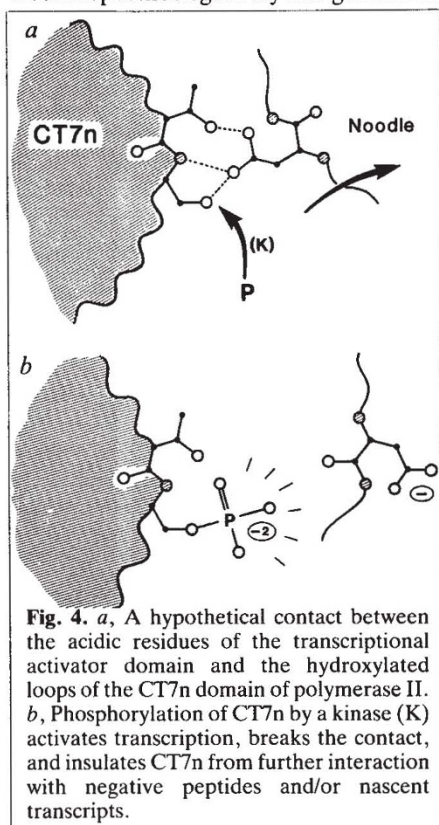


Once the components of a stable pre-initiation complex have been recruited and assembled, the polymerase must be released from the complex to proceed with transcription. The model also suggests how this may occur. The hydroxyl groups of CT7n could be phosphorylated at or near the interaction sites of the activator domains (Fig. 4b). The flexibility of the noodles and their variable patterns of attachment would allow a kinase molecule access to the abundant hydroxyl groups of the CT7n. Indeed, J. Corden and S. McKnight (personal communication) suggest that acidic residues might actually activate the phosphorylation. Insinuating negatively charged phosphate groups would repel the negatively charged noodle



**Fig. 4.** *a*, A hypothetical contact between the acidic residues of the transcriptional activator domain and the hydroxylated loops of the CT7n domain of polymerase II. *b*, Phosphorylation of CT7n by a kinase (K) activates transcription, breaks the contact, and insulates CT7n from further interaction with negative peptides and/or nascent transcripts.

and possibly other inhibiting factors. Moreover, phosphorylation would prevent potential 'pausing' or 'braking' interactions caused by hydrogen bonds between the hydroxylated CT7n and the newly synthesized transcript. Thus, phosphorylation would disassemble the pre-initiation complex while activating the transcriptional function of the enzyme.

The model has been left vague about the role of the important TATA-binding factor. Evidence reviewed at a recent meeting\* suggests that the binding of this class of proteins to the TATA element of certain promoters is augmented by remotely bound *trans* activators (R. Roeder, Rockefeller University). However, if the TATA factor is a globular protein of modest size, it is difficult to imagine

how it could make significant direct contact with a large and indefinite number of diverse structures. Difficulties of this sort generally reflect insufficient information. Until more is known of its structure and function, the exact role of the TATA factor(s) will remain elusive. Promising biochemical and genetic studies of the yeast TATA factor(s) by S. Hahn in Guarente's laboratory (MIT) should provide valuable insights.

The activation of polymerase II transcription is not the only case in which extended polypeptides of ill-defined tertiary structure mediate important interactions. Exported or integral membrane proteins have similarly loosely defined sequences that specify their destination and orientation; the unstructured basic amino-terminal arms of the viral capsid subunits help anchor the protein to the underlying nucleic acid.

*Cro*,  $\lambda$  and *trp* repressors have flexible carboxy- and amino-terminal arms that contribute to DNA affinity. All these systems share with the transcriptional initiation complex the need for a mechanism by which many and various proteins can interact with a common cellular element. These flexible and variable contact patterns depart from the traditional view of specific molecular interactions gained from studying assemblies of globular molecules that give crystalline images. Whereas crystal structures at atomic resolution are crucial to our understanding of the physical chemistry and dynamics of specific molecular interactions, we can imagine many assemblies like the eukaryotic transcriptional initiation complexes whose function requires strong but less precisely defined arrangements than the ones we have seen crystallographically. The model presented here will certainly be wrong in many details, but it typifies the need for a less traditional view of molecular assemblies and new types of structural experiments to close the gap in our chemical understanding of cellular regulatory systems. □

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## Daedalus

### Cash in hand

THE cashless society, in which all transactions are carried out by inserting a plastic card into a computer terminal, is slow in arriving. One reason is its great vulnerability to theft and misuse of the cards. Now Daedalus proposes an unstealable cash-card: the user's own thumbnail.

A nail has a smooth and uniform surface. A small focused laser moving over it in a dot-matrix could easily emboss small white thermal decomposition marks in the body of the nail (such marks sometimes occur naturally). A bit larger than the dots on a compact disc, they will be easily optically readable, but shielded from chance abrasion. A nail has no nerves, so laser-writing will be quite painless.

Every day a nail grows about 0.1 mm, enough to record perhaps ten new transactions; the user of the system will accumulate on his thumbnail a running financial statement which will act in effect as a continually updated password. Each time he inserts his thumb into a terminal to validate a transaction, the system will check that statement against its files. If everything matches, it accepts the new transaction and prints it below the previous ones. But if there is a suspicious mismatch, the terminal sounds the alarm and clamps down on the suspect thumb, trapping the fraudster till the police arrive.

Thus fraud is powerfully discouraged. The only feasible way to cheat the system might be for a crooked manicurist to photograph a client's thumbnail, and use it to make a forged thumb. But by the time it was ready, the victim would probably have used the system again, so the forgery would not bear the latest data. It would be detected, and trapped by the terminal into the bargain, for the police to study later as evidence.

The system also imposes a certain financial prudence on its users. The spendthrift who fills his thumb up with wild transactions will soon be choked off by sheer lack of space. But diseases that arrest nail-growth (like mumps and measles) will rapidly threaten bankruptcy. And wearing one's finances on one's thumbs will have its own risks, for secrecy will be hard to maintain. Gigolos with magnifiers may revive the old gallantry of hand-kissing; palmists will scan both sides of your hand; business executives of both sexes may take to wearing opaque nail-varnish, and start consigning their nail-clippings to a microshredder. And a death in the family will have the worried relatives hastily falsifying the deceased's thumbs with a laser scrambler, before some unscrupulous undertaker or body-snatcher can copy or remove them in order to steal their encoded legacy.

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\* The UCLA Symposium DNA-Protein Interactions in Transcription was held in Keystone, Colorado on 4-10 April 1988.