

32 and 62-94), though most of the chymotryptic peptides have been analyzed.

In view of the frequent occurrence of interchanges in the NH_2 -terminal portion, the remarkable feature of the COOH -terminal portion is the probable identity in sequence of the last 106 amino acids except for the Val-Leu interchange at position 189, which was independently observed by Hilschmann and Craig (6) for the two proteins they studied (7). This agreement begins at position 106 after the "switch peptide," in which four homologous interchanges occur in the three proteins (8). Although the switch point involves two basic amino acids, it has no other unique features.

The conclusions reached by comparison of the sequence data for Ag and Roy are supported by the limited data available for the third protein, Cu. Although positions at only 37 residues can be assumed from end-group data on the tryptic peptides, these include four definite homologous interchanges with either Ag or Roy (positions 1, 102, 105, 189) as well as two nonhomologous interchanges (55 and 72). In agreement with that of Hilschmann and Craig (6), our comparative data suggest that there are many other interchanges, both homologous and nonhomologous, in the NH_2 -terminal half of this protein. Some of these involve the replacement by arginine and lysine in specimens Cu and Ag of amino acids present in Roy for which trypsin lacks specificity; this, of course, leads to different tryptic peptides. Although sequence data are not available for the Cu protein, our data for Ag support the hypothesis of Hilschmann and Craig (6) that its entire sequence from 106 to 212 is like that of Roy.

The possibility of widespread rearrangement in amino acid sequence has obvious significance for antibody structure since Bence Jones proteins are abnormal products of a tumor of cells (plasmacytes) that have the normal function of antibody synthesis. We have other results that indicate that at least four different NH_2 -terminal tryptic peptides may be obtained from different type I Bence Jones proteins and L-chains. This appears to exclude the mechanism of chromosomal rearrangement through a single event of unequal but homologous crossover ascribed to Lepore-type hemoglobins, since only two different NH_2 -terminal

sequences could arise by such a mechanism.

The multiple structural differences reported here for Bence Jones proteins are incompatible with the concept of single point mutations now accepted for the abnormal hemoglobins. We favor the hypothesis of somatic chromosomal rearrangements in the genes controlling antibody structure. In Smithies' hypothesis of γ -globulin variability (10), he postulates that the γ -globulin genes contain local inverted duplications of base sequence that permit intragenic crossing over. One possible consequence of duplications within a gene is the expression as repeated amino acid sequences, but the number of these does not seem significant in our data (11). Complete analysis of amino acid sequence of a number of Bence Jones proteins of each antigenic type will be needed for an experimental test of the Smithies hypothesis and of other theories of γ -globulin variability.

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5. Abbreviations for amino acid residues: Lys, lysine; His, histidine; Arg, arginine; Asp, aspartic acid; Asn, asparagine; Thr, threonine; Ser, serine; Glu, glutamic acid; Gln, glutamine; Pro, proline; Gly, glycine; Ala, alanine; Val, valine; Met, methionine; Ileu, isoleucine; Leu, leucine; Tyr, tyrosine; Phe, phenylalanine; Try, tryptophan; CyS, half-cystine. In Fig. 1 Ilu is used instead of Ileu for typographic reasons.
6. N. Hilschmann and L. C. Craig, *Proc. Nat. Acad. Sci. U.S.* **53**, 1403 (1965).
7. Through independent experiments we have verified the sequence Leu-Ser-Ser-Thr at positions 173 to 176 which is reported in a different order by Hilschmann and Craig (6). Our sequence is in accord with that expected from the specificity of chymotrypsin and the composition of the chymotryptic peptides in this region.
8. The sequences Val-Val-CyS-Leu at positions 130 to 133 and Tyr-Ala-CyS-Glu at positions 190 to 193 accord with the sequence reported by Milstein (9) for the peptic peptide containing the disulfide bridge present in all type I L-chains and Bence Jones proteins he examined.
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11. In our data the dipeptide sequences Lys-Val and Pro-Ser recur three times and Leu-Ser four times.
12. We thank Caroline W. Easley for peptide maps and consultation. Supported by grants CA-02803 and H-02966 from NIH. Reprint requests should be addressed to the authors at the Division of Biological Sciences, Indiana University, Bloomington.

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Liquid Waves by Computer

Abstract. *A numerical, fluid-dynamics technique for high-speed computers is described and illustrated. It applies to the solution of problems dealing with incompressible viscous fluids and involving nonsteady motions in several dimensions in space. The ability to handle free-surface boundary conditions allows waves to be studied through all phases of breaking and splashing, as well as a number of related phenomena.*

We have developed a new technique for numerically solving problems in fluid dynamics. It is particularly applicable to studies of waves and of other phenomena that are associated with the motion of an incompressible fluid with a free surface. Examples are the flow of water from a broken dam, the generation of water waves by an explosion, the formation of breakers on a beach, and the splash of a jet of liquid hitting a plate.

The application illustrated in Fig. 1 is to the surge of water under a sluice gate. The initial frame (top left) shows the water at rest immediately after the gate has quickly opened; the deep reservoir (left) is subjected to a surface pressure in addition to that produced by gravity and the shallow pond (right) is initially quiescent. Subsequent frames show the formation of a backward breaker, in which the flow is partly smooth, partly irregular.

The problem was scaled to give unit density to the water. The downward gravitational acceleration was also of unit magnitude, while the scale of distance is determined by the initial height of the reservoir behind the sluice gate, 2.9 distance units. In these dimensions, the applied surface pressure was 2.5, the coefficient of kinematic viscosity was 0.01, and the times of the six frames are $t = 0, 1.0, 1.5, 2.0, 2.5$, and 2.73.

The elements of fluid are represented in the calculations by marker particles. Determination of the trajectories of the particles is based on a finite-difference approximation to the full, nonlinear, Navier-Stokes equation for a viscous, incompressible fluid. The finite-difference equations are related to a Eulerian mesh of cells not shown in the figure. The cells cover the entire region of interest, amounting to 1500 in this case.

The computing method has been designed for use with a high-speed computer. The present program is run on

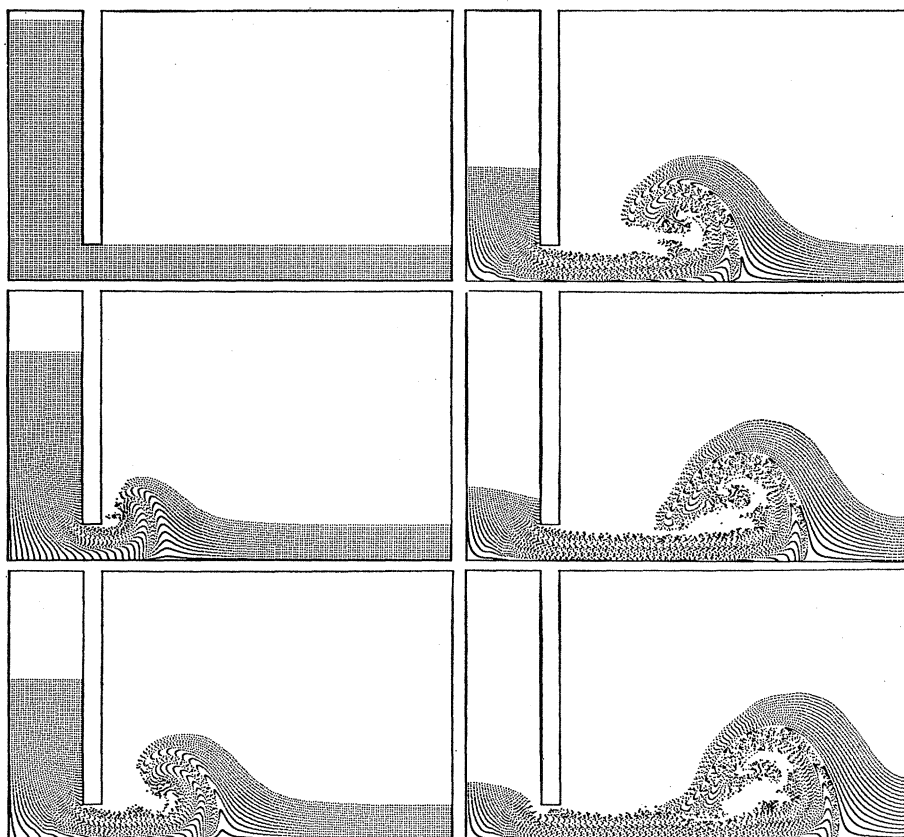


Fig. 1. Sequence of frames, produced by a computer, depicting the escape of water under a newly opened sluice gate into a tranquil pond; frames progress downward and from left to right.

the IBM 7030 (Stretch); a typical problem requires approximately 20 to 60 minutes. Available computer memories limit our studies to two space dimensions, but the method is equally applicable to three-dimensional problems. Configuration plots, such as those in Fig. 1, are obtained directly from the computer through the Stromberg-Carlson microfilm recorder and are not retouched.

The results are generated by the computer through a succession of small time steps or cycles, resembling the frames of a motion picture. The frames shown in Fig. 1 were selected from among hundreds that were obtained in the complete run. The sequence of processes necessary to accomplish the solution for each new frame is as follows:

1) The cycle begins with the full availability of velocity for each cell and of position for each marker particle; velocities and positions either are left over from the previous cycle or have been supplied as initial conditions. The velocities satisfy the conservation equation for the flow of incompressible liquid.

2) Pressures are calculated through-

out the fluid in such a way that the resulting accelerations produce a velocity field that, at the end of the cycle, still satisfies the incompressibility equation; this requires the solution of a finite-difference Poisson's equation, accomplished by an iterative procedure.

3) Accelerations and corresponding new velocities are calculated.

4) The marker particles are moved with the velocity of the fluid.

The equations, boundary conditions, and techniques for solution (1) are related to those used by Fromm (2), but they have required modifications appropriate to a different set of primary dependent variables; Fromm employed the stream function and vorticity, variables that never enter directly into this pressure-velocity technique.

The results of such calculations have been compared with experiments, showing excellent agreement in every case. A study of the water motion from a broken dam, for example, proved that all aspects of the flow can be obtained at least as accurately as experiments could measure them (1). An advantage of the calculations is that they give more detailed data than can be obtained from experiments. In some cases, costly or time-consuming experimental studies can even be avoided by the careful use of such computer studies. Even more important, computer studies often provide a valuable basis for analytical studies of physical processes, giving both new ideas for models and bases for comparing the results of analysis of the models.

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3. This work was sponsored by the Atomic Energy Commission.

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Turnover of Ribosomal RNA in Rat Liver

Abstract. After a single injection of radioactive orotic acid and a "chase" of nonradioactive precursor, the specific activity of ribosomal RNA in rat liver decreases logarithmically at a rate corresponding to a half-life of about 5 days. The possible significance of this result is discussed with regard to control of protein synthesis.

In dividing bacteria (1) and in L cells growing in tissue culture (2), ribosomal RNA (rRNA) turns over slowly, if at all, with respect to the generation time of the cells. This report shows that in normal rat liver, where the generation time of the cells is long, rRNA has a half-life of about 5 days and hence is replenished many

times during the lifetime of a cell.

The existence, in the intact animal, of RNA-precursor pools of unknown size and number makes it difficult to estimate the turnover rate of rRNA from the rate of appearance of radioactivity after the administration of a radioactive precursor. For this reason the turnover of rRNA has been esti-