Showing My work:

Species:	HIV	Malaria	Homo
Population:	10^{20} to 10^{22} per last 25 years	10^{22} per last century	10^{12} since chimp divergence
Mutation Events:	$3x10^{19}$ to $3x10^{21}$	$2x10^{19}$	$6x10^{13}$
Evolution:	a few new binding sites	0 new binding sites, resistance to several drugs each caused by a one or more aa substitutions	280 to 1400 genes of novel function, many arising from non-coding DNA, likely just as many new binding sites. Dozens without homologs?

HIV:

1. In 2010, 34m people have HIV :(,
2. "[HIV] has a viral generation time of ~2.5 days and produces ~10^{10} – 10^{12} new virions each day", The causes and consequences of HIV evolution (Nature, 2004)
3. "the FDC-associated pool of HIV RNA would be about 10^{11} copies in a 70-kg HIV infected individual",Quantitiative Image Analysis of HIV-1 Infection in Lymphoid Tissue, (Science, 1996)
4. $3x10^{6}$ people x (10^{10} to 10^{12}) viruses x 365x25 / 2.5 days per replication = about 10^{20} to 10^{22} virons over the last 25 years.
5. HIV point mutations occur at a rate of about one nucelotide per 1-3 generations for a total of around $10^{20}$to 10^{22} mutation events.
6. During this time it has had a gene duplication event as well as a some new binding sites.

Malaria (p. falciparum):

1. According to Antimalarial drug resistance (J Clinical Inv, 2004) "Resistance to chloroquine in P. falciparum has arisen spontaneously less than ten times in the past fifty years. This suggests that the per-parasite probability of developing resistance de novo is on the order of 1 in 10^{20} parasite multiplications."
2. In Plasmodium falciparum chloroquine resistance, (Mol MicroBiology, 2005) the authors describe the necessary mutations in p. falciparum's PfCRT gene: "the critical Lys76→ Thr mutation is accompanied by an Arg220→ Ser mutation in all CQR lines except for some (the P2a/P2b types) from the Philippines, where this mutation appears to be replaced by the paired Ala144→ Thr and Leu160→ Tyr mutations" A DNA codon tableshows that Lys→ Thr and Arg→ Ser each require only one nucleotide substitution.

3. With about 10^{20} organisms existing per year, or 10^{22} in the last century. With a genome size of 23m and point mutation rate of about 10^{-10} per replication, that comes to 10^{22} * 23m * 10^{-10} = roughly 2.3 * 10^{19}mutation events
4. In Michael Behe's Book, Edge of Evolution, p143, Malaria is listed as having no new binding sites develop. Neither in the NCSE's rebuttal, in Ian Mosgrove's 7 part rebuttal, or anywhere else have I been able to find anyone challenge this.

Homo:

1. In 6 million years and ~300k generations of hominids among populations of millions (let's say 3.3, so we get an even result), and you get 300k*3.3m = 10^{12} (a trillion) human ancestors since the chimp/bonobo divergence; times 60 mutations per generation is about 6^{13} mutation events.
2. In Jerry Coyne's, Why Evolution is True: "More than 6 percent of genes found in humans aren't found in *any form* in chimpanzees. There are over 1400 novel genes expressed in humans but not chimps."
3. "Our results indicate that the human genome contains 1,418 genes—6.4% of all genes—that do not have orthologs in the chimpanzee genome (689 gains in humans+729 losses in chimpanzee/22,000 total genes). ... Furthermore, if we include differences in the size of gene families that are unique to the primates (such that we cannot polarize changes as gains or losses), this would add an additional 566 genes that do not have orthologs between the two species. ... Our results provide evidence for a high number of extinctions and creations of whole gene families, no matter how families are defined. ... our results demonstrate that humans and chimpanzees differ by ~6% at the level of gene complement. ", The Evolution of Mammalian Gene Families, PLoS One, Dec 2006
4. "Remarkably, we also identified a number of human-specific genes which are expressed in the prefrontal cortex, which is implicated in complex cognitive behaviors. The **young genes upregulated in the early developing human brain play diverse functional roles**, with a significant enrichment of transcription factors. Genes originating from different mechanisms show a similar expression bias in the developing brain. Moreover, we found that the young genes upregulated in early brain development showed rapid protein evolution compared to old genes also expressed in the fetal brain. Strikingly, genes expressed in the neocortex arose soon after its morphological origin. ... These data demonstrate a striking recruitment of new genes into the early development of the human brain. ... Our data reveal that evolutionary change in the development of the human brain happened at the protein level by gene origination and also via evolution of regulatory networks, as intimated by the enrichment of primate-specific transcriptional regulators in our dataset. ... Exon array profiling of 13 fetal brain regions showed that up

to 576 (39%) young genes are upregulated in the neocortex, relative to non-neocortical regions of the brain such as the cerebellum or striatum (Materials and Methods). In contrast, only 10% of young genes are more abundantly expressed in non-neocortical regions. ... human young genes do not show a lack of regulatory elements such as insulators or enhancers relative to old genes, **suggesting that the majority of these genes are functional** ... We next investigated the evolutionary mechanisms underlying the origination and subsequent evolution of the fetal brain biased genes. First, we examined whether these genes are generated by relatively few mutational events, e.g. segmental duplications, which would violate assumptions of the FET test in Table S1, as the genes are not statistically independent of each other. We found these genes are scattered across the whole genome, **demonstrating that they are generated by many independent events.** ... Examination of the gene structure and homology further revealed that these genes were generated by DNA-mediated duplication, RNA-mediated duplication (retroposition), and de novo origination (which created a protein without a parental locus)" The study was comparing the human and mouse genomes, but they realized that that "Up to 54 of [neocortal genes] were human-specific, i.e. they originated after human lineage diverged from the other hominoids." "Previous analyses of the molecular evolution of the human brain did not find consistent evidence of rapid evolution in the protein-coding genes expressed in the adult human brain. ... However, we noticed that all these analyses were based on the adult brain, just one stage of brain development. ... Our analyses revealed an unexpected pattern: the expression patterns and protein sequences of new genes appear to contribute to the early (fetal and infant) brain development of humans. ... However, we also observed that young genes were associated with diverse functions, ranging from nuclear pore proteins to ribosomal proteins", Accelerated Recruitment of New Brain Development Genes into the Human Genome, PLoS Biology, 2011. Emphasis mine.

5. Summary of the study above: "By comparing the order and orientation of genes along chromosomes across multiple mammalian species—spanning humans to mice—the researchers noticed several striking patterns. ... Finally, 54 of the 280 genes found to be unique to humans were also highly expressed in the developing prefrontal cortex, which grew considerably in humans after the human chimpanzee lineages broke off ... We were very shocked that there were that many new genes that were upregulated in this part of the brain",New Genes, New Brain, The Scientist, 2011
6. In another study, a large number of genes are excluded from databases, because they have no homologs: "The remaining 1,177 cases were declared to be orphans, because they lack orthology, paralogy, or homology to known genes and are not obvious artifacts. We note that the careful review of the genes was essential to obtaining a “clean” set of orphans for subsequent analysis. ... If the orphans represent valid human protein-coding genes, we would have to conclude that the vast majority of the orphans were born after

the divergence from chimpanzee. Such a model would require a prodigious rate of gene birth in mammalian lineages and a ferocious rate of gene death erasing the huge number of genes born before the divergence from chimpanzee. We reject such a model as wholly implausible. ... Among the orphans, there are only 12 cases with reported experimental evidence of an encoded protein. These cases, which comprise ≈0.06% of the gene catalog, have similar RFC and nucleotide identity scores to neutral sequence and have no similarity with any mouse or dog genes, suggesting these are truly novel inventions." Distinguishing protein-coding and noncoding genes in the human genome, PNAS 2007

7. Another study suggested genes without homologs: "A total of 69 genes were excluded from our analysis as the ancestral state of the human specific mutation was not conserved in chimpanzee and orangutan.", De Novo Origin of Human Protein-Coding Genes, PLoS Genetics, 2011