

Translational Regulation in Frogs and Flies

In amphibian oocytes, the 5' and 3' ends of many mRNAs are brought together to form repressive loop structures by a protein called maskin (Stebbins-Boaz et al. 1999; Mendez and Richter 2001). Maskin links the 5' and 3' ends into a circle by binding to two other proteins, each at opposite ends of the message. First, it binds to the cytoplasmic polyadenylation-element-binding protein (CPEB) attached to the UUUUUAU sequence in the 3' UTR; second, maskin also binds to the eIF4E factor that is attached to the cap sequence. In this configuration, the mRNA cannot be translated (Figure 1A). The binding of eIF4E to maskin is thought to prevent the binding of eIF4E to eIF4G, a critically important translation initiation factor that brings the small ribosomal subunit to the mRNA.

Mendez and Richter (2001) proposed an intricate scenario to explain how mRNAs bound together by maskin become translated at about the time of fertilization. At ovulation, a kinase activated by progesterone phosphorylates the CPEB protein. The phosphorylated CPEB can now bind to the cleavage and polyadenylation specificity factor, CPSF (Mendez et al. 2000; Hodgman et al. 2001). The bound CPSF protein sits on the 3' UTR and complexes with a polymerase that elongates the polyA tail of the mRNA. The important aspect of this model is that the length of the polyA tail is what is being manipulated to control translation. In oocytes, a message having a short polyA tail is not degraded, yet such messages are also not translated. Once the tail is extended, however, molecules of the polyA binding protein (PABP) can attach to the growing tail. PABP stabilizes the eIF4G to eIF4E interaction (outcompeting maskin) to facilitate ribosomal assembly around the mRNA and initiate translation (Figure 1 B).

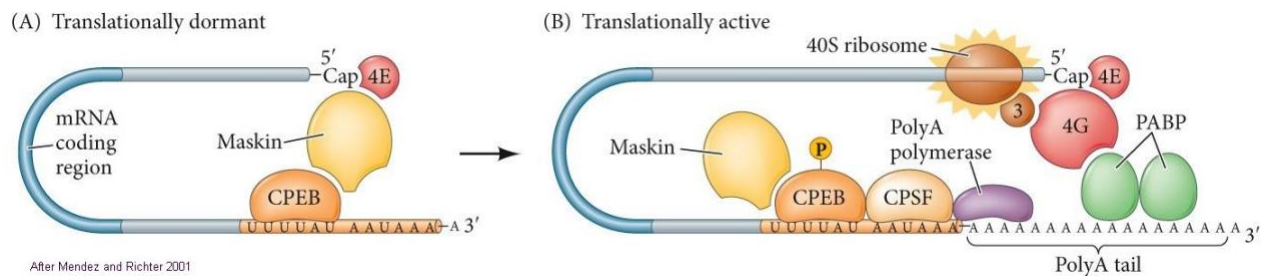


Figure 1 Translational regulation in oocytes. (A) In *Xenopus* oocytes, the 3' and 5' ends of the mRNA are brought together by maskin, a protein that binds CPEB on the 3' end and eukaryotic initiation factor 4E (eIF4E) on the 5' end. Maskin blocks the initiation of translation by preventing eIF4E from binding eIF4G. (B) When stimulated by progesterone during ovulation, a kinase phosphorylates CPEB, which can then bind CPSF. CPSF can bind polyA polymerase and initiate growth of the polyA tail. PolyA binding protein (PABP) can bind to this tail and then bind eIF4G in a stable manner. eIF4G can then bind eIF4E and, through its association with eIF3, position a 40S ribosomal subunit on the mRNA. (After Mendez and Richter 2001.)

In the *Drosophila* oocyte, Bicoid protein initiates head and thorax formation. Bicoid can act both as a transcription factor (activating genes such as *hunchback* that are necessary for forming the fly anterior) and as a translational inhibitor of those genes such as *caudal* that are critical for making the fly posterior (see Chapters 2 and 9). Bicoid inhibits *caudal* mRNA translation by binding to a "bicoid recognition element," a series of nucleotides in the 3' UTR of the *caudal* message. Once there, Bicoid can bind with and recruit another protein, d4EHP, which can compete with eIF4E protein for

the cap. Without eIF4E, there is no association with eIF4G, and *caudal* mRNA becomes untranslatable. As a result, the *caudal* message is not translated in the anterior of the embryo (where Bicoid is abundant) but is active in the posterior portion of the embryo.

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