shape of the moving cells, SEM reveals details of surface configuration that are important for motility, but cannot be recognized at the light microscopy level. This approach, 'dynamic morphology', has revealed that the two types of motility distinctly influence cell shape and surface architecture [1].

Stationary or surface motility is characterized by the appearance and disappearance of cytoplasmic extensions of varying sizes and shapes. During this activity the cell neither changes its position nor becomes polarized. In our experience the only exception regarding polarization are some types of white blood cells: leukemic blasts, stimulated lymphocytes and granulocytes. They can display stationary motility in a polarized configuration by producing a single major extension. This is used for fastening the cells on the substrate or on other cells and for making bending movements into all directions; we call it 'on spot motility'. [2].

During translocative motility, locomotion, the cells are always polarized. Although manner and degree of polarization can be different from one cell type to the other, most cells achieve it by the continuous development of cytoplasmic extensions at the front part. While the rear end of blood cells frequently shows a tail-like single extension, flattened cells tend to assume a trapezoid shape.

What has been said so far is based on studies performed under *in vitro* conditions, and we have, therefore, to ask whether these observations have any relevance to cellular behavior in the living organism. Microcinematography *in vivo* is technically difficult. For this reason we have chosen a model that stands halfway between *in vitro* and *in vivo* conditions: the rat mesentery after intraperitoneal injection of leukemia cells [3]. Once the leukemia cells have penetrated into the mesentery in the host, the organ is removed and placed into a culture chamber. We could show that leukemia cells within the mesentery move in the same overall manner as on glass. The cells exhibit surface motility and locomotion in their known polarized configuration [4]. However, the histologic structure of the mesentery imposes a locomotive activity that is characterized by short tracks and frequent changes in direction. In addition, the model reveals that besides propulsion, locomotion within a tissue forces a cell to pronounced adaptations of its shape to its momentary environment.

In summary it can be said that cells under identical *in vitro* conditions can exhibit two types of motility, stationary and translocative, and stay spherical or flattened according to their origin. These features combine in a way that both spherical and flat cells are able to develop stationary and/or locomotive activity. In the living tissue, a further ability is indispensable: changes of shape that allow movement despite the presence of a restrictive structured environment.

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Biochemistry and Immunochemistry of Cytoplasmic Filamentous Structures

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The cytoplasmic matrix contains at least 3 different filamentous structures (microtubules, intermediate filaments and microfilaments) which, in their entity, participate in cell motility, the maintenance of cell shape, attachment to substratum, nuclear anchorage, transport of organelles, cell division and secretory processes. Electron microscopy and, later on the use of specific antibodies in the immunofluorescent technique have revealed these cytoplasmic structures in almost all eukaryotic cells.

Microtubules (MT)

These are hollow structures with a diameter of 24 nm and a clear lumen of 15 nm, which extend radially from the nucleus (microtubular organizing centers) and terminate near the cell surface. Microtubules are sensitive to low temperature and alkaloids (such as colchicine, podophyllotoxin and vinblastine), which causes them to dissemble to dimers of mol. wt 115,000, called tubulin. Tubulin has been shown to consist of two similar subunits (α and β) of mol. wt 55,000. Thirteen of the dimeric subunits assemble, probably via ring and ribbon structures, into the microtubular wall. Microtubular associated proteins are indispensable for this polymerization step. Antibodies against sperm flagellar or brain tubulin are used in immunofluorescent studies to visualize MT in tissue culture cells. The cytoplasmic MT disappear during the onset of mitosis, they may then assemble into the spindle (respective literature [1, 2]).

Intermediate filaments (IF)

There may be a possible association between microtubules and the cytoplasmic filaments to be discussed next, since IF are usually located outside a clear zone surrounding MT [3]. In addition, the disassembly of MT by colchicine will cause an 'elastic recoil' of IF towards the nucleus. IF are long and hollow with a diameter of 10 nm; they occur as individual strands of loose fascicles that follow a curving course. These filaments are insoluble in buffers of low or high ionic strength and in non-ionic detergents. Originally, they were considered to be closely related in all cells, and only recently has their heterogeneity been pointed out and some grouping been attempted [4]. Immunological studies indicate that IF are preserved during mitosis.

(1) *Tonofilaments.* These are found in most (if not all) epithelial cells, with a polypeptide composition in the mol. wt range of 45,000–68,000. Biochemically and immunologically, they resemble pre-keratins from tonofilament–desmosome preparations [5]. They are insensitive to colchicine and may increase in certain pathological states. Auto-immune antibodies against these filaments were found in rabbits [6].

(2) *Neurofilaments.* These are also composed of subunits of mol. wt 50,000–55,000 [7], which have recently been claimed to be breakdown products of higher mol. wt subunits [8]. They are sensitive to colcemide. Their relationship to glial filaments is still being disputed; also their possible immunological relationship to smooth muscle IF.

(3) *Smooth muscle IF.* These were originally isolated by P. Cooke [9], also have a subunit of mol. wt 53,000–55,000. This polypeptide is named 'desmin' [10] or 'skeletin' [11], respectively. These filaments are also sensitive to colcemide. Antibodies against the SDS-denatured protein subunit [12] react with smooth muscle cells, endothelial cells, the Z-disc of striated muscle but not with fibroblasts, neurons or glial filaments.

(4) *Mesenchymal cell IF.* These filaments also have subunits of mol. wt 50,000–60,000. It has yet to be established if the proteins from hamster fibroblast filaments [13] and the BHK filaments [14] are immunologically related. There are also autoimmune antibodies against intermediate filaments [15], which do not seem to discriminate between the above groups.

Microfilaments (MF)

The basic component of the 5–7 nm MF is G-actin, a globular protein with a mol. wt of 42,000. The amino acid sequence has been highly conserved during evolution; there is only a 6% difference between actin from bovine heart and Acanthamoeba. By isoelectric focussing, at least three actin isomers can be distinguished: α (characteristic for striated muscle; β (preponderant in cytoplasmic microfilaments) and γ (predominant species in most smooth muscle cells). α and γ are closely related in sequence [16]. In our hands, antibodies against α and γ actins are immunologically related and, since they do not react with platelets, fibroblast and endothelium, different from the β-species.

G-actin polymerizes to form the double-stranded helix of F-actin with a half pitch of 35 nm. Filamentous actin seems to concentrate in submembranous structures. In cultured cells MF and MF bundles ('stress fibres') run parallel to the axis of the cell and insert into the membrane via α-actin in patches. Tropomyosin is also present in non-muscle cells, it is somewhat smaller than in muscle (mol. wt 30,000). Myosin, resembling smooth muscle myosin (HC mol. wt 200,000 $LC_1 + LC_2$, mol. wt 17,000 and 20,000), makes up 1–4% of the total protein (against 35% in striated and 4–8% in smooth muscle). Immunological studies showed association of

tropomyosin [17] and myosin [18] with microfilaments. Our anti-myosin (prepared against chicken gizzard myosin) does not react with myosin from non-muscle cells as shown by immunofluorescence and immunoelectron microscopy. Non-muscle cell myosin structures will, however, react with an antibody against uterine myosin, since the immunogen seems to consist of muscle type and non-muscle type myosin.

Little is known about the contractile mechanisms in non-muscle cells, although a possible regulator protein (calcium dependent regulator) has recently been described and has been localized in association with stress fibers. [19].

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In the next section, four cell classes are presented, two of them normal, two neoplastic. In each class, the emphasis is put on a different expression of the interaction of motility, shape, and fibrillar organelles. Activated blood platelets show an intense stationary motility coupled with conspicuous shape changes and alterations of microfibrillar organelles. The main regulator of this characteristic series of events is Ca^{2+}. In no other cell type has the role of this cation been so extensively analyzed, and it appears timely to apply experience on calcium in thrombocytes to motile phenomena in other cells. For instance to the locomotion of fibroblasts. In these cells, studies on the interaction of adhesion and contraction for generating translocative motility are well advanced. They allow us to envisage a first rough concept of the mechanics of locomotion in this particular cell type. For other expressions of cell motility, e.g., the projection of growth cones in neuroblastoma cell, other mechanisms, based on polymerization–depolymerization processes rather then on contraction, must be taken into consideration. Studies on the interrelation of motility, shape and fibrillar organelles are particularly promising in leukemia. In leukemia cells processed for electron microscopy, the functional state—rest or locomotion—in the moment of fixation is revealed by the spherical or polarized configuration. Thus, electron microscopic findings concerning shape and fibrillar organelles of fixed cells can be directly related to the motile behavior of living cells.

Regulation of the Contractile System of Blood Platelets

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ALTHOUGH platelets generally do not show locomotion, they nevertheless contain large amounts of actomyosin, which is essential for many aspects of platelet activity [1]. Upon activation the disk-shaped platelet generally undergoes a fast transformation to a 'spiny sphere', whereby long filiform pseudopodia are formed. Activation is brought about by a wide variety of agents, such as thrombin, collagen and ADP, but also by surface and cell–cell interaction in closely packed platelets. 'Rapid shape change' involves the temporary disappearance of a ring of microtubules which is localized in close proximity to the inner surface of the plasma membrane. Under physiological conditions, shape change is linked to cell aggregation and followed by the contraction of formed pseudopodia. During this process, the aggregates are drawn together. With higher concentrations of inducer, aggregation is accompanied by the release of a variety of substances from at least two types of specific storage organelles.

By the use of ionophores for Ca^{2+} ions, such as A 23187, it has been possible to show that all manifestations of platelet activity are due to the mobilization, in the cytoplasm, of Ca^{2+} ions [2]. It is most likely that this mobilization occurs in three different steps, namely:

(1) From the stimulated plasma membrane [3]: the local appearance of small amounts of the cation would be causative for the induction of the contraction of a performed network of submembranous filaments leading to morphological changes ('rapid shape change') and to the disappearance of the microtubular ring. (2) Upon more extensive stimulation, Ca^{2+} ions are mobilized from cytoplasmic vesicles, termed the dense tubular system (DTS) and corresponding to the sarcoplasmic reticulum of muscle cells [4]. Concomitant with this step, large amounts of F-actin are formed throughout the cytoplasm from a dispersed precursor [5], and gross contractile activity sets in. Simultaneously, two other important manifestations of platelet activity are initiated: the release reaction and prostaglandin (PG) synthesis. (3) Concomitant with the release reaction the plasma membrane acquires permeability for Ca^{2+} ions. It must be noted, though, that this influx of Ca^{2+} is not the trigger for platelet activity: shape change and the release reaction occur also in Ca^{2+}-free systems.

Although the essential role of the Ca^{2+} ions is well established, very little is known about the nature of the membrane signal which induces their mobilization. Perhaps cluster formation of membrane constituents is the essential event [6]. Shape change and release-