



Modeling reveals protein channel's function

KIMM FESENMAIER
Caltech Science Writer

Chemists at the Caltech have managed, for the first time, to simulate the biological function of a channel called the Sec translocon, which allows specific proteins to pass through membranes. The feat required bridging timescales from the realm of nanoseconds all the way up to full minutes, exceeding the scope of earlier simulation efforts by more than six orders of magnitude. The result is a detailed molecular understanding of how the translocon works.

Modeling behavior across very different timescales is a major challenge in modern simulation research. "Computer simulations often provide almost uselessly detailed information on a timescale that is way too short, from which you get a cartoon, or something that might raise as many questions as it answers," says Thomas Miller, an assistant professor of chemistry at Caltech. "We've managed to go significantly beyond that, to create a tool that can actually be compared against experiments and even push experiments—to predict things that they haven't been able to see."

The new computational model and the findings based on its results are described by Miller and graduate student Bin Zhang in the current issue of the journal *Cell Reports*.

The Sec translocon is a channel in cellular membranes involved in the targeting and delivery of newly made proteins. Such channels

are needed because the proteins that are synthesized at ribosomes must travel to other regions of the cell or outside the cell in order to perform their functions; however, the cellular membranes prevent even the smallest of molecules, including water, from passing through them willy-nilly. In many ways, channels such as the Sec translocon serve as gatekeepers—once the Sec translocon determines that a given protein should be allowed to pass through, it opens up and allows the protein to do one of two things: to be integrated into the membrane, or to be secreted completely out of the cell.

Scientists have disagreed about how the fate of a given protein entering the translocon is determined. Based on experimental evidence, some have argued that a protein's amino-acid sequence is what matters—that is, how

many of its amino acids interact favorably

with water and how many clash. This argument treats the process as one in equilibrium, where

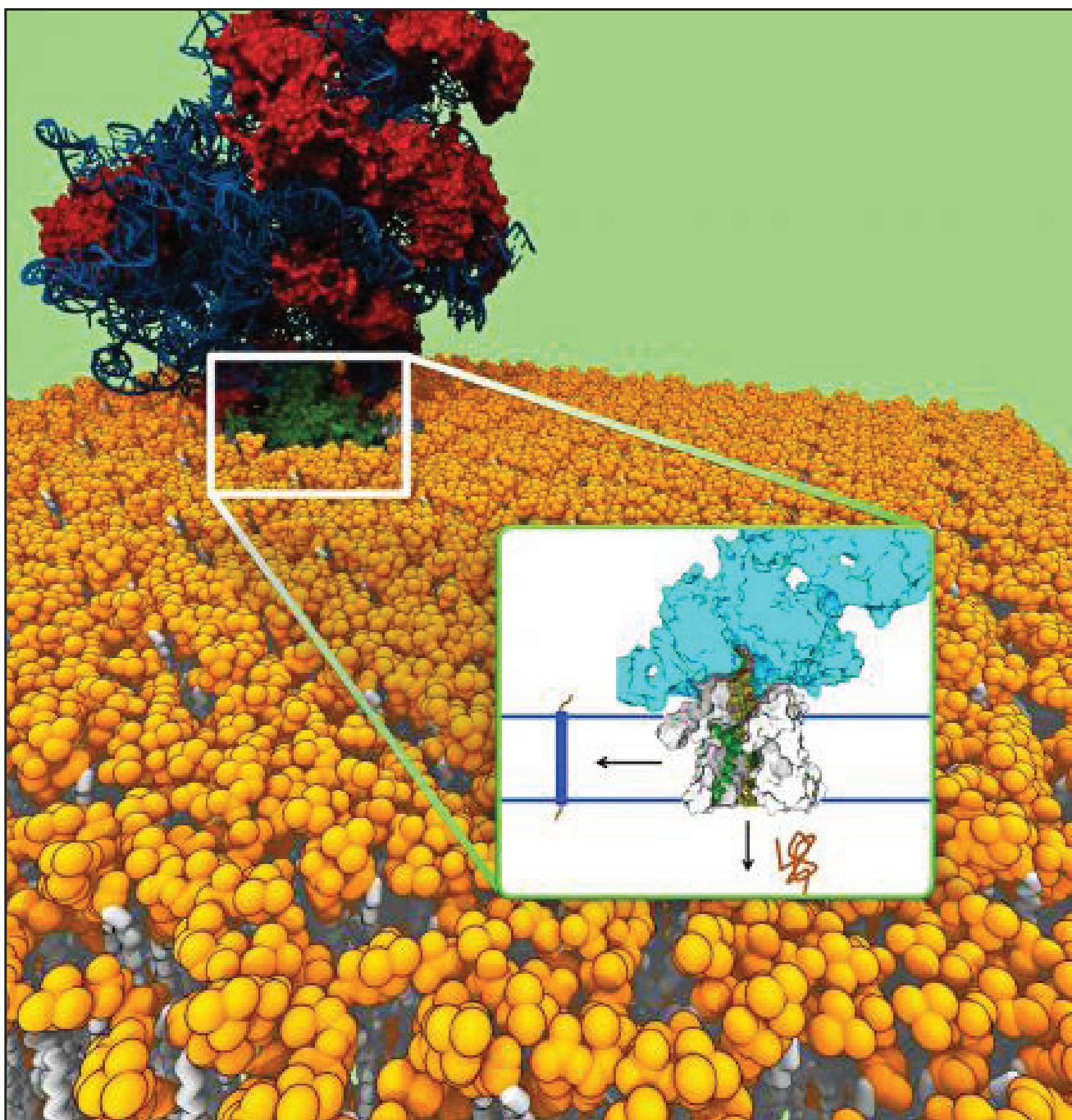
the extremely slow rate at which a ribosome adds proteins to the channel can be considered infinitely slow.

Other researchers have shown that slowing down the rate of protein insertion into the channel actually changes the outcome,

suggesting that kinetic effects can also play a role.

—Bin Zhang and Thomas Miller

Continued on page 3



The ribosome (red, blue) in complex with the translocon channel (green), which is embedded in the cell membrane (yellow, white). Proteins that are inserted via the ribosome into the channel can either be laterally integrated into or secreted across the cell membrane (inset).

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News briefs from around the globe

Helping readers burst out of the Caltech bubble

Need to know

< **100** words about the world this week – topics sorted from good to bad

by *The Tech Eds*

Jordan foils al-Qaeda plot **11** people arrested, targets included the U.S. Embassy in Amman [WP]

Ryan photo-op helps poor **\$11,000** raised for soup kitchen after original donors withdrew [HP]

Pope names new saints **7** chosen in attempt to revive Catholic faith among followers [FoxNews]

Castro makes appearance **86**-year-old former president of Cuba meets ex-VP of Venezuela [NYT]

Former senator dies **90**-year-old George McGovern served as a Dem in South Dakota [CNN]

Lebanese official killed **3** dead after bombing in Lebanon, US vows to help investigate [BBC]

Homicide in Wisconsin **4** dead and 4 injured in Milwaukee spa shooting, including shooter [CNN]

Food with Mannion!

Do you like eating food?

How about free food at nice restaurants?

Ever want to tell the world exactly what you think of said food?

The Tech will be beginning a new column to chronicle the foodie experiences of new writers every other week... The Catch: They'll be going head-to-head with Tom Mannion who will be reviewing the same restaurant. If you have ever thought you were more of a gourmand than our resident master chef, now's your chance to prove it!

Email us for a spot on the list at tech@caltech.edu

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ASCIT Minutes

Minutes for October 18th, 2012. Taken by Allika Walvekar

Officers present: Diego Caporale, Christian Rivas, Pushpa Neppala, Mario Zubia, Michelle Tang, Puikiei Cheng, Allika Walvekar

Officers Absent:

Call to Order: 8:41

President's Report (Diego): Diego would like to remind the student body that it is responsible for the upkeep of houses. Any damage accrued is reported to the deans. Diego would like to remind everyone that ASCIT meetings are open to the public, and this term they are at 8:30PM in SAC 15. If you have something specific to discuss email the secretary at sec@donut.caltech.edu so the topic can be added to the agenda.

Officers' Reports:

Secretary (Allika): Talked to DevTeam about an ASCIT Screening Room Reservation system on Donut. Designed a new poster for the Olive Walk with descriptions of the various BoD positions. Will be finalizing the design in the coming week.

Social Director (Michelle): Met with Big I reps to discuss their budget. Fall Harvest moved to 11/10. Dabney Drag Show, Fleming Frosh Party, and Page Interhouse are all coming up soon.

Treasurer (Puikiei): Continuing to fund for Big I. Puikiei will now approach Graduate Student Council (GSC), Student Affairs, and smaller companies with Caltech Alums for funding.

Director of Operations (Mario): Club funding will take place on 10/21. Clubs have to turn in their registration 10/19. The results of Club funding will be announced once club approval has finished. The assignment of the new club storage will be included in the club funding process. If the clubs absolutely cannot attend Club funding on 10/21, they can come to the ASCIT meeting on 10/25 instead.

V.P. of Non-Academic Affairs (IHC Chair: Christian): Rotation happened quite smoothly. The Deans received the statistics that compared freshmen's choices with the house they actually rotated in. Overall, most people were very satisfied with the house they were put in.

V.P. of Academic Affairs (ARC Chair: Pushpa): Interviewing frosh reps on 10/20. Pushpa would like to emphasize that the course complaint box should be used for specific, tangible issues that the student has towards a class, rather than general derogatory comments that are difficult act upon. Lucas Carreno has been reinstated to the ARC. Puspha is working with the alumni association to facilitate alumni feedback for the SFC.

Agenda for Thursday Oct 18 Meeting:
- ASCIT Meet & Greet

Meeting Adjourned: 9:54

Obituary: Farewell to delicious Dreyer's

North House ice cream machine spurts out its last frozen treat

JONATHAN WEBSTER
CDS Associate Director

North Kitchen Dreyer's Machine dispensed its last serving of soft-serve Friday

to some serious health issues, North Kitchen Dreyer's Machine moved to the warmer climate of the Caltech campus in 2007, working part time to pay for its room and board.

stopped making the tubes that fit this very special machine). Alas, North Kitchen Dreyer's Machine must cease its service to the world.

North Kitchen Dreyer's Machine leaves a legacy of cold

“

North Kitchen Dreyer's Machine was stubborn as a mule and strong as an ox. When one of its chambers blew out in an unfortunate ultimate Frisbee accident, it went on serving three flavors as though nothing was wrong.

”

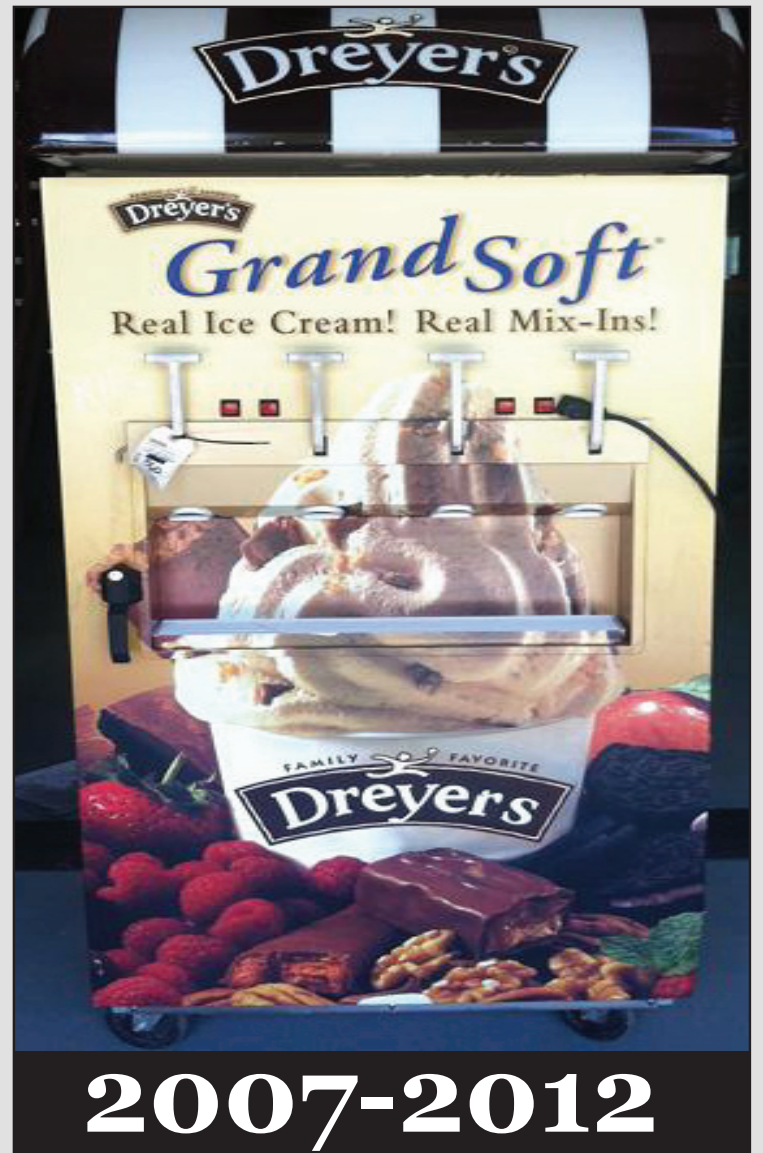
October 19, 2012. North Kitchen Dreyer's Machine was a stalwart in the Caltech community providing comfort and gastronomical bliss for at least five years. North Kitchen Dreyer's Machine was born sometime in the '80's and spent its formative years perfecting the art of dispensing softly frozen confections at JPL. Due

North Kitchen Dreyer's Machine was stubborn as a mule and strong as an ox. When one of its chambers blew out in an unfortunate ultimate Frisbee accident, it went on serving three flavors as though nothing was wrong.

Unfortunately, there is only so much soft-serve that an aging machine can dispense (no seriously...the manufacturer

deliciousness that would be hard for any machine to follow. However, after an exhaustive international (Google) search for a successor, Caltech Dining Services has found a suitable successor.

While we hope you will not immediately forget North Kitchen Dreyer's Machine, we hope that you will welcome Sani Serv Model 501 to the Caltech Community.



North Kitchen Dreyer's Machine will be missed by many.

- backpage.com

Caltech uncovers mechanism of translocon

Continued from page 1

“There was this equilibrium picture, suggesting that only the protein sequence is really important.

And then there was an alternative picture, suggesting that kinetic effects are critical to understanding the translocon,” Miller says. “So we wondered, could both pictures, in some sense, be right? And that turns out to be the case.”

In 2010 and earlier this year, Miller and Zhang published papers in the Proceedings of the National Academy of Sciences and the Journal of the American Chemical Society describing atomistic simulations of the Sec translocon.

These computer simulations attempt to account for every motion of every single atom in a system—and typically require so much

computing time that they can only model millionths of seconds of activity, at most.

Meanwhile, actual biological processes involving proteins in the translocon last many seconds or minutes.

Miller and Zhang were able to use their atomistic simulations

and to calculate how much energy it costs those parts to move in ways that allow proteins to pass through.

In this way, they were able to build a simpler version of the simulation that modeled important groupings of atoms, rather than each individual atom.

“There was this equilibrium picture, suggesting that only the protein sequence is really important. And then there was an alternative picture, suggesting that kinetic effects are critical to understanding the translocon. So we wondered, could both pictures, in some sense, be right?”

- Thomas Miller

to determine which parts of the translocon are most important

Using the simplified simulation, they could simulate the translocon's

activity over the course of more than a minute.

The researchers ran that simplified model tens of thousands of times and observed the different ways in which proteins move through the channel.

In the simulation, any number of variables could be changed—including the protein's amino-acid sequence, its electronic charge, the rate at which it is inserted into the translocon, the length of its tail, and more.

The effect of these alterations on the protein's fate was then studied, revealing that proteins move so slowly within the tightly confined environment of the translocon that the pace at which they are added to the channel during translation—a process that might seem infinitely slow—can become important.

At the same time, Miller and Zhang saw that other relatively fast processes give rise to the results associated with the equilibrium behavior.

“In fact, both equilibrium and kinetically controlled processes are

happening—but in a way that was not obvious until we could actually see everything working together,” Miller says.

Beyond elucidating how the translocon works and reconciling seemingly disparate experimental results, the new simulation also lets the researchers perform experiments computationally that have yet to be tried in the lab.

For example, they have run simulations with longer proteins and observed that at such lengths—unlike what has been seen with shorter proteins—the equilibrium picture begins to be affected by kinetic effects.

“This could bring the two experimental camps together, and to have led that would be kind of exciting,” Miller says.

The new Cell Reports paper is titled “Long-timescale dynamics and regulation of Sec-facilitated protein translocation.”

The work was supported by the U.S. Office of Naval Research and the Alfred P. Sloan Foundation, with computational resources provided by the U.S. Department of Energy, the National Science Foundation, and the National Institute of General Medical Sciences.

Caltech Couture: A day in the life of a Techer

NINA BUDAIEVA
Staff Writer

Several weeks ago I mentioned that Caltech has a very distinct sense of fashion.

Analyzing the subject further, I have come to the Eureka-worthy revelation that dressing is only a small fraction of a greater phenomenon found here.

Besides adopting a rather specific clothing style that sets Techers apart from the rest of humanity, the Techer community has evolved a new form of behavior that further secures its uniqueness.

Examples of this behavior may be observed in activities from mere walking to more complex patterns of social interactions. One word that summarizes this style: minimalism.

To a Techer, many things are all about efficiency, and walking seems to be one of these. When a Techer walks from his room to the C-store, he walks from point A to point B.

He does not look around, barely even looks ahead of himself and instead focuses on the ground one foot in front of the other as he makes his trek. When walking right up to the C-store entrance in this fashion and face-planting onto the glass door to read a note

politely informing him the store is closed for the next five minutes, the baffled Techer is at a loss. What is he to do?

Usually in such a situation, the Techer awkwardly sits down at one of the tables five feet away from the entrance and waits rigidly for the door to magically open.

If he came with a group, he might consider attempting casual small talk.

The situation is absolutely terrible. The C-store is closed, so the efficiency of his journey to the oasis is being decimated by the second!

He took the path of minimal length and minimal physical exertion, he refrained from saying hello to anyone he passed, and he didn't stop to smell the flowers blooming on campus.

He sacrificed all of these small joys in order to make his quest to the C-store as streamlined as possible.

And now, he must sit and wait!

What a waste, what a despicable waste! The Techer must now die of boredom.

What is he to do when his glorious plan of quickly attaining the booty and scurrying back to his room is interrupted by such a rude closing of the C-store? It was all for nothing.

The next day I see the same Techer, barely recovered from the previous night's C-store calamity,

the C-store. She kept him good company, for they were both suffering together.

To his surprise last night, he noted that he found her company agreeable and was almost sad that the C-store opened so quickly. Now he is not the type to fall for immature and misleading feelings

all. Oh math class ... It was such a great class!

Oh wait, math class! He is on his way to the library to check out a book, wait, which book? Ah yes! The hero has recovered from his dangerous daydream and is now in full possession of his \$50K-per-year-valuable wits. He strides on towards the library but doesn't notice that he fumbled and actually cracked his voice to say hi to the sweet girl that comforted him through the agony of last night.

Of course he never made eye contact with her. If he did, he would suffer the same fate as all of Medusa's victims and become a soulless stone-cold statue frozen forever.

No, he must be Perseus.

He must not fall victim to the wrath of Medusa and he must not look her in the eye. In fact, he must avoid her for he knows that if he looks her in the eyes, he will be done for. What will the world do without his brain?

No, he must walk on and check out that book. Then he must go back to his room and not think about the Medusas. He must not waste any energy on silly, uncomfortable things. That is not efficient. And the Techer marches on.

“

Besides adopting a rather specific clothing style that sets Techers apart from the rest of humanity, the Techer community has evolved a new form of behavior that further secures its uniqueness...One word summarizes this style: minimalism.

”

walking across campus. Always doing things with a purpose, the Techer is walking in order to check out a book from the library. He walks, or rather marches (for he is on a mission), past a girl he unwillingly met last night while suffering through the wait for

such as admiration, especially not admiration of girls! So it cannot be that he actually likes the girl.

He was teased very much in third grade for liking the sweet girl sitting in front of him in math class and he had learned his lesson about liking girly girls once and for

All Serious Physical Science Students
A must read

Foundations of Physics

By
Joseph M. Brown
Ph.D., Purdue University, 1952

- Starts with basic Newtonian particles
- Derives conservation of mass, momentum, and energy
- Derives Newton's equations of motion
- Shows why Maxwell-Boltzmann gas parameters v_r and v_m arranged as $[(v_r - v_m)/v_m]^2 = (\sqrt{3\pi/8} - 1)^2 = 1/137.1$ is fundamental to quantum mechanics
- Shows how neutrinos develop 10^6 newton thrust
- Proves that Newtonian particles can form stable inhomogeneous states – the neutrinos
- Shows why fundamental angular momentum has one value – $1/2$ Planck's constant
- Shows what produces the magnitude of the proton mass
- Shows how hydrogen is formed
- Shows what causes electric charge
- Derives the strong nuclear force
- Shows how matter motion is accomplished
- Shows what causes matter waves and magnetism
- Derives superconductivity
- Derives the neutron and what causes nuclear decay
- Shows exactly what a photon is
- Shows what causes gravitation
- Shows how atoms are formed
- Shows how stars are formed
- Shows why photons decay with travel
- Shows why matter we see was formed 10^{10} years ago

Other books by Dr. Brown

The Grand Unified Theory of Physics,
ISBN 9780971294462, 2004, \$29.95

The comprehensive unified theory showing what the neutrino structure must be

The Chemistry and Mechanics of Human Aging,
ISBN 9780971294486, 2008, \$19.95

An increment of torsional strain is induced in DNA at each division – probably the cause of aging.

Photons and the Elementary Particles,
ISBN 9780971294455, 2011, \$29.95

The detailed structure of the photon is derived.

The Neutrino,
ISBN 9780971294479, 2012, \$29.95

Finally a rigorous proof is obtained of the neutrino structure which is a counter example to the second law of thermodynamics. The neutrino is a translating tornado-like stable flow pattern.

Principles of Science,
ISBN 0-9626768-0-2, 1991, \$39.95

Language and mathematics foundations are derived. Also an outline of a unified science theory is presented.

See the destruction of age-old misconceptions of the Universe

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Caltech Library
library.caltech.edu

The screenshot shows the Nook app interface for Caltech Library. At the top, it says "Read all your newstand favorites" and "nook by Barnes & Noble". Below that, there's a navigation bar with "library", "Most Recent", and a grid icon. The main content area is titled "Magazines (13)" and displays a grid of magazine covers including Newsweek, The New Yorker, U.S. News Weekly, The Economist, TIME Magazine, and Popular Mechanics. At the bottom, there's a search bar and a call to action: "Check it out @ SFL • 72 hours • Full Color".

SIEMENS | Foundation



The Siemens Competition in Math, Science and Technology is coming to the California Institute of Technology!



The Siemens Competition takes great pleasure in inviting you to the following events:

Student Project Exhibition (Refreshments will be served)

Date: Friday, November 9, 2012
Time: 5:00 pm – 6:15 pm
Location: Dabney Lounge Dabney Hall
Pasadena, California 91106

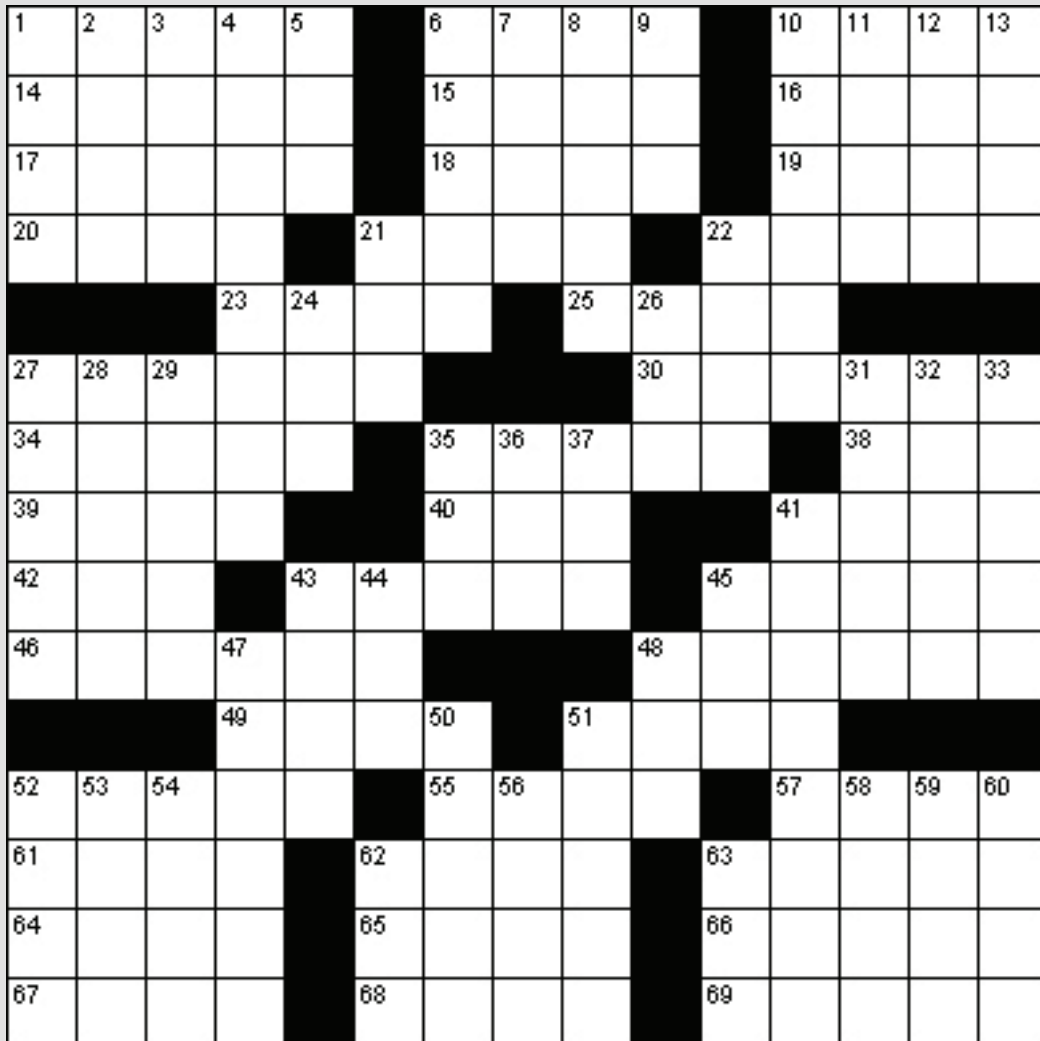
Student Oral Presentations

Date: Saturday, November 10, 2012
Time: 8:15 am – 1:15 pm
Location: Ramo Auditorium
Pasadena, California 91106

Please RSVP by Friday, November 2, 2012:
<http://tinyurl.com/SiemensCompetition2012>

www.siemens-foundation.org

Today's Puzzle: Crossword



[<http://www.puzzlechoice.com/>]

Across

1. Lariat
6. Exchange
10. Vessel
14. Change
15. Aura
16. Encryption
17. Gaze
18. Public violence
19. Part
20. Ripped
21. Ego
22. Card game
23. Requirement
25. Peel
27. Resuscitate
30. File holder
34. Selected as the best
35. Toward the stern
38. Anger
39. Prying
40. Breed of dog
41. Break suddenly
42. Appropriate
43. Aquatic birds
45. Taunt
46. Lacking lightness
48. Cask
49. Annul
51. Remedy
52. Equine animal
55. Plan

57. Small cut

61. Adjoin
62. Dread
63. British peer
64. Proboscis
65. Type of song
66. Worship
67. Cervid
68. Arrow
69. Regenerate

Down

1. Final
2. Singing voice
3. Leading actor
4. Peacefulness
5. Metal-bearing mineral
6. Tatter
7. Howl
8. Upward
9. Cooking implement
10. Gyre
11. Short swinging punch
12. Not in action
13. Look searchingly
21. Understand
22. Secret plan
24. The night before
26. Not in operation
27. Relating to the kidneys
28. Run away secretly to marry
29. Panorama
31. Currency of Tunisia
32. Wipe out
33. Repluse
35. Simian
36. Form of transport
37. Historic period
41. Sing and play for somebody
43. DNA segment
44. Conclusion
45. Seafarer
47. Cleaning material
48. Small rounded bread
50. Musical drama
51. Unit of weight for precious stones
52. Crew member
53. Woodwind instrument
54. Artifice
56. Den
58. Golf club
59. Center of an object
60. Was cognizant
62. Fashion
63. Saloon

*Caltech Public Events is now hiring student ushers.
\$15 per hour to work concerts, performances, lectures, films
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*For info on Caltech Public Events visit: [www.caltech.edu/
content/public-events](http://www.caltech.edu/content/public-events)*

Caltech volleyball ends losing streak



Rockin the always in fashion concussion head band, Caltech's Paige Logan obliterates a volleyball in front of an audience so stunned, they vanished into thin air

-gocaltech.com

gocaltech.com

PASADENA, CA – The Caltech women's volleyball team snapped a 56-match losing streak as they posted a 3-0 (25-16, 25-18, 25-13) win over Mills College. The Beavers last win came early in the 2010 season when they knocked off Mills.

Caltech came out of the gates strong as they grabbed a 14-1 lead in the opening set and never looked back in cruising to a 1-0 lead in the match.

The second set proved to be more of a tussle between the two schools. Caltech broke a 4-4 tie and nudged out to an 11-6 lead. However the Cyclones fought

back with a 3-0 scoring spurt to get within two points at 11-9. The Beavers wouldn't let the visitors get any closer as they scored nine of the next 12 points en route to taking the frame.

In the final set Mills took their first lead of the match when they won the opening point of the stanza. Caltech wouldn't let them

have another lead during the afternoon contest. Caltech went on an 8-2 scoring spree to take a five point advantage at 8-3. Mills got their deficit down to two points at 11-9 but couldn't pull any closer as the Beavers took the triumph.

Paige Logan had match high 17 kills and a .577 hitting percentage. Her hitting mark was a season high

while her kills total was her second best tally on the year. Catherine Jamshidi chipped in a nine-kill performance while Megan Jackson played solid along the back row with a 12-dig effort.

As a team the Beavers had 35 kills on 82 swings while committing just seven errors en route to hitting a season best .341.

From the desk of the sports editor: Opposing fans and why they suck

AMOL KAMAT
Sports Editor

Maybe because I've been here too long and have started entering that "creepy senior grey area," I've started noticing other people's conversations a lot more. I know that sounds bad, but bear with me. My favorite targets are opposing fans at Caltech sporting events. Last week, I talked about a woman and a comment about a banana, which was all in good fun, as I think she was aware of how ridiculous she was (although, you never know with some of those SCIAC parents). But, not all fans are so good-natured.

For example, this Saturday, the Caltech soccer team played at Chapman, losing 2-0. I've heard my fair share of taunts (I almost got into a fight during a high school tennis tournament, which, by the way, is one of the least manly places to fight someone), but some

of the things these fans were saying actually got to me. I don't think I'm allowed to print most of their comments.

I'm perfectly fine with jeering at an opposing team. At soccer, basketball, and volleyball games, even we seek out strange names and hometowns. But, when you make fun of a team for allowing girls to play and use pretty bad adjectives to describe said female, even I get offended. As much as I hate the "Yeah, well at least we go to a real school and are gonna be super rich" cheer, I think it would have been fine to pull out against Chapman.

Now, I know we're not perfect fans, either (although now that certain seniors have graduated, I think we've toned it down a bit), but I like to think we keep things in check (Evan Zhao excluded, of course). My point is, SCIAC sports should be fun, and cheering for your DIII school should be

fun, but when OH MY GOD THE NORTH KITCHEN ICE CREAM MACHINE IS DEAD?! WHY IS THIS HAPPENING TO ME?! DO THEY SERIOUSLY EXPECT US TO LIVE ON REGULAR PLAIN OLD VANILLA SOFT SERVE FROM THE SOUTH KITCHEN?! YOU KNOW, THE ONE THAT ONLYWORKS5%OFTHETIME?! GOD, EVERY TIME I THINK THINGS ARE PICKING UP HERE, SOMEBODY JUST KILLS AN ICE CREAM MACHINE OR POOPS IN A DRYER. THIS IS WHY WE CAN'T HAVE NICE THINGS, BECAUSE THE MAN DOESN'T WANT US TO HAVE NICE THINGS. I DON'T EVEN REMEMBER WHAT I WAS RANTING ABOUT BEFORE. THIS IS THE ONLY THING I'VE EVER CARED ABOUT EVER. I DON'T EVEN oh, wait, oh. I guess we're getting another one. Is that true? I think that's true. I—I don't...ok.

Weekly Scoreboard

Men's Soccer
at Chapman
L, 2-0 Final

Women's Volleyball
vs. Mills
L, 3-1 Final

Men's Water Polo
vs. La Verne
L, 13-10 Final

Women's Volleyball
at Chapman
L, 3-0 Final

Women's Volleyball
vs. Mills
W, 3-0 Final

COKE ADVENTURE

BY NICK J GREICKLER



Nominate your favorite professor for the Feynman Teaching Prize!

Here's your chance to nominate your favorite professor for the 2012-13 Richard P. Feynman Prize for Excellence in Teaching! You have from now until January 2, 2013 to submit your nomination package to the Provost's Office to honor a professor who demonstrates, in the broadest sense, unusual ability, creativity, and innovation in undergraduate and graduate classroom or laboratory teaching.

The Feynman Prize is made possible through the generosity of Ione and Robert E. Paradise, with additional contributions from an anonymous local couple. Nominations for the Feynman Teaching Prize are welcome from faculty, students, post-doctoral scholars, staff, and alumni.

All professorial faculty of the Institute are eligible. The prize consists of a cash award of \$3,500, matched by an equivalent raise in the annual salary of the awardee. A letter of nomination and detailed supporting material, including, but not limited to, a curriculum vitae, course syllabus or description, and supporting recommendation letters should be directed to the Feynman Prize Selection Committee, Office of the Provost, Mail Code 206-31, at the California Institute of Technology, Pasadena, California, 91125. Nomination packages are due by January 2, 2013.

Additional information including guidelines for the prize and FAQ may be found at <http://provost.caltech.edu/Feynman-TeachingPrize>. Further information can also be obtained from Karen Kerbs (626-395-6039; kkerbs@caltech.edu) in the Provost's Office.

*For more photos,
videos, and archives
of previous issues,
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