that any sulphide ores remain unannealed in nature. It leads us to suspect that they may be a good deal less static than has been generally thought, and, in fact, that they are being more or less continuously deformed and annealed. It follows from this, at least for "massive" ores, that present textures are unlikely to indicate the original physical nature of a deposit or the processes by which it was formed.

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MOLECULAR STRUCTURE

Interaction between Model Compounds of Actinomycin *D* and DNA: DNA Dependent RNA Synthesis

DIMETHYL-actinocinyl-*bis*-(carboxylate) (AMD 1) and dimethyl-actinocinyl-*bis*-(L-threonate) (AMD 2) bind to the double stranded DNA (see following article) by a mechanism similar to that suggested for aromatic hydrocarbons[1]. The binding sites may be related to conformational defects the concentration of which can be drastically reduced by addition of spermidine. This is very likely the result of a re-ordering of the Watson and Crick model in solution caused by a stereospecific complex between the polyamine and DNA (refs. 2 and 3).

This conclusion strongly suggests that in contrast to actinomycin *D* (ACT *D*), no specific sites are involved in the binding of AMD 1 and AMD 2 to DNA. Some correlation has been found to exist for actinomycin between interaction in specific binding sites and inhibition of DNA-dependent RNA synthesis in the presence of RNA polymerase[4], and so we decided to study this reaction in the presence of AMD 1 and AMD 2.

For this purpose, DNA–AMD 1 and DNA–AMD 2 complexes to be used as templates in the RNA synthesis were prepared by equilibration of fine crystals of the two compounds with DNA (Sigma, Type 1) solutions in the cold (4° C) for 4 days and centrifugation, as described in the following article. A sample of DNA solution was treated in the same way and used as control. RNA polymerase (Miles) from *Micrococcus lysodeikticus* with an enzyme activity of 700 U/mg (ref. 5) was used. Reactions were performed at 30° C, 10 min in a final volume of 0·3 ml. containing 0·1 molar *tris* pH 7·5, 2·5 mmolar $MnCl_2$, 1·6 mmolar spermidine hydrochloride (Fluka), 1 mmolar CTP, GTP, UTP and ^{14}C-ATP (2,100 c.p.m./mμmole), and 200 mμmoles of DNA control or DNA-AMD 1 or DNA-AMD 2 and 4 μg of the enzyme. The inhibition of RNA synthesis by actinomycin was studied in the same experimental conditions, by adding to the DNA control increasing amounts of actinomycin *D* (a gift from Merck, Sharp and Dohme Research Laboratories).

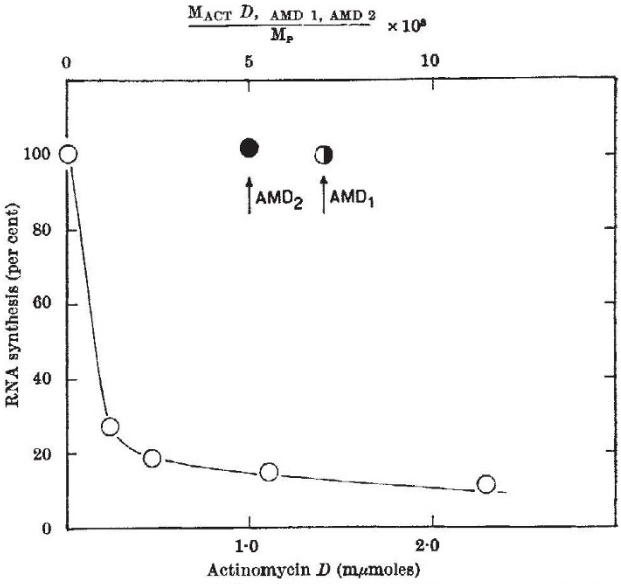

Fig. 1. Percentage of RNA synthesis in presence of: ○, actinomycin *D*; ◑, AMD 1, and ●, AMD 2. 100 per cent corresponds to the incorporation of 2 mμmoles of ^{14}C-AMP. For experimental details see text.

The reaction was terminated by chilling in ice and adding an equal volume of cold 10 per cent trichloroacetic acid; the precipitate was collected on a 'Millipore' filter and washed extensively with cold 5 per cent trichloroacetic acid. The filters were dried and counted in a liquid scintillation counter (Nuclear Chicago). The results of these experiments are shown in Fig. 1. Compounds AMD 1 and AMD 2 do not inhibit the DNA-dependent RNA synthesis and give the same results as the DNA control at concentrations comparable with those of actinomycin *D* which inhibits the reaction more than 80 per cent. In absence of spermidine the extent of the RNA synthesis is 25 per cent lower for both DNA control and DNA-AMD 1 or DNA-AMD 2.

These results indicate that specific binding of actinomycin *D* to DNA which causes inhibition of RNA synthesis must necessarily involve the peptide lactone, although the isolated aromatic moiety of actinomycin can also interact with DNA.

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Interaction between Model Compounds of Actinomycin *D* and DNA: Physicochemical Studies

THE remarkable inhibitory effect of actinomycin *D* on DNA dependent RNA synthesis has been correlated with its ability to interact in a specific way with the DNA template[1]. The nature of the sites of interaction has