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# A proposal for the definition of terms related to locomotion of leucocytes and other cells

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Active locomotion of cells or organisms depends on intrinsic cellular mechanisms which are influenced by factors from the environment. Responses to environmental stimuli which take the form of directed orientation reactions are called taxes; those which take the form of undirected locomotion are called kineses (for review, see 1). The words chemotaxis (2) and chemokinesis (3) may be used to describe such reactions when the stimulus from the environment is chemical. Chemotaxis and chemokinesis play a considerable role in cell locomotion particularly in leucocytes (4, 5 & 6). Analysis of leucocyte locomotion in the presence of a source of a chemical attractant shows that these cells (a) become morphologically oriented in the concentration gradient and (b) migrate directionally towards the source of the gradient (7). Cells exposed to certain chemical stimuli in the absence of a gradient show enhanced locomotion whose speed is determined by the stimulus but which is not directional (8, 9, 10 & 11). It remains to be evaluated whether and to what extent chemotaxis and chemokinesis can be mediated by identical factors. This capacity for active locomotion is a prerequisite for leucocyte emigration into inflammatory sites and influx of these cells into such sites may be regulated by changes in speed and/or directionality of the cells. Therefore, experimental tests of cell function must be capable of distinguishing these different modes of leucocyte locomotion. Present methods measure fairly complex phenomena such as 'random locomotion' and 'directional locomotion'. Further analysis of these complex phenomena will yield information on leucocyte functions such as intrinsic locomotor capacity, chemokinesis or chemotaxis.

There is currently serious confusion of terms relating to locomotion of leucocytes. In particular the term chemotaxis has been used in a variety of ways, so that it often becomes impossible to discern what the author had in mind. Frequently the term 'chemotaxis' has been used interchangeably with 'directional locomotion' or even to describe any form of movement of leucocytes (e.g. into filters) in the presence of chemical substances (see 6). The terms 'random migration' or 'random locomotion' have been used interchangeably to express different qualities such as intrinsic locomotor capacity, changes in the speed of locomotion or just undirected movement. A standardized precise and adequate use of the relevant terms is however indispensable for the analysis of the basic mechanisms controlling leucocyte locomotion under experimental as well as clinical conditions. Such terms must allow for a clearcut distinction between: (1) basic forms of behaviour (e.g. random or directional locomotion) on the one hand and the interpretations derived from such measurements in terms of leucocyte function such as intrinsic locomotor capacity, chemokinesis, chemotaxis etc. on the other; (2) the basic 'intrinsic locomotor capacity' of a cell on the one hand and reactions to environmental influences such as chemokinesis and/or chemotaxis on the other; (3) different types of reactions (chemokinesis, chemotaxis) to environmental influences.

The evaluation of terms currently used in biology to describe locomotion of cells or organisms shows that they meet these requirements, provided the terms are used in a well-defined and standardized way.

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The present proposals are mainly concerned with leucocytes because these cells show chemokinesis as well as chemotaxis and because the confusion of terms is particularly obvious in this field. The same criteria should however be applied to all cells or organisms. We believe that such a uniform scheme would encourage a more complete evaluation of cell behaviour and permit valid comparisons of the behaviour exhibited by different cells or organisms. In the following section we present a proposal for such a standardized terminology with particular reference to responses to chemical stimuli and discuss the use of the different terms.

## NOMENCLATURE

*Definition of basic forms of locomotor behaviour. Random locomotion.* A type of locomotion that is random in direction. The axis of the moving cell or organism is not orientated in relation to the stimulus. The term random locomotion includes two meanings (12 & 13). (1) Random direction in relation to the surrounding of the cell i.e. non-directed locomotion. For instance, the cells may move in persistently straight paths but randomly directed in relation to the environment. (2) Locomotion according to a 'random walk' model (13), in which if the course of the cell is expressed in straight-line segments separated by turns, there is an equiprobable distribution of intersegmental angles; and in which the mean square displacement of the cells is proportional to time. Locomotion random in the first sense may or may not be random in the second.

*Directional locomotion.* Locomotion with preference for or avoidance of a particular direction. The axis of the migrating cells or organisms is orientated in relation to the stimulus.

*Definition of some particular functions which influence cell locomotion. Intrinsic locomotor capacity.* An intrinsic capacity of the cell to perform active locomotion.

The expression of intrinsic locomotor capacity may depend on other functions such as adhesion of cells to the substrate (14) and conceivably deformability (15).

*Chemokinesis.* A reaction by which the speed or frequency of locomotion of cells and/or the frequency and magnitude of turning (change of direction) of cells or organisms moving at random is determined by substances in the environment. Chemokinesis is said to be positive if displacement of cells moving at random is increased and negative if displacement is decreased.*

In analogy to chemotactic mediators (see below), chemokinetic mediators can be called cytokinesins or chemokinetic substances or factors.

Two forms of kinesis have been distinguished (1): ortho-kinesis, a reaction by which the speed or frequency of locomotion is determined by the intensity of the stimulus, klino-kinesis, a reaction by which the frequency or amount of turning per unit time is determined by the intensity of the stimulus.

*Chemotaxis.* A reaction by which the direction of locomotion of cells or organisms is determined by substances in their environment.

If the direction is towards the stimulating substance, chemotaxis is said to be positive, if away from the stimulating substance, the reaction is negative. If the direction of movement is not definitely towards or away from the substance in question, chemotaxis is indifferent or absent (16).

Positive chemotaxis can result in attraction towards the stimulating agent or in retaining the cells in high concentrations of the active substances by avoidance of low concentrations. Chemotaxis is increased when the directionality of locomotion is increased; if directionality is decreased, chemotaxis is said to be decreased. Terms such as necrotaxis (17) have been proposed in order to characterize the source of the attractant. Chemotactic mediators have been termed cytotaxins (18) or more vaguely chemotactic substances (19) or factors (20).

## APPLICATIONS OF TERMS

The terms which have been defined above should not be used without experimental demonstration of these forms of behaviour. If the experimental data do not provide for such a precise description, non-

* This expresses the meaning of the term chemokinesis as first proposed by Rothert (3). The present formulation is based on McCutcheon's definition of chemotaxis (16) (see below).

committal descriptive terms should be used. Where the only information is that cells have responded to an agent with increased movement, e.g. increased penetration into the filter, non-committal terms such as 'stimulated movement' or 'increased movement' should be employed (21).

*Distinction between basic forms of locomotor behaviour and functions*

None of the current methods provides for a direct measurement of functions such as intrinsic locomotor capacity, chemokinesis or chemotaxis. These functions have to be determined by analysis of complex phenomena such as random and/or directional locomotion.

*Examples.* The fact that cells or organisms accumulate in response to a chemical gradient is not sufficient proof for directional migration or chemotaxis. The analysis of the behaviour of individual cells or organisms has shown that such a phenomenon can be due to biased random locomotion in the form of klinokinesis (22 & 23) or to directional locomotion in the form of chemotaxis (7, 16 & 17).

Decreased random locomotion can reflect either defects in the intrinsic locomotor capacity, e.g. due to structural defects in the contractile system of the cell (24), or negative chemokinesis due to regulatory substances such as neutrophil immobilizing factors (25 & 26).

Decreased directional locomotion may reflect defects in the intrinsic locomotor capacity, a decrease due to negative chemokinesis and/or decreased chemotaxis e.g. due to deactivation with cytotaxins (20) or to cellular defects of chemotaxis (4).

*Distinction between intrinsic locomotor capacity and reactions to environmental factors such as chemokinesis and chemotaxis*

The distinction presents no problem if chemicals are evaluated for their activity on moving cells *in vitro*. It is also easy to distinguish changes in chemotaxis from altered intrinsic locomotor capacity by measuring random locomotion concomitantly. It is however more difficult to decide whether e.g. cells obtained from a patient show impaired locomotion because of intrinsic defects in the cell or due to immobilizing factors.

*Examples.* The analysis of leucocytes from patients with the 'lazy leucocyte' syndrome on the basis of the proposed terms shows that these cells exhibit decreased random locomotion but no defect of chemotaxis (6).

Cells may behave like 'lazy leucocytes' because of intrinsic defects e.g. in their contractile system (24) or as a result of regulatory chemokinetic influences (25, 26). It is still uncertain which of these possibilities applies to the actual 'lazy leucocyte' syndrome (27). In such a situation additional experiments evaluating cell adhesion, deformability, contractile structures and metabolic processes in 'lazy leucocytes' or the presence of cytokinesins in the circulating blood of these patients have to be performed to determine the cause.

*Distinction between chemotaxis and chemokinesis*

Experimental and clinical studies indicate that chemokinesis and chemotaxis can be regulated by different factors and mechanisms (4 & 16). The distinction between chemokinesis and chemotaxis can be made on the basis of parallel measurement of random and directional locomotion using comparable techniques. Exclusive assessment of directional locomotion does not permit this differentiation.

*Examples.* Certain substances have been reported to have an exclusive effect on chemotaxis (16 & 28), while e.g. neutrophil immobilizing factors (25 & 26) can affect the rate of locomotion without exerting a chemotactic effect.

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