

Natural Selections

A NEWSLETTER OF THE ROCKEFELLER UNIVERSITY COMMUNITY

Inside the Science Research Program

DISAN DAVIS



SRP students gather to present their summer research to colleagues, friends, and family. Credit: Zach Veilleux

Through this summer's Science Research Program (SRP) here at Rockefeller University (RU), 57 high-school students got the opportunity to experience hands-on, cutting-edge science, working with graduate students, postdocs, and researchers. While there may be an impression that these students come from privileged backgrounds, 50 different schools were represented, with 30 percent of the students accepted into the program coming from disadvantaged backgrounds and 69 percent from public schools; half were women. The program also included three teachers from public schools around the city.

The director of the program, Ted Scovell, has taken extra measures to reach out to students from disadvantaged schools around the city in order to include more communities that might not be aware of an opportunity such as this. Other Rockefeller programs such as the Summer Neuroscience Program and Science Outreach Days have increased students' knowledge

of and excitement for this program.

Through an Internet survey of participants in the program from 1995-1998, the program has been able to follow up with about two-thirds of the students and found that 55 percent of them have entered a graduate program in a scientific field (M.D., Ph.D., M.P.H., or M.S.). While there is no control for what these students would have done without this research experience, it's clear that this opportunity was a stepping-stone for a new generation of smart, successful, scientifically minded people.

I had the unique opportunity to meet weekly with the three teachers who took part in the summer research program. In addition to doing research with a lab, they had the huge added challenge of simultaneously processing the concepts involved in their work and turning these ideas into fully established lesson plans for their classrooms. For example, we discussed the logistics of incorporating groundbreaking obesity research into a seventh-grade

class studying body systems, while simultaneously realizing that body systems is only one of about ten broad science topics to be covered in the seventh-grade curriculum... and that many of the seventh graders don't yet know how to use a ruler. The other teachers were in labs that prompted them to develop different lesson plans: one on the ethics of animal research in science, and the other on the fundamental chemical principles that underlie protein structure.

However, science is also about the process of asking a question, designing experiments, and analyzing the results for clues to lead us forward. How do we incorporate this fundamental, underlying concept into our science curricula?

Especially when we also want students to understand obesity, scientific ethics, and the importance of chemistry in life. I would love for students graduating high school to understand important scientific breakthroughs and the ways that science is relevant to our lives and to our world; but first, I want them to understand simply that science is fun, creative, and inspiring. After all, that's why we do what we do.

For the students, the culmination of the summer research program is a poster session where they share what they've accomplished with their mentors, peers, friends, and families. The excitement and pride on their faces demonstrates the joy and enlightenment they've experienced through the program. This program allows scientists, teachers, and students to bring together scientific knowledge and new discovery. I hope that science outreach programs similar to this model can continue to bring students closer to science as well as to bring more science into schools. ◊

Concert Review: Paul McCartney, Yankee Stadium, July 15, 2011

BERNIE LANGS

I had two great realizations about the music and the body of work of Paul McCartney during his incredible show at Yankee Stadium this summer. The first occurred early in the concert. I was overwhelmed at how beautiful the sound that was pouring through the massive space was. The rich harmonies and the textured instrumentation were the greatest sounds I'd ever heard in all my years of attending rock and classical concerts. McCartney opened with a Beatles tune, "Hello, Goodbye," and when he began to play songs from his solo oeuvre, I thought to myself, "I understand the solo years now. I finally understand." I had always joined the chorus of critics who felt that McCartney's genius had never been equaled after his years with The Beatles. *The New York Times* has been particularly cruel to McCartney in the last 40 years, once dubbing him a "marshmallow," and on another occasion describing his talents in such an unflattering way, I will not repeat it. (Ironically, the *Times* loved this concert.) When I heard the pulsating rhythm of the Wings's song, "Junior's Farm," I understood that McCartney has been all about the music all along: about the craft of rock and roll, about structuring a good solid tune, and about making it sound so very gorgeous for a crowd of people who want to be entertained. And he had succeeded with this in every aspect. I didn't even understand this when my own first band had performed that same song in 1974. It all made sense now, standing in Yankee Stadium, and I felt very much like a fool on a hill for doubting this consummate musician.

The Beatles had made it impossible for themselves because of the incredible heights to which they'd risen. I, too, placed them on a ridiculously high pedestal, believing that they played a large part in my having had such a fun childhood and being forever in their debt for teaching me, through osmosis, how to write a melodic pop song. I also believed that their music was the only artistic



Paul McCartney, 2010. Credit: Wikipedia

achievement comparable to Michelangelo's (roll over Beethoven). My second realization at McCartney's concert came towards the end of the evening, during a great rendition of a Beatles ballad, "Golden Slumbers." Of all the members of the Fab Four, it was McCartney who really was the one who believed the music came first, and that the image, the legacy, and the relationships within the band, were all secondary. The Beatles changed the world, but to expect their members to maintain that intensity and that importance past their years together is asking too much. John Lennon used to say to people who wanted the band to get together again something along these lines: "You want me to get back on the cross, just because you missed it the first time?"

As McCartney sang the song from *Abbey Road* that night, I felt his soul saying, "This is all I've ever wanted to do: to sing great music to people who want to enjoy it." It was McCartney who had been pushing the other Beatles to return to live concerts at the end of the days of The Beatles. John Lennon never had a solo tour (though he was mired for years in

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legal problems). George Harrison toured the states just once. Ringo Starr is closest to McCartney's spirit of playing live and has toured often through the years.

At Yankee Stadium, once McCartney had sung songs such as "The Night Before" and "Nowhere Man," I knew that the whole concert was going to be a delight and a joy for the ears. I just took it all in. He performed a total of 35 songs and played about a half dozen instruments without taking a break, for nearly three hours. One of the peaks of the show was his moving rendition of Harrison's beautiful song, "Something." McCartney's on-stage banter was also quite funny and lighthearted. He completely understood the mood of the crowd and kept it relaxed between tunes. You could feel the appreciation and the emotion of his audience as he crooned lovely ballads such as "I Will," "The Long and Winding Road," and "Blackbird." When he performed my favorite song, "Hey Jude," I fondly remembered hearing it for the first time in 1968 as a lad of eleven years.

McCartney closed the show with the final medley from the *Abbey Road* album. When he sang the famous last line, "And in the end, the love you take/Is equal to the love you make" I thought about all the joy that Paul McCartney has brought into the lives of so many millions of people throughout the world. That's quite a lot of love he's given. I was glad the audience was able to give some back. ◉

PDA Corner—The Retreat: Two Days of Science and Fun

ISABEL KURTH

It does not happen very often that we go to a conference where almost every talk is not from our field. It happens even less that we go to a conference where the average age of participants is 32 and where the quality of largely unpublished science easily matches—and sometimes even exceeds—the quality found at the conferences considered to be the best in the field. But once a year it does happen, as it did on August 3 and 4 during our postdoc retreat, held at the Ocean Place resort on the beautiful New Jersey shore. For two days, 96 postdocs left their normal bench routines and came together to share their research, learn about other people's work, and, well, socialize. As small as Rockefeller University (RU) is, it often seems that meeting one another is not that easy—unless one spends every night at the faculty club and runs from one campus party to the next. This year, we were especially excited to have several outstanding scientists join us for the retreat. We were joined by Marc Tessier-Lavigne, our new president; Nina Papavasiliou, professor at RU; our keynote speaker, Tom Maniatis, professor at Columbia University; and Shaun Muthian, Director of the Center for Therapeutic Innovation at Pfizer. They all interacted, mingled, and socialized with us in a very relaxed atmosphere.

As always, high-quality science was the centerpiece of the retreat—we had fourteen excellent talks across many areas spanning immunology, structural biology, virology, cancer biology, and neurobiology. There was something new to learn for everyone. Three of the best talks were rewarded with Amazon gift certificates, which were well deserved. The first prize of \$150 went to Nicholas Stavrapoulos, from Mike Young's lab, for his talk on "insomniac," a newly discovered mutant in *Drosophila*. "Insomniac" animals only sleep the equivalent of two to three hours per day, as compared to a human time scale. Nick showed that "insomniac" is regulating sleep in neurons through a pathway distinct from the circadian clock, but one that involves a protein degradation mechanism. The second prize of \$75 went to John LaCava, from Mike Rout's lab. John developed a strategy to purify affinity-tagged protein complexes in a 96-well plate set-up, where purification conditions are varied systematically to screen for the optimal condition to re-

tain pure native protein complexes. The goal is to transition from extract to biochemistry within one hour. Patrick McGrath, from Cori Bargmann's lab, received the third prize of \$50 for his work on the regulation of dauer, a long-lived diapause in many species of *Caenorhabditis*. Using a quantitative genetics approach, Patrick identified a hotspot of microevolution in domesticated strains of *C. elegans* and *C. briggsae*. Mutants in two chemoreceptors that sense one of the pheromones driving dauer formation have been repeatedly fixed in strains grown at high-density.

While many scientists are famous and well known beyond their fields, few reach the fame of this year's keynote speaker. Without his pioneering work in developing tools for molecular biology, biomedical science probably would not be where it is right now. The biggest impact that Tom Maniatis might have made on all of our lives was through his book, *Molecular Cloning: A Laboratory Manual*, which belongs in any lab as much as a centrifuge or PCR machine does. It was a great honor to have Tom Maniatis join our retreat.

His charismatic lecture on the generation of single-cell diversity in the brain showed us how his work has been constantly evolving through solid science and through an interest in fundamental questions. These days, his focus is on the mechanisms of transcription and RNA splicing in the nervous system and how they relate to neuronal connectivity and neurodegenerative diseases.

The first intense day ended with a relaxing reception on the terrace of the resort. The beach view and the

drinks definitely made up for the many hours spent in the packed seminar room, and helped to transition from science to social. The dinner was followed by a trivia game and some happy hours of dancing and drinking. If it hadn't been for the rain, more people probably would have continued their night in the ocean but the Jacuzzi wasn't a bad option either for those who didn't want to sleep yet.

The second day started with a generous brunch buffet to get everyone back into gear before moving to the morning sessions. Talks competed with the sun and the beach for participants, but as the morning proceeded, the seminar room filled up. After lunch,



we concluded the scientific part of the retreat with a lively panel session with our guest speakers on “The Future of Scientific Collaborations.” According to Tom Maniatis, science has changed since his generation started out. Collaborating is becoming a bigger part of science, and he encouraged our group to engage collegially. “Sometimes you have to give up something in order to advance in science,” he said, addressing the fact that collaborations also lead to shared fame. Marc Tessier-Lavigne talked about his own experience collaborating, which played a big part in his discovery of netrins, a novel class of proteins involved in axonal guidance, setting up his career. When asked what the most important part of a collaboration is, he answered, “people, people, people.” He explained how important it is to work with someone whom you feel you can trust and with whom you share views and ideas on the project you are working on. According to Nina Papavasiliou, an important aspect of collaborations is communication. She encouraged us to share our ideas, concerns, and thoughts, with our PIs in particular. This approach will lay the groundwork for successful relationships in both present and future collaborations. A different angle on the topic was broached by Shaun Muthian, who talked about collaborations between academia and companies. The gap between the “good” and the “dark” sides of science has become smaller over the past years, with more research grants available from companies to support basic science, and more postdoctoral programs at biotech companies. A great example of this is the Center for Therapeutic Innovation, a new research concept that Pfizer has developed with the goal to establish partnerships with academic institutions,



Credit: Yingpu Yu

in order to accelerate drug discovery and development. Dr Tessier-Lavigne was excited about this new concept and supported the idea enthusiastically. We are all curious to see where the future will take us and how we will be a part of it.

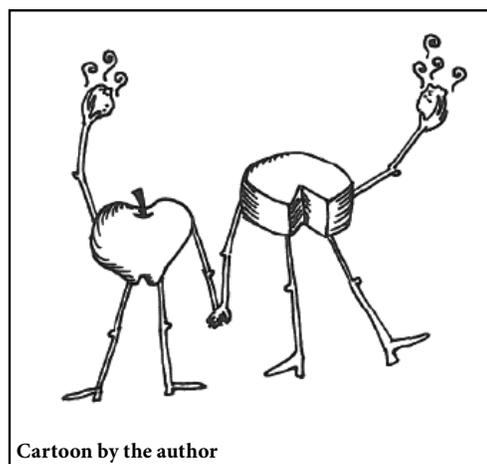
Everyone was looking forward to the last part of the retreat: free time. The water was warm enough; the volleyball nets were up and ready; and the weather was showing its sunniest side. These few hours passed rapidly and ended with tasty hamburgers and beer on the beach.

Thanks to everyone who came out for making this retreat a great success. We, at the PDA, look forward to seeing you again next year! ◊

Natural Confections

CARLY GELFOND

Let’s get one thing straight: I love this city. Really, I do. It’s a city like no other, a place where I can see a documentary about bodybuilders, then go eat dim sum on the second floor of a Chinese fashion boutique. There are plenty of reasons I love New York, but generally speaking, the weather isn’t one of them. I went to college in central New York, so I know things could be worse, but when I’m walking to the office mid-winter through



Cartoon by the author

inches of motor oil-glazed slush, I tend to get caught in the moment. Summer, too, is not for the faint of heart. I might liken the experience of descending into a New York City subway station in the dead of August to what a lobster might feel as it’s thrown

mercilessly into a simmering pot. So, if you’re anything like me, the morning you awaken to find your city at last (however briefly!) awash in a brilliant autumnal sheen—all cool breezes and acorns crunching underfoot—you can barely wait to get out of the house and revel in that hard earned blissful temperate comfort. Take to the streets! Head for the park! It will be winter before you know it.

Once the mercury has leveled off, if you’re looking for me, I’m probably at the farmer’s market, happily sampling pumpkin butters or deliberating over root vegetable empanadas. People, if you have never wandered beneath the glorious tents at a New York City farmer’s market in the fall, it’s time we had a chat.

Here’s why: collectively called the “Greenmarket,” this city’s outdoor urban farmer’s market network is incredible, having grown to become the largest of its kind in the country. New York is home to 53 markets, in which more than 230 family farms and fishermen participate, their goods coming from over 30,000 acres of farmland protected from development. Cruising the local farmer’s market is like taking a stroll around the tri-state area—the green, grassy parts, where your brussels sprouts and cheeses and milk come from. Behind the tables stacked high with the most gorgeous golden apples you’ve ever



New York State of Mind

This Month Natural Selections interviews Charles Gilbert, Professor, Head of the Laboratory of Neurobiology.
Country/State of origin: United States, NY

1. How long have you been living in the New York area? 28 years.

2. Where do you live? Brooklyn.

3. Which is your favorite neighborhood? In Brooklyn, Atlantic Avenue and Cobble Hill are great for finding a wide variety of restaurants and food markets; in Manhattan, SoHo, especially early on a weekday when the crowds haven't yet shown up.

4. What do you think is the most overrated thing in the city? And underrated? Underrated: the pleasure of just walking around the city; Overrated: street fairs—they're all the same, regardless of the neighborhood.

5. What do you miss most when you are out of town? The quality and variety of food.

6. If you could change one thing about NYC, what would that be? In the realm of when pigs fly, I'd like to have New York upgrade to a first class school system, with rebuilt schools, smaller class sizes, an advanced curriculum for math and sci-

ence, and the best teachers available. That would be expensive but would pay us back manyfold in the future.

7. Describe a perfect weekend in NYC. Getting up and out early, a bike ride around the green belt, exploring a new neighborhood and finding a great new restaurant.

8. What is the most memorable experience you have had in NYC? Discovering a lot of hidden and not so hidden gems—a tour of the Brooklyn Navy yard, including Steiner Studios, a park on a pier in Red Hook, the food carts on the soccer fields, the Boardwalk Empire set in Greenpoint, the waterfront by the Verrazano Bridge, the East River water taxi, the High Line, dinner at Per Se, dinner and opera at the Met, seeing Philip Bosco in *Copenhagen* on Broadway.

9. If you could live anywhere else, where would that be? In the mountains or on a cliff overlooking the ocean—in beautiful natural surroundings, though it would be

tough to be separated from the resources available in an urban environment.

10. Do you think of yourself as a New Yorker? Yes, though I've lived in many places, I was born in New York, and have lived here longer than anywhere else. Also, it has the best of everything—architecture, museums, music and theater, and, of course, food. ◉



Continued from page 4

seen, growers and purveyors are generally happy to tell you as much as you want to know, and—even better!—will typically let you sample the goods. Since the weather is fine, why not? Try an apple! Try some cheese! Could there be anything better than these?

APPLE AND CHEDDAR SCONES

Adapted from SmittenKitchen.com, originally tweaked from *The Perfect Finish*

Makes 6 scones

- 2 firm tart apples (about 1 pound), such as Granny Smith
- 1 ½ cups all-purpose flour
- ¼ cup sugar plus 1 ½ tablespoons for sprinkling
- 1 ½ teaspoons baking powder
- ½ teaspoon salt plus additional for egg wash
- 6 tablespoons unsalted butter, chilled and cut into ½-inch cubes
- ½ cup sharp white cheddar, shredded
- ¼ cup heavy cream
- 2 large eggs

Position a rack at the center of oven and preheat oven to 375 °F. Line baking sheet with parchment paper.

Peel and core apples, then coarsely chop them into chunks. Place them in a single layer on the baking sheet lined with parchment paper and bake them until they brown slightly and feel dry to the touch, about 20 minutes. They will be about half-baked. Let them cool completely. (You can speed this up in the fridge.) Leave oven on.

Sift or whisk flour, sugar, baking powder, and salt together. Set aside. Place butter in the bowl of an electric mixer with a paddle attachment (or, alternatively, use a hand mixer) along with cooled apple chunks, cheese, cream, and one egg. Sprinkle flour mixture over the top and mix on low speed until the dough just comes together. Do not overmix.

Generously flour your counter top and place the scone dough on top of it. Sprinkle with flour. Use a rolling pin to gently roll (or use your hands to pat) the dough into a 1 ¼-inch thick, 6-inch circle. Cut circle into 6 wedges. Transfer them to a baking sheet that has either been buttered or lined with a fresh sheet of parchment paper. Leave at least 2 inches between each scone.

Beat remaining egg in a small bowl with a pinch of salt. Brush the scones with egg wash and sprinkle them with the remaining tablespoon of sugar. (Be careful not to let the egg drip onto the baking sheet or it will burn.) Bake until firm and golden, about 30 minutes. With a spatula, lift scones to a wire rack to cool for 10 minutes. ◉

A Week That Was for the (Humming)Birds

JEANNE GARBARINO



A recipe for (hummingbird) success.

Given the incredible infrequency with which hummingbirds have graced my presence (I have seen this species a mere three times), I have always considered their appearance to be equally spectacular and special. However, as I sit typing this article, in the middle of the woods, in Maine, I am no more than four feet away from an attractive red feeder jar filled with simple syrup—one part water and one part sugar—and my ears are becoming intermittently fixated on the characteristic hum that gives these miraculous birds their name.

In an effort to try and describe the defining noise of a hummingbird, a member of the Trochilidae family, perhaps it would be appropriate to draw a parallel to a more familiar organism. As this bird whips by, I can only think of bees. More specifically, I imagine putting my ear to a mason jar filled with several bees, all buzzing in unison, except that the buzz emitted from the hummingbird is occasionally interrupted with the tiniest (and very cute) squeak.

Though one might associate a hummingbird with adjectives like adorable, pretty, and/or delightful (all very true), the biomechanics of hummingbird flight are actually quite impressive. In fact, the

aerodynamics of hummingbirds have been extensively studied, with some results featured in *Nature*, and despite their avian body plan, hummingbird flight is more akin to insect flight than bird flight. Because of their ability to rotate their wings in a circular fashion, hummingbirds generate a series of vortices in their wake—a phenomenon that has been documented using stereo-photography and helium-filled soap bubbles. This gives the hummingbird amazing versatility, allowing them to fly forwards, backwards, or side-to-side. Furthermore, these creatures are the only group of birds that can hover in mid-air.

But what puts the hum in hummingbird? This buzz is actually the result of the flapping of hummingbird wings. To be more specific, hummingbirds can flap their wings between 12 and 90 times per second (depending on hummingbird species). The maintenance of hummingbird flight is extremely demanding metabolically: the heart rate of

these birds can reach up to 1,260 beats per minute! Because of these huge energy requirements, hummingbirds must drink the nectar from hundreds of flowers per day. This probably explains why there were hummingbirds frequenting our sugar-filled feeder every few minutes, from dusk until dawn. Interestingly, when food is scarce, hummingbirds can enter a state of torpor—a hibernation-like status that is characterized by both slowed breathing and heart rate, thus reducing the need for food (nectar).

Speaking of nectar, hummingbirds have been categorized as “nectarivores” and the size of their beaks are closely related to the lengths of the flowers on which they feed, all suggesting co-evolution. Typically, hummingbirds are most attracted to flowers that are red, orange, and fuchsia, explaining why most hummingbird feeders are bright red. However, these tiny birds are able to see colors that fall into the near-ultraviolet portion of the light spectrum.

Although I spent a week watching this awesome avian species, seeing a hummingbird will still elicit a feeling of excitement, especially knowing just how incredible these tiny vertebrates really are. ☉



Capturing the Ruby-throated hummingbird was no easy task!



Going in for a drink. All photos by the author.

Historic Instrument of the Month: Lyman C. Craig's Countercurrent Distribution Machine

JOSEPH LUNA

Some machines, like the pH meter discussed in last month's issue, we primarily remember for their unit of measurement—that wondrous shorthand that is the culmination of arduous theory and experimentation. The history of science is peppered with such units brought on by great minds and new technologies, and it is often that their theoretical or their practical pioneers receive the honor of having these units named after them. Celsius, Ampere, Dalton, and Svedberg are but a few such names etched into the brains of practically any biomedical bench scientist. Yet while their names live on in text and in lab notebooks, there remains an encyclopedia of names that are defined less by a new “how” to measure than by a related and incessant doubt: “How do I know I’m measuring what I want to measure?”

The problem of separating and isolating specific substances from a mixture has been a central headache for chemistry since its modern start on Lavoisier's lab bench. For later nineteenth and twentieth century chemists inclined to think of biological molecules, this headache often turned into a migraine. For if an organism is composed of thousands of different nucleic acids, lipids, proteins and peptides, sugars, minerals, salts, and soluble ions, how is it even possible to conceive of isolating a pure and single type of molecule from such an extraordinarily complex mixture? (This seems one of those rare problems whose difficulty isn't easier to grasp with hindsight.)

More pressing concerns during WWII, however, propelled one chemist to make such a seemingly impossible task for small molecules a reality. In 1943, Rockefeller chemist Lyman C. Craig published a single-author paper outlining a method for the separation of complex chemical mixtures.¹ If an unknown mixture of interest were mixed in two known immiscible solvents, compounds in the mixture could be purified on the basis of how well they partitioned into one solvent or the other upon separating. If this mixing then separating were repeated sequentially, one could observe the unique distribution of each pure compound among the fractions, even if the compounds were highly related. Craig applied these techniques—later called Coun-

tercurrent Distribution (CCD)—to mixtures of the anti-malarial drug quinicrine (atabrine), which was then in use by the US Army in the Pacific. Using CCD, Craig was able to isolate microgram amounts of quinicrine from blood and urine samples of treated patients, and was, as a result, able to inform clinicians of the pharmacological profile of the drug for the first time.

That, of course, was only the beginning. From the late 1940s through the 1960s, Craig applied CCD techniques to purify and to analyze many other useful compounds,

ceed through up to 1000 separation cycles in a single run! Simple in theory, these machines were quite elaborate and technically impressive, and what is most striking is their apparent dynamism: they were meant to move. To see them operate must've induced a combination of awe and excitement at such wizardry; it is little wonder that the Craig lab on the sixth floor of Flexner historically had no shortage of interested post-docs and students.

In the end, you might be wondering why this technology didn't survive. Around the time Craig published his paper on what is essentially an extraction scheme from two liquid phases, a British pair of scientists proposed doing something similar though slightly different by immobilizing one liquid phase on a gel.³ Dubbed “partition chromatography” by their inventors A. J. P. Martin and R. L. M. Synge, this advance marked the beginning of modern chromatographic methods of separation (affinity, thin layer, high-pressure, etc.) and ultimately proved easier and more effective than Craig's labor-intensive technique. Martin and Synge would go on to win the 1952 Nobel Prize in Chemistry for their invention, an honor that, at first glance, makes Craig's 1963 Lasker Award appear prosaic. But this is not the case. As Stanford Moore wrote in Craig's biography for the National Academy of Sciences, “Craig always kept in mind the principle that methods are a means to an end and not an end in themselves.” For Craig, proper purification was just a starting step for further analyses, a theme evident in his bibliography of 300 or so papers. Whether it was an important chemical structure or a pharmacokinetic study of drugs or hormones, Craig's energy remained focused on biological problems that could be addressed with the methods of chemistry. And when no methods were available, he was fearless in designing newer, and seemingly magical, means of separation. ◊

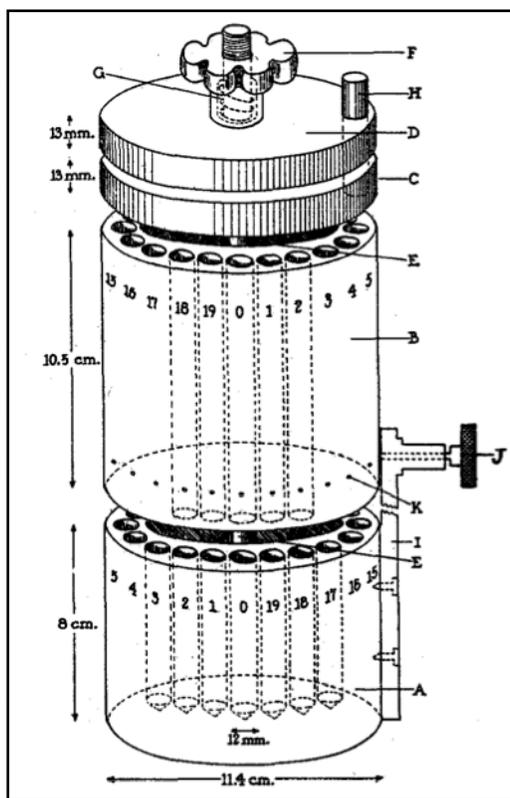


Figure 1, Craig, L.C. (1944) *J. Biol. Chem.* 155, 519-534

from the antibiotics gramicidin, tyrocidine, bacitracin, and various penicillins, to fatty and bile acids, to insulin and other hormones. Two of his famed CCD machines with which much of this work was done are on display in the museum in Caspary Hall. The original, a stainless steel cylinder with counter-rotating drums (Accession no. 39A), was built by Craig and his technician Otto Post, and allowed for twenty mixing and extraction cycles in a single run.² Later models (Accession nos. 39B; C) relied on intricate glass separation funnels that could be rocked such that a mixture could pro-

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