

Researchers generate first complete 3-D structures of bacterial chromosome

October 21 2011

A team of researchers at the University of Massachusetts Medical School, Harvard Medical School, Stanford University and the Prince Felipe Research Centre in Spain have deciphered the complete three-dimensional structure of the bacterium *Caulobacter crescentus*'s chromosome. Analysis of the resulting structure -- published this week in *Molecular Cell* -- has revealed new insights into the function of genetic sequences responsible for the shape and structure of this genome.

Scientists know that the three-dimensional shape of a cell's chromosome plays a role in how genetic sequences and genes are regulated. However, technical challenges have limited genome-wide analysis of a chromosome's architecture that would allow for simultaneous identification of the elements involved in shaping it and analysis of specific features of the [structure](#). In this study, researchers used high-throughput chromatin interaction detection; next-generation DNA sequencing; computational modeling; and fluorescent microscopy to build the first 3D model of the architecture of the bacteria's chromosome and analyze the resulting structures. This new experimental approach revealed novel characteristics of a specific [genetic sequence](#) called the parS site, which helps to define the chromosome's shape.

"What we've shown is that it's possible to combine [molecular biology](#) with 3D modeling technology to perform studies that tell us novel things about how genomes fold and identify the genetic sequences that are responsible." said Job Dekker, PhD, a pioneer in chromosome interaction detection technologies, professor of biochemistry &

molecular pharmacology at the University of Massachusetts Medical School, and one of the authors on the study.

Dekker and colleagues used "5C" technology to map more than 28,700 contact points in the *Caulobacter crescentus*'s genome and used these contacts to approximate spatial distance in the folded chromosome. Plugged into a computational model, these contact points yielded a structural model of the bacterial chromosome which was strikingly beautiful: ellipsoidal in shape with arms helically arranged on either side.

Marc A. Marti-Renom, PhD, a computational biologist who leads the Structural Genomics Laboratory at the Prince Felipe Research Center in Spain, and study author said "This work demonstrates that hybrid methods combining 5C maps with the Integrative Modeling Platform can produce genome-wide 3D models of unprecedented resolution, which for the first time allows for spatially pinpointing regulatory elements responsible of organizing the structure of a genome."

The resulting 3D models of the *Caulobacter crescentus* genome, in conjunction with fluorescent microscopy, illustrate that the parS sequence, located in the pole of one arm of the chromosome, potentially served as an anchor for the genome and were instrumental in defining its overall structure.

To unravel the role the parS site plays in the 3D organization of the chromosomal structure, Dekker and colleagues constructed mutant bacteria in which the parS site had been moved away from its normal position. Building 3D models of the shape of the mutated bacteria, they observed a change in the chromosome's structure; the entire genome had rotated clockwise.

Changing the position of the parS site had resulted in a large-scale reorganization of the chromosome's shape that repositioned these sites at

the cell's poles. Mark Umbarger, a post doctoral fellow at Harvard Medical School and study author notes, "Strikingly, we found that moving sequence elements which are no larger than 500 base pairs, led to a change in the conformation of all of the 4 million base-pairs of the chromosome!"

"Our study is the first to test the effect of altering chromosome architecture. We were able to show that a very simple system, with a single anchor, can orient the whole chromosome inside of the cell." said Esteban Toro, PhD, one of the study authors and now a post doctoral fellow at the University of Pennsylvania. "These results suggest that the *parS* site in *Caulobacter crescentus* determines the orientation and global structure of the entire chromosome and are the only sequence elements that stably anchor the chromosome to the cell."

The ability for scientists to perform structure function studies on [chromosomes](#) has the potential to yield powerful new insights into the biology of genomes. "When we began this project, most scientists were assessing the positions of a handful of genomic loci and attempting to derive general conclusions about genome structure. We were unhappy with this approach and sought to develop an integrated experimental approach to generate higher-resolution, and genome-wide insights," Umbarger said.

"This isn't something we could have predicted from just looking at the DNA sequence," said Dekker. "This study illustrates how an investigation of 3D genomic structure can provide insights into how the complex relationships between genome sequence and structure can impact function. By studying genomic architecture we can potentially identify new classes of genomic sequences that are important in chromosome function and structure that we otherwise couldn't."

Provided by University of Massachusetts Medical School

Citation: Researchers generate first complete 3-D structures of bacterial chromosome (2011, October 21) retrieved 5 May 2024 from <https://phys.org/news/2011-10-d-bacterial-chromosome.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.