**2 Background**

**2.1 Structure of the Chromosome**

To fully appreciate the discussion on epigenetic modifications and the simulation work performed in this project, it is important to understand how the DNA is stored within a (eukaryotic) cell. The DNA is located within the cell nucleus and is organised into highly compact structures called chromosomes. At the elementary level, the DNA is packaged into nucleosomes similar to a bead-on-a-string structure (see Figure XX). The core of each nucleosome is the histone octamer, which contains two copies of four kinds of histone proteins (H2A, H2B, H3, H4). The octamer is wrapped around by roughly 150 base pairs (bp) of DNA sequence. There are ~50 bp of DNA between two nucleosomes and the H1 histone protein binds to this region. The nucleosomes organise themselves into higher order structures by associating with each other to form the chromatin fibre. The fibre further compacts itself by proposed mechanisms such as forming loops and rosettes (cite). It is only during cell division (metaphase specifically) that the fibre condenses itself into the well-known X-shape structure to prepare for the separation of the genetic materials.

**2.2 Epigenetic Modifications**

As mentioned in the introduction, epigenetic modifications are heritable changes associated with gene expression without modifying the underlying sequence of the DNA. These modifications tend to be reversible, meaning that they can be added and removed from the genes throughout the lifetime of the cell. Two well-known types of epigenetic modifications are DNA methylation and histone modifications. Both have significant influence on the biological functions of a cell by regulating its genetic expression – whether a particular gene should be active or inactive.

DNA Methylation

DNA methylation refers to the addition of the methyl group (CH3) to a particular nucleotide, the basic unit of the genetic code, of the DNA. Most commonly, methylation occurs to the cytosine within the cytosine-guanine (CG or CpG) pair in the genetic sequence. Studies have shown that CpG methylation is associated with various biological processes including transcriptional repression, X-chromosome suppression in female mammals,

Histone Modifications

Histone modifications, which is the type of epigenetic modification of interest in this project, refer to the biochemical modifications that are applied to the histone proteins in the nucleosomes. As with other proteins, histone proteins are composed of amino acids, which are the basic building blocks any protein molecules. Each histone molecule has an extended tail which is composed of a thread of amino acids. Different functional groups can be bind to the amino acids of the tail to modify the histone protein. The three common types of modifications observed are acetylation (addition of CH3CO), methylation (addition of CH3), and phosphorylation (addition of PO43-). It can be seen that these modifications allow information to be stored in addition to the genetic sequence. These modifications have been thought as forming a “histone-code” which

The addition and removal of functional groups on histone tails are carried out by different classes of enzymes. Specifically, the addition and removal of acetyl group are done by histone acetyltransferases (HATs) and histone deacetylases (HDACs), while the addition and removal of methyl group are done by histone methyltransferases (HMTs) and histone demethylases (HMDs).

**2.3 Relation between Epigenetic Modifications and Dynamics of Chromatin**

It is understood that epigenetic modifications have the function of regulating the activity of different genes within the DNA. A possible mechanism by which these modifications affect gene expression is through the control of how tightly the chromatin fibre is compacted together. An active gene means that it is possible for transcription factor. Indeed, there are evidences which support this proposed mechanism. For instance, it has been shown that acetylation of lysine 16 on histone H4 (H4K16Ac) hinders the compaction of nucleosomes into a very tight chromatin fibre and [knaak2006].

**2.4 Mechanisms for the Establishment and Maintenance of Epigenetic Marks**

The main focus in epigenetic modifications .

**3 Methodology**

**3.1 Simulation Model**