Objective

The study of biological processes at the single-molecule level has greatly influenced our view of the molecular mechanisms that define life. However, studies so far have mainly focused on individual, purified proteins in non-physiological environments. Since cellular processes are typically not mediated by single proteins, but rather by large complexes of dynamically interacting components, the development of the tools to study such large complexes with single-molecule sensitivity is an important direction.

With our initial successes in developing the single-molecule tools to study DNA replication, we have begun to open the field of single-molecule biophysics to the study of large, multi-component complexes. Here we describe how we will develop new single-molecule approaches to study the physical interactions and molecular mechanisms that control the DNA replication machinery, both in simple model systems and in higher organisms.

By measuring the elastic properties of DNA and simultaneously visualizing fluorescently labeled replication proteins acting on the same DNA we will be able to relate the physical structure and composition of the replication complex to its mechanism of action. We will also develop the tools to study the replication machinery in cellular extracts of higher organisms; an environment that is compatible with our nanomanipulation and fluorescence tools, but faithfully mimics the complex environment in which these processes normally take place.

Our objective is to arrive at a complete molecular understanding of how DNA replication works. We will use the tools described in this proposal to address a number of poorly understood issues: What is the
mechanism of coupling between DNA unwinding and synthesis? How are the two DNA polymerases coordinated? How does replication deal with roadblocks on the DNA? Our approach to obtain “molecular movies” of the replication process represents an entirely novel strategy to understand these issues.

Field of Science

/humanities/arts/modern and contemporary art/film
/natural sciences/biological sciences/biophysics
/natural sciences/biological sciences/biochemistry/biomolecules/proteins

Programme(s)

FP7-IDEAS-ERC - Specific programme: "Ideas" Implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

Topic(s)

ERC-SG-LS1 - ERC Starting Grant - Molecular and Structural Biology and Biochemistry

Call for proposal

ERC-2011-StG_20101109

See other projects for this call

Funding Scheme

ERC-SG - ERC Starting Grant

Principal Investigator

Antonius Martinus Van Oijen (Prof.)

Host institution
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**Principal Investigator:** Antonius Martinus Van Oijen (Prof.)

**Administrative Contact:** Dick Veldhuis (Dr.)

**Website**

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