

The Epigenetic Alphabet

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Introduction

Cells are really small, so small that we cannot see them with our eyes. Our whole body is made out of these tiny cells but we spend our life looking at our hands and we never see one of the cells that they are made out of. When we look at our skin all we see is this a flat, unbroken, surface. Cells are so small they are entirely outside of our field of vision.

These cells are not empty; far from it. Inside each of our cells are thousands and thousands of even smaller things. Each of our cells has tiny proteins floating around inside of them. Proteins are so small that we can fit thousands of them inside something that is so small we cannot see it.

Our cells have different compartments that perform different functions: there are particular places where proteins are made, particular places where proteins are modified and readied for work, and there is a particular place where all of our DNA is. Our genetic information is inside a part of our cells called the nucleus.

The nucleus is a subcompartment of a cell. Cells are so small we cannot see them. You could spend your whole life staring at your hand and you would never see one of the cells your hand is made out of. Inside this, inside the thing so small we cannot even see it, is an even smaller thing that houses all our DNA. There is a problem with this type of organisation: our DNA is billions of pieces long.

It is true that the building blocks of DNA are very small but even with how small these units are the whole of our DNA, our genome, is monstrously long. There is just so much of it. If you laid out your genome in a straight line it would be metres long. Inside a small compartment inside the thing that is so small we cannot see it there is a metres long string. How could you possibly fit something so large inside something so small?

Our genome is instructions for how to make things, mainly proteins. A cell reads a stretch of DNA and builds a protein based on what the DNA said. Everything our cells do they do with proteins: if a cell wants to eat it needs to use a specific protein and if it wants to breathe it needs to use a different specific protein. Some proteins are essential so if a cell becomes unable to make a specific protein it will die soon afterwards. The cell needs to be able to access the DNA so it can make the proteins it needs to make. Because the genome is so long the cell has to do strange things to fit it inside the nucleus.

The DNA is put through an incredibly harsh packing process: first it is wrapped around things called histones and then the resulting DNA:histone complexes are wrapped around themselves. This wrapping and squashing process is so extreme that the cell manages to fit the metres long genome inside the microscopic nucleus.

Because the DNA has been wrapped and squashed the cell does not have instant access to it. It needs to use the DNA to make the proteins it needs to survive but the DNA is wrapped around histones so the cell cannot read it. The only way the cell can read the DNA is taking it off the histones. Because the DNA is wrapped around histones the cell cannot use it quickly and efficiently.

DNA is four elements repeated over and over; it is just the same four things repeated in various combinations. It is a code that is impossible to crack, impossible to read. DNA is almost entirely incomprehensible, as in you can't look at a stretch of DNA and tell anyone what protein it will make.

Imagine a cell wants to make a specific protein called protein A. If the cell does not make this protein in the next hour it will die. Cellular machinery in the nucleus goes to the DNA and starts looking for the gene that codes for protein A. How can the cellular machinery find the exact stretch of DNA it needs when every part of the genome looks exactly the same?

We think there are about twenty thousand genes in the human genome. There are too many genes. The cellular machinery doesn't have time to search through the whole genome all to find the one gene it needs.

If the cellular machinery was simply presented with billions of the same four things over and over it would have absolutely no idea what to do. DNA on its own is completely unusable because there is so much of it. If there are twenty thousand genes in the human genome and the cell needs to make one specific gene how would it go about this task? How would it find the gene it needs? How would it ensure it reads the one gene it needs instead of the twenty thousand other genes? The cellular machinery needs help because the mass of DNA is so monstrous it has no idea how to approach it.

The cellular machinery needs to be helped to read the DNA in some way. The problem is even more serious than I have suggested so far because there is a huge amount of genetic information in our genome that is not genes. There is just too much DNA for the cellular machinery to be able to approach and use the genome effectively.

If someone gives you a book and tells you to read it then you will read the book. If someone gives you twenty thousand books and tells you to read them you will not read any of the books. What is the point? The task is impossible. The task the cell has to perform is like this: it cannot read twenty thousand things. The cell needs help; it needs to be told what to read. The genetic information needs to be organised so the cell knows how to use it. Genetic information is organised through a process called epigenetics.