mRNA molecule is not a straight, linear molecule as depicted in Fig. 1, but rather that the 5' and 3' ends of the mRNA could be physically associated by protein-protein or protein-mRNA interactions to form a 'closed-loop'¹¹.

The realization that the rates of both deadenylation and decapping can contribute to the stability of an mRNA provides us with an insight into what properties of an mRNA molecule set its intrinsic rate of turnover. For example, the sequence and/or structural features of an mRNA may have either a direct or indirect effect on the rate at which the

decapping enzyme is able to bind to the m⁷G cap and cleave it from the mRNA (Fig. 2). The decapping enzyme must also compete with the translation-initiation factor complex eIF4F for the cap. Although the mechanism by which the PABP-poly(A) complex inhibits decapping remains to be elucidated, Beelman *et al.* have also identified two other genes (*MRT1* and *MRT3*) whose products are required for deadenylation-dependent decapping (manuscript submitted).

Although the mist is beginning to clear from the mRNA degradative pathways in yeast, a shroud of it stills lies over the

mammalian pathways. Can we assume that similar, if not identical, pathways exist in mammalian cells? That deadenylation and loss of PABP precedes degradation of mammalian mRNAs¹² would suggest that the answer is yes, but it must now be established how the mRNA is then degraded. Undoubtedly, even as you read this article, PCR machines are churning out *XRN1* and *DCP1* homologues from higher eukaryotic cells. □

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NEUROBIOLOGY

Tales of the unexpected

MONKEYS, like humans, do not take kindly to having their hopes raised only to be dashed, as illustrated in this cartoon. It depicts a classic experiment, published by O. L. Tinklepaugh in 1928, in which a monkey is shown a food reward that is then concealed. The monkey must remember the location of the reward for several seconds before receiving a cue to uncover and collect it. The monkey prefers banana, but will settle for lettuce; if, however, it expects banana but finds lettuce instead, it becomes angry, indicating that it remembers not only the location but also the nature of the expected reward.

On page 629 of this issue, Masataka Watanabe provides new insight into

how the brain stores such expectations, by recording from single forebrain neurons as monkeys perform delay-reward tasks similar to Tinklepaugh's. In some cases, the monkey could actually see the food reward in advance, while in others its location was cued by a light, and only from previous trials does the monkey know which reward to expect. It is known that neurons in the dorsolateral prefrontal cortex store information about location of hidden cues; this so-called delay activity is thought to underlie short-term spatial working memory. Watanabe now shows, however, that these neurons also store information about the nature of the expectation.

Some neurons fire selectively in antic-

ipation of a particular type of reward (for instance, cabbage versus raisin), some are selective for its location (left versus right), and some are influenced by whether the reward has actually been seen rather than merely inferred from experience. It is possible to see how learning affects their activity; Fig. 4b of the paper (page 631) illustrates how one neuron's response to a light cue changes as the monkey realizes that the cue now predicts potato rather than grape juice. The combined activities of many such neurons could in principle encode a detailed description of the expected reward, which could then be used to control goal-directed behaviour.

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