



CRAIG J. BENHAM, PH.D.

Professor

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PERSONAL EDUCATION

Ph.D. in Mathematics, 1972, Princeton University

AFFILIATION

Biomedical Engineering Graduate Group

RESEARCH INTEREST

Craig J. Benham's research group has developed statistical mechanical methods to analyze computationally the occurrence of structural transitions in stressed DNA molecules. When these methods are used to analyze genomic DNA sequences, they make highly precise predictions of the locations at which the DNA duplex is destabilized and the amount of destabilization experienced. Several experiments have been performed to date to assess stress-induced DNA destabilization in specific DNA sequences, both in vitro and in vivo. In all cases, the methods used correctly predicted the locations and extents of separated regions at single base pair resolution as functions of the level of imposed superhelical stress. This quantitatively close agreement enables our computational methods to be used with confidence to analyze other sequences, on which experiments have not been performed.

The group has analyzed a wide variety of genomic DNA sequences in this way, including the complete genomes of *Escherichia coli* and *Saccharomyces cerevisiae*.

This work has shown that the susceptibility to stress-induced destabilization is closely associated with several classes of DNA regulatory regions, including promoters and terminators, replication origins, nuclear matrix attachment sites, DNase hypersensitive sites, and hotspots for translocation, retrotransposon integration, or recombination. Working in collaboration with experimental groups, researchers have found that this approach is providing unprecedented new insights into the precise mechanisms governing numerous biologically important events, including eukaryotic nuclear scaffold attachment to c-myc oncogene regulation, activation of transcription from IHF-regulated genes in *E. coli*, transcription termination in yeast, and activation of replication of a mutant, encephalopathy-producing JC virus.

RESEARCH PAPERS

G. W. Hatfield and C. J. Benham, 2002, "DNA topology-mediated control of global gene expression in *Escherichia coli*." *Annual Review of Genetics*, 36: 175-203.

C.J. Benham, A. Savitt, and W.R. Bauer, 2002, "Extrusion of an imperfect palindrome to a cruciform in superhelical DNA: Complete determination of energetics based upon a statistical mechanical model," *Journal of Molecular Biology* 316: 563-580.

MAJOR RESEARCH INTEREST

Mathematical and Computational models of regulatory mechanisms, pathways, systems and networks, Bioinformatics, DNA mechanics.

Biomedical Engineering

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