An appreciation of genius

The Calculus Gallery by William Dunham introduces the major contributors to the growth of this mathematical branch

S ANANTHANARAYANAN

Calculus is a mathematical technique, taught in high school and largely mastered by the time a science student graduates, and it is now the basis and foundation of the physical sciences and technology. The present form of calculus, however, has come about with the work of many, since the 17th century, when Isaac Newton sowed its seeds, and the path by which it got here shadows the explosion in science since then.

The Princeton University Press has brought out a new edition of *The Calculus Gallery*, a 2005 masterpiece by William Dunham, from Bryn Mawr College in Pennsylvania. The author introduces the major contributors to the growth of calculus, and, like the history of art can be described by selected works of the masters through the ages, he explains each mathematician with classic pieces of the mathematician's work, which refined or grew out of calculus, all the way till the 20th century.

As Dunham says in a first "interlude" in the book, where he reviews the progress in the first century of calculus, calculus marked the transition, in perspective, from the geometric to the analytic. This is to say that the study of shapes and surfaces, even the path of the planets in their orbits, which were studied on the basis of Euclid, now moved to the abstraction of algebraic expressions. The paths of the planets had long been considered to be perfect circles, and Kepler, who showed they were ellipses, described the changing speed of the planet by areas swept out by the line from the sun to the planet. Galileo had studied the motion of a falling object, and arrived at a form of the equation of motion, but based on a geometric construction.

It was Isaac Newton who analysed the path of planets, or falling objects in terms of a relationship of position, speed and how they changed with time. And then the way the shape of a curve changed along its length, in terms of numbers and ratios. It was along this course of study that Newton developed the idea of the 'fluxon', or the instantaneous rate of change of a quantity that changed with time, like the speed of a falling body, not over a period, but at any instant. The idea could be adapted to other mutually dependent values, like the length of the circumference of a circle or the area, traced by a radius, for different angles through which the radius turns. This problem had been approached by the Greeks using geometric methods. But the method of fluxons permitted generation of a formula (the familiar, 2 pi r or pi r2, for the radius going all the way round).

With this method of dealing with smooth, or continuous changes, Newton was able to work out an analytical expression for the path of body that was in motion under a central attractive force, like a planet, and the data, and Kepler's results, showed that the force must be one that reduces by the square of the distance - the law of Gravitation.

While Newton is thus credited with discovery of calculus, the same method, with greater mathematical finesse, had been developed at the same time by the German philosopher, polymath, Gottfried Wilhelm Leibniz. Leibniz' versatility extended to history, jurisprudence, languages, theology, logic and diplomacy. When just 27, Dunham writes, Leibniz was elected to the Royal Society, for inventing a mechanical calculator that could perform all the operations of arithmetic!

The calculus that Leibniz developed was very much closer to calculus as we know it, to the extent of the notation, and was formally a method to examine the behavior of an mathematical function without the need to physically plot its values. And then, more clearly than Newton's way, to do the reverse, to identify a function, given its behavior.

Dunham goes on, before he takes the first interlude, to explain and provide samples of the work of Newton and Leibniz, the Bernoulli brothers, and then Euler, which covered almost a century from the time of Newton.

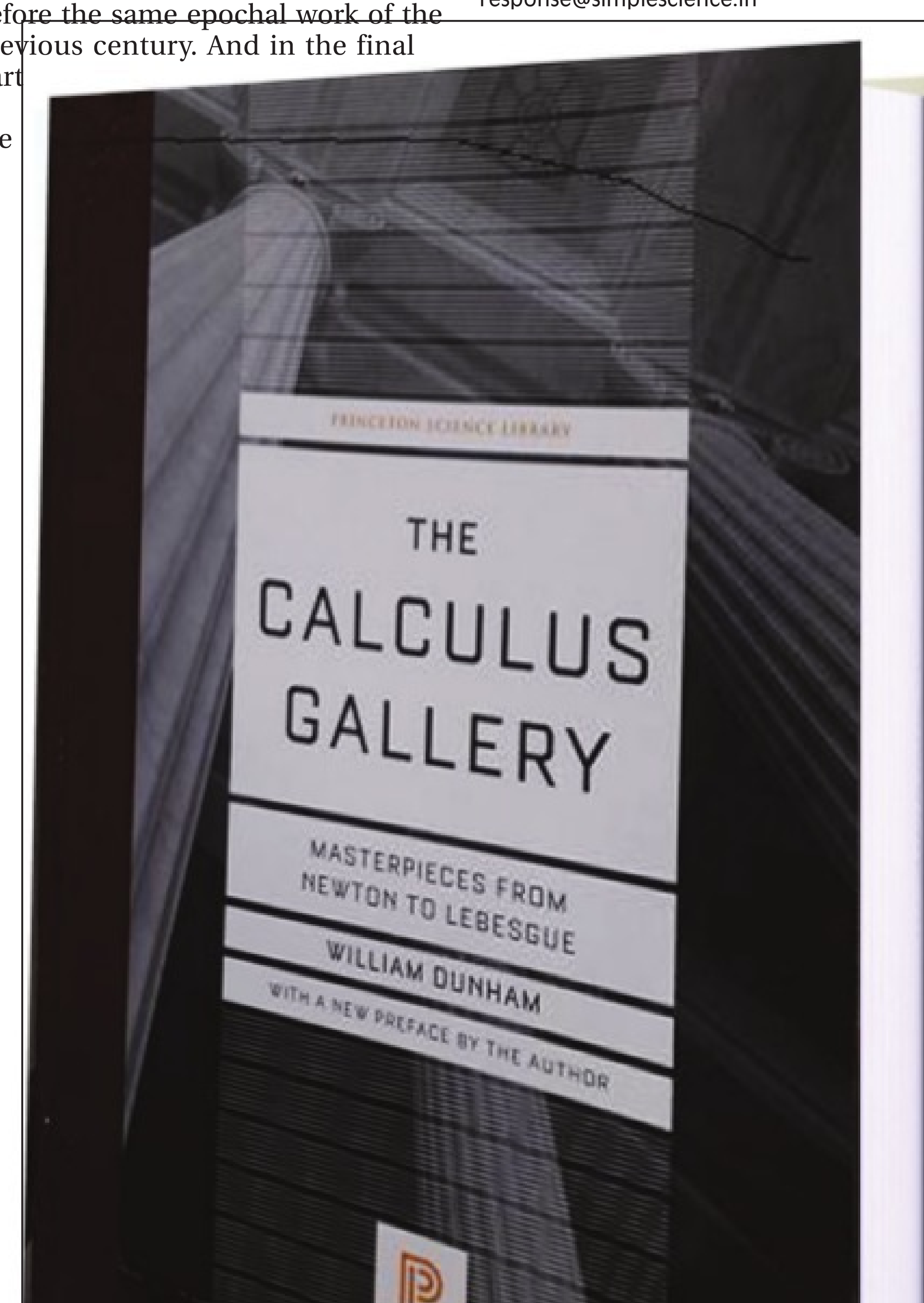
The work done during this period had first examined continuous processes as if they were step processes, which could be understood by conventional mathematics, and then by reducing the steps till they were 'vanishingly small'.

This computational device, of considering things that were 'infinitely small', was new and its validity was suspect. The process consisted of taking in hand a ratio, the ratio of changes in a pair of variables, and reducing, proportionately, the values of the numerator and denominator. As smaller and smaller changes are considered, the ratio approaches a final value, at which point, the numerator and denominator reduce to zero and vanish!

The approach invited attack and criticism. The Irish philosopher, George Berkley "ridiculed those scientists who accused him of proceeding on faith and not reason, yet themselves talked of infinitely small or vanishing quantities ,' Dunham says in the interlude.

Although Berkley did not dispute the results that calculus produced, he said the thinking was incorrect and "error may bring forth truth, but it cannot bring forth science." Capable mathematicians did their best to firm the foundations of calculus, but Berkley held the field and "the 18th Century ended with the logical crisis still unresolved," says Dunham.

Dunham then describes the work of Cauchy, Reimann, Liouville and Weierstrass, which did put calculus on robust conceptual bases, by the year 1873, nearly a century after Euler. The work, of "unprecedented care, taking pains to define their terms exactly and to prove results that had hitherto been accepted uncritically, succeeded in putting to rest the objections raised by Berkley and placed calculus on unassailable bases. And then, in the last quarter of the 19th Century, Dunham says, the work gave rise to questions that could not have been conceived before the same epochal work of the previous century. And in the final part of the book, Dunham describes Cantor, Volterra, Baire and Lebesgue.



Cantor went back to the basis of calculus, that ratios could be considered at the vanishingly small limit, and worked on the nature of fractional (called "real") numbers. He then brought about a change in the direction of analysis, by considering the principles of a grand generalization, the Set Theory, and 'small' and 'infinite' sets. The ideas were followed through by Voterra, Baire and Lebesgue, who "pushed analysis ever further towards generality and abstraction" and left the subject, as Dunham says, revitalised and the platform from which the advances in the 20th Century were launched.

In many disciplines, Dunham notes, there is a tradition of studying illustrious predecessors, like Shakespeare, in Literature or Bach, in music. As this tradition is not often seen in mathematics, his book, Dunham says, is an assembly of masterpieces that reflect the excellence that has gone before, and appreciation of genius.

The writer can be contacted at response@simplescience.in

Enabling protein synthesis

Only polypeptides with ER signal sequences can be inserted into or across the ER membrane as their amalgamation proceeds

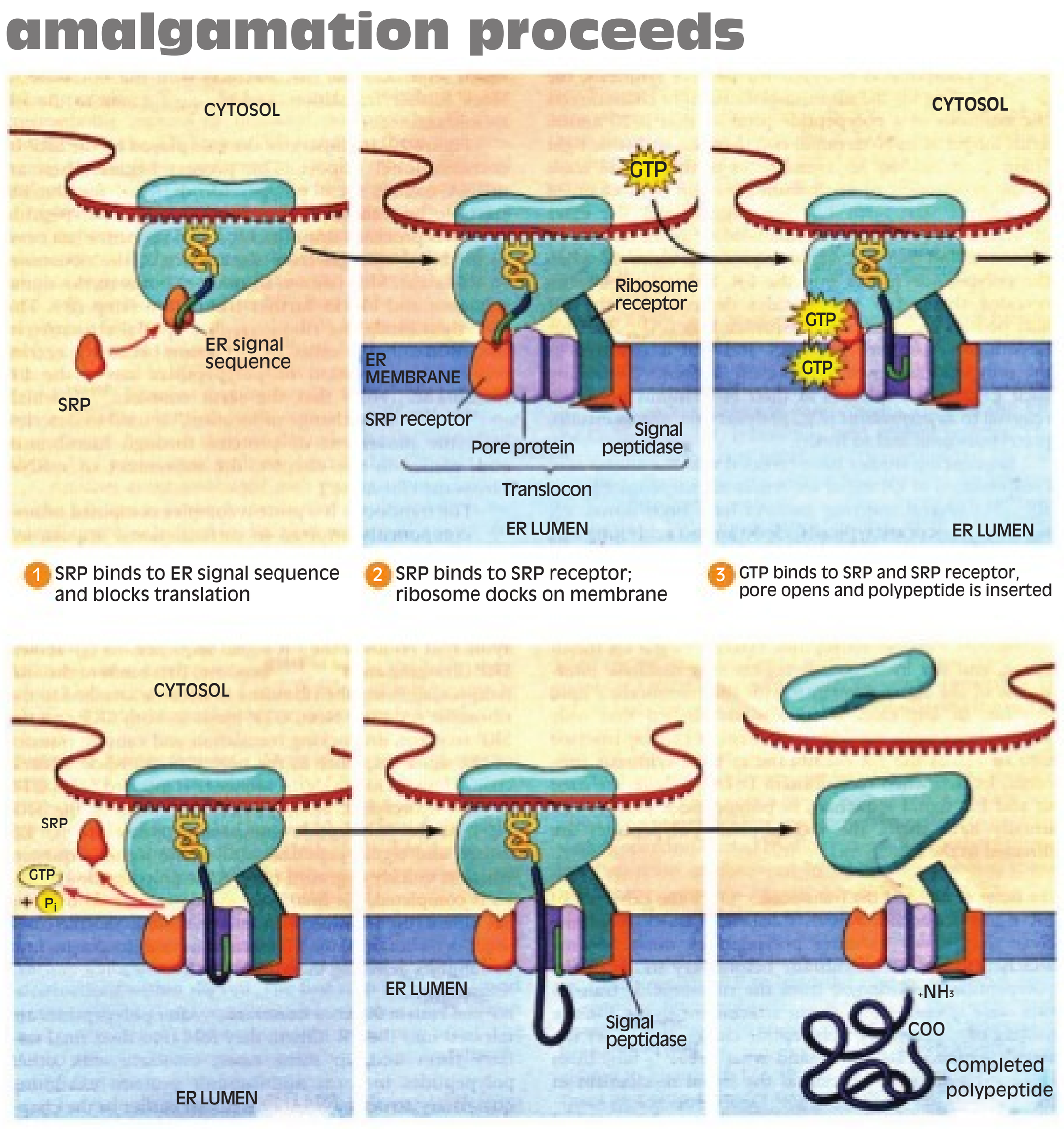


Figure B

TAPAN KUMAR MAITRA

The idea that the ER is involved in transporting newly synthesised proteins to various locations within the cell first emerged from studies by Colvin Redman and David Sabatini of protein synthesis in isolated vesicles of rough ER (ER vesicles with attached ribosomes).

After briefly incubating rough ER vesicles in the presence of radioactive amino acids and the other components required for protein synthesis, they added the antibiotic puromycin to halt the process. In addition to blocking further protein synthesis, puromycin causes the partially completed polypeptide chains to be released from the ribosomes. When the ribosomes and membrane vesicles were then separated and analysed to see where the newly made, radioactive polypeptide chains were located, a substantial fraction of the radioactivity was found inside the ER lumen. Such results suggested that some newly forming polypeptides begin to pass into the lumen of the ER as they are being synthesised, allowing them to be subsequently routed through the lumen of the ER to their correct destinations.

If some polypeptides move directly into the lumen of the ER as they are being synthesised, how does the cell determine which polypeptides are to be handled in this way? An answer was first suggested in 1971 by Güinter Blobel and David Sabatini, whose model was called the signal hypothesis because it proposed that some sort of intrinsic molecular signal distinguishes such polypeptides from the many polypeptides destined to be released into the cytosol.

This hypothesis has had such a profound impact on evidence that proteins synthesised on ribosomes attached to ER membranes pass directly into the ER lumen. ER vesicles containing attached ribosomes were isolated and incubated with radioactive amino acids to label newly made, polypeptide chains.

Next, protein synthesis was halted by adding puromycin, which also causes the newly forming polypeptide chains to be released from the ribosomes. The ribosomes were then removed from the membrane vesicles and the amount of radioactive protein associated with the ribosomes and in the membrane vesicles was measured.

The graph shows that after the addition of puromycin, radioactivity is lost from the ribosomes and appears inside the vesicles, suggesting that the newly forming polypeptide chains are inserted through the ER membrane as they are being synthesised, and puromycin causes the chains to be prematurely released into the vesicle lumen.

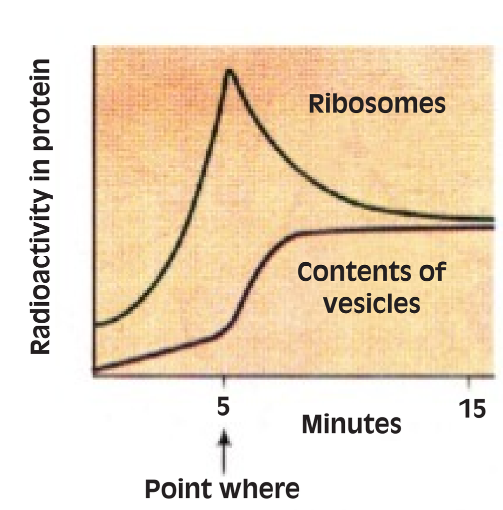


Figure A

The field of cell biology that Blobel was awarded the Nobel Prize in 1999 for his many years of work in demonstrating the validity and widespread relevance of the idea that proteins have intrinsic signals that govern their transport and localisation within the cell. The signal hypothesis stated that for polypeptides destined for the ER, the first segment of the polypeptide to be synthesised, the N-terminus, contains an ER signal sequence that directs the ribosome-mRNA-polypeptide complex to the surface of the rough ER, where the complex anchors at a protein "dock" on the ER surface.

Then, as the polypeptide chain elongates during mRNA translation, it progressively crosses the ER membrane and enters the ER lumen. Figure B shows a current model for the signal mechanism. It is now well established that the growing polypeptide translocates through a hydrophilic pore created by one or more membrane proteins. The complex of membrane proteins that carry out translocation is called the translocon.

Evidence for the actual existence of ER signal" sequences was obtained shortly thereafter by Cesar Milstein and his associates, who were studying the synthesis of the small subunit, or light chain, of the protein immunoglobulin G.

In cell-free systems containing purified ribosomes and the components required for protein synthesis, the mRNA coding for the immunoglobulin light chain directs the synthesis of a polypeptide product that is 20 amino acids longer at its N-terminal end than the authentic light chain itself.

Adding ER membranes to this system leads to the production of an immunoglobulin light chain of the correct size. Such findings suggest that the extra 20-amino acid segment is functioning as an ER signal sequence, and that this signal sequence is removed when the polypeptide moves into the ER.

Subsequent studies revealed that other polypeptides destined for the ER also possess an N-terminal sequence that is required for targeting the protein to the ER and that is removed as the polypeptide moves into the ER. Proteins containing such ER signal sequences at their N-terminus are often referred to as preproteins (e.g., prelysozyme, preproinsulin, pretrypsinogen, and so forth).

Sequencing studies have revealed that the amino acid compositions of ER signal sequences are surprisingly variable, but several unifying features have been noted. ER signal sequences are typically 15 to 30 amino acids long and consist of three domains: a positively charged N-terminal region, a central hydrophobic region, and a polar region adjoining the site where cleavage from the mature protein will take place.

The positively charged end may promote interaction with the hydrophilic exterior of the ER membrane, and the hydrophobic region may facilitate interaction of the signal sequence with the membrane's lipid interior. In any case, it is now established that only polypeptides with ER signal sequences can be inserted into or across the ER membrane as their synthesis proceeds.

In fact, when recombinant DNA methods are used to add ER signal sequences to polypeptides that do not usually have them, the recombinant polypeptides are directed to the ER.

The writer is associate professor and head, department of botany, Ananda Mohan College

PLUS POINTS

Reducing air pollutants

A rabbit gene has been inserted into common houseplants, giving them the power to filter toxic pollution from the air. Scientists hijacked a process that breaks down alcohol in the liver to create plants that could make ordinary households safer.

Homes accumulate small pollutants known as volatile organic compounds, produced by everyday activities and items ranging from smoking to furniture. These substances tend to be overlooked, but some, such as benzene and chloroform, have been linked with cancer.

To remove these pollutants, a team of scientists harnessed the power of genetic engineering and the ability of mammals to eradicate harmful substances using a naturally occurring protein. This substance is able to break down benzene and chloroform into harmless byproducts.

Known as 2E1, the protein is present in all mammals, including humans, but as it is found inside the liver and is switched on when processing alcohol it does not protect them from air pollution.

To achieve this, the scientists made a copy of the gene that codes for 2E1 protein in rabbits, and inserted it into the popular houseplant pothos ivy.

To test how their plants performed as living air filters, they placed them in glass tubes filled with potentially harmful household pollutants.

They found that within six days chloroform was virtually undetectable, while benzene levels had dropped by three-quarters after eight.

As a comparison, the scientists repeated the experiments with unmodified plants and found the concentration of these gases did not change at all over this period.

The results were published in the journal Environmental Science and Technology. As pothos ivy does not flower in temperate climates, the researchers reasoned that there was a low risk of their genetically modified creations spreading their pollen into wild populations.

Even unmodified plants can play a vital role in cutting other forms of air pollution, and "living walls" have been recommended for polluted schools in London to protect children.

The independent

Plunge for love

In the bird world, males often go to extremes to attract females through dance, colour and sophisticated home decor, for instance.

Hummingbirds are no exception. Broad-tailed hummingbirds (Selasphorus platycercus) fly up to 30m in the air before diving down towards a perched female, then climb up for a subsequent dive in the opposite direction.

At the Rocky Mountain Biological Laboratory in Gothic, Colorado, home to a population of breeding broad-tailed hummingbirds, researchers from Princeton University have been investigating how these tiny dynamos combine speed, sound and colour in their displays. Their work appears in the journal Nature Communications.

To explore how the different components fit together, and what a dive might look and sound like to a female, Hogan and Mary Caswell Stoddard, an assistant professor of ecology and evolutionary biology and the study's senior author, created video and audio recordings of 48 dives performed by wild male hummingbirds. They used image-tracking software to estimate each male's trajectory and speed throughout the dive, said Princeton University in a statement.

Using multi-angle imaging and an ultraviolet-sensitive camera, they created special photographs, which were combined with a model of hummingbird colour vision and details of the U-shaped flight path, allowing the researchers to estimate a female "bird's-eye view" of the male's iridescent throat feathers.

The straits times/ann