

ROLE OF ACTIN SUPERFAMILY IN THE FORMATION OF POLYMERS

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ABSTRACT

The alternative of an appropriate polymer template is an imperative aspect in polymer-backed reactions. The primary prerequisite for the enlargement of a solid-phase synthesis was a appropriate sustain. The corporeal proprietorship of the maintain can put forth a strapping authority on the recital of the reagent. The sustain, in totaling to asset the thoughtless groups, plays an significant role in formative the reactivity of reagent affiliations.

The sustain used may be moreover hydrophobic polymer resulting from styrene and its hydrophilic polymer like polyacrylamide or polyvinyl pyrrolidone). Polystyrene cross linked with unreliable amounts of divinylbenzene is the most deliberated and most utilized surrounding substance for polymeric reagents. The profitable accessibility, alleviate of fictionalization and conflict to degenerative chain scission make polystyrene a suitable sustain on polymer aided reactions line to the muscular hydrophobic nature, it appeared to be mismatched with polar solvents and substrates. Still despite the fact that the polystyrene based reagents persist to govern the field, reagents based on polyamides, poly(methyl methacrylate), polyvinyl pyridine) and poly(N-acrylyl pyrrolidine) were also imported. These polymeric supports were set up to be a great deal greater to those based

on polystyrene due to improved hydrophobic/hydrophilic steadiness they could afford. The current article highlights the role of actin super family in the formation of polymers.

KEYWORDS:

Polymer, Actin, Chemical

INTRODUCTION

The effortlessness of chemical alteration of a resin and accomplishment of its succeeding submission as a reagent or catalyst, depend significantly on the corporeal proprietorship of the resin which in turn depend on the amount of cross connecting of the resin and the circumstance working for the training of the resin. Both linear and cross linked polymers are used as supports for various purposes. One of the striking features of the polymer backed is their capability to present separation of reaction sites. Imprudent sites have been productively secluded on exceedingly cross linked polymer backed. In distinction, with unconsciously cross linked polymer matrices inter-resin site separation is not achieved Cross linked polymers can be primed as blob which are exceedingly swell able in macrobiotic solvents such as dichloromethane. For the reason of the solvation and swelling of the blob, the reactions are hasty.

Postponement polymerization is the frequent method engaged for the research of cross linked polymers. They can also be primed by popcorn polymerization. In suspension or postponement polymerization, there are assorted factors which resolve the constituent part size of the polymer blob. Less significant particles are obtained by mounting the

water/monomer fraction or diluting the crude phase with a solvent. Temperature is also an significant aspect. Conversely, the two mainly significant factors are the selection of the dispersing mediator and the inspiring process. Popcorn polymerization consequences in white and opaque glassy polymers .These are inexplicable and tremendously permeable materials.

Cross linked polymers display significant difference in propriatorship depending on the grade of cross linking and the technique of research. Two parts of cross linked polymers are the gels and macro porous resins. Gel polymers are also known as micro porous resins, for the reason that, the liberty among the cross links engaged by the bulge solvent are measured as small pores. They are usually primed by deferral or suspension polymerization and are flippantly cross linked (1-5%). On using a 'good solvent,' far-reaching salvation of the polymer chains effect the blob to swell comprehensively. As the scale of cross linking is amplified, the mobility of polymer chain is condensed. Macro porous resins are moreover primed by deferral or suspension polymerization using higher amounts of cross concerning agent (5-6%). These macro porous resins are swell able in fine solvents. The major benefit of macro porous resins is their hefty interior plane area within outsized pores which allows trouble-free admittance of the reagents which is critical for reactivity. An additional benefit of macro porous resins is their extent steadiness which makes them idyllically appropriate for column applications.

Functionalized polymers can be used in two fields of recent attention i.e importance— asymmetric synthesis and combinational chemistry. Enantioselective epoxidation via chiral (salen) Mn(III) has befall a functional preparatory technique in organic synthesis

Siva ram and Dhal have broadcast the research and relevance of the polymer-supported chiral (salen) Mn(III) complex. Lamaire and co-workers have primed two polymer-bound rhodium catalysts for arbitration of enantioselective hydride reassign. Levason has investigated the research of polymer-supported o-phenylene(diphosphine) folklore. Sherrington urbanized a polyimide-supported molybdenum (IV) epoxidation medium. Cross linked poly (acenaphthylene) is urbanized as an proficient support for arrange oxidizing reagents. Reactions via functionalised poly acenaphthylene are of importance for the reason that acenaphthyl residues in these polymers could be more effortlessly customized by electrophilic substitution reactions and they are start to be more inflexible, chain motions are fewer recurrent, and some degree of site seclusion can be achieved.

A functionalized polymer is a artificial macromolecule to which chemically vault purposeful groups are append, which can be utilized as reagents, catalysts, defending groups etc. The macromolecule can be moreover a linear type which is soluble or a cross linked species, insoluble but swell able. The affection of efficient groups to polymers is recurrently the foremost pace towards the research of specialty polymers, for illustration, for biomedical relevance or as supported reagents. Functionalized polymers can be primed by chemical adaptation of polystyrene either beneath orthodox circumstances or using segment transfer catalysis method. The obligatory imprudent functional group can be introduced on to the polymeric sustain either by the (1) polymerization of the monomer containing the preferred functional group 01 and by (2) chemical amendment of preformed polymer.

Several functional linear polymers can be primed by the previous technique by cationic

and free-radical polymerization. But cross linked polymers are extra constructive than the linear ones. Cross linked polymers can be primed in superior corporeal form by suspension polymerization. The supplementary acknowledged technique is the chemical adaptation of the preformed polymer as it allows a superior power of the degree of functionalisation of the resin. It is predominantly striking for the research of cross linked polymers, for the reason that one can initiate with commercially obtainable micro porous or macro porous polymer blob of fine substantial form and dimension with a acknowledged proportion of cross linking and porosity. The artifact polymer has the similar corporeal form as the novel polymer.

ALLOSTERY AND MONOMER CONTACTS WITHIN AN ACTIN-LIKE FILAMENT

When embedded within a filament, actin-related monomers make extensive contacts with one another. These include head-to-tail contacts between monomers within individual protofilaments and contacts between the two filament strands. In most actin-like polymers, the location of the head-to-tail monomer contacts within the protofilaments are conserved: subdomain Ia in one monomer interacts with residues in subdomain Ib in the next monomer in the series, while subdomain IIa interacts with subdomain IIb in a similar way. Even in FtsA, which is missing subdomain Ib, the longitudinal contacts appear to be conserved; an insertion into subdomain Ia takes the place of subdomain Ib within a presumed polymer.

thus these contacts may be essential across actin-related proteins to enable the formation of dynamic filaments, because nucleotide binding shortens the distance separating subdomains Ib and IIb, matching the distance between subdomain Ia and IIa.

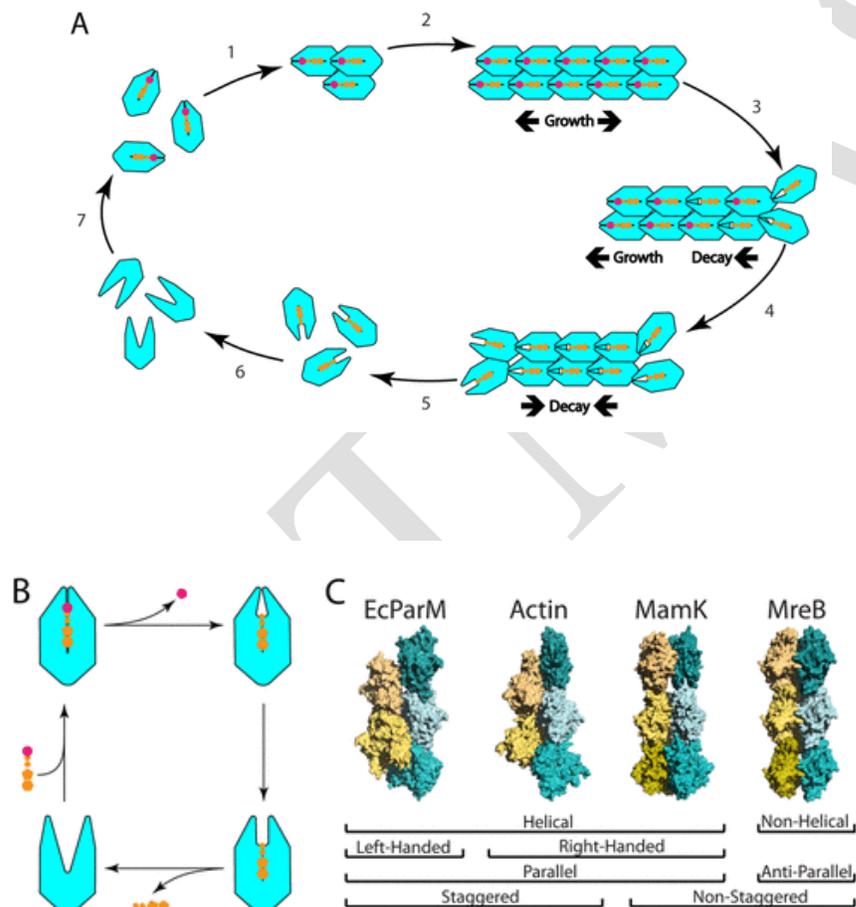


FIGURE 1: Polymer formation is a repeated feature within the actin superfamily

(A) Polymerization of actin homologues requires the formation of a filament nucleus (1). Once a nucleus has formed, filament elongation is rapid (2). Once monomers incorporate into a growing filament, they begin to hydrolyze ATP (3) until the filament end(s) is(are)

composed of ADP-bound monomers (4). Filaments initially grow in both directions. Under certain conditions, some filaments can grow from one end and shrink from the other (a process referred to as treadmilling). Eventually, lower affinity between ADP-bound monomers allows for filament disassembly from the ends (5). ADP then dissociates from ADP-bound monomers (6), which then rapidly rebind ATP (7).

(B) ATP hydrolysis, phosphate release, ADP/ATP exchange are associated with changes in monomer conformation that influence filament architecture and actin on/off rates. (C) Among actin-like filaments, the contacts within individual protofilaments vary little. By varying lateral contacts between protofilaments, different filament structures with different properties and behaviors can be generated. A subset of these structures is displayed here. *E. coli* ParM is a parallel, left-handed, helical filament whose protofilaments are staggered.

As a result of these contacts, changes in the conformation of individual monomers that result from ATP hydrolysis and phosphate release can be felt by neighboring monomers in the filament. As well as making actin an excellent chassis for use in the generation of cytomotive filaments (filaments that generate force via polymerization or depolymerization), this type of monomer–monomer communication may enable actin-related proteins to act as allosteric enzymes with high cooperativity. It is therefore formally possible that some members of the enzyme/chaperone actin subfamilies form polymers. This would not be without precedent, as other enzymes have been shown to assemble into filaments that regulate their activity: one of the best examples being the non–actin related protein, CTP synthetase.

VARIATION IN THE STRUCTURE OF ACTIN-RELATED FILAMENTS

Even though all members of the actin superfamily appear similar at the monomer level, they differ greatly in their filament structure. Much of this variation comes from changes in the lateral contacts between protofilaments. This can alter helical pitch and filament handedness and can determine whether filament strands lie parallel or antiparallel to one another. Because of this, filaments built from monomers with a similar fold can have very different properties.

In the case of eukaryotic actin, two parallel filament strands twist around one another like rope to form a right-handed helical filament that is both chiral and polar. Many of these structural features of the polymer are essential for actin's function. For example, filaments must be polar to be used as a substrate for directed molecular motors, like myosin. However, the protofilament polarity, pitch, handedness, and degree of stagger between protofilaments varies across polymers within the actin superfamily.

MreB polymers are involved in bacterial cell wall synthesis and maintenance of prokaryotic rod shape. MreB forms two-stranded, antiparallel, nonhelical filaments, with no stagger between the subunits in each protofilament. The lack of a twist is essential to MreB function in two ways. First, because MreB associates with the membrane through a single face, the absence of filament twist enables adjacent monomers to form tight contacts with the membrane. Furthermore, because MreB lacks a helical twist, MreB filaments can sustain an intrinsic curvature—something that appears to be crucial for its function in the regulation of bacterial cell shape.

MamK organizes the cellular distribution of magnetic organelles (magnetosomes) within magnetotactic bacteria. MamK filaments form parallel helical filaments like actin but with no stagger between the subunits, leaving an open cavity between the protofilaments. This raises some interesting questions about how these structural differences influence MamK polymer dynamics, the interaction of the polymer with magnetosomes, and how the lack of stagger affects the mechanical properties of MamK filaments.

ParM from the *Escherichia coli* R1 plasmid (*EcParM*) forms parallel, twisted filaments, but unlike actin, has a left-handed twist. In contrast, ParM from the *Bacillus thuringiensis* pBMB67 plasmid (*BtParM*), forms two-stranded, supercoiled, *antiparallel*, helical filaments. Interestingly, in the presence of its DNA adaptor protein (ParR), these filaments associate to form a four-stranded nanotubule with an open core; a structure reminiscent of microtubules. While this structure's mechanical properties have not been studied, it is likely that these filaments are stiffer than two-stranded filaments, again reminiscent of the mechanical properties of microtubules or of stiff fascin–cross-linked actin bundles seen in many eukaryotic cells.

EVOLUTION OF POLYMERIZATION IN THE ACTIN SUPERFAMILY

Having established a likely common ancestry for all known actin-like proteins, we next inferred a phylogenetic tree to determine the relationships among the subfamilies and to assess the number of times that polymerization has evolved. A prerequisite for this phylogenetic analysis is sufficient similarity among sequences to permit alignment. Thus we limited our tree inference to the set of actin-like families for which all pairs show

significant pairwise sequence similarity (with an E-value cutoff of $< 10^{-5}$): a set that includes the polymers actin, MreB, FtsA, ParM, and PilM; and the enzymes DnaK, type II secretion protein L, diol dehydratase reactivase, peptidase M22, BcrAD-BadFG, glutamate mutase, 2-hydroxyglutaryl-CoA-reductase, EutA, FGGY carbohydrate kinase, AnmK, GDA1-CD39, and PPX GPPA phosphatase.

The maximum-likelihood phylogeny (Figure 2) resolves the filament-forming actin families into a single clan or lineage on the tree, so the split occurring between polymers and monomers receives good (93) bootstrap support. This result strongly suggests that polymerization evolved once during the evolution of actins and that all filament-forming actins are descended from an ancestral polymer-forming, actin-like protein.

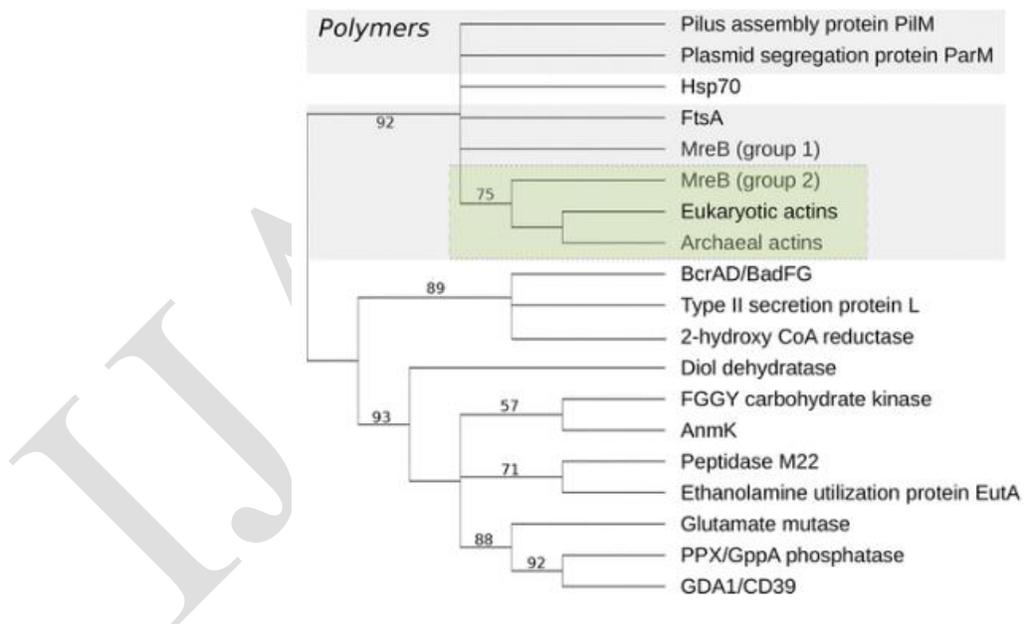


FIGURE 2: Evolutionary relationships among members of the actin superfamily

The phylogeny was inferred under the LG+C20+G+F model in IQ-Tree, and branch supports are maximum-likelihood bootstrap values. All polymer-forming actins cluster together in the tree, suggesting that the capacity to form filaments arose once during the evolution of the actin fold. Interestingly, the molecular chaperone DnaK/Hsp70 falls within the polymer lineage, suggesting that it may have evolved from an ancestral polymer-forming actin by loss of polymerization. The actin-like proteins of Crenarchaeota and the Asgard archaea (indicated as “Archaeal actins”) are the closest prokaryotic relatives of bona fide eukaryotic actins, consistent with a close relationship between the Asgard superphylum and the archaeal host cell for the mitochondrial endosymbiont.

The archaeal actins and the eukaryotic actins together form a lineage that is most closely related to the cell shape-determining protein MreB, found in rod-shaped bacteria. Our phylogenetic analysis suggest that actins are nested within the diversity of MreB proteins (green box), although statistical support for the specific relationship is low.

We have depicted the actin tree as unrooted: the divergences between superfamily members are ancient, with some likely occurring before the time of the last universal common ancestor. It nonetheless seems reasonable to suppose that the polymer-forming actins evolved from an ancestral monomer, suggesting that the root may lie somewhere among the monomeric actins. Among modern actin-like proteins, only two proteins, both monomeric—benzoyl-CoA reductase (BcrAD/BadFG) and hydantoinase (not depicted in this tree, due to high levels of sequence divergence)—are broadly distributed in bacteria, archaea, and among some eukaryotic lineages and may represent good candidates for the

oldest extant members of the superfamily; both also perform functions that may have been important during the evolution of early life. A complete version of this schematic tree is available in the Supplemental Material.

CONCLUSIONS AND PERSPECTIVES

In this review, we have examined the similarities in the structure and function of actin-like proteins across the tree of life. Importantly, our evolutionary analysis suggests that the known polymer-forming actin-like proteins from bacteria, archaea, and eukaryotes have all arisen from a single ancestral polymer-forming protein. This makes actin and its relatives an ancient protein. Importantly, much of the structural variation that appears to underpin changes in the biological function of actin-related proteins across domains is based on changes in lateral contacts between protofilaments, yielding changes in twist, packing, curvature, and polarity. In addition, it is clear that there are wide differences in the dynamics of polymer formation and disassembly across the clade. More work needs to be done to survey the variations in kinetic properties of different actin-like subfamilies (MreB, actin, MamK, ParM, etc.) to understand how subtle differences in the context of a similar fold can lead to dramatically different behaviors. For the one well-studied case of ParM, a weakening of the cross-protofilament contacts occurs when filaments are ADP bound. In addition, our analysis raises the question of whether Hsp70/DnaK can form polymers or has lost that capability during evolution.

It seems remarkable that so many of the cytomotive filaments used to generate intracellular forces, to order cellular organization, and to drive cell division across living

systems are based on this single scaffold. This reflects the role of evolution as tinkerer. It may also point to the special properties of the actin fold within the polymer-forming enzymes. Actin couples ATP hydrolysis and phosphate release to large-scale changes in conformation, altering monomer–monomer contacts in the context of a filament, giving rise to polymer dynamics and the capacity to do work. Of course, there are instances in which biological polymers appear to have evolved from nonpolymerizing proteins.

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