Chapter 1. Historical background, pattern duplications and information compression.

Since a fertilised egg can grow into an adult, this single cell must, in some sense, contain the full complexity of the adult organism. Hartsoeker's preformation hypothesis of 1694 addressed this paradox by postulating the presence of miniature homunculi within sperm heads [1]. This hypothesis specified where the developmental information came from in any given generation. Each subsequent generation, however, must be simpler than the previous one; until, like a set of Russian Matryoshka dolls, the succession of nested homunculi becomes exhausted, Fig. 1.

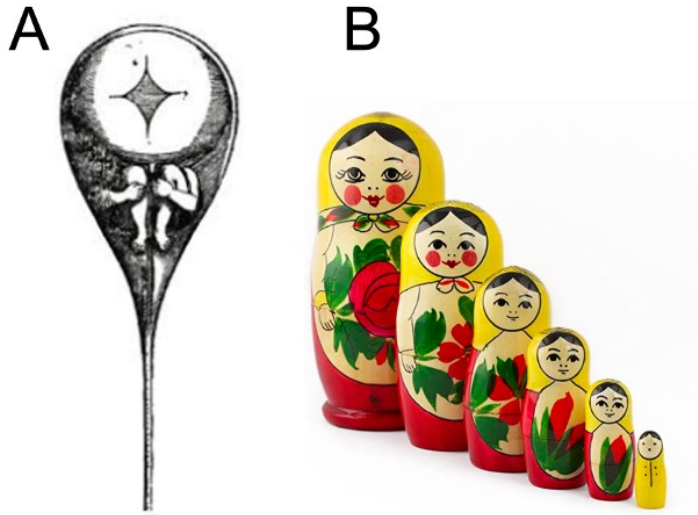

Fig. 1. Hartsoeker's hypothesis. A. Pre-patterned homunculi are transmitted in sperm heads. However, the ever-smaller homunculi would become depleted in successive generations, like a set of Matryoska dolls **B.**

Major advances in understanding developmental mechanisms were made by the early 20th century embryologists [2] [3]. In particular, the "organiser" region of Mangold and Spemann induced mirror-image duplications when transplanted between amphibian embryos. These pioneering studies gave rise to the concept that growth is regulated within morphogenetic fields, with the implicit assumption that the initial patterning processes take place on epithelial surfaces. Epithelial topography may be convoluted, but surfaces are critical, even when they are not flat.

Turing's theoretical analysis of chemical reaction/diffusion mechanisms formed the basis for modern morphogenetic models [4]. This model was extended by Wolpert's hypothesis that concentration gradients could assign "positional values" to individual cells within a morphogenetic field [5]. On this hypothesis, "positional information" provides a background pre-pattern that allows the differentiation of specialised cell-types with precise spatial patterns. The compelling attraction of a gradient model is that it can supply vectorial information, both the direction of flow and the concentration of a morphogen. Transmission of vectorial information must be essential during development. However, for the positional value of each cell to allocate a unique individual fate would impose a tremendous information load on the genome. This paradox leads back to Hartsoeker's postulated homunculi: in its original formulation Wolpert's hypothesis fails to address the requirement for genetic information compression.

While Turing's analysis of reaction/diffusion mechanisms addresses the transmission of morphogenetic information, his earlier work on computable numbers provided the theoretical basis for coding algorithms and information compression. Turing's hypothetical "machine" could read one symbol on a tape and interpret this as an instruction to move either forwards, or backwards, to scan adjacent symbols [6]. By introducing recursive, re-iterative loops, a sequence

of symbols can be used to encode complex data. In principle, the encoded information could contain a set of instructions to manufacture another Turing machine. It is not possible, however, for the tape to encode a set of instructions that will both build a Turing machine and replicate the tape it carries. From Turing's viewpoint, the DNA "tape" of a yeast cell could not contain its full description. Instead, its highly organised cellular structure is transmitted as an intact, functioning unit. The DNA encodes only the information required to maintain and replicate a pre-existing cell. Each daughter cell utilises the mother cell as a template on which to build itself, and thence to read the replicated tape. Maintaining and accessing epigenetic information must be essential as the morphogenetic programs of multicellular organisms unfold. To construct a fly's eye, or the human brain, requires that information encoded in the linear DNA sequence be transcribed, translated and displayed on cytoplasmic interfaces, before the assembly of differentiated adult tissues.

Summary:

Morphogenetic interactions direct the proliferative growth of epithelial sheets, the allocation of differentiated cell fates, and the assembly of 3D tissues from 2D templates.

References:

1. Hill, K. A. Hartsoeker's Homunculus: a corrective note. *J Hist Behav Sci* 21, 178–179 (1985).
2. Spemann, H. Die Erzeugung tierischer Chimaeren durch heteroplastiche embryonale Transplantation zwischen Triton cristatus u. taeniatus. *Wilhelm Roux Arch Entwicklungsmech Org 48 533–570* 48, 533–570 (1921).
3. Weiss, P A. *Principles of Development*. Henry Holt and Company (1939).
4. Turing, A. The chemical basis of morphogenesis. *Philos. Trans. R. Soc. Lond. Ser. B-Biol. Sci.* 237, 37–72 (1952).
5. Wolpert, L. Positional information and the spatial pattern of cellular differentiation. *J. Theor. Biol.* 25, 1–47 (1969).
6. Turing, A. On computable numbers, with an application to the Entscheidungsproblem. *Proc. Lond. Math. Soc.* 42, 230–265 (1937).