the line of sight AE i.e, the line joining it and the enemy ant (see *Figure 2*). It moves in a straight line along this direction until its path intersects the radial line OR, emanating from the centre O of the closed area, which is parallel to the initial line of sight AE. From here it continues in the same direction AR through a distance equal to it and reaches the new position A'. By this time the enemy ant would have moved to a different position E'. Now A locates the new line of sight A'E' and repeats the whole procedure. By successive applications of this method, the ant A can avoid the enemy ant E eternally. In the process A's own path will be a squiral, i.e, a spiral with successive line segments. More on this problem can be found in Ian Stewart's article in *Scientific American.*

Bruckstein's work not only sheds light on what is going on in the world of ants but is also useful in the world of robotics. We conclude from his work that globally optimal solutions for navigation problems can be obtained as a result of near neighbour co-operation between simple agents or robots. It is very expensive and technically difficult to make a single robot that can find the shortest path around obstacles. Instead of making a single sophisticated robot we gain considerably by making many simple robots. These can find the best path through a mere pairwise nearest-neighbour interaction.

Next time you seen an ant, approach it in all humility. It is not for nothing that the Bible says

Go to the ant, thou sluggard; consider her ways, and be wise.

(Proverbs 6,6.)

Long live the members of Formicidae.

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Hickory Dickory Dock

Molecular Clues to the Control of Circadian Rhythms

T R Raghunand

Most time keeping systems are based on the sun, reflecting age old patterns of human activity. For most practical purposes, according to our social contract, a day starts when the sun rises and ends when it sets. But the organisation of activity into day and night cycles is not merely an arbitrary agreement for setting clocks; it is also a biological imperative. (Recall Geetha's experiences in a timeless environment: ***Resonance*** Vol.1, No.3, 1996.) Most organisms - animals, plants and even microbes, have internal clocks that dictate daily or *circadian* (from the Latin *circa*, about, and *dies*, day) rhythms of a myriad life

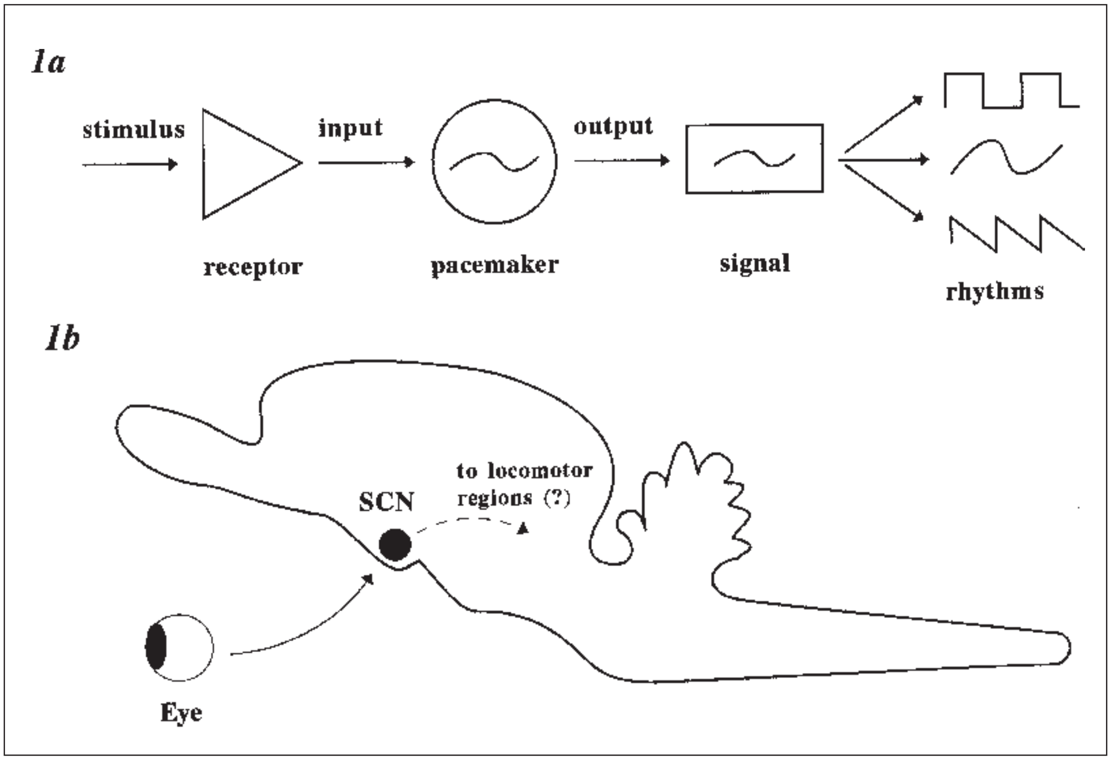


Figure (1a) Schematic representation of the three essential elements of a circadian system. (1b) In rats, the pacemaker is the suprachiasmatic nucleus (SCN) present in the brain.

processes like metabolic, cellular and reproductive activity as well as the sleep and wakefulness cycles. The biological clock, like the human artefact, follows the 24 hour cycle of the earth's rotation. Mice are most active at night, while most birds are active during the day. Bees visit the same flower at the same time each day. Photosynthesis in plants is not merely light driven, but follows a circadian rhythm, even when plants are exposed to constant light. Exactly how the internal clock keeps time is a mystery, as is the identity of most of the molecular wheels and gears that make it tick. Although the internal clock itself does not require environmental inputs to maintain a period of approximately 24 hours, light is an important criterion in synchronising that period with the solar day. All circadian systems therefore require at least three elements. First, a sensory pathway to receive cues from the environment. Second, a pacemaker or clock, that lies at the heart of the system, to generate the rhythm. Finally, an output pathway through which the pacemaker regulates the rhythms of organismal activity (*Figure 1a*).

As a general feature it appears that pacemakers help to anticipate the needs of the organisms through the cyclic regulation of specific

Early studies have indicated that the underlying mechanisms of circadian rhythms involve intracellular and biochemical processes .

target genes. Early studies have indicated that the underlying mechanisms of circadian rhythms involve intracellular and biochemical processes . Today it is clear that the activity of several genes in various organisms oscillates following a circadian cycle. One question concerns whether they oscillate as a consequence of a general circadian rhythm or whether they are responsible for it, and are therefore a part of the molecular architecture of the endogenous clock. The paramount questions are — how does the clock itself run, how is it reset, and how does the output regulate cellular activity?

In all organisms studied so far, there is a pathway that is sensitive to light. But the receivers of this cue are varied due to the anatomical diversity of systems. In most animals light hits the eyes, and the information is then transmitted to the appropriate region of the brain containing the circadian pacemaker. In single-celled organisms, light acts directly on photosensitive compounds, which in turn activate other cellular pathways. In many higher organisms a special pine-cone shaped structure called the pineal gland, is found very close to the surface of the head where it is exposed to light. It not only receives information about light but is also known to set the pace for circadian rhythms in certain fish, reptiles and birds .

The SCN has been identified as the pacemaker for mammals

In mammals, the pineal gland is buried deep within the centre of the brain and has lost its ability to be light sensitive. Its role in circadian rhythms has been superseded by a cluster of nerve cells located at the base of the brain called the suprachiasmatic nucleus (SCN). The SCN has been identified as the pacemaker for mammals where rhythms are both set and maintained. In rats, the SCN is believed to send a signal to the locomotor regions of the brain, where it determines periods of physical activity and inactivity (*Figure 1b*). Recent studies have shown that individual cells of the pineal gland of some birds and the SCN of mammals can maintain their rhythmic oscillations even when removed from the animal. One conclusion drawn from this is that each oscillating cell contains all the components necessary to maintain the rhythm, requiring no input from adjacent cells. Technically the oscillations are said to be 'cell autonomous'.

The Molecular Basis of Rhythms — Clues from the Fly

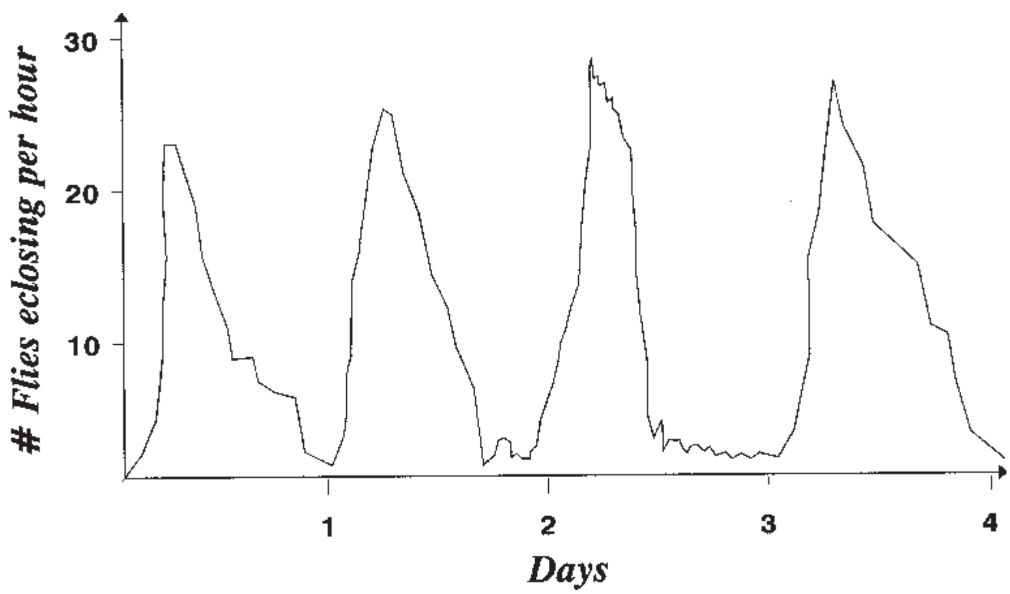
Molecular genetics is a powerful tool that has been used to identify key elements in the generation and maintenance of rhythms. In

(*per* and *tim* refer to the genes; *PER* and *TIM* refer to the proteins.)

Rhythms in Drosophila

Rhythms in Drosophila are primarily analysed by examining patterns of eclosion (emergence of adult flies from pupae) and locomotor activity.

The eclosion profile which shows a 24 hour period in wild type flies is depicted below graphically. (Data taken from Konopka and Benzer's Clock mutants of *Drosophila melanogaster*. *Proc. Natl. Acad. Sci.* USA, 68: 2112-2116 (1971).) In mutants (e.g per, tim) flies, this rhythm is altered (arrhythmic, short period or long period) (not shown).



the early 70's Ronald Konopka, a student of Seymour Benzer, in a pioneering genetic approach, identified a gene that controlled rhythm in the fruit fly *Drosophila melanogaster*. He named the gene *per* for period, since mutations in this gene upset the 24 hour cycle of the fly . For over 10 years since the gene was isolated, molecular biologists have been looking at its expression with the hope of understanding how a single gene controls circadian rhythms. Researchers studying the first step leading to PER protein synthesis, the production of messenger RNA (mRNA) by the gene, found that *per* activity cycled with a 24 hour period. Cycling seemed to be controlled in part by the PER protein itself, a phenomenon called *autoregulation*. As the levels of *per* mRNA increased, cells produced more PER protein, which then went into the nucleus and shut off its own gene. That caused the mRNA and protein levels to drop and eventually released the gene from its self imposed repression, allowing it to be active again. But this by itself couldn't constitute a clock since a pro-

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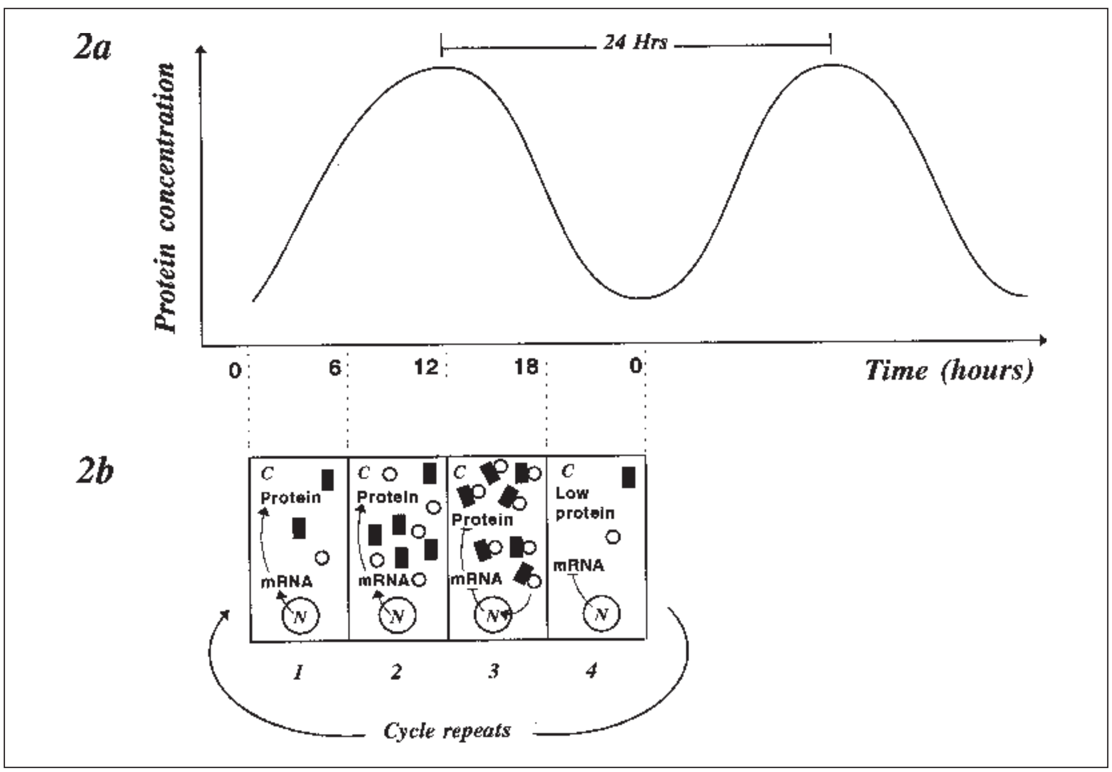
tein with an autoregulatory loop would damp out concentration swings, reaching some relatively constant level rather than end up cycling in an endless rhythmic fashion. A second player had to be involved to complete the puzzle.

Towards Completion of the Jigsaw

Yet another vital component of the clock was discovered in November 1995, marking one of the most exciting finds in clock research. Two groups of workers independently cloned a

Figure 2 Proposed model for creating a rhythm or oscillation based on recent experimental results in the fruit fly. (a) A graphical representation of cyclic variation in protein concentration against time. (b) The probable molecular events. N-nucleus, C-cytoplasm, PER protein, ▮ TIM protein ○. The concentration of proteins builds up (1 & 2); the two associate at a critical concentration and the dimers enter the nucleus to shut off their own synthesis (autoregulation), resulting in the decline of PER and TIM in the cytoplasm (phase 3); decreased levels of the proteins in the cytoplasm (phase 4). Absence of the PER-TIM dimer allows repression to be lifted, leading to the next oscillation.



Two groups of workers independently cloned a gene called *timeless (tim)* and showed that the protein made by this gene interacts with the PER protein

gene called *timeless (tim)* and showed that the protein made by this gene interacts with the PER protein (*Science* **270** :732-733, 1995). Sure enough its mRNA levels cycled up and down every 24 hours just like the *per* mRNA ! In addition, mutations in *per* upset *tim* mRNA cycling and vice versa, suggesting that under normal circumstances TIM and PER somehow work together to turn down both of their genes. To regulate the genes, PER apparently should first accumulate in the cytoplasm until something triggers its move to the nucleus. Moreover accumulation of PER and its subsequent migration into the nucleus of the cell seemed to be blocked in mutants lacking a functional TIM protein. All these findings led to the proposal that the binding of the two proteins to each other played a role in the timing of PER nuclear entry, and thus the circadian cycle itself. According to the model (*Figure 2*), the PER protein is relatively unstable when first made in the cytoplasm. As a result, the protein molecules accumulate slowly till they run into TIM proteins, being made at the same time. The proteins then bind one another, forming stable dimers that enter the nucleus. There they shut down the expression of their own genes in association with yet unidentified nuclear partners, and may affect other genes as well. The identification of these genes would be the next logical step in the quest to delineate the pathway by which rhythms are manifested.

As more clock components and more mechanisms become defined, and the field of circadian rhythms continues its demystification process, we may perhaps very soon be able to answer the eternal question: "What makes us tick?"

In addition to the fly, clock genes have been identified in a host of organisms such as the bread mould Neurospora (*frequency*), mouse (*clock*), and hamsters (*tau*), ushering in a revolution in clock research. As more clock components and more mechanisms become defined, and the field of circadian rhythms continues its demystification process, we may perhaps very soon be able to answer the eternal question: "What makes us tick?"

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Environmental Chemists Share the 1995 Chemistry Nobel Prize

An Honour for Unearthing the Secrets of our Ozone Roof

S Parthiban

> "The whole of my remaining realizable estate shall be dealt with in the following way: the capital, invested in safe securities by my executors, shall constitute a fund, the interest on which shall be annually distributed in the form of prizes to those who, during the preceding year, shall have conferred the greatest benefit on mankind."
>
> — *from the will of Alfred Nobel.*

The 1995 Nobel prize for chemistry to the trio — Paul Crutzen, Mario Molina and Sherwood Rowland — is the first chemistry Nobel for any environmentally related work. While the announcement came as a surprise to many, the Nobel committee had clearly adhered to the will of Alfred Nobel. By detailing the delicate balance that maintains the ozone layer and showing how human activity on the earth is perturbing it, "the three researchers contributed to our salvation from a global environmental problem that could have catastrophic consequences," reads the citation from the Royal Swedish Academy of Sciences.

Leaky Roof over the Living Room

Ozone (O_3), a molecule composed of three oxygen atoms, is found primarily in the stratosphere between 12 and 50 km above the Earth's surface. The formation of ozone from molecules of oxygen in the upper atmosphere is part of a cyclic series of chemical reactions that prevents the sun's ultraviolet (UV) radiation from reaching the earth. The steps are illustrated in the following mechanism, proposed by Chapman in 1930.

$$O_2 + UV\ (\lambda < 242\ nm) \longrightarrow O + O$$
$$O + O_2 + M \longrightarrow O_3 + M$$
$$O_3 + UV \longrightarrow O + O_2$$
$$O + O_3 \longrightarrow O_2 + O_2$$

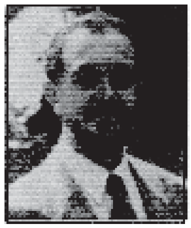
where M represents another molecule of oxygen or nitrogen that is unchanged in the reaction.

Why worry about the ozone layer? Without it human beings would suffer serious biological effects from solar radiation, including a large increase in the incidence of skin cancer and irritating eye disorders. Light-skinned people, especially children, are most at risk. Closer to the earth, however, ozone is a harmful pollutant that causes damage to lung tissue and plants.

Why worry about the ozone layer? Without it , human beings would suffer serious biological effects from solar radiation, including a large increase in the incidence of skin cancer and irritating eye disorders.

1995 Nobel Laureates in Chemistry

Paul J Crutzen (1933-)



Mario J Molina (1943-)

F S Rowland (1927-)

"the three researchers contributed to our salvation from a global environmental problem that could have catastrophic consequences."

After years of observation and experimentation, it seems clear that the ozone layer is affected by natural and man-made activities. Scientific measurements have documented a downward trend in the total column amount of ozone over mid-latitudes, as well as substantial ozone loss over polar regions during the spring seasons.

Theories to Explain the Ozone Thinning

Theoreticians came up with three competing models to explain the ozone depletion. One group of scientists blamed the 11-year solar cycle — the periodic waxing and waning of the sun's energy output. A second group suggested that natural changes in stratospheric winds were responsible. But a third theory held man-made chemicals as the culprits. The fast paced research of the last two decades proved that ozone in the stratosphere is removed predominantly by catalytic cycles involving gas phase reactions of active free radical species in the HO_x, NO_x, ClO_x, and BrO_x families.

Crutzen was instrumental in establishing the nitrogen oxide chemistry in 1970. The following year, Johnston made the connection between supersonic transport emissions and the ozone layer. Until then, it had been thought that the radicals H, OH and HO_2 (collectively called HO_x) were the principal catalysts for ozone loss. The next leap towards a better understanding of ozone chemistry was in 1974, when Rowland and Molina first suggested that chlorine from chlorofluorocarbons (CFCs) was destroying the ozone layer. At that time, several papers had been published indicating that CFCs were excellent tracers in the troposphere.

CFCs set the Chlorine Atoms Free

CFCs is the name traditionally given to the group of fully halogenated methanes. They were invented in 1928 as safe alternatives to ammonia and sulphur dioxide refrigerants. Rowland and Molina recognized that once CFCs are released into the troposphere, they will remain there until transported to the

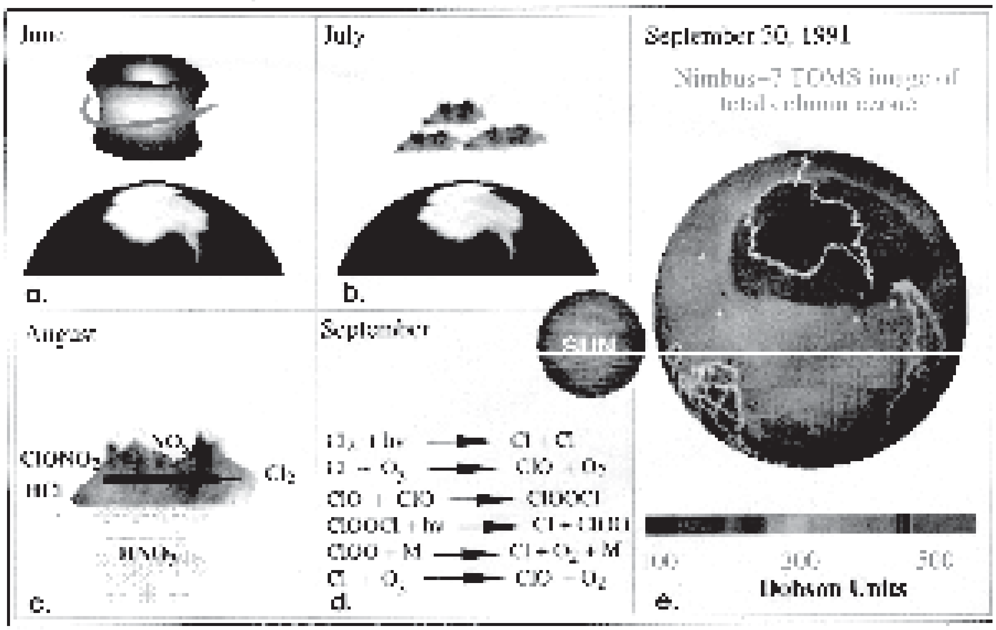


Figure 1 The sequence involved in the formation of the ozone hole. a) Polar vortex circles Antarctica in winter. b) Temperatures drop low enough to form clouds known as polar stratospheric clouds (PSCs). c) PSCs denitrify and dehydrate the stratosphere through precipitation and convert HCl and $ClONO_2$ into more reactive chlorine. d) The arrival of the sun photolyses the Cl_2 to radicals that can catalyse ozone destruction. e) The ozone hole is completely established in September and October (1 Dobson Unit = 2.69×10^{16} molecules of ozone cm^{-2}). The polar vortex breaks down in November and the ozone level attains normal values in December (not shown in the figure).

stratosphere and decomposed by solar UV radiation.

$$CCl_2F_2 + UV\ (\lambda < 220\ nm) \longrightarrow CClF_2 + Cl.$$

The atomic chlorine released reacts with ozone as follows:

$$Cl + O_3 \longrightarrow ClO + O_2$$
$$ClO + O \longrightarrow Cl + O_2\ .$$

The chlorine atom thus freed, can participate once again in the breakup of ozone molecules. The net effect of this pair of reactions is the conversion of atomic oxygen (O) and ozone into molecular oxygen (O_2).

$$O + O_3 \longrightarrow 2O_2\ .$$

The quantitative aspects of the ozone hole, however, could not be explained by this cycle. As a result, several other proposals have been made for the catalytic mechanism linking halogen radicals to the chemical destruction of ozone. The catalytic cycle that is considered

Milestones in Ozone Research

1839 - Schonbein discovered ozone using a chemical test with potassium iodide paper.

1880 - Hartley recognized that the 293nm cutoff in the solar UV radiation at the Earth's surface corresponds very closely with the UV absorption spectrum of O_3.

1926 - Dobson developed an ultraviolet spectrophotometer to measure the total column ozone.

1930 - First qualitative photochemical theory for the formation and decomposition of ozone in the atmosphere was formulated by Sidney Chapman.

1950 - Bates and Nicolet drew attention to the role played by H, OH and HO_2 (products of photolysis of water vapour) in the catalytic reduction of odd oxygen above 60km.

1970 - Paul Crutzen suggested that additional important processes must be taken into account in order to correctly describe the photochemistry of the atmospheric ozone.

1971 - Johnston made a connection to supersonic transport emissions. This resulted in a very intensive debate among researchers as well as among technologists and decision makers.

1974 - Rowland and Molina established the possibility of major stratospheric ozone depletion from CFCs.

1978 - Nimbus-7 satellite was launched. It contains the 'Total Ozone' Mapping Spectrometer that measured the daily ozone concentration globally till 1993.

1985 - The British Antarctic Survey announced their startling discovery of an 'ozone hole' over Halley Bay, Antarctica.

1987 - Molina and his wife Louisa proposed a chlorine chain involving ClO dimer formation which is now thought to account for the massive ozone destruction.

1995 - Crutzen, Molina and Rowland were jointly awarded the Nobel Prize in Chemistry for their pioneering work on the subject of formation and decomposition of ozone.

currently involves the formation of ClO dimer at low temperatures followed by photolysis or thermal decomposition (*Figure 1d*) proposed by Molina and his wife Louisa.

A Hole has Opened in the Southern Sky

Anxiety deepened when a continent-sized hole (as wide as the United States of America and as deep as Mount Everest) which had eroded the ozone from 40 km above the Earth and eventually extended downwards to 15-20 km in the ozone layer was detected in the 1980s over Antarctica by a British team. Unravelling the reasons for this massive destruction of ozone has involved a vast collaborative effort, in which the three laureates have remained active. The series of processes currently seen as responsible for the ozone hole formation are presented in *Figure 1*. Some of them occur simultaneously in parallel stages.

The Antarctic ozone hole, once a mystery, is now one of the best understood aspects of the entire subject thanks to the pioneering research by Crutzen, Molina, Rowland and several others. It is now accepted that chlorine chemistry is responsible for the ozone depletion. Yet chlorine photochemistry alone cannot explain the entire ozone loss; chemists believe that Antarctica's unusual meteorology is also responsible for setting up conditions that allow photochemical ozone destruction.

Early Sign of Coming Doom

Although a fairly solid picture has emerged about the global ozone loss, many pieces of the ozone puzzle are still missing. Will new ozone problems develop in the near future? Despite the complexities and uncertainties, almost everyone agrees on the following: Chemistry is central to understanding any phenomenon associated with ozone layer depletion.

Under the auspices of the United Nations, the major industrial countries have agreed to cease production of CFCs. The United Nations Environment Programme and the Ozone Secretariat invited the world community to observe 16 September, 1995 as the first-ever International Day for the preservation of the ozone layer. This day was designated to commemorate the signing, in 1987, of the Montreal Protocol on substances that deplete the ozone layer.

At last, the world is waking up to protect the ozone shield for future generations! Scientists are now involved in developing safe substitutes for CFCs. It is only fitting that the 1995 Nobel prize in chemistry has been awarded to the researchers who played a key role in identifying the chemicals and mechanisms by which the ozone destruction occurs.

Men and women carry on:
making more of self is fun.
But before all world is gone
something drastic must be done.
Is there still a little chance
of putting end to doomsday dance?

(-L.O. Bjorn)

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