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# NEW TRENDS IN POLARITY
# I. TRANSPORT POLARITY AND CYTOSKELETAL COMPONENTS[1]

BY

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ABSTRACT

**New trends in polarity. I. Transport polarity and cytoskeletal components. –** These Trends are devised to update our general knowledge of Polarity with a biais on Biopolarity. Cytoskeletal components are first singled-out and vectorially motive in the establishment of intracellular polarizations.

## INTRODUCTION

The primordial electrical bipolarity (+/–), *intrinsic* to inert matter since the confinement of quarks into the first H atom, has been evolutionarily taken over in living matter by ways in which polar structures are at the molecular level made themselves felt macroscopically in the various polar biopatterns (Turian, 1994). These ways which involve the expression of positional information leading to biopolarizations modulated by *extrinsic* factors are being progressively unraveled. Their most fertile Trends will be annually reviewed, thereby complementing our general survey of Polarity (Turian, 1989-1992) in close correspondence with its sequence of chapters. Our two first Trends (I and II) will be focussed on nucleocytoplasmic processes of polarity transport which exploit the intrinsic polarity of the long, proteinaceous polymers of the cytoskeleton, actin and tubulins.

### A. *Polarity of transport*

As motile, *intracellular* functions, exocytosis and endocytosis play an important role in the organization of cell architecture (Bershadsky and Vasiliev, 1988; Lloyd, 1991; Kreis and Vale, 1993). The *exocytotic* (secretory) pathway is composed of the

[1] Chapter IV. C and E (Table of contents, Turian, 1989-92)

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endoplasmic reticulum, the Golgi apparatus, the endosomal/lysosomal system, and the plasma membrane, which is polarly separated into apical and basolateral domains in epithelial cells, and various vesicular and tubular intermediates that connect dynamically these membrane compartments. Selective targetings of proteins to the various compartments of the exocytotic pathway are governed by complex molecular mechanisms and signals. *Endocytotic* carrier vesicles which derive from peripheral early endosomes are thought to transport endocytosed materials to more centrally located late endosomes. A role for microtubules for the delivery of endocytosed molecules to the pericentriolar late endosomes via endocytotic carrier vesicles has been suggested by Gruenberg *et al.* (1989). A new protein, CLIP-170 (Pierre *et al.*, 1992), would also additionally play a role as a linker between endosomes and microtubules (Scheel *et al.*, 1993).

Nuclear uptake of *Agrobacterium* spp. T-complex (Citovsky *et al.*, 1992; Zambryski, 1992) and nuclear export of BR hnRNPs (Mehlin *et al.*, 1992) are transported *intercellularly* in a polar fashion. Polarity of TmG cap signals in pol II U snRNPs (Hamm *et al.*, 1990) suggests that these nucleic acid-protein complexes are also transported directionally. Such a vectorial transport may be required for immediate processing — integration, translation, etc. — of the emerging complex. According to Citovsky and Zambryski (1993), transport polarity is potentially determined by a specific signal associated with one end of the transported nucleic acid molecule (e.g. VirD2 protein in *Agrobacterium* spp. T-complex and TmG in snRNPs).

As linear molecules, single-stranded nucleic acids are polar and, being less rigid and easily coated by SSBs, have certain advantages over transport of double helix. Intercellular moving plant viruses (presumably through plasmodesmata) possess a single-stranded genome or replicate via a single-stranded nucleic acid intermediate (ref. in Citovsky and Zambryski, 1993) as are also most of the transported nucleic acids (*Agrobacterium* spp. T-strand, RNA, and genomic nucleic acids of many animal viruses).

### B. *Cytoskeletal components*

The microtubule cytoskeleton is thought to be intimately involved in generating and maintaining cell polarity and can generate many different morphological structures from a few structural elements (Goldman *et al.*, 1976 and Gottlieb *et al.*, 1981, both in Schulze & Kirschner, 1988).

A model for cytoskeletal reorganization responsible for the polarization of pseudopodia has been proposed by Bershadsky and Vasiliev (1993) which implicates the stabilization of the signal-induced polarization of pseudopodia.

*In vivo*, some microtubules depolymerize up to a specific point and then either regrow along exactly the same path or abruptly reverse their direction of growth. Schulze and Kirschner (1988) have also suggested that certain cytoplasmic components stabilize microtubules and exert strong influence on the direction of growth of microtubules. Because of their cellular distribution and well established association with

microtubules, mitochondria are ideally suited to serve such a function. On this basis, Gupta (1990) has proposed a new model for *in vivo* microtubule assembly.

As departing centre of intracellular transports, the nucleus has also its own skeleton, a network of insoluble protein fibers known as the nuclear matrix (Berezney and Coffey, 1960s-1970s, in Hoffman, 1993). In it, complex nuclear processes are at work, which in turn, are influenced by cytosolic signals of intra- and extracellular origin which induce biochemical cascades that result in modification of gene expresssion (see Marx, 1993 and Whiteside and Goodburn, 1993, in Bustamente, 1994).

Nuclear *actin* and its role in cells have long been a controversial issue (Volkman *et al.*, 1992) because contamination is difficult to rule out. Nevertheless, it has be found in many cases in the nucleus both in plants and animals as well as in molds (ref. in II). Systems suited to solve the problem are, however, still rare but nucleus-specific actin-binding proteins have been discovered which are reliable indicators (Ankenbauer *et al.*, 1989; Rimm & Pollard, 1989).

A direct example of the possible function of intranuclear actin has been provided by injection of anti-actin antibodies into the germinal vesicles of *Xenopus laevis* oocytes which suggested to Rungger *et al.* (1979) an actin function in chromosome condensation. A functional role for such nuclear actin in gene expression has also been suggested by transcription blockage of the lampbrush chromosome loops by microinjected actin antibodies and actin-binding proteins (Scheer *et al.*, 1984). However, "the function of nuclear actin and myosin remains enigmatic" (Milankov & De Boni, 1993). Results by Nakayasu & Ueda (1985) had suggested that rapidly-labelled RNAs anchor on the actin filaments in the nuclear matrix. It has further been proposed by De Boni (1994) that intranuclear actin and myosin represent the motor driving chromatin motion. According to Sahlas *et al.* (1993), snRNPs are associated with actin in the nuclear matrix suggesting that "both actin and snRNPs may be involved in the processing and transport of transcripts".

Other long but more rigid polymers of globular proteins, α and β *tubulins* assembled as microtubules are not only closely associated with the intranuclear onset of the bipolar mitotic spindle, but also constitute an important part of the cellular scaffold or cytoskeleton. Thereby, they provide a network of "rails" or tracks for active intracellular polar transports.

The organized dynamical activities of microtubules might involve information processing tentatively explained by Hameroff *et al.* (1986) by a microtubule automaton behavior based on coherent dipole oscillations within microtubule subunits (Hameroff & Watt, 1982; Smith *et al.*, 1984) .

Formation of a microtubule network lies in a process of out-of-equilibrium aggregation or polymerization called "dynamical instability" (Mitchison & Kirschner, 1984) which involves a GTP conversion to the diphosphate GDT. This model has been further analyzed by Dogterom & Leibler (1993) within a simple theoretical model in which the polymers are nucleated by a flat surface. According to Maddox's opinion (1993), the essence of the model must be a mechanism for switching between the state

of growth and of shrinkage of the microtubules, the "treadmilling" process previously described by Margolis & Wilson (1978, see Turian, 1989) supposed to be a random process. However, to more fully understand the underlying molecular mechanism of microtubule dynamic instability which concerns the kinetic properties of tubulin-GTP and tubulin-GDP (see reviews by Gelfand & Bershadsky, 1991 and Erickson & O'Brien, 1992), it should be additionally taken in account that tubulin GTP is present in dynamic microtubules in the limits of analytical detection. Quantitative numerical modelling of this instability rationalizes the transitions between microtubule growth and shortening in terms of a single terminal layer of tubulin GTP at the microtubule end as reviewed by Bayley & Martin, 1992).

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