



1. "Our results suggest that between 200 and 300 Mb (6.7%–10.0%) of the human genome is under functional constraint. This estimate was arrived at as follows. First, the amount of human genome under functional constraint is at least 200 Mb, the upper-bound estimate for human and horse made in a divergence regime associated with conservative estimations, according to our simulations. Second, the indicative higher estimate of 300 Mb was obtained by extrapolating the trend for lower-bound estimates involving human ... methods for inferring quantities of functional DNA rest upon the hypothesis that in functional sequence most nucleotide changes are detrimental, causing such changes to be purged from the species' populations, which results in evolutionarily conserved sequence. ... the true quantity of functional material in mammalian genomes may be around 300 Mb (10% of the human genome) ... these values may underestimate the true level of constraint" [Massive turnover of functional sequence in human and other mammalian genomes](#), Genome Research, 2010
2. In addition, in this phase of ENCODE we did sample broadly but nowhere near completely in terms of cell types or transcription factors. We estimated how well we have sampled, and our most generous view of our sampling is that we've seen around 50% of the elements. There are lots of reasons to think we have sampled less than this (e.g., the inability to sample developmental cell types; classes of transcription factors which we have not seen). A conservative estimate of our expected coverage of exons + specific DNA:protein contacts gives us 18%, easily further justified (given our sampling) to 20% [ENCODE: My own thoughts](#), Ewan Birney's Blog, 2012
3. "...all ENCODE classes display evidence of negative selection in these unique-to-primate elements. Furthermore, even with our most conservative estimate of functional elements (8.5% of putative DNA/protein binding regions) and assuming that we have already sampled half of the elements from our transcription factor and cell-type diversity, one would estimate that at a minimum 20% (17% from protein binding and 2.9% protein coding gene exons) of the genome participates in these [primate] specific functions, with the likely figure significantly higher." [An Integrated Encyclopedia of DNA Elements in the Human Genome](#), Nature, 2012