Ideas on Protein Synthesis (Oct. 1956)

The Doctrine of the Triad.
The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it.

That is, we may be able to have

\[ \text{DNA} \rightarrow \text{RNA} \rightarrow \text{Protein} \]

but never

\[ \text{DNA} \rightarrow \text{RNA} \rightarrow \text{Protein} \]

where the arrows show the transfer of information.

Requirements for protein synthesis.

(a) a passive template i.e. one which does not turn over in the process. This can be RNA or DNA.

(b) mixed intermediates of ribose nucleotides and amino acids. (The most favoured ones have the general formula:

\[ \text{Base} - \text{base} - \text{base} - \text{base} - \text{base} \]

\[ \text{Sugar} - \text{phos} - \text{sugar} - \text{phos} - \text{sugar} - \text{phos} - \text{phos} - \text{amino acid} \]

DNA makes DNA by a special process not involving RNA and only involving proteins is a non-template manner (e.g. as enzymes, or
as structural supports). Presumably the Kornberg system.

DNA is held in a configuration by histone so that it can act as a passive template for the simultaneous synthesis of RNA and protein. None of the detailed "information" is in the histone. (My guess is that in this configuration the DNA bases have been unpaired).

RNA only acts as a template for protein synthesis when in a microsomal particle. The protein of the particle carries none of the detailed "information"; it is made of identical sub-units. Different particles (i.e. making different proteins) contain different RNA but (usually) the same protein sub-units. They hold the RNA by its phosphate-sugar backbone, not by the RNA bases.

New RNA is usually produced in protein synthesis, but unless it is stabilized by combining with the structural protein to make a microsomal particle, it is broken down. Chloramphenical uncouples the joining up of the protein.

Thus of the arrows shown in the first diagram all but the dotted one are allowed in this scheme. It is implied that the configurations of the passive templates, whether RNA or DNA, are always much the same, so that the same ribotide-amino acid intermediates can always be used to absorb onto them.

This scheme explains the majority of the present experimental results!