# MORPHOGENS

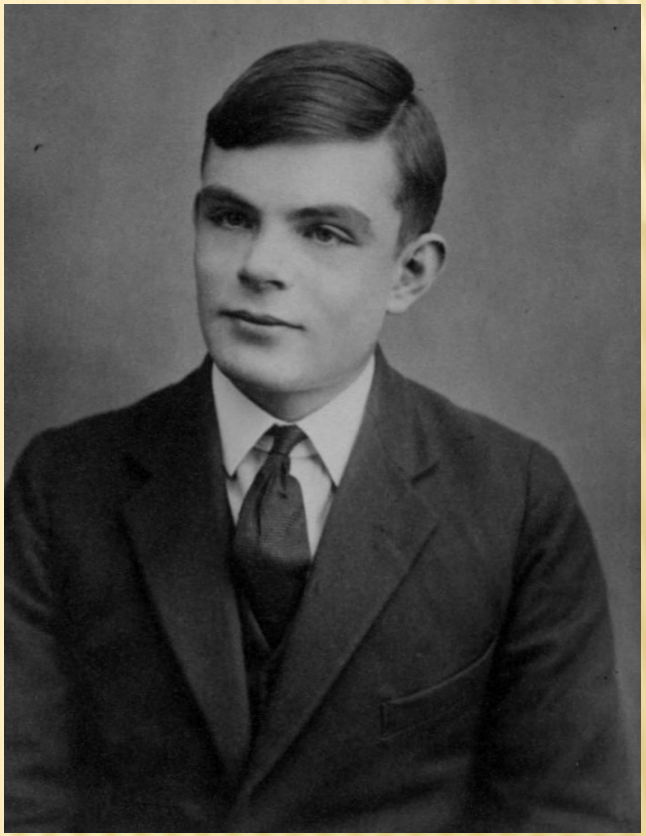
A MORPHOGEN IS A SUBSTANCE GOVERNING THE PATTERN OF TISSUE DEVELOPMENT IN THE PROCESS OF MORPHOGENESIS, AND THE POSITIONS OF THE VARIOUS SPECIALIZED CELL TYPES WITHIN A TISSUE. MORE SPECIFICALLY, A MORPHOGEN IS A SIGNALING MOLECULE THAT ACTS DIRECTLY ON CELLS TO PRODUCE SPECIFIC CELLULAR RESPONSES DEPENDING ON ITS LOCAL CONCENTRATION.

SINCE MORPHOGENS DIFFUSE THROUGH THE TISSUES OF AN EMBRYO DURING EARLY DEVELOPMENT, CONCENTRATION GRADIENTS ARE SET UP. THESE GRADIENTS DRIVE THE PROCESS OF DIFFERENTIATION OF UNSPECIALISED (STEM) CELLS INTO DIFFERENT CELL TYPES, ULTIMATELY FORMING ALL THE TISSUES AND ORGANS OF THE BODY.

## THOMAS HUNT MORGAN

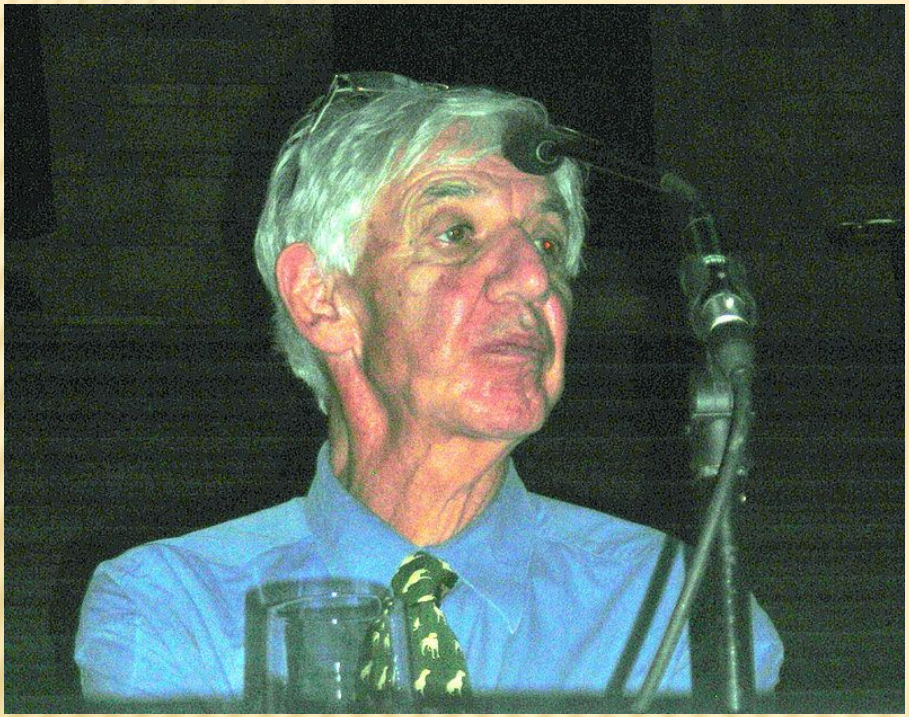
The concept of the morphogen has a long history in developmental biology, dating back to the work of the pioneering Drosophila (fruit fly) geneticist, Thomas Hunt Morgan, in the early 20th century.

## ALAN TURING



The term was coined by Alan Turing in the paper, The chemical basis of morphogenesis where he correctly predicted a chemical mechanism for biological pattern formation.

## LEWIS WOLPERT



## PETER LAWRENCE

LEWIS WOLPERT REFINED THE MORPHOGEN CONCEPT IN THE 1960S WITH HIS FAMOUS FRENCH FLAG MODEL, WHICH DESCRIBED HOW A MORPHOGEN COULD SUBDIVIDE A TISSUE INTO DOMAINS OF DIFFERENT TARGET GENE EXPRESSION (CORRESPONDING TO THE COLOURS OF THE FRENCH FLAG). THIS MODEL WAS CHAMPIONED BY THE LEADING DROSOPHILA BIOLOGIST, PETER LAWRENCE.

## CHRISTIANE NUSSLEIN-VOLHARD

## MORPHOGENESIS OF DROSOPHILA FRUIT FLIES WAS INTENSIVELY STUDIED IN THE LABORATORY

CHRISTIANE NUSSLEIN-VOLHARD WAS THE FIRST TO IDENTIFY A MORPHOGEN, BICOID, ONE OF THE TRANSCRIPTION FACTORS PRESENT IN A GRADIENT IN THE DROSOPHILA SYNCITIAL EMBRYO. SHE WAS AWARDED THE 1995 NOBEL PRIZE IN PHYSIOLOGY AND MEDICINE FOR HER WORK EXPLAINING THE MORPHOGENIC EMBRYOLOGY OF THE COMMON FRUIT FLY. GROUPS LED BY GARY STRUHL AND STEPHEN COHEN THEN DEMONSTRATED THAT A SECRETED SIGNALLING PROTEIN, DECAPENTAPLEGIC (THE DROSOPHILA HOMOLOGUE OF TRANSFORMING GROWTH FACTOR BETA), ACTED AS A MORPHOGEN DURING THE LATER STAGES OF DROSOPHILA DEVELOPMENT.

# FRUIT FLY

Drosophila melanogaster has an unusual developmental system, in which the first thirteen cell divisions of the embryo occur within a syncytium prior to cellularization. Essentially the embryo remains a single cell with over 8000 nuclei evenly spaced near the membrane until the fourteenth cell division, when independent membranes furrow between the nuclei, separating them into independent cells. As a result, in fly embryos transcription factors such as Bicoid or Hunchback can act as morphogens because they can freely diffuse between nuclei to produce smooth gradients of concentration without relying on specialized intercellular signalling mechanisms. Although there is some evidence that homeobox transcription factors similar to these can pass directly through cell membranes, this mechanism is not believed to contribute greatly to morphogenesis in cellularized systems.

In most developmental systems, such as human embryos or later Drosophila development, syncytia occur only rarely (such as in skeletal muscle), and morphogens are generally secreted signalling proteins. These proteins bind to the extracellular domains of transmembrane receptor proteins, which use an elaborate process of signal transduction to communicate the level of morphogen to the nucleus. The nuclear targets of signal transduction pathways are usually transcription factors, whose activity is regulated in a manner that reflects the level of morphogen received at the cell surface. Thus, secreted morphogens act to generate gradients of transcription factor activity just like those that are generated in the syncitial Drosophila