Possible Interaction Between Epigenetics, Genetics and Quantum Mechanics

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ABSTRACT

The human genome consists of roughly 23000 genes which cannot explain the enormous diversity of proteins or behavior. A second epigenetic code warrants adaptive variation of gene expression. The rationale of this variation are transfer reactions such as methlyation, acetylation or phosphorylation of DNA, RNA or histones including reverse reactions. Enzyme activity and especially transferases are supposed to integrate tunnel effects of protons or electrons in order to overcome energy barriers. The paper discusses the theoretical involvement of tunnel effects as the base of transferase activity and hence adaptive epigenetic gene expression.

Key Words: epigenetics, methyl transferase, DNA, histone, tunnel effect

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Introduction

How do we become the individuals who we are and how do we behave as we behave with such a low number of genes? Man has approximately 23,000 genes, i. e. less than a mouse. Insects (fire ant) have about 16,600 genes, nematodes (caenorhabditis elegans) even 19,000 and plants about astonishing 27,000 (Genlisea tuberosa) genes (Pray, 2008). Man cannot "compete" with Trichomonas vaginalis, which possesses whopping 60,000 genes. Therefore, genes cannot by far explain the variety of proteins, human behavior and moreover complex diseases we may suffer from, respectively. Many hopes were set into the human gene project but this attempt yielded some kind of new sobriety. However, nature has invented a new strategy to warrant sufficient diversity.

Nature developed a sophisticated solution called epigenetics. We have a genetic code on the one side and an epigenetic code on the other side, which implies modulation of the DNA itself but also of histones and RNA or even mitochondrial DNA (Golbabapour *et al*., 2011; Kegel, 2016; Stimpfel *et al*, 2018). The DNA coils around the basic histone protein complex being composed of H2A, H2B, H3 and H4 histone proteins. In addition, a linker histone (H1) connects the nucleosome to the DNA (Yan *et al*.,2003). Approximately 30 millions of DNA-histon complexes (nucleosomes) exist in humans. Four major enzyme complexes transfer functional groups - e.g. methyl groups - to either DNA or histones thus gradually modifying gene expression. In general, acetylation and deacetylation, methylation and demethylation or phosphorylation and dephosphylation among other groups can change gene expression substantially.

Biology and Epigenetics

There are numerous biological examples how epigenetics can modulate gene expression and therefore life. The suppressed X chromosome in women (Barr body) is probably the most common epigenetic phenomenon by DNA methylation or histone deacetylation (Tycko and Ashkenas, 2000). The best known animal phenomenon is the development

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of the bee larva (Apis melifera) to the queen instead to a worker by feeding the bee with royal jelly by the nurse bees. Here, the modified methlyation pattern and the alternative splicing - thereby producing completely different gene products - play together. In the European sea bass (Dicentrachus labrax) male animals develop at temperatures in the sensitive phase of the egg over 17 ° C, otherwise - with lower temperature - females will be the offspring. The reason for this different temperature dependent gene expression is the methylation of the aromatase gene (formation of androgens) at higher temperatures. The common toadflax (Linaria vulgaris) completely changes its flower form due to methylation with a complete different appearance (phenotype). The same gene code is modified by an epimutation due to methylation of the LCYC (Linaria cycloidea gene) gene (Kegel, 2016).

A very important epigenetic issue is spermatogenesis in mammals and other species (Ge *et al*., 2017; Cui *et al*., 2016; Jenkins *et al*., 2017). Apart from DNA methylation, non-coding RNAs and histone acetylation plays a decisive role to control the histone-protamine transition during spermatogenesis. Initially, transition proteins occur and testis specific histones and are step by step replaced by basic protamines 1 or 2 (PRM1, PMR2). In sperms about 90% of the histones have been replaced by protamines which warrant adequate condensation of the nucleosomes. This very complex vulnerable transition process in sperm development may lead to diseases such as the Fragile X-syndrome but is necessary to reset the sperm to a status of totipotency (Ge *et al*., 2017).

Enzyme Activity

Enzyme activity has been associated with quantum mechanical effects such as tunneling via an energetic wall (Marais *et al*. 2018; Alleman and Scruton, 2009). The classical example of tunneling in physics is the alpha-decay but tunneling of protons in the DNA are renowned quantum biology examples which were and are supposed to cause spontaneous mutations (Löwdin, 1963; Trixler, 2013). The reason for tunneling is that the wave function flattens after the barrier but never disappears. The number of particles *dN* which overcome the barrier during the time interval *dt* is statistically derived from the wave function being according to Meschede (2010)

$dN = -f_0 DNdt$

f_0 (frequency of trials to overcome the barrier) is given by

$f_0 = h/2ma^2$, h being the Planck constant, m the mass of the particle and a the width of the barrier. D denotes the probability of passing the barrier (Fig. 1).

In clear terms D corresponds to

$$D = e^{-\left(\frac{2d}{h}\right)\sqrt{2m(U-E)}}$$

or $= \varphi_{after}2 / \varphi_{before}2$. d is the depth of the barrier being roughly – as the width – a magnitude of 1 Å and U - E stand for difference between the potential (height) of the barrier and the energy of the particle, respectively. For the mass of an electron (0.9 10^{-27} g) and a = b = 1 Å and ΔU = 1 eV the exponent will be 1 and f_0 being about 10^{16}/sec (Meschede, 2010). The probability of passing the barrier can be interpreted as the ratio of amplitudes of the wave functions φ after and before the barrier. As the mass of the particle is decisive we learn that the chance to overcome the barrier is lower for heavier particles such as protons also depending on the geometry of the tunnel.

An important enzyme involved in epigenetic modulation is the DNA-methyl-transferases (DNMT1) which has Zn++binding sites which have proved to have several quantum mechanical regions (Zhang and Bruce, 2006; Yang *et al*., 2019). Quantum mechanical effects influence the methylation of DNA especially at 5´postitions in CpG-rich islands (Cytosin-Guanin; p stand for the prime coding strand) of the DNA (Smith *et al*., 1992) (Fig. 2). In general, methylation of the DNA causes silencing of a gene and demethylation activates a gene (Kegel, 2019). On the contrary, methylation of histones can activate or deactivate a gene, depending on the histone considered (Fischer, 2016). Additionally, acetylation and phosphorylation of histone complexes usually activate gene expression.

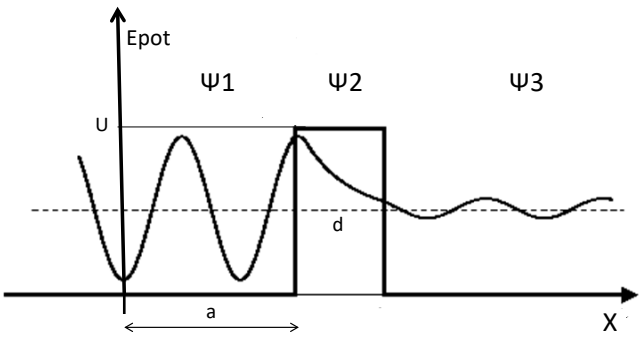

Figure 1. Schematic diagram of the tunnel effect. Adapted according to the notation of Meschede 2010.

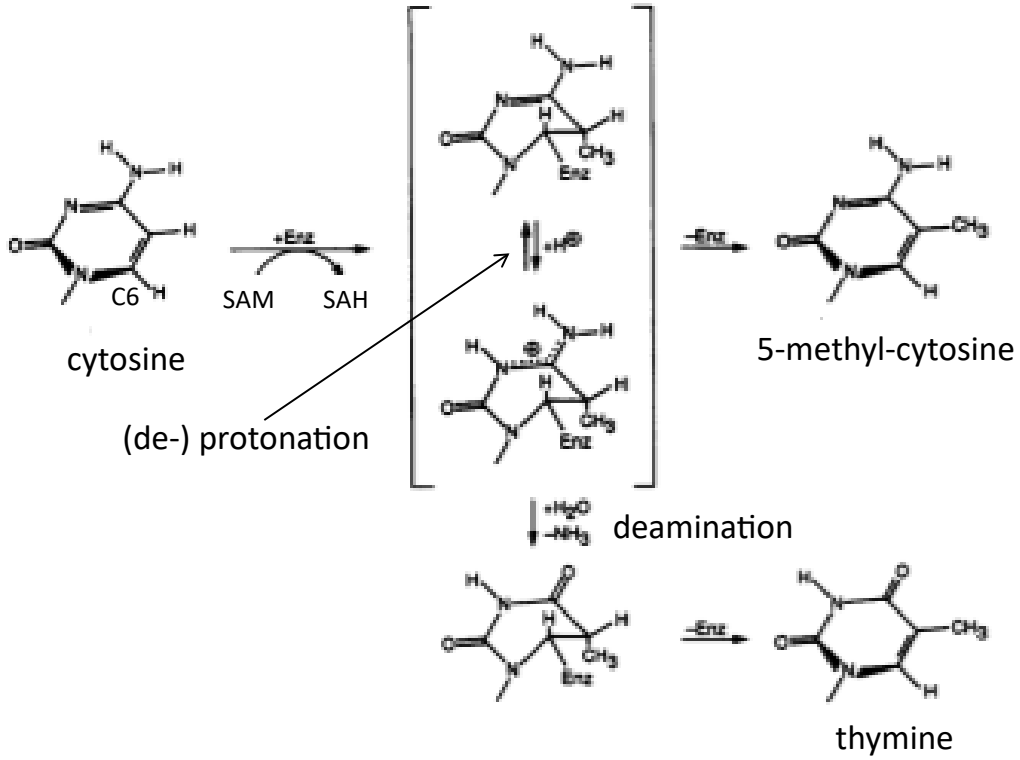

Figure 2. Potential mechanism of DNA methylation in human. After a nucleophilic attack at C6, C5 of cytosine becomes a methyl-acceptor by saturating the double bond. Alternatively, the protonated intermediate can be deaminated and form thymine (modified according to Smith et al., 1992). Abbreviations: SAM: S-Adenosyl methionine; SAH: S-Adenosyl homocysteine, enz: enzyme

Several authors dealt with the relation of quantum mechanics and enzyme activity concerning both with regard to electron or proton tunnel effect (Marais *et al*., 2016; Al-Khalili and McFadden, 2015; Brooks, 2017) and have underlined the possible role of the tunnel effect for enzyme activity. Allemann and Scrutton (2009) focused on the quantum mechanical tunneling of hydrogen (proton), which leads us directly to the activity of methyltransferases and possibly acetylation and other epigenetic reactions. If we calculate f_0 using the mass of a proton (mass ratio about 1830) we get roughly 5.5 10^{12}/sec, which still should explain tunneling compared to alpha decay or tunneling of other heavy nuclei. So it seems rather reasonable, that the tunnel effect is also associated in epigenetic transferase processes as well.

Conclusion

The diversity of life and especially human life is warranted by the epigenetic code. This code is adaptive and requires instant transferase activity to turn on or turn off gene expression. Tunnel effects in epigenetic coding may not only be important in somatic cells but are probably also involved in development in germ cells and embryogenesis. It seems rather reasonable that tunnel effects, particularly concerning electrons or protons, are involved in this process of biodiversity and human evolution.

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