SiH species exist in the material produced under the latter circumstances.

Carlson, Wronski, and their colleagues at RCA are the only group that has reported on solar cells at present. The Dundee group reportedly has been unable to get support for this kind of research, and American laboratories may be going slow until the strength of RCA's patent position is clarified.

The RCA group has found that the best solar cell configuration is that of the Schottky barrier, which has an estimated theoretical efficiency of about 15 to 20 percent. As made by RCA, the solar cell consists of undoped, hydrogenated amorphous silicon onto which a thin transparent layer of metal, such as platinum, is evaporated. At the junction between the silicon and the platinum, an internal electric field exists—the Schottky barrier. Absorption of sunlight passing through the metal layer by the silicon results in the creation of equal numbers of free electrons and holes. The electric field drives the electrons across the silicon away from the junction, whereas it pulls the holes toward the junction. A second thin layer of amorphous silicon doped with phosphorus sits across the cell from the junction. The purpose of this layer is to collect the photogenerated free electrons and transmit them to a stainless steel substrate on which the entire assembly resides. No barrier must exist at the junction between the stainless steel and doped silicon because it would give rise to an electric field that would drive the free electrons back into the silicon. The accumulation of free electrons and holes on opposite sides of the cell gives rise to a voltage, hence the name photovoltaic solar energy.

Wronski of RCA points out that there are a number of differences between amorphous and crystalline silicon solar cells. As has long been known, amorphous silicon absorbs sunlight much more strongly than crystalline material. Thus, thin films of amorphous silicon of the order of 1 micrometer or less can make efficient solar cells, whereas much thicker cells of crystalline silicon are needed. The addition of hydrogen has relatively little effect on the absorption of sunlight.

What is not yet so well appreciated is that doped amorphous silicon seems to contain new defects introduced by the doping process itself. These defects hamper the transit of free electrons and holes through the silicon, reducing the efficiency of the cell greatly. For this reason, unlike the case in crystalline cells, the most efficient cells must be made largely from undoped amorphous silicon, and the doped layer needed for facilitating a good electrical contact between the silicon and the stainless steel substrate is made as thin as possible.

The development of useful solar cells awaits better understanding of the properties of amorphous silicon. For example, a major factor limiting solar cell efficiency is the tendency of the photogenerated holes to become trapped in the silicon before reaching the Schottky junction. Understanding why the holes are trapped and how to prevent them from being so is high on the agenda of the RCA researchers. Moreover, Peter Zanzucchi, Wronsky, and Carlson have shown that the type of glow discharge (whether it is d-c or high-frequency a-c) is one more parameter that affects material quality. And David Staebler of RCA and Wronski have found that long-term exposure to light can also change the behavior of amorphous silicon. A systematic sorting out of the effects of different preparation and operating conditions is sorely needed before the results of researchers in different laboratories can be meaningfully compared.

In the meantime, investigators of amorphous silicon are elated and point gleefully to an analogy between the present state of knowledge of amorphous semiconductors and that characterizing crystalline silicon 25 years ago—just before the solid state revolution began.

—ARTHUR L. ROBINSON

Viral Messenger Structure: Some Surprising New Developments

A recent discovery about the synthesis of some of the messenger RNA's of two unrelated animal viruses has excited molecular biologists. The findings* appear to confirm what many investigators have long suspected but have had difficulty proving; that is, that the control of gene expression in higher organisms is different from that in more primitive bacterial cells. Several groups of investigators have independently found that there is a major structural difference between the animal viral messengers and those of well-characterized bacterial systems.

In all cells, gene expression occurs when the DNA of the genes directs the synthesis of messenger RNA's (mRNA's), a process called transcription, and the mRNA's in turn direct the synthesis of proteins (translation). In bacteria, as far as is known, transcription is straightforward in that it begins at a start signal on DNA, continues along the DNA molecule, often for a length of several genes, and terminates at a stop signal. The resulting messengers undergo few, if any, structural modifications before being translated into protein structures—in fact, they are exact copies of the transcribed DNA without any missing regions.

A similar mechanism probably also operates in the nucleated cells of higher organisms, but investigators have now found that certain mRNA's synthesized by adenovirus 2 and SV40 consist of contiguous segments that are coded for by widely separate portions of the viral DNA. They think that what they are learning about the viral messengers probably applies to at least some of those of the animal cells where the viruses multiply, because the same cellular enzymes synthesize both kinds of messengers.

Although there are at least four possible mechanisms that might account for the synthesis of mRNA's with these unusual structures, the researchers think that the evidence currently favors the hypothesis that the entire stretch of DNA, encompassing both the segments found in the viral messengers and those that are missing, is copied to form large mRNA precursors. The appropriate intervening sequences are then excised to produce the actual messengers.

Some of the investigators postulate that, during the excision, the regions of the RNA that will become adjacent are brought together by a looping-out of the intervening sequences, and the regions are subsequently joined by an intramolecular ligation reaction (Fig. 1b). The mechanism that accomplishes the specific joining of the sequences is unknown, and further work will be needed to confirm whether the hypothesis is correct. But even if the viral mRNA's prove to be synthesized by another process, the structural findings indicate that the messengers of these animal viruses—and possibly those of the cells they infect—are produced in a manner unlike any described previously. Provided that a similar phenomenon does not turn up in bacteria, the current findings support the hypothesis that there may be fundamental

*Most of the articles on which this news account is based are in press at *Cell*, the *Journal of Biological Chemistry*, and the *Proceedings of the National Academy of Sciences*.

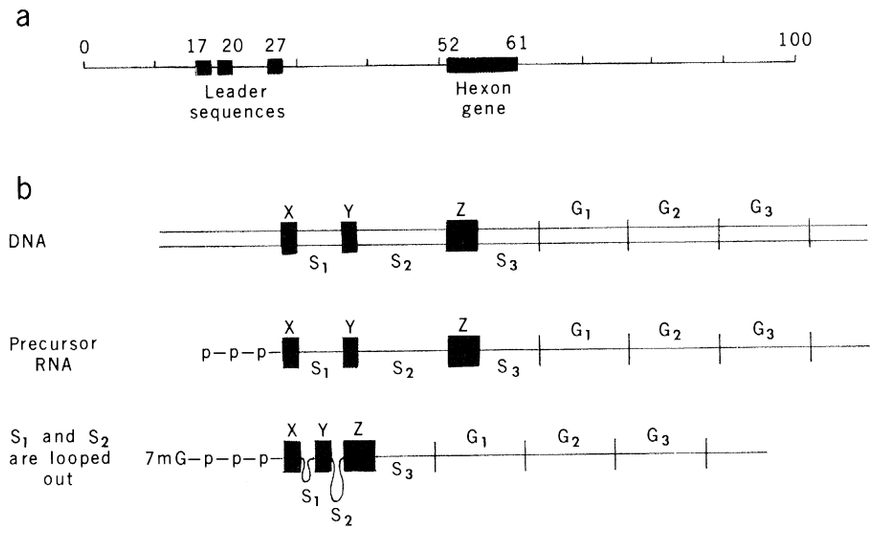

Fig. 1. (a) Diagram of the linear adenovirus 2 chromosome, which is arbitrarily divided into 100 map units. The three segments of DNA coding for the sequences that make up the leader are located at map positions 17, 20, and 27; the gene coding for the viral coat protein (the hexon gene) lies between map units 52 and 61. (b) Loop-out model for synthesis of late adenovirus mRNA's. The three regions coding for the leader segment (X, Y, and Z) and the genes coding for protein structure (G_1, G_2, and G_3) are separated by the spacer regions (S_1, S_2, and S_3). Synthesis of the precursor RNA begins near region X and continues along the genome. Three phosphates are attached to the first nucleotide on the precursor and are eventually capped with a nucleotide containing the unusual base 7-methyl guanosine (*7mG*). The leader is formed by the looping-out of S_1 and S_2, and will be coupled to the appropriate structural region by the further looping-out of intervening sequences (S_3, or S_3 and G_1, and so forth). There will also have to be a mechanism for removing unwanted structural regions from the right-hand end of the precursor and for adding the tract of adenine nucleotides to this same end. [Fig. 1b is adapted from Daniel Klessig, Cold Spring Harbor Laboratory]

differences in the ways in which primitive and more advanced cells synthesize their messengers and control gene expression.

Direct study of gene expression in the nucleated cells of higher organisms has proved frustrating because of their complexity. For example, most of these cells produce many different messengers, and isolation of a particular one in quantities sufficient for analysis is difficult. For this reason, investigators have turned to the study of simple viruses that infect and multiply in animal cells. During infection, relatively large amounts of viral products, including mRNA's, are produced and can be easily separated from cellular components. Usually the expression of the different viral genes follows an orderly time schedule. Some genes may be turned on early in infection whereas others may not be expressed until later. Most of the current investigations have focused on viral messengers synthesized in abundance late in the infective cycles of adenovirus 2 and SV40.

The differences between these two viruses are substantial. Adenovirus 2 has a linear chromosome that codes for the synthesis of about 25 proteins; the chromosome of SV40 is circular and only big enough to code for about a half-dozen products. But the results with regard to the structures of their late messengers are strikingly similar. In both cases, a sequence of about 150 nucleotides (nucleotides are the building blocks of nucleic acids) somehow becomes attached during messenger synthesis to the RNA sequences that code for the structure of viral proteins. The DNA segments corresponding to the 150-nucleotide sequence and to the sequences coding for protein structure are some distance apart on the viral genomes; however, the order of the different regions in the RNA molecules is the same as the order of the corresponding segments in the DNA.

The 150-nucleotide sequence, called a "leader," is at the end of the messenger which is synthesized first. After synthesis of both cellular and viral mRNA's, this end becomes "capped" with an unusual nucleotide that is not normally found in the interiors of the molecules. The other end is modified by the addition of a string of 100 or so adenine nucleotides.

The picture developed thus far for some late messengers of adenovirus 2 is especially complicated because three separate regions on DNA are needed to code for just the leader, according to investigators at the Massachusetts Institute of Technology (MIT) and Cold Spring Harbor Laboratory. The evidence for this conclusion comes from both biochemical and electron microscopic studies.

Susan Berget and Phillip Sharp and their colleagues at MIT observed that neither end of a messenger for a viral coat protein appears to be copied from the DNA adjacent to the protein gene. While they were not surprised that this was true for the end with the string of adenine nucleotides, because these are added after transcription, they say they were surprised about the segment at the capped end. Further experimentation bore out their initial conclusion and they went on to show in electron microscopic studies that the leader sequence is itself composed of three regions that map at positions 16.8, 19.8, and 26.9 on the adenovirus genome; the protein gene maps between positions 51.9 and 61.2 on adenovirus DNA (Fig. 1a).

Meanwhile, several groups of researchers† at Cold Spring Harbor Laboratory were pursuing independent lines of investigation all leading to the same conclusion about the structure of adenovirus messengers. For example, Louise Chow, Richard Gelinas, Thomas Broker, and Richard Roberts used electron microscopy to show that the leaders of eight different messengers consist of three regions that map at positions 16.6, 19.6, and 26.6 on adenovirus DNA; the genes for the proteins coded for by the mRNA's map beyond position 36.

This finding suggests that these different mRNA's all carry the same leader, and agrees with results obtained earlier by Gelinas and Roberts and by Daniel Klessig that show that different late messengers of adenovirus have identical nucleotide sequences on their capped ends. Gelinas and Roberts determined that enzymatic treatment of a mixture of late adenovirus messengers released only one oligonucleotide from the capped ends, even though the mixture was known to contain at least 12 messengers.

Experiments by Klessig ruled out the possibility that the oligonucleotide analyzed by Gelinas and Roberts was somehow just a contaminant of the mRNA mixture. He isolated two of the messengers and determined that the base compositions of the first 11 nucleotides on their capped ends were identical to each other and to that found by the other two investigators.

†Because of space limitations, the individual contributions of all the investigators cannot be summarized here. The investigators doing the biochemical and electron microscopic studies include Carl Anderson, John Atkins, Thomas Broker, Louise Chow, Ashley Dunn, Richard Gelinas, John Hassell, James Lewis, Daniel Klessig, John Manley, Richard Roberts, and Sayeeda Zain.

Evidence from several laboratories shows that late SV40 messengers are also composed of contiguous sequences that are coded for by separated segments of the viral genome. Again, a leader of about 150 to 200 nucleotides is spliced to the structural sequences of the messengers.

Only two major mRNA's are produced during the late stages of SV40 infection. The larger one is thought to be a precursor of the smaller mRNA. Investigators from the laboratories of Yosef Aloni at the Weizmann Institute of Science in Israel and of George Khoury at the National Cancer Institute (NCI), working in collaboration, determined that the leader sequence of both mRNA's is complementary to the DNA between map units 0.72 and 0.76 on the SV40 genome (Fig. 2). They mapped the DNA sequence corresponding to the structural portion of the larger RNA between 0.77 to 0.17 map units and that for the smaller one between 0.95 to 0.17 map units. Ming-ta Hsu and John Ford of the Rockefeller University obtained almost identical figures for the map positions of the DNA that is complementary to the different segments of the two messengers.

Direct comparison of the nucleotide sequence of SV40 DNA with the sequences of the RNA's prepared from the cytoplasm of infected cells confirms that the nucleotides at the capped end of the smaller RNA could only be coded for by sequences between map positions 0.72 and 0.77, according to Sherman Weissman and his colleagues at Yale University Medical School. They say that nucleotides between map positions 0.77 and 0.95 were not represented in the RNA molecule but, as predicted, the messenger did carry nucleotides complementary to those mapping between 0.95 and 0.17 units on the SV40 DNA. Thus, for SV40 messengers, just as for adenovirus messengers, there has been a remarkable convergence from several laboratories of results that all paint the same picture.

The researchers point out that it is unlikely that RNA molecules are copied separately from several different DNA segments and joined to form a single messenger. James Darnell and his colleagues at Rockefeller University have evidence that the transcription of several late adenovirus messengers is initiated between map positions 15 to 20 on the genome. This is the same segment that codes for the first two regions of the leader sequence. Similarly, the NCI-Weizmann investigators have determined that there is only one major initiation site for transcription of the late SV40 messengers. This site is near map position 0.67, not far from the region coding for the leader sequence and also close to the origin of replication for the viral chromosome. Individual transcription of the different DNA regions would require the existence of more than one initiation site and is not compatible with these results.

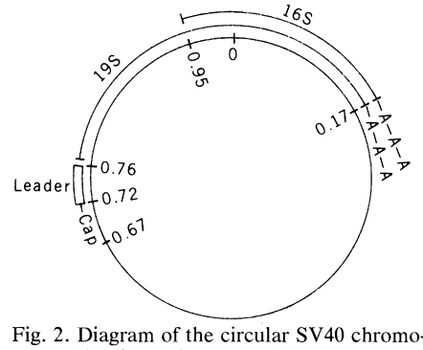

Fig. 2. Diagram of the circular SV40 chromosome. The single site cut by the restriction enzyme called Eco RI is arbitrarily designated as 0 on the map. The origin of replication for the viral DNA is at 0.67 map units. The initiation site for transcription of the late messengers, which proceeds clockwise around the genome to map position 0.17, is near the same position. Transcription of the early SV40 messengers, which proceeds in the counterclockwise direction, also begins around map unit 0.67. The sequences of the genome corresponding to the leader sequence, and the structural portions of the two messengers, are indicated outside the circle. The larger and smaller messengers are, respectively, designated as 19*S* and 16*S* RNA. [Modified from Yosef Aloni of the Weizmann Institute and George Khoury of NCI]

The role of the caps and leaders on the mRNA's is not known, but the best guess now is that they function somehow in regulating gene expression. They do not appear to code for protein structure. The region between map units 0.72 and 0.76 on the SV40 genome does not code for any known SV40 proteins. Broker says that he thought that the adenovirus leader might code for protein structure, but experiments by John Manley of Cold Spring Harbor indicate that the initiation signal for translation is beyond the leader, making its translation unlikely.

The fact that the regions coding for the leaders map near the initiation site for transcription is consistent with a potential role for these DNA sequences in regulating the initiation of messenger synthesis. In addition, protein synthesis begins somewhere near the leader end of mRNA's and proceeds in the direction toward the end bearing the string of adenine nucleotides. Thus the leaders could also help to regulate translation. Additional possibilities include a role for the leaders in transport of the messenger out of the nucleus or in attachment to the ribosomes, small particles in the cytoplasm and the actual sites of protein synthesis.

Moreover, the results indicate that several late adenovirus mRNA's carry the same leader sequence. If all these messengers are formed by excising the appropriate segments from a single precursor, then the control of the synthesis of several proteins may be coordinated. The late viral proteins of SV40 may be under similar coordinated control. Coordinated control of the synthesis of several proteins is a common occurrence in bacteria, but the mechanism for achieving it differs considerably from the one postulated for the viruses.

However, not all of the late adenovirus messengers have leader segments that are complementary to DNA sequences between map positions 16 and 27. James Lewis, Carl Anderson, and John Atkins of Cold Spring Harbor Laboratory found that the mRNA's for three viral proteins, the genes for which are located between map positions 4 and 17, did not appear to contain them. Thus, the control of these genes may differ from that of genes located beyond map position 36.

Nevertheless, electron microscopic studies done by Chow, Gelinas, Broker, and Roberts indicate that two of these messengers also consist of spliced segments. In addition, Heiner Westphal and his colleagues at the National Institute of Child Health and Human Development have evidence that four adenovirus messengers produced early in infection consist of spliced-together regions, with each of the four messengers having its own characteristic leader. At least for adenovirus, the attachment of leader sequences to those coding for protein structure may be a general phenomenon.

The nuclei of mammalian cells contain a class of RNA's, the heterogeneous nuclear RNA's (hnRNA's), that are not found in bacteria. These RNA's are a diverse group of short-lived molecules, some of which are very large. Some investigators think that the large hnRNA's are the original transcription products and the precursors of the actual mammalian messengers. Following transcription, the hnRNA's would have to be shortened to form the messengers which are then transported to the cytoplasm where protein synthesis occurs.

This hypothesis about the role of hnRNA's has not been universally accepted because not everyone has agreed that the evidence for it is convincing. The new work, however, provides additional support for the idea that shortening of RNA transcripts occurs, but the

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looping-out model, if it is correct, is an unexpected development. Darnell, who is one of the investigators studying the hnRNA's, thinks that the new results are compatible with his views about their role but says that he was surprised to learn that interior sequences, not just those on the ends, might be removed from the molecules.

If several interior sequences are excised from the precursors, then it might be possible to detect a series of hnRNA's that show progressive loss of interior nucleotide segments. The experiments are extremely complicated, but Sharp and Berget have preliminary evidence for the existence of these intermediates in RNA prepared from the nuclei of cells infected with adenovirus.

So far, the bulk of the evidence indicates that during messenger synthesis, noncoding sequences become attached to sequences coding for proteins. But splicing may also occur within structural sequences themselves. Weissman and his colleagues say that the section of SV40 DNA that codes for the T antigen, a large viral protein produced early in infection, contains a number of termination signals whose presence in messengers normally stops protein synthesis. Weissman says that, if the size estimate for the T antigen is correct, either there is selective suppression of the termination signals during translation of the T antigen messenger or else the messenger must be synthesized in such a way that the signals are excluded from it. Further work will be required to determine whether this situation is comparable to the intramolecular splicing seen with the late viral messengers.

The big question is whether a similar phenomenon occurs during gene expression in nucleated cells themselves. The existence of spliced cellular mRNA's has not been demonstrated directly, but several of the investigators doing the viral work cite recent results from other laboratories that could be interpreted as supporting the existence of spliced mammalian messengers. However, the researchers who are actually doing this work currently disavow any such interpretation. They say that other possible explanations have not been eliminated. Nonetheless, the recent developments will no doubt stimulate a lot of new research and encourage investigators who until now have experienced more frustration than success in their studies of gene expression in the cells of higher organisms.

—JEAN L. MARX

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Lectures on Structure and Significance of Science. H. Mohr. Springer-Verlag, New York, 1977. xii, 228 pp. $16.80. *To order this book circle No. 480 on Readers' Service Card.*

Legacies in Ethics and Medicine. Chester R. Burns, Ed. Science History Publications (Neale Watson), New York, 1977. viii, 326 pp. $7.95.

Mineralogy of Arizona. John W. Anthony, Sidney A. Williams, and Richard A. Bideaux. University of Arizona Press, Tucson, 1977. viii, 256 pp., illus. Cloth, $22.50; paper, $9.75.

The National Health System in Denmark. A Descriptive Analysis. Dorte Gannik, Erik Holst, and Marsden Wagner. National Institutes of Health, Bethesda, Md., 1977 (available from the Superintendent of Documents, Washington, D.C.). vi, 86 pp. Paper, $1.15. A Publication of the John E. Fogarty International Center for Advanced Study in the Health Sciences.

The Nation's Use of Health Resources. 1976 Edition. National Center for Health Statistics, Rockville, Md., 1977. x, 104 pp. Paper.

Principles of Zoology. Willis H. Johnson, Louis E. Delanney, Eliot C. Williams, and Thomas A. Cole. Holt, Rinehart and Winston, New York, ed. 2, 1977. xii, 748 pp., illus. + plates. $16.95.

Problem Solving with FORTRAN. Donald D. Spencer. Prentice-Hall, Englewood Cliffs, N.J., 1977. xiv, 320 pp., illus. Paper, $9.95.

Problems in Calculus and Analytic Geometry. Richard J. Palmaccio. J. Weston Walch, Publisher, Portland, Me., 1977. iv, 148 pp. Spiral bound, $3.50.

Proceedings of the Second International Symposium on Clinical Enzymology. Norbert W. Tietz, Albert Weinstock, and Denis O. Rodgerson, Eds. American Association for Clinical Chemistry, Washington, D.C., 1976. xiv, 338 pp., illus. $15.

The Sewing Machine. Its Invention and Development. Grace Rogers Cooper. Published for the National Museum of History and Technology by Smithsonian Institution Press, Washington, D.C., ed. 2, 1976. x, 238 pp., illus. $14.95.

Social Networks. A Developing Paradigm. Samuel Leinhardt, Ed. Academic Press, New York, 1977. xxxiv, 466 pp., illus. $17.50. Quantitative Studies in Social Relations. *To order this book circle No. 481 on Readers' Service Card.*

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World Economy and East-West Trade. Papers from a workshop, Vienna, Oct. 1975. F. Nemschak, Ed. Springer-Verlag, New York, 1976. 208 pp. Paper, $19.80. East-West European Economic Interaction Workshop Papers, vol. 1. *To order this book, circle No. 485 on Readers' Service Card.*