A model based upon minimization of surface energy is proposed as an explanation for compaction and internalization of cells during mammalian embryo development. The model is used to simulate and graphically display these phenomena on a computer.

1. Introduction. The first three divisions of the mammalian egg cell result in eight spherical, equivalent and totipotential cells (Burgoyne and Ducibella, 1977; Garner and McLaren, 1974; Kelly, 1979) that constitute the early morula. Morulae become blastocysts, bodies with two cell types: trophoblast cells and inner mass cells. These cells can be distinguished by their enzyme (Izquierdo et al., 1980; Izquierdo and Ebensperger, 1982) and immunoprotein (Solter and Knowles, 1975; Wiley and Calarco, 1975; Muggleton-Harris and Johnson, 1976) contents, by their morphology (Van Blerkom et al., 1973; Ducibella et al., 1975) and by their relative positions with respect to each other (inner mass cells surrounded by trophoblast cells). Each cell type normally gives rise to a particular descendancy. In general, embryonic structures are derived from inner mass cells whereas extra-embryonic structures (placental membranes) are trophoblast derivatives (Surani and Barton, 1977). Thus blastulation constitutes the first cell differentiation in the organism. Differentiation and morphogenesis are complex biological processes underlying development and related to the processes of tumorigenesis and wound-healing. The morula–blastocyst transition constitutes one of the simplest cases of these phenomena that can be studied both theoretically, because it starts with identical cells in a spherical shape, and experimentally because the cells can be cultured in a medium of known composition.
At the cellular level, the transition from morula to blastocyst requires that each cell of the morula opt for one of the aforementioned two types of cells found in the blastocyst. What determines this choice for a cell is not yet clear. There is ample evidence to support the hypothesis that this choice is not determined by genetic factors alone. For example, morulae can be developed into a normal embryo even with missing or destroyed blastomeres (Hogan and Tilly, 1978a, b; Rossant and Lis, 1979; Rossant and Vijh, 1980; Fernandez and Izquierdo, 1980) or into blastocysts of only one cell type after a treatment (e.g. exposure to Li⁺) that slows down the rate of cell divisions (Izquierdo and Becker, 1982). Furthermore, the choice for a cell must be influenced by the other cells (the whole) since a morula deprived of the outer cells can achieve a normal development by replacing them from inner cells.

It should be pointed out that Tarkowski and Wroblewska (1967) hypothesized that the fate of a cell is determined by its relative position just before blastulation occurs: the inner cells of the morula give rise to inner mass cells of the blastocyst while the outer cells develop into trophoblast cells. Their hypothesis does solve the problem of fates of blastocyst cells by the inclusion of a positional signal before blastulation occurs and a response which forces the genetic content to express one phenotype at the blastocyst stage. However, it doesn’t provide an answer to the question of whether the inner cells of the morula are there by a genetic program or whether their positions depend on a mechanism that can adapt to new circumstances, nor does it specify the nature of the positional signal.

To understand the mechanism whereby a cell is chosen and its eventual role in morphogenesis is determined, it is fruitful to analyze the transition between the early and late morula. This transition includes several phenomena (Van Blerkom and Motta, 1979; Sutherland and Calarco-Gilam, 1983): cell divisions, compaction, peripheral sealing and the appearance of inner cells (completely surrounded by other cells). Compaction is a process whereby the contact area between blastomeres is increased to the point that all the intercellular space necessarily found between close-packed spheres is eliminated (through deformation of the initially individual spherical blastomeres), while the whole embryo takes on a spherical shape (Calarco and Brown, 1969; Ducibella, 1977; McLachlin et al., 1983; Lo and Gilula, 1979; see Fig. 1). The time at which compaction occurs is independent of the number of cells (Fernandez and Izquierdo, 1980). After compaction, cells develop junctions which allow the interchange of small molecules between cells and which seal off the intercellular surfaces along the lines where the external cell membranes pass between pairs of cells (Ducibella and Anderson, 1975). Inner cells appear shortly after compaction (Ducibella, 1977; McLachlin et al., 1983), and this is followed by peripheral sealing of the