

## **NUCLEAR ACTIN AND MYOSINS: LIFE WITHOUT FILAMENTS**

Primal de Lanerolle and Leonid Serebryanny  
Department of Physiology and Biophysics  
University of Illinois at Chicago  
Chicago, IL 60612

Corresponding author:  
Primal de Lanerolle  
Department of Physiology and Biophysics  
University of Illinois at Chicago  
835 South Wolcott  
Chicago, IL 60612  
[primal@uic.edu](mailto:primal@uic.edu)

## **ABSTRACT**

Actin and myosin are major components of the cell cytoskeleton, with structural and regulatory functions that impact many essential cellular processes. Actin and myosin were traditionally thought to function only in the cytoplasm. However, it is now well accepted that actin and multiple myosins are found in the nucleus. Increasing evidence on their functional roles has highlighted the importance of these proteins in the nuclear compartment.

## **INTRODUCTION**

Myosins are a large family of motor proteins that interact with actin, a major cytoskeletal component, and use the energy released from ATP hydrolysis to power muscle contraction, cell motility and organelle movement<sup>1,2</sup>. Decades of studying actin and myosin II have led to two major concepts: actin and myosin must form filaments<sup>1</sup> to do work and they are only found in the cytoplasm<sup>2</sup>. The discovery of myosin I by Pollard and Korn<sup>3</sup> challenged the former and the discovery of an isoform of myosin I in the nucleus<sup>4,5</sup> challenged the latter. However, nuclear myosin I (NMI) does not form filaments and nuclear actin filaments are only observed under specialized conditions. Thus, the question of how actin and myosin perform physiologically relevant functions in the nucleus persists. This review will present evidence in support of the physiological functions of nuclear actin (Figure 1) and myosins (Figure 2 and Table 1) and describe some of the important questions regarding molecular motors in the nucleus.

## **NUCLEAR ACTIN**

### **Nuclear actin structure**

Although the existence of nuclear actin is now undisputed, the absence of nuclear actin filaments<sup>6</sup> is perplexing. Filamentous actin in the cytoplasm is routinely visualized by staining with phalloidin. Despite exceeding the critical concentration for polymerization<sup>7</sup>, phalloidin-stained nuclear actin filaments are rarely seen. Filamentous structures have been observed in the nucleus only with antibodies that recognize unique actin conformations, and then only in specific cell types and under specific conditions<sup>8,9</sup>. This extends to the multiple types of nuclear actin in plants<sup>10</sup>. While nuclear actin is predominantly monomeric, ~20% of actin in the nucleus has

characteristics of a very dynamic polymeric population, which might represent oligomers<sup>11</sup>, and has led to the use of the term "polymeric actin" in reference to nuclear actin.

Interestingly, Latrunculin A, an actin polymerization inhibitor, causes the formation of actin rods that stain with phalloidin<sup>9</sup> by increasing monomeric actin in the cytoplasm and the nuclear translocation of actin/cofilin complexes. Similarly, several stress related conditions, including DMSO treatment<sup>12</sup>, heat shock<sup>13</sup> and ATP depletion<sup>14</sup>, also generate nuclear actin rods. Physiologically, mutations in the  $\alpha$ -skeletal muscle actin gene lead to intranuclear rod myopathy, a disease characterized by the formation of nuclear rods containing actin and  $\alpha$ -actinin<sup>15</sup>. Actin rod formation decreases the mitotic index and may contribute to the muscle weakness seen in this myopathy<sup>35</sup>. Thus, the formation of intranuclear actin rods may represent a stress response that includes a decrease in transcription.

Nuclear actin filaments appear to play a crucial role in viral infection<sup>16</sup>. Baculovirus infection results in the translocation of the host ARP2/3 complex to the nucleus, where it interacts with a viral WASp-like protein to stimulate actin polymerization<sup>17</sup>. Pseudorabies virus and herpes virus infections also result in the formation of nuclear actin filaments<sup>16,17</sup>. Although the mechanism by which viruses induce the formation of actin filaments is not known, a viral kinase may be involved<sup>16</sup> and the physical association of nuclear actin filaments with Herpes viral capsids appears to be necessary for the correct formation of viral assembly sites and viral transcription<sup>18</sup>. Viral capsid proteins co-localize with myosin V, suggesting that viral capsids travel along nuclear actin filaments using myosin V as a motor<sup>18</sup>. Herpes simplex virus replication involves the formation of replication compartments that grow, move and merge with each other in a nuclear actin and NMI dependent manner<sup>19</sup>. Collectively, these data suggest that viruses may use actin and different myosins to accomplish specific objectives.

## Nuclear actin regulation and functions

The absence of canonical nuclear actin filaments under physiological conditions could be due to post-translational modifications or regulation by actin binding proteins (ABPs) and actin related proteins (ARPs) that bestow actin with nucleus-specific properties. However, although SUMOylation has been implicated in the nuclear retention of actin<sup>20</sup> and despite undergoing many other post-translational modifications in the cytoplasm<sup>21-26</sup>, whether actin is similarly modified in the nucleus and how such modifications affect the structure, function or trafficking of nuclear actin is unknown.

The nuclear roles of ABPs and ARPs and their influences on actin have been studied more intensely. Two actin-binding proteins, cofilin and profilin, have been implicated in the import/depolymerization and the export/polymerization of actin, respectively<sup>27</sup>. Actin does not contain a nuclear localization signal and its nuclear import appears to require an interaction with cofilin<sup>28</sup>. In contrast, nuclear export involves exportin 6, a channel dedicated to the translocation of actin and actin-profilin complexes<sup>29</sup>. The actin regulatory protein CapG was shown to localize to the nucleus and nucleolus and may therefore affect nucleolar actin dynamics<sup>30</sup>.

The roles of ABPs and ARPs in the nucleus also hint at the functions of actin. Actin partners such as supervillin<sup>27</sup>, gelsolin<sup>27,31</sup>,  $\alpha$ -actinin<sup>27,32</sup> and nuclear myosins<sup>31</sup> interact with liganded steroid receptors and act as transcriptional coactivators<sup>27</sup>. The actin nucleating ARP2/3 complex has also been implicated in transcription by RNA polymerase II *in vitro* and *in vivo* in association with a neuronal Wiscott-Aldrich syndrome protein (N-WASp) complex<sup>33,34</sup>. Actin and ARPs are important in recruiting chromatin remodeling complexes<sup>35-39</sup> and many chromatin remodeling complexes associate with at least one ARP and actin<sup>35,39</sup>, further supporting a transcriptional role for actin.

Indeed, actin is functionally involved in virtually all the steps of transcription. Actin binds to all three polymerases<sup>40-42</sup> and may be needed to form the active forms of RNA polymerase I and II. Exogenous actin stimulates the rate of *in vitro* transcription by RNA polymerase II more than eight-fold, technically making it a transcription factor<sup>42</sup>. Actin is also involved in forming high order structures required for export and conformational changes of mRNA through its association with pre-mRNP (messenger ribonucleoprotein) or hnRNP (heterogeneous RNP) particles in *C. tentans* and rat liver nuclei<sup>43,44</sup>. The interaction of actin with hnRNPs regulates RNA polymerase II elongation and the recruitment of histone acetyltransferases (HATs) in a transcription dependent manner<sup>45,46</sup>. Specifically, a complex of hnRNP U, actin and other proteins binds to the Ser2/5- and Ser2-phosphorylated C-terminal tail domain of RNA polymerase II (CTD), along with PCAF HAT, to couple the elongation phase of transcription with the processing of transcripts<sup>36,37</sup>. Furthermore, the interaction between Cdk9, which phosphorylates Ser2 of the RNA polymerase II CTD, and actin stimulates RNA polymerase II transcription by promoting chromatin remodeling<sup>38</sup>.

### **Actin connecting the cytoplasm and nucleus**

Ultimately, the nucleus has to respond to environmental changes that are initially detected by cell surface receptors and communicated via the cytoskeleton<sup>47</sup>. One mechanism for connecting the nucleus to its external environment involves the binding of proteins that have nuclear functions to the actin cytoskeleton. PREP2<sup>48</sup>, a transcriptional activator, and YY1<sup>49</sup>, a transcriptional repressor, bind to actin filaments in the cytoplasm and translocate to the nucleus when actin is depolymerized. In contrast, the transcriptional co-activator MAL interacts with cytoplasmic unpolymerised actin in the absence of serum and translocates to the nucleus when actin polymerization increases<sup>50</sup>. Mechanical cues can also be relayed from the cell exterior to

the nucleus by the concerted action of the cytoplasmic actin cytoskeleton and force sensors, as was recently observed with the transcriptional regulators YAP and TAZ<sup>51</sup>. Thus, changes in the physical characteristics of the cytoskeleton, resulting from changes in the environment, can directly regulate nuclear functions by sequestering or releasing specific proteins.

The connection between the cytoplasm and the nucleus can be achieved more directly through the LINC (Linkers of the Nucleoskeleton to the Cytoskeleton) complex, which includes nesprin and the SUN proteins<sup>52</sup>. This complex physically connects the nuclear lamins on the inside of the nuclear envelope to the actin cytoskeleton, microtubules<sup>53</sup> and intermediate filaments<sup>47</sup> in the cytoplasm. Lamins form a meshwork under the inner nuclear membrane that binds to chromatin, providing a relatively direct pathway for transducing cytoskeletal changes to the nuclear interior. Indeed, cells lacking lamins A and C have decreased nuclear stiffness<sup>47,54</sup> and lamin A mutants result in progeria, muscular dystrophies and other diseases<sup>47</sup>. Nuclear lamins also bind the spectrin repeat protein, emerin<sup>54</sup>. Emerin associates with proteins involved in signaling, RNA processing, chromatin remodeling and DNA replication<sup>55</sup> and also stably interacts with spectrin, NMI and actin-ADP<sup>55</sup>. Thus, emerin, like other spectrin repeat proteins, has the capacity to link actin and the nucleoskeleton<sup>54</sup>. These results highlight the complex mechanisms that cells employ to communicate extracellular events to the nucleus via the cytoskeleton.

## **NUCLEAR MYOSINS**

### **Nuclear Myosin I**

NMI is an isoform of myosin IC that has a 16 amino acid N-terminal sequence that is essential for its nuclear localization<sup>5</sup>. Class I myosins are the largest group of unconventional

myosins<sup>56</sup> and are characterized by three domains: an actin-binding head that hydrolyses ATP to move along actin filaments, a linker neck domain that is regulated by calmodulin binding and a tail that, unlike myosin II, is too short to self-aggregate into filaments<sup>56</sup>. The myosin IC tail does, however, contain regions, such as a positively charged domain and a putative pleckstrin homology domain, that can bind various molecules, including DNA<sup>57</sup> and phospholipids<sup>58</sup>.

Although both NMI and actin have been implicated in transcription by RNA polymerase I<sup>59-61</sup> and II<sup>6,62</sup> (Figure 3), subtle differences have been noted in their functions. NMI is necessary for forming the first phosphodiester bond during transcription initiation and purified NMI stimulates transcription by RNA polymerase II<sup>62</sup>, but not as much as actin<sup>42</sup>. Like actin, NMI interacts with RNA polymerase I<sup>59-62</sup> and ribonucleoproteins to aid in elongation and rRNA maturation<sup>59,63</sup>. Immunoelectron microscopy has shown that NMI is found in the dense fibrillar component of the nucleolus, the site of active rDNA transcription<sup>4,64,65</sup>. In contrast, actin is found largely in the nucleolar fibrillar center, the site of inactive RNA polymerase I<sup>66</sup>, even when transcription is inhibited<sup>64,65</sup>. Actin binds RNA polymerase I directly, whereas the interaction of NMI is indirect and mediated by TIF-1A, a transcription factor phosphorylated by growth associated kinases<sup>61</sup>. The NMI-TIF-1A interaction suggests that NMI plays a role in the growth dependent regulation of rDNA transcription<sup>60,61</sup>.

The motor function of nuclear actin and myosin I is crucial for the functional compartmentalization of the nucleus. The nuclear centre includes early replicating chromosomes while the periphery contains late replicating heterochromatic chromosomal regions<sup>67</sup>. How this compartmentalization is established and how genes on different chromosomes are coordinately expressed have been open questions in cell biology. Chuang *et al.* revealed that the movement of an engineered chromosome locus is an active process powered by actin and NMI by showing



that actin and NMI mutants inhibit the repositioning of the gene locus<sup>68</sup>. Other studies have corroborated these results by demonstrating that chromosome repositioning requires an NMI-containing motor complex<sup>69-71</sup>.

ATP hydrolysis by actin and NMI has also been implicated in regulating the association of the transcription machinery and the rate of transcription. Ye *et al.* showed that NMI motor activity and stabilized polymeric actin are necessary for efficient rDNA transcription<sup>60</sup>. They also reported that a mutant NMI lacking the tail domain, reduced the level of RNA polymerase I found at both promoter and transcribed regions, but had no effect during elongation. These studies, along with data from multiple ChIP assays using different antibodies, suggest that NMI adopts different conformations when associating with the promoter or transcribed regions<sup>60,61,72</sup>. These findings have revealed small parts of what could be an elegant motor function coupled to transcription or a dynamic platform for structural regulation.

NMI also interacts with topoisomerase II<sup>73</sup> and with the chromatin remodeling complex WSTF/SNF2h<sup>74</sup>, indicating additional roles for NMI in DNA damage repair and chromatin regulation and highlighting the multifunctionality of this motor.

### **Other nuclear myosins**

Embryonic myosin II heavy chain is found in the nuclei of proliferating myoblasts and is down-regulated during differentiation<sup>75</sup>. Myosin Va and b have also been observed in the nucleus. Myosin Va is phosphorylated by calcium-calmodulin dependent protein kinase II and phospho-myosin Va localizes in nuclear speckles, the sites of RNA processing in transcriptionally active cells<sup>76</sup>, raising the possibility that it is involved in splicing. Myosin Vb, in contrast, interacts with  $\beta$ -actin and RNA polymerase I in the dense fibrillar component of nucleoli<sup>77</sup>. This association can be altered by blocking RNA polymerase I, suggesting a role for

myosin Vb in rRNA transcription. These observations, along with the role of myosin Va in viral infection<sup>16-18</sup>, reinforce the idea that myosins have separate functions in the nucleus.

Myosin VI has also been implicated in transcription by RNA polymerase II<sup>78</sup>. ChIP assays demonstrated its recruitment to the promoter and intergenic regions of active genes. Moreover, myosin VI depletion down-regulates gene expression and antibodies against myosin VI inhibit transcription in a runoff assay<sup>78</sup>. The presence of both NMI and myosin VI in RNA polymerase II complexes is intriguing. In contrast to NMI, myosin VI has a large and highly variable step size and can act as an anchor at high mechanical loads<sup>79,80</sup>. Myosin VI is also a backward motor<sup>79</sup>, raising the possibility that these two myosins are involved in separate aspects of transcription.

Myosin XVI, another nuclear myosin, contains an ankyrin repeat domain in the N-terminal head region that mediates an interaction with protein phosphatase 1<sup>81</sup>. Expression of different domains of this myosin demonstrated that the C terminus is necessary for nuclear localization. The N terminal ankyrin repeat domain targeted the protein to the nucleolus and the tail region of myosin XVI associated with stress induced nuclear actin rods and nuclear profilin, indicating that different regions may direct the protein to function in distinct nuclear compartments. Indeed, myosin XVIb localizes in a nuclear compartment that contains proliferating cell nuclear antigen (PCNA) and cyclin A, and over-expressing the full length protein or the tail region decreases BrUTP incorporation and delays S-phase progression. Together, these data suggest that myosin XVI may affect the cell cycle and proliferation<sup>81</sup>.

Myosin XVIIIb is principally found in cardiac and skeletal muscle<sup>82</sup>. Although it is cytoplasmic in myoblasts, a fraction localizes in the nucleus upon differentiation. Myosin XVIIIb is necessary for myofibrillar development<sup>83</sup> and a candidate tumor suppressor gene<sup>84</sup>

because mutations in this protein have been found in a variety of cancers<sup>85</sup>. This myosin interacts and co-localizes with the HOMER2 protein in membrane protrusions and stress fibers and the expression of HOMER2 enhances the ability of myosin XVIIIb to suppress anchorage independent growth<sup>84</sup>. Because its nuclear functions remain undefined, it is unclear how these data relate to the nuclear form of myosin XVIIIb.

## **DISCUSSION**

### **Outstanding questions**

The available data raise a number of important questions. The first of these relates to the form of actin in the nucleus. Elucidating whether nuclear actin is primarily monomeric or polymeric, how it is affected by post-translational modifications, ARPs and ABPs, how it relates to different myosins and where it is located in pre-initiating and elongating transcription complexes will greatly increase our understanding of how motors work in the nucleus. The absence of a reasonable picture of how actin and myosins associate with each other and with other nuclear components is one of the factors retarding progress in this field. Fortunately, the technology related to super resolution microscopy is evolving rapidly and 3D images of the nucleus could clarify these interactions.

A related question is *why* there are no canonical actin filaments in the nucleus. It is possible that technical limitations have prevented their visualization to date. Another possibility is that canonical actin filaments in the nucleus confer a developmental disadvantage. Thin filaments found in sarcomeres of skeletal and cardiac muscle are the most stable<sup>1,2</sup> actin filaments in any cell type. They are an excellent example of form following function because the structure of the sarcomere enhances both reliability and speed of muscle contraction. Cell

motility is much slower in comparison and requires a dynamic cytoskeleton. Thus, bacteria and archaea have unusually dynamic filaments<sup>86</sup> and motile cells sacrifice speed and dependability for flexibility and plasticity. Nuclear actin can be visualized as part of a structural and evolutionary continuum that stretches from thin filaments in muscle cells to filopodia and other dynamic actin structures in motile cells to actin polymers in the nucleus. In this continuum, thin filaments are the most highly organized, least plastic and evolutionarily most recent adaptation. In contrast, the organization of actin in the nucleus would be the most plastic and evolutionarily oldest. The nature of this organization, how it is regulated and how it serves the nuclear functions of actin are prime issues to be addressed in future work.

The absence of nuclear actin and myosin filaments is also consistent with the evolution of these proteins. Evolution depends on adapting new functions for existing proteins. Actin<sup>87</sup> and myosin<sup>88,89</sup> developed separately and almost certainly had separate functions, and because actin and myosin have to work together to perform as a motor, their initial, individual functions were probably structural in nature. Moreover, two of the three earliest myosins<sup>88</sup> are found in the nucleus (myosin I and myosin V) and neither forms filaments. It is conceivable that, at some point, actin and myosin co-operated to perform a function that provided an advantage to a cell. This event is likely to have triggered the evolution of multiple myosin families, diverging in their ability to form filaments. In this context, having non-mutually exclusive structural and motor functions in the nucleus seems reasonable.

The lack of filamentous actin and myosin questions how force is generated in the nucleus. The sliding filament model of muscle contraction is central to our understanding of force production and filaments clearly enhance the efficiency and speed of force generation<sup>1</sup>. However, force could also be generated if myosin anchored to a nuclear component pulled on an

actin molecule bound to something else. For instance, actin binds to all three polymerases, indicating that it is “anchored” to them and NMI can bind to DNA through its tail domain<sup>57</sup>, suggesting a potential binding partner during transcription. The specificity and stability of these interactions could be increased by DNA binding proteins, ABPs or transcription factors, but whether the strength of these interactions and the amount of force they generate is sufficient to support transcription remains unclear.

### **Future directions**

Understanding how nuclear actin and myosin are regulated is equally important. The actin-myosin II interaction in muscle contraction is regulated by calcium. Likewise, calcium transients have been demonstrated in the nucleus<sup>90</sup> and may contribute to nuclear dynamics<sup>91</sup>. Nuclear myosin II is reportedly regulated by calcium-dependent phosphorylation<sup>92</sup> and phosphorylated myosin Va is found in the nucleus<sup>76</sup>. PIP<sub>2</sub> and PIP kinases associate with nuclear speckles and nucleoli<sup>93-95</sup> suggesting that proteins with lipid binding domains, such as myosin or ABPs, can localize to speckles to mediate the aggregation of actin by altering its organization, capping, or polymerization. Nuclear PIP<sub>2</sub> also regulates chromatin remodeling activity<sup>35</sup>. Based on its regulation of the cytoskeleton, PIP<sub>2</sub> could control interactions of nuclear actin with myosins, gelsolin, cofilin, profilin, and WASp<sup>7</sup>, which have all been identified in the nucleus<sup>27</sup>.

Finally, two of the greatest challenges in the future will involve describing all the nuclear myosin isoforms and obtaining an integrated picture of how they interact with each other and with nuclear actin. Sequence analysis has shown that myosins VII, IX, X and XV in mammals have putative classical nuclear localization signals (Wilma A. Hofmann and Primal de Lanerolle, unpublished) and future work on their subcellular localization and activities will provide a complete picture of their physiological functions. An important consideration in these studies

will be to determine how the characteristics of individual myosins, such as step size, number of heads, processivity and cargo binding domains, fit with the requirements of individual nuclear processes. The available literature supports the notion that specific myosins perform distinct nuclear functions and paints a picture of nuclear actin and myosins regulating multiple processes that are crucial for key cellular functions. Learning more about the molecular details of the nuclear roles of actin and myosin will undoubtedly increase our understanding of both the nucleus and molecular motors, and will perhaps change how we think about them.

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## FIGURE LEGENDS

**FIGURE 1. THE ROLES OF ACTIN IN THE NUCLEUS:** Monomeric, G-actin can polymerize to form canonical actin filaments (F-actin) in the cytoplasm. Actin in complex with cofilin can enter the nucleus via nuclear pore complexes (NPC), while profilin-actin complexes are exported via exportin 6. Nuclear actin appears to be highly dynamic. It can interact with all three polymerases and engage in transcription, it can undergo post-translational modifications, like SUMOylation, or it can form actin polymers (shown as groups of three or fewer monomers to differentiate from F-actin in the cytoplasm). Helical rod bundles consisting of actin and cofilin have been detected in the nucleus under various stressful conditions and in the disease intranuclear rod myopathy. The formation of actin rods or polymers and the recruitment of nuclear myosin I or myosin Va appear to be important in viral replication. LINC complexes, which bind to lamins inside the nucleus and to actin filaments in the cytoplasm, appear to be important in outside-in nuclear signaling. The cytoplasmic actin cytoskeleton can also influence nuclear activity. The transcription factors PREP2, YY1 and MAL bind to cytoplasmic actin and changes in actin polymerization can sequester, or release these factors so that they can enter the nucleus to regulate transcription. Steroid receptors that translocate to the nucleus following binding of their activating ligands also interact with actin, actin binding proteins and myosins and act as transcriptional co-activators of genes regulated by steroid hormones.

**FIGURE 2. MYOSIN IN THE NUCLEUS:** Myosins are involved in many nuclear functions. NMI and actin are important for transcription by RNA polymerase II and I, through structural roles, motor functions or a combination of the two. Myosin VI is also implicated in transcription

by RNA polymerase II (see also Figure 3A). The motor activity of NMI and actin is also critical for positioning and organizing chromatin and the expression of estrogen receptor-activated genes. In the nucleolus, NMI and Myosin Vb are localized in a transcription dependent manner to the dense fibrillar component, while actin is in fibrillar centers. Myosins are also part of nuclear scaffolding complexes containing lamins and emerin. The latter associates with actin, NMI, myosin II heavy chain, spectrin and others, thus providing a link to the nucleoskeleton and chromatin. Myosin XVIb may regulate the cell cycle by interacting with cyclin A and proliferating cell nuclear antigen (PCNA), whereas binding to protein phosphatase 1 (PP1) may control its activity and its nuclear transport through the nuclear pore complex (NPC). Adult and embryonic myosin II have also been described in the nucleus, with functions in regulation of gene expression and differentiation, respectively. Myosin XVIIIb has also been implicated in the transcription of genes required for differentiation. Myosin Va is found in speckles and is thought to be involved in RNA processing.

### **FIGURE 3. ACTIN AND MYOSINS IN TRANSCRIPTION:**

**Panel A: Transcription by RNA Polymerase II:** Actin interacts with RNA polymerase II and is necessary to form the pre-initiation complex. The actin binding protein WASp has been discovered in the nucleus and modulates transcription independently or with the ARP2/3 complex. Actin is needed to enhance the activity of several chromatin remodeling proteins and the elongation machinery, including BAF, PCAF, Cdk9, P300, and P-TEFB, following phosphorylation (P) of the C-terminal domain of the polymerase. Actin also induces the activity of hnRNP U, a post-transcriptional modifier of mRNA. Nuclear myosin I (NMI) is needed to create the first phosphodiester bond in transcription initiation. Myosin VI (MVI), a backwards

motor, has also been implicated in transcription, posing the intriguing possibility that NMI and MVI have counteracting motor functions (represented by white arrows). Myosin Va has been discovered in nuclear speckles, suggesting a role in splicing.

**Panel B: Transcription by RNA Polymerase I:** Actin also binds to polymerase I and a polymerized form of actin is suggested to be necessary for rRNA transcription. NMI is recruited by phosphorylated (P) TIF-1A and the binding of the phospho-TIF-1A-NMI complex results in an initiation competent form of polymerase I. NMI also has a role in chromatin remodeling by the WSTF/SNF2h complex and rRNA maturation. Actin is proposed to act in concert with NMI, either as a structural complex or a supplemental motor in transcription. Myosin Vb has also been implicated as a regulator of polymerase I transcription.



**TABLE 1 MYOSINS IN THE NUCLEUS**

<b>Myosin Type</b>	<b>Abbreviation</b>	<b>Potential Nuclear Functions</b>
Nuclear Myosin I	NMI	Transcription by RNA pol I <sup>4,59-61</sup> and II <sup>5,62</sup> ; DNA damage repair <sup>73</sup> ; Chromosome translocations <sup>67-70</sup> ; Virus replication <sup>19</sup>
Myosin II	MII	Embryonic MII in myoblast differentiation <sup>75</sup> ; Adult MII in pre-initiation <sup>92</sup>
Myosin Va & Vb	MVa and MVb	MVa: Splicing <sup>76</sup> ; Virus replication <sup>18</sup> ; MVb: Transcription by RNA pol I <sup>77</sup>
Myosin VI	MVI	Transcription by RNA pol II <sup>78</sup> ; DNA damage repair <sup>96</sup>
Myosin XVI	MXVI	Cell cycle and proliferation <sup>81</sup>
Myosin XVIII		Myofibrillar development <sup>82,83</sup> ; Putative tumor suppressor gene <sup>84,85</sup>

Figure 1: Actin in the Nucleus

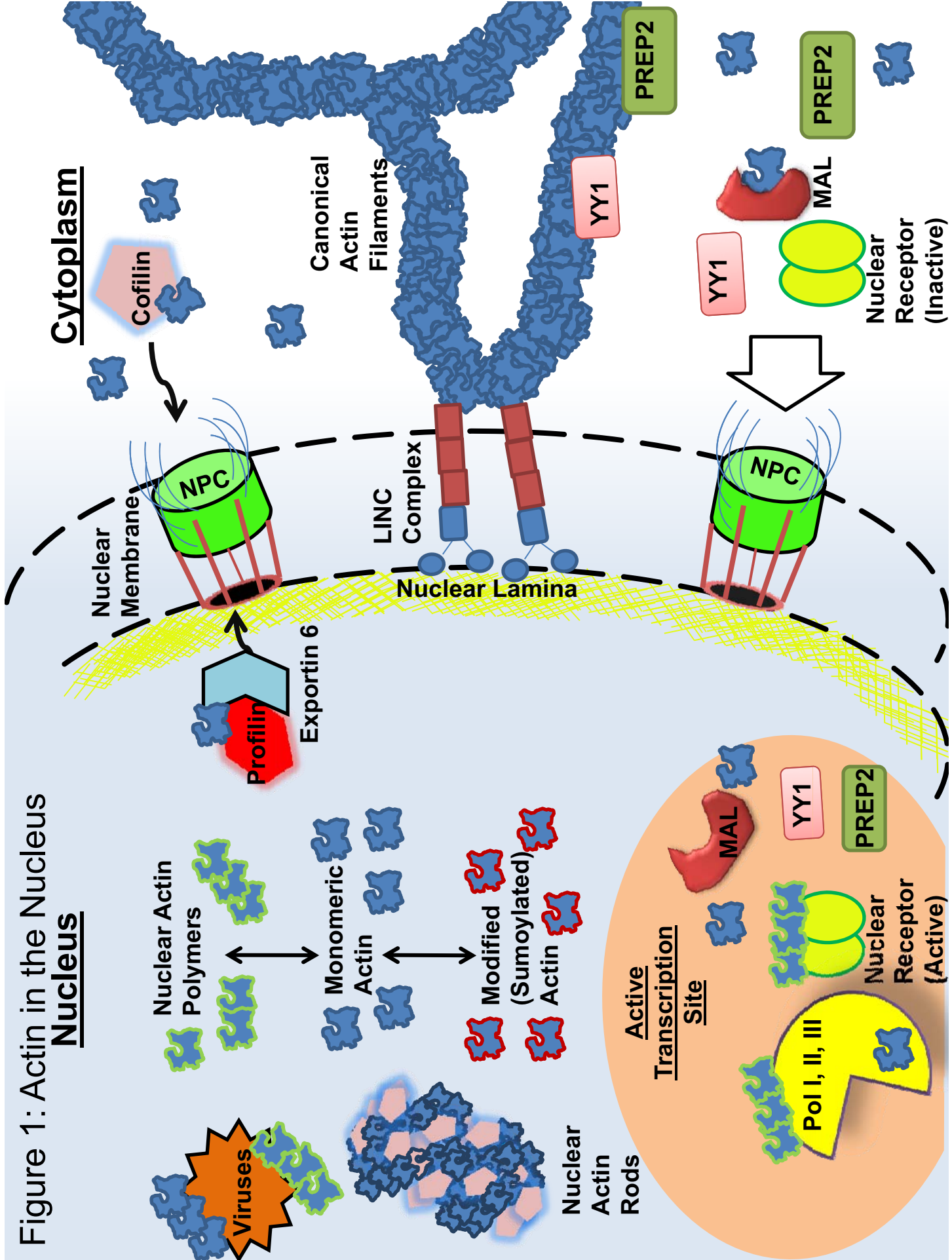


Figure 2: Myosins in the Nucleus

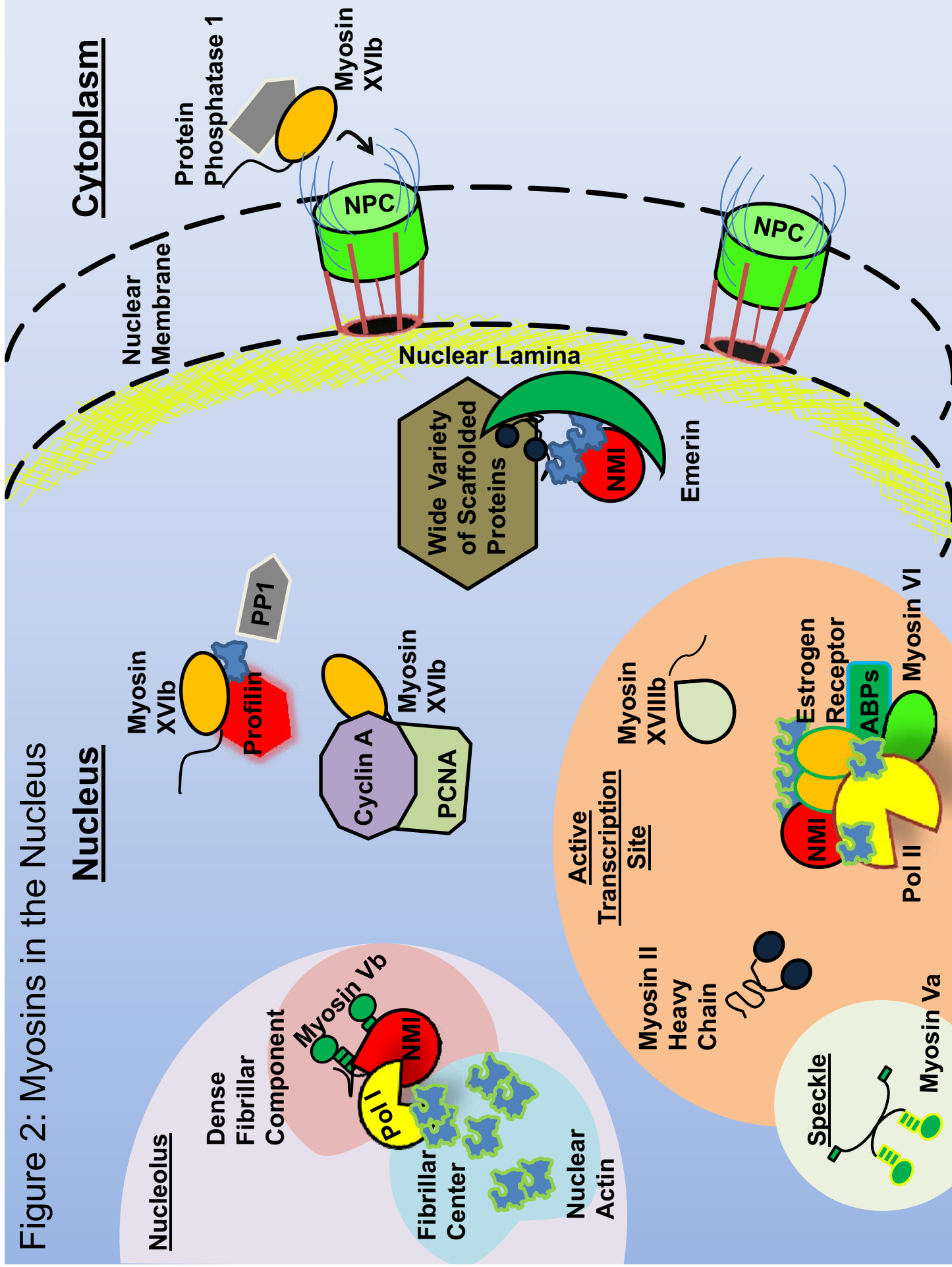


Figure 3a: Actin, Myosins and Interacting Proteins  
In Transcription by RNA Polymerase II

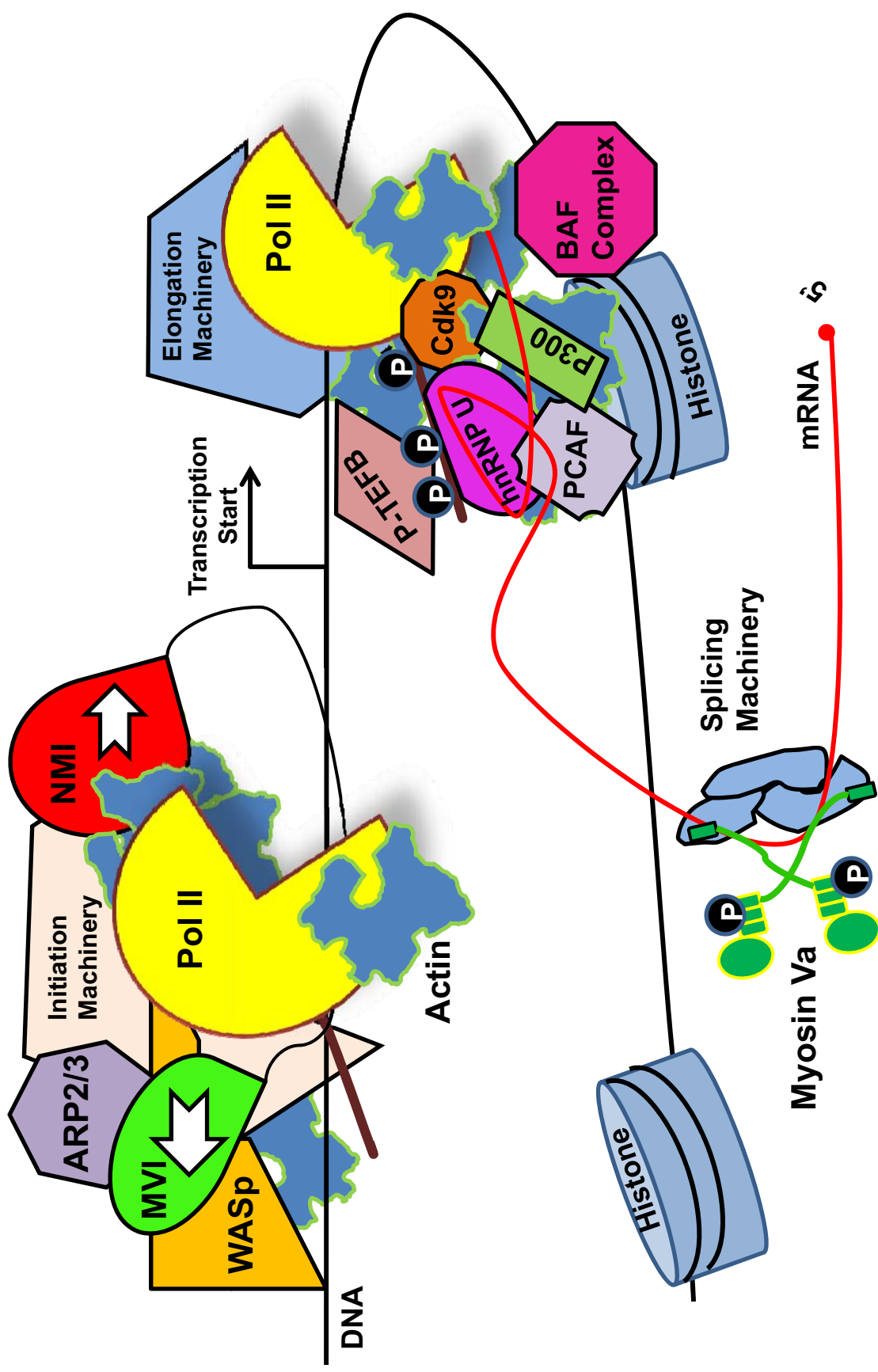


Figure 3b: Actin, Myosins and Interacting Proteins  
In Transcription by RNA Polymerase I

