) that inactivated them. So the transgenes are not producing any full-length Agrobacterium protein but rather a truncated product with no serious functional consequence in the affected plants. This inactivation may explain why the transgenes have been tolerated by the plant.

"Producing a genetically engineered plant in the laboratory is quite different. You insert a transgene(s) that is specifically designed to persist in the plant and express. Over the past few years this has been helped along by a genetic engineering procedure called codon optimization, which in some cases can lead to higher levels of transgene protein production.

"In addition, when you have your GM plant, you introduce it into an artificial environment – agriculture.

"But with natural HGT, the consequences are selected for over an evolutionary timescale and in a natural environment, which brings to bear very different pressures of survival. And in this natural environment, in the majority of the "natural GMO" plants studied in the new research, the consequences were inactivation of the invading genes. Perhaps the plants that did not manage to inactivate the transgenes did not survive. And we simply don't know what happened to humans or animals that consumed them.

"Thus, the new research does not show that either HGT in nature or genetic engineering in the laboratory is safe, either for the plant that is engineered or the humans and animals that consume it."

"GMO sweet potato" quotes still apply:

Here's what scientists told GMWatch in 2015 at the time of the sweet potato research publication and subsequent wave of hype. It equally applies to the latest PR messaging over the so-called "natural" GMOs.

Michael Hansen, senior scientist, Consumers Union, said:

"This paper validates what GMO critics have said all along: that horizontal gene transfer (HGT) is a potential risk of GM

and must be considered as part of the risk assessment – yet it misleadingly presents this fact as showing that GM technology is safe.

"Historically, GMO seed companies have denied that HGT happened or claimed it was unimportant, since they were arguing against having to look for any unintended consequences due to the insertional mutagenesis associated with HGT.

"Indeed, I wrote the report, 'Genetic engineering is not an extension of conventional plant breeding', in January 2000 to draw attention to the risk of unintended consequences due to the insertional mutagenesis associated with HGT.

"The US FDA explicitly recognized this risk in 2001, when it proposed requiring companies to notify the government at least 120 days before commercializing a transgenic plant variety and named insertional mutagenesis as potential problem: 'Because some rDNA-induced unintended changes are specific to a transformational event (e.g. those resulting from insertional mutagenesis), FDA believes that it needs to be provided with information about foods from all separate transformational events, even when the agency has been provided with information about foods from rDNA-modified plants with the same intended trait and has had no questions about such foods. In contrast, the agency does not believe that it needs to receive information about foods from plants derived through narrow crosses [in traditional breeding].'

"The notion that this natural engineering of sweet potatoes shows that GM technology is perfectly safe is false. Since we weren't around to document the early history of these sweet potatoes, we have no idea if they caused problems.

"Let's assume that the first 'natural' GM sweet potato, in addition to having some of the Agrobacterium DNA present, also, as an effect of insertional mutagenesis, caused a gene to be turned on that produced birth defects, sterility, or reduced fertility. As the further breeding occurred there would be variable levels of this particular toxin among sweet potatoes. People eating the sweet potatoes with high levels of the toxin would have fewer viable offspring, so the process of natural selection (the co-evolution of people and the food plants they are domesticating) would result in a shift toward decreasing the level of the toxin in sweet potatoes, due to the strong selection pressure against higher toxin levels.

"Since the Agrobacterium DNA has no direct link to the toxin, there would be no selection pressure to remove the Agrobacterium DNA.

"Similar arguments have been raised regarding GM golden rice. Golden rice needs to be evaluated to see if levels of retinoic acid (a known teratogen), or any other potentially toxic retinoids, have increased in golden rice as an unintended effect. GMO proponents have argued that if high beta-carotene levels could lead to high retinoic acid levels and increased birth defects, why haven't we seen such problems with people eating carrots, or other foods high in beta-carotene? The answer is that humans have co-evolved with their food plants over time, so that if there had been varieties of carrots that caused such problems, there would be negative selection pressure against those traits so the toxin level would decline over time. With golden rice, there has been no co-evolution, so that's why it must be checked for potentially increased levels of potentially toxic retinoids.

Dr Michael Antoniou said:

"Maybe Agrobacterium genes did insert into the sweet potato genome. But then the genetic alteration was selected for fitness, advantage, and crucially, food safety for humans and animals over evolutionary time. This does not happen with GM crops. And the discovery that Agrobacterium gene sequences have ended up in the sweet potatoes does not equate with the artificial combinations of DNA sequences that make up the GM gene units that are introduced into GM crops. So this natural event cannot be likened to GM technology."

Professor Jack Heinemann, University of Canterbury, New Zealand, said:

"This is an example of horizontal gene transfer (HGT). There is nothing unanticipated in this discovery because the process

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has been known to occur for decades and many other processes of HGT from bacteria to multicellular organisms have been demonstrated in the laboratory. So we've known for over a half century about HGT, even between kingdoms of organisms. Agrobacterium DNA in sweet potatoes isn't 'natural transgenics'; it's the outcome of a natural process.

"Ironically, especially in the 1990s many who were developing or selling GM crops attempted to minimise the frequency or effects of HGT. Indeed, they also tried to define it in ways that were so restrictive and unusual that it would be difficult to prove. When contradictions to this view inevitably appeared, it was reconstructed as evidence that HGT is common and therefore HGT from or to GM crops was no different than HGT from anything else. That somehow equated to it not being a new risk.

"The point is that when we move genes, we create organisms with no history of safe use and they should be tested for safety, consistent with international agreements. When people move genes into plants, we move constructs that we have pieced together from an average of 8 different species simultaneously. In my 25 years of work on HGT, I've seen no precedent for this kind of transfer so quickly. When HGT occurs in nature, nature has a chance to react, respond and adjust over many millennia to initially very small descendant populations. When we do it, nature is immediately bombarded by millions of hectares of new organisms in only a few years.

"Of course nature can also create organisms – by HGT or other means – that are capable of causing us harm. But that is no reason for us to do it unwittingly to ourselves. Nature can squash us with a rock from space, causing injuries indistinguishable from a car crash. This is not a reason to stop motor vehicle safety testing or recommend removing seat belts."

Dr Ignacio Chapela, associate professor, University of California, Berkeley, said:

There is nothing new here, and no surprises. We have known about this for almost forty years.

"What the authors of the new paper — and the reporters writing about it — claim as a surprise is based on the existence of a sequence incorporated over evolutionary time into the genome of a plant. This introgression implicated long processes of trial-and-error in a complex context which cannot be reproduced in the genetic engineering laboratory. The 'thing' resulting in the end may look similar, but the process and context through which that 'thing' came to be is what really matters.

"The people writing this paper know nothing about what processes led to the genomic transformation they encountered. They also know nothing about the processes (ecological, evolutionary, social) that these things may influence.

"They are content with describing the 'thing' instead of the process. At this level, they are right, just as defenders of crop genetic engineering are right when they make up true but irrelevant arguments to avert scrutiny of the safety of their work. They say, 'DNA is DNA is DNA', as if the chemical reality of the molecule was all that we needed to know — without acknowledging the role played by many other aspects, such as the DNA sequence.

"By this logic, a play by Shakespeare would be equivalent to an article in the tabloid press, on the grounds that both are made up of letters. But that would be nonsense. It is the sequence of letters, the words, sentences and paragraphs, and the context in which they are all placed that makes each work different from the other and lends a specific identity and function to each.

"This confusion between 'thing' and 'process' has been there all along since a policy decision was made in the US defining by decree and against reason that GMOs were 'substantially equivalent' to non-GM crops on the basis of their chemistry, not the biology of the transgenic manipulation."

Let's hope that this time, the scientists' message hits home and the Cornell Alliance for Science abandons this particular thread of deceptive reporting.

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