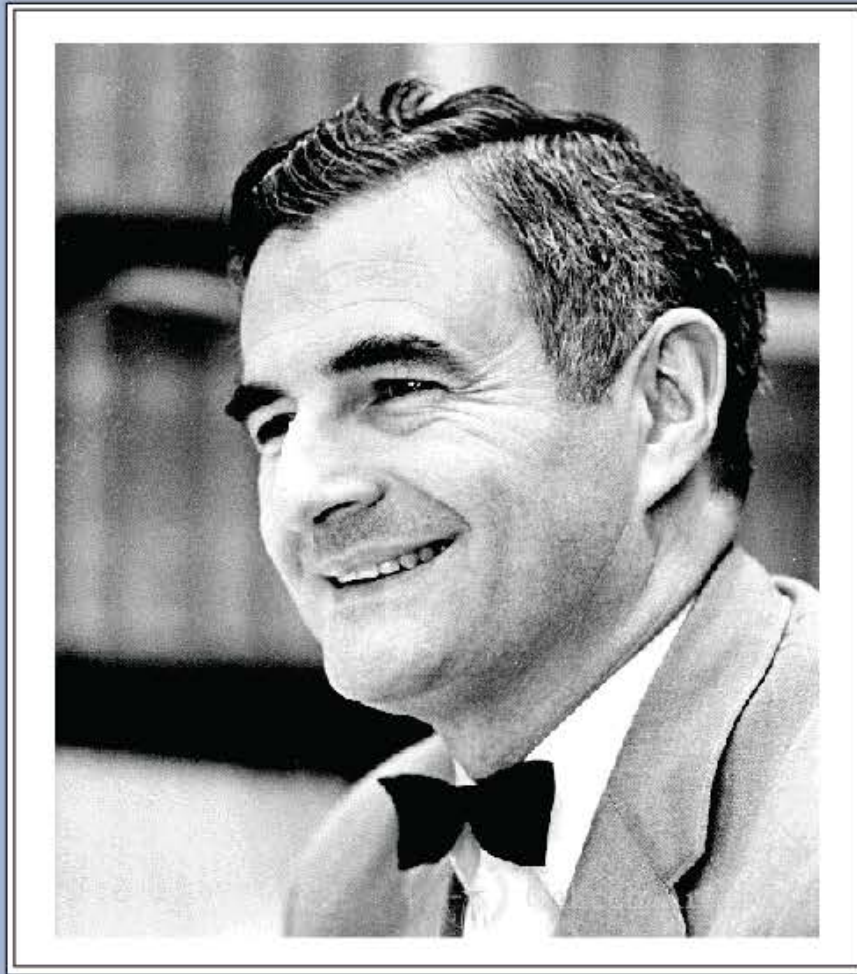


Robert Louis Sinsheimer

February 5, 1920-April 22, 2017



*A memorial celebration of life at the University of California, Santa Barbara  
July 15, 2017*

# First Paper, Nature, 1947

4.8	6		
6.3	7		
6.3	8		
7.8	9		
7.8	11		
7.9	12		
8.2	13		
10.0	18		
10.6	25		
11.1	28		
11.1	29		
11.3	30		
13.7	56		
13.8	70		
15.0	71		
13.9	72		
15.2	102	8.8	
15.3	103		-1.877

\*  $p$  = pressure difference across jet in cm. mercury,  $t$  = time of flow in seconds. The permanent decrease of the  $(\eta t)$ -values of very long molecules (length of the order of 1 per cent of the diameter of the jet) is always larger than the permanent viscosity-loss measured at low rates of shear because turbulence arises with these long molecules even at very low Reynolds' numbers. With the degradation of the molecules this tendency to turbulence becomes reduced.

With an apparatus<sup>1</sup> giving mean rates of shear of the order of  $10^5 \text{ sec.}^{-1}$  under laminar flow conditions, long-chain molecules of molecular weights above 100,000 were broken down (Table 1), yielding an exponential type of decay curve for the percentage permanent viscosity-loss plotted as a function of the number of cycles of forcing the solution in individual drops through a jet. The mechanical degradation was assessed by the *permanent* viscosity-loss of the solutions at low rates of shear, by the accompanying increase of the viscosity-temperature coefficient of the solutions and by the displacement of the transition region from laminar to turbulent flow towards higher values of the rate of shear as the result of rupturing the largest molecules.

According to the simplifying assumptions made for the calculations, the stretching forces reached their

<sup>1</sup> Morris, W. J., and Schnurmann, R., *Rev. Sci. Instr.*, 17, 17 (1946).

## Christiansen Filters for the Ultra-Violet

Gaydon and Minkoff<sup>1</sup> have described a Christiansen filter designed to isolate the 2537 Å. resonance line of mercury. We have been working for some time upon the general problem of the design of Christiansen filters for the isolation of various spark and discharge tube lines to be used in ultra-violet microscopy. We have amplified the work of Kohn and von Fragstein<sup>2</sup>, and developed a series of filters employing benzene-alcohol mixtures with fused quartz chips, which can span the region 3000–4000 Å.

The absorption of benzene prevents the use of this combination below 3000 Å. Therefore, we have developed a set of filters employing mixtures of purified decahydronaphthalene and cyclohexane,

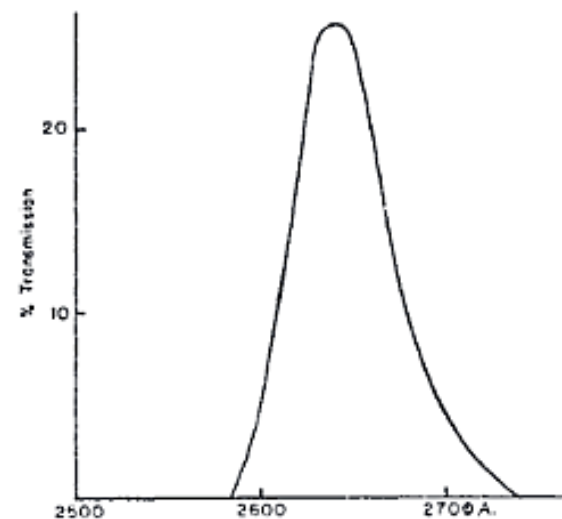


Fig. 1

# First paper from Iowa

When one compares the usual human dose, 5 ml 4% (0.2 g), with the LD<sub>50</sub> for mice (2.26 g/kg), it is evident that there is a large safety factor involved even if the dye should inadvertently be injected intravenously. Furthermore, when one considers that most of the stained area is removed during surgery, it is probable that the total amount of residual dye is of no practical importance. Applying the toxicity criteria of Hodge and Steiner (6) reveals that Pontamine Sky Blue would be classed as a slightly toxic material.

A full report of the clinical utility and duration of skin staining caused by Pontamine Sky Blue will be reported in detail elsewhere.

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## Ion Exchange Separation of Desoxyribonucleotides<sup>1</sup>

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As has been implied by Cohn (1), the ion exchange methods developed by him for the separation of ribonucleotides (2) may be readily adapted to the separation of desoxyribonucleotides. Since no procedure for this separation has been published, it would seem worth while to outline the technique developed in our

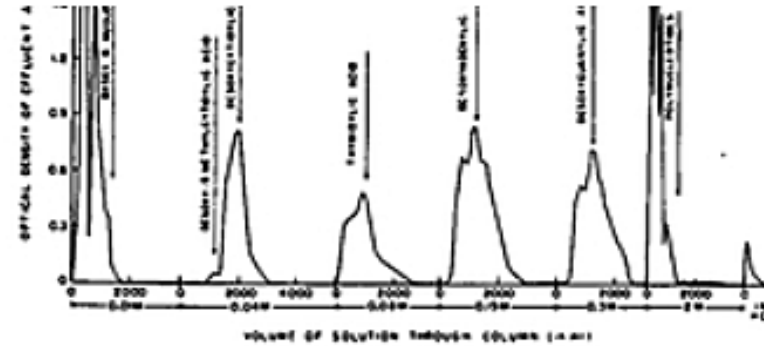


FIG. 1.

nuclease preparation from intestinal mucosa, in the presence of arsenate to inhibit alkaline phosphatase also present in the preparation. The pH of the digest resulting from the action of the pancreatic enzyme was adjusted to 8.5 with 2 N NaOH. To the digest were added 10 ml 0.36 M Na<sub>2</sub> (AsO<sub>4</sub>)<sub>2</sub>, 10 ml 1 M NH<sub>4</sub>OH · (NH<sub>4</sub>)<sub>2</sub> SO<sub>4</sub> buffer, pH 8.5, and 10 ml of a solution containing 17 mg/ml of the intestinal enzyme, prepared according to Klein, as modified by Brady (5). Digestion was carried out for 20 hr at 37° C under hexane, with constant stirring.

The pH of the digest was adjusted to 4.7 with glacial acetic acid to precipitate the intestinal preparation, which was then centrifuged out. The centrifugate was washed with 0.01 M acetate buffer, pH 4.7, and the washings were added to the previous supernatant. The pH of the combined solutions was adjusted to 9.0, and the volume made up to 250 ml.

This solution, containing mixed bases, nucleosides, nucleotides, and some undigested polynucleotides, was then added to the ion exchange column, π cm<sup>2</sup> × 11 cm, Dowex A-1 resin, 250-500 mesh<sup>3</sup> in the acetate form. Because of the marked lability of the purine desoxyribonucleotides to acid, it is desirable to employ procedures that avoid any prolonged contact with solutions of low pH. For this reason, elution from the ion

## Light Scattering by Tobacco Mosaic Virus Nucleic Acid

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(Received June 18, 1953)

The molecular weight of ribonucleic acid separated from tobacco mosaic virus by heat denaturation of the protein has been measured by light-scattering techniques and found to correspond to the weight of all the nucleic acid in a virus rod. The nucleic acid disintegrated rapidly at room temperature, most probably by enzymatic action.

### INTRODUCTION

THE molecular weight of ribonucleic acid (RNA) isolated from tobacco mosaic virus (TMV) has been determined in the past by measuring various physical properties of its solutions. Among the properties measured<sup>1</sup> have been osmotic pressures, sedimentation constants, viscosities, and diffusion constants. The weight obtained has varied with the method of separating the nucleic acid and with the physical method employed. The highest weight reported by Cohen and Stanley<sup>1</sup> was  $2.9 \times 10^5$ . Their preparations disintegrated spontaneously. In the present work, the weight of the virus RNA has been determined by light-scattering techniques and the instability studied.

### THEORY

The theory of the angular distribution of light scattered from solutions of optically isotropic large or

In a solution  $n_e^2 - 1$  must be replaced by  $n_e^2 - n_0^2$ , where  $n_e$  is the index of the solution and  $n_0$  that of the solvent. Martin<sup>5</sup> proves that  $\rho_u = 2\rho_v / (1 + \rho_v)$ , where  $\rho_v$  is the depolarization ratio for vertically polarized incident light. In addition  $v = cN_0/M$ , where  $c$  = concentration of solute in gm/ml,  $N_0$  is Avogadro's number, and  $M$  is the molecular weight of the solute particles.  $(n_e^2 - n_0^2)^2/v$  can be replaced by a derivative. With these changes, expression Eq. (1) becomes

$$Kc(1 + \cos^2\theta)/R(\theta) = F(\theta, \rho_v)/M \quad (2)$$

where

$$K = 2\pi^2 n_0^2 \left[ \frac{\partial n_e}{\partial c} \right]^2 \lambda^{-4} N_0^{-1} \quad \text{and} \quad R(\theta) = I(r, \theta) r^2 / I_0 V,$$

$$F(\theta, \rho_v) = (3 - 4\rho_v)(1 + \cos^2\theta) / 3[1 + 3\rho_v + (1 - \rho_v)\cos^2\theta].$$

A correction to Eq. (2) must be made if the particles are not small compared to the wavelength. This can be

## First Steps toward a Genetic Chemistry

Robert L. Sinsheimer

The development of a genetic chemistry—a chemistry of the genetic substance—will undoubtedly be a long and exacting and inspiring task. As genetics is a central theme in the science of biology, so we may expect genetic chemistry to become, in time, an integrating core for cellular biochemistry.

The goals of a genetic chemistry, to

When I was preparing this article, I thought back to what was said about my subject—that is, about the physical nature of the *genie*—in the course in elementary genetics which I had some years ago. To the best that I could recall, nothing was said about it. I attributed this curious result to the passage of years and to an overcrowded memory, so I

istry of the gene with the chemistry of DNA is at present necessarily circumstantial. Such must be the case until we become sufficiently advanced in our understanding that we are able to demonstrate the action of a gene *in vitro*. But circumstantial evidence can be of varied degrees of credibility. The value of circumstantial evidence is, roughly, inversely proportional to the number of alternative explanations that one can advance for the observed phenomenon. The following eight lines of evidence, which are listed in a rough order of increasing significance, are, I believe, important in establishing a correlation that links DNA and the hereditary factors: (i) the location of DNA; (ii) the specific diploid content of DNA; (iii) the metabolic stability of DNA; (iv) the complementary structure of DNA; (v) the similarity of the ultraviolet absorption spectrum of DNA and the ultraviolet action spectra for mutation; (vi) the nature of the transforming factor; (vii)

## Purification and Properties of Bacteriophage $\phi$ X174††

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*(Received 4 November 1958)*

Procedures are described for the isolation in pure form of the bacterial virus  $\phi$ X174. This virus is shown to have a particle weight of  $6.2 \times 10^6$  and to contain 25 % by weight of DNA.

At neutral pH, the purified virus forms a discrete aggregate, probably a tetramer. This aggregate dissociates either upon dilution or at alkaline pH.

Lysates produced by  $\phi$ X174 contain a second particle, antigenically related to the virus, but not infective and of lower sedimentation rate and lesser DNA content.

The DNA of  $\phi$ X174 appears to have an unusual structure in that it reacts with formaldehyde (even before extraction from the virus) and in that the atomic efficiency of inactivation of the virus by decay of incorporated phosphorus-32, calculated by combining our data and that of Tessman, is 1.0.

The results of ultrafiltration and radiosensitivity experiments have indicated the existence of a class of very small bacterial viruses including notably S13 (Lea & Salaman, 1946; Zahler, 1958) and  $\phi$ X174 (Sertic & Bulgakov, 1935; Sertic, 1937*a* and *b*; Bulgakov & Bonét-Maury, 1944; Bonét-Maury & Bulgakov 1944; Frilley,