Downloaded from rstb.royalsocietypublishing.org

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Spreading and Locomotion of Tissue Cells: Factors Controlling the Distribution of Pseudopodia

J. M. Vasiliev

Phil. Trans. R. Soc. Lond. B 1982 **299**, 159-167
doi: 10.1098/rstb.1982.0122

Email alerting service Receive free email alerts when new articles cite this article - sign up in the box at the top right-hand corner of the article or click **here**

To subscribe to *Phil. Trans. R. Soc. Lond. B* go to: **http://rstb.royalsocietypublishing.org/subscriptions**

This journal is © 1982 The Royal Society

Downloaded from rstb.royalsocietypublishing.org

Phil. Trans. R. Soc. Lond. B **299**, 159–167 (1982)
Printed in Great Britain

Spreading and locomotion of tissue cells: factors controlling the distribution of pseudopodia

By J. M. Vasiliev

Cancer Research Centre of the Academy of Medical Sciences of the U.S.S.R. and Laboratory of Bioorganic Chemistry and Molecular Biology, Moscow State University, Moscow, U.S.S.R.

The spreading and locomotion of cells on substrata can be regarded as a result of the interaction of two groups of processes: pseudopodial attachment and stabilization. Stabilization processes integrate the results of previous pseudopodial reactions and determine the sites of further extensions. Stabilization mechanisms are probably based on the changes in the distribution of cytoskeletal elements. Usually the direction of pseudopodial extensions is approximately parallel to the predominant orientation of actin microfilaments in the nearby cortex. Two variants of stabilization can be distinguished: microtubule-independent and microtubule-dependent processes. Contact paralysis of the upper surfaces of epithelial sheets is possibly a special case of microtubule-independent stabilization. In the course of spreading, the cell may acquire a polarized or discoid shape depending on the efficiency of attachment.

Introduction

The spreading of cultured cells on the substratum may be regarded as a prototype of a major group of morphogenetic processes by which the cells acquire non-spherical shapes and become attached to extracellular matrices. The crawling movement of cells on the substrata can be regarded as a continual, polarized, non-isotropic spreading. The main reaction involved in spreading is the pseudopodial attachment reaction: extension, attachment and contraction of pseudopodia. In the course of spreading, numerous pseudopodial attachment reactions transform spherical epitheliocytes and fibroblasts into discoid or elongated polarized cells. Flattening is accompanied by the differentiation of cell cytoplasm into central endoplasm and peripheral lamelloplasm. Pseudopodial attachment reactions not only change the cell shape, they also re-organize further pseudopodial activity so that it becomes restricted to certain zones of the lateral cell edges, called active edges. All the outer edge is active in discoid cells, while the outer edge of polarized cells is divided into several discrete active and inactive zones. The distribution of many components and functional activities within the substratum-spread cells is closely correlated with the distribution of endoplasm, lamellae and active edges. Thus microtubules radiate from perinuclear centres in endoplasm into lamelloplasm. The network of actin microfilaments has a somewhat different pattern of organization in endoplasm, in lamelloplasm and at the zone of active edges (Temmink & Spiele 1980). In the endoplasm and lamellae of polarized cells this network is stretched in such a way that many large and small bundles of microfilaments are oriented approximately parallel to the lateral stable edges of the cell. The spread cells exert traction on the substratum to which they are attached (Harris 1982); most probably, this traction is exerted by the stretched cortical microfilamental network, through microfilaments anchored directly or indirectly to membrane components participating in cell–substratum

The Royal Society is collaborating with JSTOR to digitize, preserve, and extend access to *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences.*
www.jstor.org

Downloaded from rstb.royalsocietypublishing.org

attachment. Centripetal movements of certain surface and cytoplasmic components are also oriented along the same axes, i.e. from the active edges through the lamelloplasm toward endoplasm. In particular, ruffles, surface-attached particles and membrane receptors patched with corresponding ligands move in this direction. Cell–substratum and cell–cell adhesions are usually only formed by the pseudopodia at the active edges (for review see Vasiliev & Gelfand 1981). To explain the vectorial organization of spreading cells, Dunn (1980) developed the hypothesis of a continuous contraction of an actin network: the non-polymerized actin and other materials are transported toward the active edges, microfilaments are polymerized within the region of active edges, then the newly formed network contracts toward the nuclear region and is dissembled in the endoplasm. As yet, there are no direct proofs for all the postulates of this hypothesis but they seem to be in good agreement with the data available at present. In particular, the role of active edges in centripetal movement of receptors and in adhesion is well explained by the suggestion that these regions may be the special sites where new microfilaments are formed and anchored to membrane components (for review see Vasiliev 1982). The polarized organization of the substratum-spread cells is both stable and dynamic: the cells can maintain certain orientation and direction of locomotion for a long time (Trinkaus 1982) but at the same time they are able to change the distribution of their edges and direction of locomotion, especially in response to external stimuli. In this paper I shall discuss mechanisms controlling this directionality of spreading and locomotion.

Cytoskeleton-dependent stabilizations of the edge

The cytoplasmic fragment is the simplest system in which division of the edges into active and inactive zones can be observed. We (Vasiliev & Shekutjeva 1982; O. Y. Ivanova, unpublished results) obtained these fragments of normal mouse fibroblast by a method similar to that of Albrecht-Buehler (1980): mouse fibroblasts were transferred into a medium containing cytochalasin B (10 μg/ml) and the substratum-attached distal parts of their elongated processes were detached from the main cell body either with a micromanipulator or by centrifugation. When the cultures were transferred into a cytochalasin-free medium, these elongated fragments (about 20–40 μm long and 10–15 μm wide) developed pseudopodial activity and small lamellae at the two opposite edges, while their lateral edges remained inactive. When incubated with Concanavalin A, the surface of lamellae at the opposite ends of these small fragments usually becomes free of cross-linked receptors of this lectin. Immunofluorescent examination had shown that these fragments often do not contain microtubules but always contain thin microfilament bundles oriented along the length of fragment. Colcemid did not affect the shape of these fragments or the distribution of pseudopodial activity. Thus the differentiation of central endoplasm and of peripheral lamelloplasm as well as the differentiation of active and inactive edges can take place not only in the whole cell but even in the anuclear cytoplasmic fragment. We suppose that the distribution of the elements of microfilamental meshwork plays a leading role in these processes: pseudopodia are extended at the edges located near the peripheral ends of microfilament bundles, whereas the surface movement of the cross-linked receptors takes place in the opposite direction from the same edges. On the basis of these and many other observations the following rule can be formulated: pseudopodia can be protruded from the membrane only in the directions approximately parallel to the predominant orientation of microfilaments located near the corresponding membrane sites (figure 1). The same rule can be

Downloaded from rstb.royalsocietypublishing.org

also formulated as follows: directions of pseudopodial extension are parallel to those of contractile tensions acting within the cell. This rule imposes certain limitations upon the possible localization of active edges: an edge cannot be active if it is parallel to most microfilaments in the nearby cortex. This rule, however, does not predict the actual intensity of pseudopodial activity at the 'permitted' membrane sites; this intensity may depend on a variety of factors, e.g. contact with the substratum may be needed for the induction of extension.

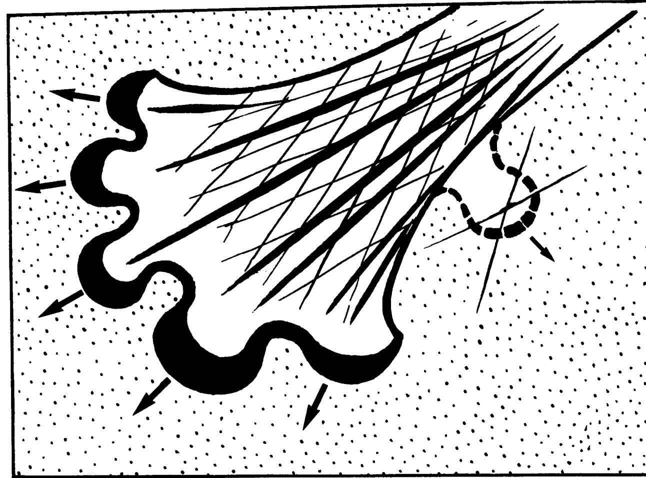

FIGURE 1. Scheme illustrating the rule of correspondence between the direction of pseudopodial extensions (arrows) at the active edges (thickened lines) and predominant orientation of microfilaments (lines in the cytoplasm). The 'prohibited' direction of the extension of the pseudopodium is shown by the broken line that has been crossed out.

Correspondence between the orientation of microfilaments and pseudopodial extensions may be the common basis of many phenomena observed in the course of spreading and locomotion. Self-perpetuation of active edges is one of these phenomena: when a pseudopodium is attached to the substratum, new microfilaments are anchored to this attachment and they may orient the further extension of pseudopodia from the nearby sites of the edge. The width of the active zone of the edge will therefore have a tendency to increase, if attachment to the substratum is effective in this zone. The active zone of the edge may exert tension on the unattached parts of the cytoplasm, orienting their microfilaments parallel to the cell surface. As a result, the edges of these stretched zones will become inactive, i.e. stabilization of lateral cell edges will take place (figure 2).

It is useful to distinguish microtubule-independent and microtubule-dependent stabilizations, i.e. the processes respectively not prevented and prevented by drugs such as colcemid or colchicine, which destroy microtubules. Stabilization of the lateral edges in cytoplasmic fragments as described above is obviously a microtubule-independent process. Usually microtubule-independent process can stabilize relatively short stretches of the edge. In contrast, microtubule-dependent processes are essential for long-range differentiation of all the cell edges into a few active and inactive zones. The difference between these two forms of stabilization is best illustrated by the observations of badly attached transformed mouse fibroblasts before and after addition of colcemid to the culture medium (Ivanova *et al.* 1980). In a control medium these cells have an elongated shape with one or two active lamellae at the two poles

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Downloaded from rstb.royalsocietypublishing.org

and with long (up to 60–100 μm each) inactive lateral sides. After the destruction of microtubules the cells become polygonal and their edges have up to 10–15 small active zones at the ends of attached cytoplasmic processes; these active zones are separated by relatively short (up to 20–30 μm long) unattached stable zones of the edge (figure 3). Directional cell movement is obviously dependent on the long-range differentiation of the leading lamella and of

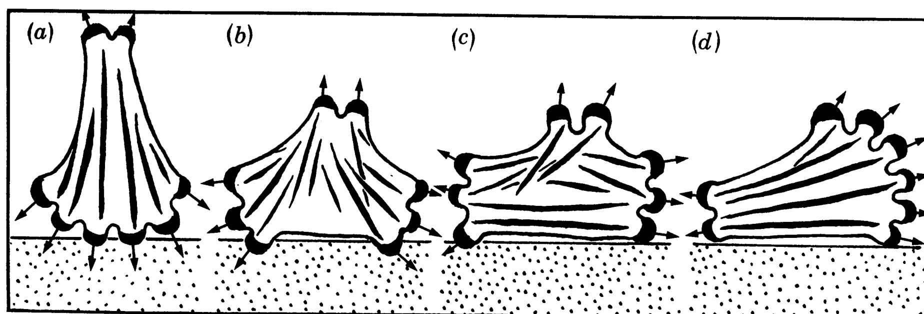

FIGURE 2. Consecutive stages of reorientation of a fibroblast moving on the adhesive substratum after contact with the boundary of non-adhesive substratum (shaded area). Designations as in figure 1. (*a*) Fibroblast before contact. (*b*) Pseudopodia in the centre of a leading active edge are not attached to the non-adhesive substratum. Successful attachment of pseudopodia at the two lateral sides of the leading edge changes the orientation of microfilaments. (*c*, *d*) The leading active edge is divided into two zones that stretch the microfilamental network in the direction parallel to the boundary of non-adhesive substratum. As a result, the cell edges parallel to this boundary become inactive. One of the two active zones acquires the leading status (*d*).

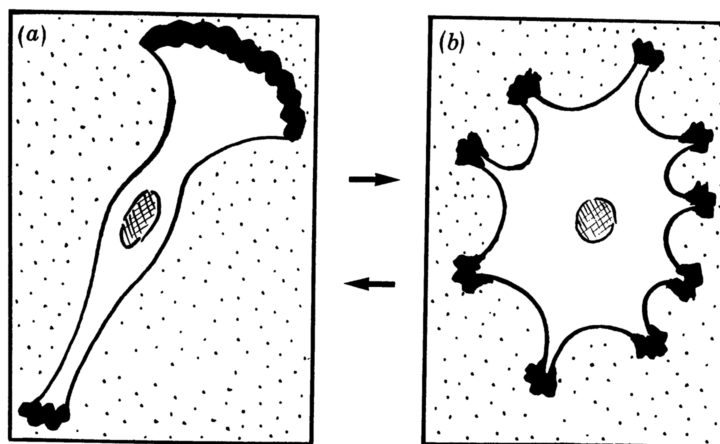

FIGURE 3. The difference between microtubule-dependent and microtubule-independent stabilization. (*a*) A transformed fibroblast with intact microtubules has only two active zones of the edges separated by long, inactive zones. (*b*) After the destruction of microtubules, numerous active zones are formed separated by relatively short concave inactive zones.

the lateral zones; colcemid-treated cells, in spite of high pseudopodial activity, are unable to perform directional translocation. Microtubule-independent stabilization is possibly based on the orientation of microfilaments: as discussed above, stretching of the microfilamentous network will prevent pseudopodial activity at the edges parallel to the direction of this stretching. The microtubule-independent process may therefore also be called stretch stabilization. It is possible that microtubules also control pseudopodial activities by stabilizing certain orientations

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Downloaded from rstb.royalsocietypublishing.org

of microfilaments. In fact, the destruction of microtubules leads to profound alterations of the orientation of microfilaments. Microfilament bundles approximately parallel to each other and to the lateral stable edges are characteristic of polarized normal mouse fibroblasts, while colcemid-treated cells without stable edges have bundles that cross each other at various angles and do not have any predominant orientation. Microtubules may act as mechanical elements

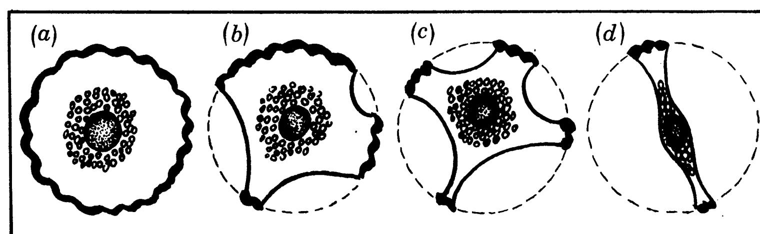

FIGURE 4. Discoid cell (*a*) with a circular active edge may aquire polarized shapes (*b*, *c*, *d*) when some parts of its active edge are detached from the substratum.

counteracting the high contractile tension developed by the stretched microfilamentous meshwork within the elongated cells and thereby preventing cell contraction. It is not, however, ruled out that microtubule-dependent stabilization has some special mechanism, unrelated to that of stretch stabilization.

RADIAL AND POLARIZED SPREADING

I have discussed intracellular mechanisms controlling the distribution of pseudopodial activities at the edges of single polarized fibroblasts. However, in the course of spreading, the cell may also achieve a radially spread state. This state is a result of isotropic spreading in all directions. Radially spread cells have a discoid shape; usually they have a circular bundle of microfilaments at the periphery and often also a 'net' of bundles approximately perpendicular to one another in the more central parts of the cell. Discoid cells, in contrast to polarized ones, do not have bundles parallel to the edges and, accordingly, they do not have stable edges. The radially spread state is an intermediate stage of spreading of normal mouse fibroblasts: spherical cells are first transformed into discoid ones but several hours later they become polarized. In contrast, the radially spread state may be the final stage of spreading of single epithelial cells; these cells are not polarized in normal conditions. The choice between radial and polarized spreading depends on the interrelations between two opposite tendencies: the tendency to widen a successfully attaching active edge and the tendency to stabilize those edges where attachment is not very effective. The cell may become discoid when pseudopodial attachments are highly effective in all active zones and these zones increase in width until they merge into a circle. In contrast, the cell becomes polarized if pseudopodial attachments are unstable and easily detached from the substratum (figure 4). These detachments may produce an initial anisotropy of spreading that is later stabilized by the mechanisms described above. Thus, other conditions being equal, transitions between polarized and discoid shapes should be correlated with alterations in the efficiency of spreading.

Our observations support this suggestion. We (Bannikov *et al.* 1982) examined a series of lines of epithelial cells (obtained from rat liver at the International Agency of Cancer in Lyon

Downloaded from rstb.royalsocietypublishing.org

(IAR series)). Single substratum-spread cells in the cultures of original non-tumorigenic lines (IAR-2, IAR-6) had a typical discoid shape with circular lamellae at the periphery. In cultures of derivative tumorigenic lines (IAR 2-31 and others) the cells became less spread and had decreased areas of lamellar cytoplasm. At the same time, these cells acquired elongated shapes with several active edges at the periphery, i.e. they became polarized. The distribution of actin bundles and of microtubules corresponded to that of the radially spread state in non-tumorigenic cultures and to the polarized state in tumorigenic ones. In the experiments of Troyanovsky (1982), transformed cells of line IAR-2-31 became better spread at the substratum after the addition of fibronectin to the medium. At the same time the shape of these cells was changed from polarized to discoid and corresponding alterations of the pattern of actin bundles were observed. Thus discoid cells may acquire a polarized shape when their spreading is decreased and vice versa. Of course, besides the efficiency of pseudopodial attachments there may be other factors controlling transitions between the discoid and polarized states. For instance, the characteristics of the microtubular system performing stabilization may be important in this respect. We do not yet know which particular factor is responsible for the difference in shapes of epithelial and fibroblastic cells.

Contact interactions of active edges

Contact of an active edge with the surface of another cell leads to contact paralysis, i.e. a local cessation of pseudopodial activity (for reviews see Abercrombie (1980) and Heaysman & Pegrum (1982)). Observations of epithelial monolayered cultures provide striking examples of contact paralysis. All the lateral contacting edges of cells forming these monolayers are locked together by firm intercellular contacts. Pseudopodia are not formed at the upper surface of monolayers; the pseudopodial activity is, however, observed at the contact-free lateral edges of monolayers. In contrast to the active surface at lateral edges, the inactive upper surface of monolayers is not adhesive for particles and cells; this surface is not cleared of patched membrane receptors (for reviews see Vasiliev & Gelfand (1981) and Middleton (1982)). On the basis of these observations it is usually assumed that pseudopodial activity is absent at the lateral edges of contacting cells of the monolayer. However, an analysis of the structure and behaviour of the monolayers of two epithelial cell lines (MPTR line of mouse kidney cells and FBT line of bovine tracheal cells) has revealed a more complex situation (O. Ivanova, E. Fetisova, I. Slavnaja & J. Vasiliev, unpublished observations). Transmission electron microscopy of the sections of monolayers has shown that two parts of the surface located above and below the belt of specialized intercellular contacts have quite different surface topographies. As might be expected, the upper surface above the belt of contacts had no cytoplasmic outgrowths except short microvilli. In contrast, lateral surfaces located immediately below the belt of contacts had numerous outgrowths varying in shape and size from microvilli 0.1–0.2 μm thick to lobopodia 3–5 μm thick. Some of these outgrowths are attached to each other or to the substratum. Thus 'contact paralysis' of epithelial surfaces has vertical asymmetry: pseudopodial activity is stopped only above the belt of intercellular contacts but not below this belt.

Vertical asymmetry of pseudopodial activity within epithelial sheets may lead to a peculiar situation: lower cell parts possibly move on the substratum with respect to those of other cells, while upper parts of the same cells form a coherent common 'roof' with inactive dorsal surfaces. This may explain the partial loss of monolayering seen in sections of epithelial sheets: the

Downloaded from rstb.royalsocietypublishing.org

lower parts of cells often overlap one another. Earlier observations of other epithelia also showed that cells within coherent sheets may extend protrusions beneath their neighbours (Di Pasquale 1975; Radice 1980). Competition of neighbouring cells for the substratum within a common sheet was obvious in our experiments with mixed cultures of two epithelia. Sheets of FBT and MPTR cells placed side by side on the substratum formed stable lateral contacts with each other, and the upper surface at the boundary of these sheets became inactive by a number of

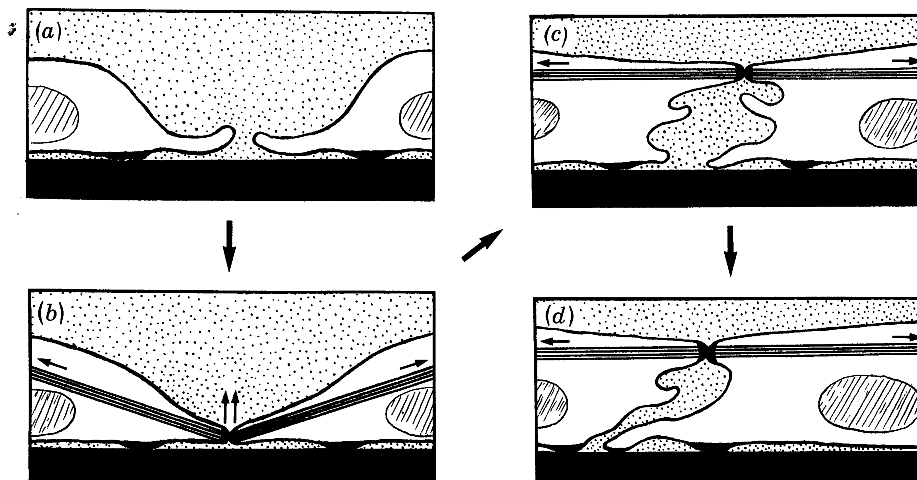

Figure 5. Scheme illustrating possible contact interactions between epithelial cells. (*a*) Two cells before the contact. Pseudopodia extended near the lower surface. (*b*) Formation of cell-cell contact between the pseudopodia. Contractile tension exerted by cortex microfilaments displaces the contact upward. (*c*) The cortex zone stretched parallel to the upper surface is formed between the contacting cells. Pseudopodia are formed only below this zone. (*d*) Pseudopodia formed near the lower surfaces of contacting cells compete for attachment to the substratum. The more successful attachment of the right cell begins to displace the left cell from the substratum.

criteria (microcinematography, non-adhesiveness for particles, inability to clear the surface of patched Concanavalin A receptors). Thus the paralysis of the upper surface was effective after the contact of heterologous cells. At the same time the boundary between the sheets was not immobile: better spread FBT cells pushed less spread MPTR from the substratum, gradually moving the boundary between the sheets in the corresponding direction. It seems very likely that this translocation of the boundary is a result of competition for the substratum between pseudopodia extended near the lower cell surfaces.

How does vertical asymmetry of pseudopodial activity within epithelial sheets arise? I suggest the following explanation (figure 5). As described above, pseudopodia are formed at lateral contact-free sides. If pseudopodia of two nearby cells touch one another, intercellular contact sites may be formed. Centripetal tensions of the upper and lower cortexes of both cells will displace firm contacts upward toward the dorsal surface. A stretched cortex zone located near the dorsal surface will be formed; the direction of tension in this zone will be parallel to that surface. This tension will be transmitted from one contacting cell to another through dorsal cell–cell contacts. The cells will continue to extend pseudopodia near their lower surface but these pseudopodia will be unable to move upwards on the dorsal surface stabilized by the stretched cortex. In other words, contact paralysis of the upper surface may be a corollary of

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES
PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Downloaded from rstb.royalsocietypublishing.org

the rule stating that pseudopodia cannot be protruded in a direction perpendicular to that of cortical microfilaments. Other cases of contact paralysis may have a similar explanation. For instance, contact of two leading lamellae of normal fibroblasts leads to the formation of layers of longitudinal microfilaments under the dorsal surfaces of both cells, and to paralysis (Heaysman & Pegrum 1982).

Conclusion

The distribution of pseudopodial activities on the cell surface is probably controlled by the distribution and orientation of the fibrillar elements of cytoskeleton. Two variants of mechanisms responsible for this control can be distinguished: microtubule-independent and microtubule-dependent stabilization. Microtubule-independent stabilization (stretch stabilization) is a short-range process, possibly based on the orientation of a stretched microfilamentous network. Microtubule-dependent stabilization is the long-range process that is essential for elongation and directional locomotion of the whole cell; possibly, microtubules stabilize an oriented distribution of microfilaments. Contact paralysis, which used to be regarded as an independent basic morphogenetic reaction (Vasiliev & Gelfand 1981), may be a special variant of stretch stabilization. The concrete roles of microtubules and microfilaments are still far from clear; the possible roles of other elements, such as intermediate filaments or the 'microtrabecular lattice' of Porter are completely obscure.

Extracellular factors may affect the shape of cells and the direction of locomotion mainly by alterations of the frequency of pseudopodial extensions and of the efficiency of the attachment of pseudopodia at various parts of active edges. This is obviously true, almost by definition, for the contact guidance by the substrata with anisotropic variations of adhesiveness. Curvature of the substratum may also affect the efficiency of protrusion and attachment of the lamellae (Dunn 1982). Effects of contact have been discussed above. An increase of the concentration of chemotactically active peptides leads to the increased formation of pseudopodia by leucocytes; these changes may be effective in orienting locomotion in chemotactic gradients (Zigmond 1982).

Each successfully attached pseudopodium exerts tension on the cytoskeleton and somewhat changes the distribution of the fibrillar cytoskeletal elements. The orientation of these elements is continually adapted to the directions in which pseudopodial attachments have been most successful. In its turn, the orientation of the cytoskeleton stabilizes the distribution of pseudopodial activities: activity is retained and increased in the most successful directions but stopped in directions where the attachment has been less efficient. At each given moment, the structure and orientation of the cytoskeleton is a statistical result of a large number of previous pseudopodial reactions and is a factor controlling future reactions. In other words, pseudopodial extensions can be regarded as exploratory trials by which a cell tests its local environment, while intracellular stabilizing mechanisms integrate and memorize the results of previous tests and direct the sites of further tests. Combination of these exploratory and memorizing mechanisms can be the basis of adaptations of cell shape and cell locomotion to the very subtle spatial differences in the properties of the microenvironment. At the same time the spreading cells continually change their microenvironment by producing and re-orienting the fibres of the extracellular matrix. The polarity of previous spreading may determine the localization of newly formed matrix fibrils (Ljubimov & Vasiliev 1982). The position of these fibrils, in its turn, may affect the distribution of further successful pseudopodial attachments. These interactions between the cells and matrix still await detailed study.

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Downloaded from rstb.royalsocietypublishing.org

The differences in the shape and pattern of locomotory behaviour of various cell types may be due to variations in the characteristics of pseudopodial reactions (the number of pseudopodia extended after various stimuli, the shape of pseudopodia, their adhesiveness to various surfaces, etc.), of the cytoskeleton (relative amounts of microtubules and microfilaments, conditions of their polymerization, properties of other cytoskeletal components, etc.) and of the matrix. Despite all these variations, the general principles of morphogenetic changes may be common for different cells: these changes are achieved by a combination of pseudopodial reactions and of cytoskeleton-dependent stabilizing processes.

I am grateful to A. D. Bershadsky for designing and preparing the drawings.

References

Abercrombie, M. 1980 The crawling movement of metazoan cells. *Proc. R. Soc. Lond.* B **207**, 129–147.

Albrecht-Buehler, G. 1980 Autonomous movements of cytoplasmic fragments. *Proc. natn. Acad. Sci. U.S.A.* **77**, 6639–6643.

Bannikov, G. A., Guelstein, V. I., Montesano, R., Tint, I. S., Tomatis, L., Troyanovsky, S. M. & Vasiliev, J. M. 1982 Cell surface and organization of cytoskeleton and surface fibronectin in non-tumourigenic and tumourigenic rat liver cultures. *J. Cell Sci.* **54**, 47–67.

Dipasquale, A. 1975 Locomotory activity of epithelial cells in culture. *Expl Cell Res.* **94**, 191–215.

Dunn, G. A. 1980 Mechanisms of fibroblast locomotion. In *Cell adhesion and motility* (ed. A. S. G. Curtis and J. D. Pitts), pp. 409–423. Cambridge University Press.

Dunn, G. A. 1982 Contact guidance of cultured tissue cells: a survey of potentially relevant properties of the substratum. In *Cell behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 225–246. Cambridge University Press.

Harris, A. K. 1982 Traction, and its relations to contraction in tissue cell locomotion. In *Cell behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 109–134. Cambridge University Press.

Heaysman, J. E. M. & Pegrum, S. M. 1982 Early cell contacts in culture. In *Cell Behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 49–76. Cambridge University Press.

Ivanova, O. Y., Svitkina, T. M., Vasiliev, J. M. & Gelfand, I. M. 1980 Effect of colcemid on the distribution of pseudopodial activity in fibroblasts. Microtubule-independent stabilization of cell surface. *Expl Cell Res.* **128**, 457–461.

Ljubimov, A. V. & Vasiliev, J. M. 1982 Distribution of fibronectin-containing structures on the surface of lamelloplasm and endoplasm of fibroblasts; hypothesis on receptor-mediated assembly of fibronectin structures. *Cell. Biol. Int. Rep.* **6**, 105–112.

Middleton, C. A. 1982 Cell contacts and the locomotion of epithelial cells. In *Cell Behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 159–183. Cambridge University Press.

Radice, G. P. 1980 Locomotion and cell–substratum contacts of *Xenopus* epidermal cells *in vitro* and *in situ*. *J. Cell. Sci.* **44**, 201–223.

Temmink, J. H. M. & Spiele, H. 1980 Different cytoskeletal domains in murine fibroblasts. *J. Cell Sci.* **41**, 19–32.

Trinkaus, J. P. 1982 Some thoughts on directional cell movement during morphogenesis. In *Cell behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 471–498. Cambridge University Press.

Trojanovsky, S. M. 1982 Effect of fibronectin on the morphology and cytoskeleton of cultured epithelial liver cells. [In Russian.] *Byull. eksp. Biol. Med.* **43**, 81–83.

Vasiliev, J. M. 1982 Pseudopodial attachment reactions. In *Cell behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 135–158. Cambridge University Press.

Vasiliev, J. M. & Gelfand, I. M. 1981 *Neoplastic and normal cell in culture*. Cambridge University Press.

Vasiliev, J. M. & Shchekutjeva, N. A. 1982 Redistribution of Concanavalin A receptors on the surface of anuclear cellular fragments. [In Russian.] *Byull. eksp. Biol. Med.* **43**, 89–91.

Zigmond, S. H. 1982 Polymorphonuclear leucocyte response to chemotactic gradients. In *Cell behaviour: a tribute to Michael Abercrombie* (ed. R. Bellairs, A. Curtis & G. Dunn), pp. 183–202. Cambridge University Press.