Chapter 27
Mechanical Models of Cell Adhesion Incorporating Nonlinear Behavior and Stochastic Rupture of the Bonds:
Concepts and Preliminary Results

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ABSTRACT

The rolling of a single biological cell is analysed using modelling of the local kinetics of successive attachment and detachment of bonds occurring at the interface between a single cell and the wall of an ECM (extracellular matrix). Those kinetics correspond to a succession of creations and ruptures of ligand-receptor molecular connections under the combined effects of mechanical, physical (both specific and non-specific), and chemical external interactions. A three-dimensional model of the interfacial molecular rupture and adhesion kinetic events is developed in the present contribution. From a mechanical point of view, this chapter works under the assumption that the cell-wall interface is composed of two elastic shells, namely the wall and the cell membrane, linked by rheological elements representing the molecular bonds. Both the time and space fluctuations of several parameters related to the mutual affinity of ligands and receptors are described by stochastic field theory; especially, the individual rupture limits of the bonds are modelled in Fourier space from the spectral distribution of power. The bonds

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are modelled as macromolecular chains undergoing a nonlinear elastic deformation according to the commonly used freely joined chains model, while the cell membrane facing the ECM wall is modelled as a linear elastic plate. The cell itself is represented by an equivalent constant rigidity. Numerical simulations predict the sequence of broken bonds, as well as the newly established connections on the 'adhesive part' of the interface. The interplay between adhesion and rupture entails a rolling phenomenon. In the last part of this chapter, a model of the deformation induced by the random fluctuation of the protrusion force resulting from the variation of affinity with chemiotactic sources is calculated, using stochastic finite element methods in combination with the theory of Gaussian random variables.

INTRODUCTION

Cell adhesion is an important phenomenon in biology, especially in immune defence, wound healing, and the growth of tissues. The ability of the cell to divide and give birth of daughter cells is certainly a fundamental feature of the living cell. It is well known that this property strongly depends on adhesion phenomena: most cells can indeed proliferate only if they adhere to a convenient surface. The development and functioning of multicellular organisms includes very often migration of cells on surfaces; this motion relies on the coordination of attachment and detachment processes of molecular bonds (Ndri, 2001). Adhesion is further a key element for the development of vectors for the targeted delivery of medicaments – such as liposomes – which are lipidic pockets transporting active elements (Marques, 2001). Adhesion is a multistep process (Bongrand & Benoliel, 1999; Bongrand, 1982, Limberg, 2002), involving the approach of the cell towards the wall, followed by the critical phase of creation of the first bond. This step is followed by a consolidation step, consisting of an adaptation of the membrane shape, the concentration of receptors in the contact zone, and eventually the reinforcement of the cell membrane in the vicinity of the adhesion zone (Bongrand & Benoliel, 1999).

Cell adhesion is a multiscale phenomenon involved in *cell rolling* and cell migration (Bongrand et al., 1982; Bongrand & Benoliel, 1999), due to the induced *cell motility*. Cell adhesion involves complex phenomena that intervene in various biological processes such as the growth of the tissues and the immune response, due to the motion of leukocyte cells (Bongrand et al., 1982). The motion of cells along a wall occurs by two different mechanisms: rolling (e.g., the movement of leukocytes along a blood vein), due to the action of the fluid flow around the cell on the contact interface (Figure 1), and protrusion and retraction, resulting from a modification of the cytoskeleton structure (Bongrand & Benoliel, 1999; Sagvolden et al., 1999). Protrusion is usually associated to the creation of lamellipods and *focal contacts* on the adherent part of the contact interface (Figure 1).

Rolling and active deformation of the cell occur, for instance, during immune defence due to the action of leukocytes, which are transported by plasma flow, captured by the wall by rolling and further move towards the infected zone by active deformations (Jones, 1996).

The creation of new connections is the result of the junction between free and specific molecules, the ligands and the receptors (Bongrand, 1982; Marques, 2001); the failure of existing connections occurs by pulling effects due to the cell motion, which result from the action of various forces. Several models have been developed in the literature in order to describe the adhesion kinetics or the deformation of the cell during the adhesion process: those models can generally be classified into probabilistic approaches (Roberts et al. 1990; Haussy and Ganghoffer 2001) or deterministic modelling strategies (Combs et al. 2004). Other modelling or experimental studies

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