













Examples of mechanisms of RNAs localization in Different Organisms and Cell types



Mechanisms 1 & 2 (combined):

The localization of maternal *nanos* mRNA at the posterior of an activated, unfertilized *Drosophila* egg is the result of two different mechanisms: generalized degradation and local protection.







Mechanism 4:

Localization of β -actin mRNA (red) in the leading lamellae of chicken fibroblast (myosin = green immunofluorescence) or in in the neurite and growth cones of a neuron. These are examples of active directional transport on cytoskeletal elements

How did researchers discover the localization of mRNAs in axons and dendrites?

A brief historical perspective







































Box 1: RNA-binding proteins acquired in the nucleus affect the cytoplasm fate of mRNAs
Aany proteins that bind to mRNAs in the nucleus have been shown to remain bound in he cytoplasm and to regulate mRNA localization and translation. Such proteins include eterogeneous nuclear ribonucleoproteins (hmRNPs), exon junction complexes (EJC) as number of other nuclear RNA binding proteins.
nRNP A2 binds an RNA element, called the A2 response element (A2RE) within the "untranslated region (UTR) of the mRNA encoding myelin basic protein (MBP) and calizes MBP mRNA to the distal processes of oligodendrocytes [96]. In neurons, L2REs mediate dendritic localization of reporter transcripts, and a subset of endritically-localized mRNAs contain A2REs, indicating a role for hnRNP A2 in endritic mRNA targeting [97].
The EJC consists of a set of nuclear proteins that bind to pre-mRNA transcripts during plicing and that have been shown to be required for the cytoplasmic localization of osi aRNA in Drosophila oocytes [98]. Many EJC components are present in neuronal endrities, where they have also been shown to bind localized mRNAs [99]. When EJC omponents are bound within coding regions, they may recruit ribosomes to promote ranslation; when they are deposited downstream of coding regions, the transcripts are sually targeted for degradation <i>irá</i> the <u>Nonsee-Mediated Decay</u> (NMD) pathway aft he first round of translation. The mRNA encoding Arc contains two conserved introns vithin its 3'-UTR and thus may be rapidly degraded by NND after the first round of ranslation [100]. Such regulation may ensure tight temporal control and a 'burst' of Arc rotein synthesis at stimulated synapses.
The zip-code binding proteins ZBP1 and ZBP2 associate with β -actin mRNA during ranscription and are required for both export and dendritic targeting of β -actin mRNA 99].
CLAV/HuD proteins, neuron-specific nuclear RNA binding proteins known to regulat nRNA stability, have been shown to associate with many localized mRNAs, including hose encoding GAP43, Homer 1a, neuritin and CamKIIa. [101].
.Sm1, an auxiliary factor for RNA degradation, and CBP80, a (pre)mRNA bindln rotein have been shown to bind to dendritically localized mRNAs β -actin, eEF1 α , an he IP3 receptor [102].











= mRNP formation, E	a) in the cytoplasm
Different r	Brown and one and porting the two type indices
Kanai et al. (2002)	immunoprecipitated RNA granules using an antibody against KIF5
(42 RBPs identified	ed from granules containing CamKII-α mRNA – NO Ribosomes!)
Table 1. Identified Proteins in th	e RNA-Transporting Granules
Function/Type (Number)	Protein Name
RNA transport (6) Protein synthesis (6) RNA helicases (3) hnRNPs (5) Other RNA associated (12)	FMR1, FXR1, FXR2, Pur α, Pur β, staufen EF-1α, elf-2α, elf-2β, elf-2γ, Hsp70, ribosomal protein L3 DDX1, DDX3, DDX5 hnRNP-A/B, hnRNP-A0, hnRNP-A1, hnRNP-D, hnRNP-U, ADP-ribosylation factor guanine nucleotide factor 6, ALY, cold inducible RNA binding protein, EWS, NonO, Nucleolin, paraspeckle protein 1, PSF, RNA 3"-terminal phosphate cyclese, RNA binding motif protein 3, SYNCRIP, TLS Ser/UT: kinase recentor associated protein 1, TSS
Other known proteins (3)	











































STEP 4 = local mRNA translation	
How is an mRNA translated at its destination?	
 (A) Formaton of mRNPs in the nucleus; (B) Cytoplasmic mRNP remodeling, oligo-merization and assembly (possible exchanges with P-Bodies, Stress Granules) 	
2. Transport of mRNPs to their destination;	
3. Anchoring of mRNPs at the destination with involvement of actin-myosin system;	
4. Local translation of delivered mRNAs and local degradation	















