The logic of life

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Even though the entire human genome has now been 'read' - the chemical composition of our DNA has been more or less mapped out, gene by gene - we still have a rather poor grasp of how living cells actually work. That's because the genome is not really a 'book of life', but is just a catalogue of the parts of the cellular machinery, rather like a list of all the electronic components in a complicated computer circuit. The key challenge for biologists in the twenty-firstt century is to figure out how those component genes are wired together. To do that, they may need help from physicists, electronic and computer scientists, and others.

On Thursday 20 April at the Condensed Matter and Materials Physics conference, organized by the Institute of Physics at the University of Exeter, Pieter Rein ten Wolde of the Institute for Atomic and Molecular Physics (AMOLF) in Amsterdam will explain how, by tracing some of the key patterns in this gene wiring, one can start to understand how 'gene logic' works. This is the first step in compiling an instruction manual that shows how the cell's components are connected up.

One of the central discoveries in this field, now called 'systems biology' was made as far back as the 1960s, when it was found that genes can 'regulate' each other, controlling the rate at which a gene is converted to its corresponding protein molecule or even switching one another 'on' or 'off' entirely. These networks of interacting genes are called gene regulatory networks and they lie at the heart of how cells work.

The functioning of gene networks looks a lot like the way components in electrical circuits might control one another. Two genes are considered

to be 'wired together' if one of them influences the activity (the rate of protein production, say) of the other. In this way, genes can be connected to act as switches or amplifiers in biochemical processes. This is why many researchers in systems biology are starting to talk about the genetic circuitry of cells using terms and concepts borrowed from electronic and computer sciences, and even to talk of cells as though they perform kinds of computation, receiving signals which they process to generate particular kinds of 'output' responses.

Ten Wolde asks whether these networks display characteristic patterns that might provide clues to how they work, or whether in contrast the wiring pattern just looks random. He has found, for instance, that genes in E. coli bacteria that regulate one another seem to be clustered closer together on the bacterial DNA than would be expected if they were just positioned at random. Sometimes, in fact, these regulatory segments on DNA actually overlap, like bits of text that run into one another. Such overlap can help to synchronize the activity of the genes - enabling one to be switched 'on' only while the other is switched 'off', say. This sort of correlated behaviour can make the gene regulatory networks less easily disrupted by random 'noise' in the biochemical system, so that they operate more effectively than if the genes were spaced randomly. Ten Wolde thinks that these improvements could provide an evolutionary selective pressure that makes the genes drift together on the genome.

Ten Wolde has also found how gene regulatory networks can do geometry. He has shown how interacting genes in a developing fruitfly embryo can locate the precise midpoint of the oval-shaped embryo, so that a protein is produced in one half of the organism but not the other. This provides a mechanism for dividing up the embryo so that the collection of initially identical cells generate compartments that follow different developmental pathways, becoming different body parts of the fly.

Source: Institute of Physics

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