Second Edition

Mitosis

THE MOVEMENT OF CHROMOSOMES IN CELL DIVISION

by Franz Schrader

Mitosis

The Movements of Chromosomes in Cell Division

FRANZ SCHRADER

DA COSTA PROFESSOR OF ZOOLOGY, COLUMBIA UNIVERSITY

COLUMBIA UNIVERSITY PRESS

New York 1953

First printing 1944
Second printing 1946
Third printing 1949

Published in Great Britain, Canada, India, and Pakistan
by Geoffrey Cumberlege, Oxford University Press,
London, Toronto, Bombay, and Karachi.

MANUFACTURED IN THE UNITED STATES OF AMERICA

Mitosis

Second Edition

NUMBER XIV OF THE
COLUMBIA BIOLOGICAL SERIES
EDITED AT COLUMBIA UNIVERSITY

Acknowledgments

In the preparation of a monograph like this discussion and criticism come to have a very special benefit. For this I am grateful particularly to Dr. Sally Hughes-Schrader, Professor K. W. Cooper of Princeton University, Dr. H. Ris of Johns Hopkins University, and to my colleagues Professor A. W. Pollister, Professor M. M. Rhoades, Dr. R. Ballentine, and Dr. F. J. Ryan.

FRANZ SCHRADER

Department of Zoology
Columbia University
New York City
October, 1943

COLUMBIA BIOLOGICAL SERIES

EDITED AT COLUMBIA UNIVERSITY

GENERAL EDITOR

L. C. DUNN, *Professor of Zoology*

EDITORIAL BOARD

HANS T. CLARKE, *Professor of Biochemistry*
SAMUEL R. DETWILER, *Professor of Anatomy*
THEODOSIUS DOBZHANSKY, *Professor of Zoology*
FRANZ SCHRADER, *Da Costa Professor of Zoology*

Preface to Second Edition

Since 1944 there has been a marked increase in the number of publications dealing with mitosis. These have resulted in so extensive a reorientation in many of our views that a treatise on the subject published in the early forties is badly in need of rejuvenation. This second edition represents an effort to bring that about.

In this, as in some other biological fields, the advances of the future will inevitably take a physicochemical direction. It is to be hoped that such mitotic researches will not lose sight of well-established cytological findings which furnish excellent guideposts along the way. Perhaps that is only saying that the time has arrived—regrettable to some of us—when we can no longer pursue our investigations alone. He is a very rare scientist who has a sound working knowledge of more than one of such disciplines as cytology, biochemistry, and physics, and for most of us the necessity of joint research work is obvious.

The last few years have seen some technical progress that is especially useful in work on mitotic problems. New techniques in cytochemistry, especially when used in conjunction with biochemistry, are contributing increasingly to our knowledge of the structure and function of cell constituents, although the results are not yet sufficiently complete or unified to apply directly to the specific problems of the mitotic process. The general adoption of the phase-contrast microscope represents a large stride forward in the study of the living cell, and the modification of the polarization microscope devised by Inoué promises to become at least as useful in the study of mitotic questions. Finally, improvements in the handling of biological materials for study with the electron microscope justify the hope that data on the submicroscopic structure of the delicate objects here involved will become increasingly available.

Since one or two of my reviewers failed to understand it, I

should like to point out again that in this treatise I am dealing with karyokinesis or mitosis in the old (and correct) sense—a division of the nucleus that involves a spindle apparatus. As such it includes meiotic mitosis but not cytokinesis. The justification for this separation of two cell processes, such as it is, can be found in the Introduction.

It is always difficult to give a just measure of the obligation that one has to fellow scientists who are genuinely helpful in an undertaking such as this. To mention the names of Dr. Sally Hughes-Schrader of Columbia University, Professor K. W. Cooper of the University of Rochester, and Professor Cecilie Leuchtenberger of Western Reserve University is therefore a very scant indication of what I owe to them.

FRANZ SCHRADER

New York City
July, 1952

Contents

Mitosis

Second Edition

I. Introduction

THE PRESENT TREATISE deals with the mitotic movements of chromosomes. Roughly speaking, the researches of only the last thirty years are considered in detail, the work of the half-century prior to that time being presented only when necessary as a background. The motive for such limitation is a practical one, for the total volume of work that has concerned itself in one way or another with mitosis is very large indeed and far beyond the compass of a monograph of this type. Moreover there exists in the compendium of Wassermann (1929) an extensive consideration of earlier publications which, though presented with his own hypothesis in mind, gives an excellent survey of the field up to that time. For the same reason the chromosome mechanics that pertain more directly to the problems of genetics are treated only briefly, though an effort is made to show that mitotic and genetic problems are indissolubly linked.

If a dispassionate discussion of the subject of mitosis is possible, it is perhaps chiefly due to the fact that our failure to solve most of its problems is so manifest. With rare exceptions we are filled with proper humility—the humility of the open mind. This has not always been so. Since about 1870 there has been a succession of periods in which triumph seemed to stand on the threshold as, first, observers of the living cell, then students of the morphology of the fixed cell, and lastly the physiologists, marshaled the evidence furnished by their different attacks. But it need hardly be pointed out that each of these periods had a corresponding aftermath of disillusion, always accompanied by a new appreciation of the difficulties of the problem.

The present, reawakened interest in the questions of mitosis owes its origin in no small degree to the development of the study of heredity. As the geneticist delves more deeply into the mechanisms that control the behavior of the chromosomes, he is ines-

capably confronted with the same problems that baffle the cytologist. But the maneuvers of the chromosomes and the complicated apparatus that is involved in their orderly distribution during cell division are equally important in almost every other field of biological research. Development and growth, be they normal or abnormal, are intimately bound to the process of mitosis, and a successful analysis of its basic mechanisms is as important to the student of embryology as to the specialist who is trying to solve the riddle of malignant growth. Similarly the biochemist and physiologist who are concerned with the functions of cells must inevitably be confronted with the series of phenomena that constitutes the mitotic cycle of the individual cell, and a knowledge of its underlying factors is involved in the solution of most of the questions of cell behavior.

Although the most obvious feature of the mitotic process lies in an orderly distribution of chromosomes to the new cells, it must be clear to every biologist that this—the anaphase—is only the culmination of a complicated but orderly series of steps. The preceding telophase, resting stage, prophase, and metaphase represent a highly involved complex of processes. We are accustomed to think of them in rather simple terms: indeed the formation of a nuclear membrane around the telophase group of chromosomes at the end of a division, the evolutions of the chromosomes during resting and prophase, and the metaphase arrangement of chromosomes in an equatorial plate with the simultaneous formation of a spindle, are well enough known in their external aspects. However, the basic significance of all these maneuvers, in so far as it pertains to mitosis, is still very obscure. Indeed, whether the biologist is conscious of it or not, our failure to solve this great problem has been a hindrance to his progress, and it is with the aim of outlining its present status that the present survey has been made.

It has frequently been argued that cell division should be regarded as a whole and that an analysis of one of its aspects to the exclusion of others can never furnish a final solution. In a sense that is of course quite true. The fact nevertheless remains that the elements which participate in the mitotic cycle frequently show a considerable independence of each other. This has long been recog-

nized and was emphasized for instance by Boveri (1897) who showed that the division cycle of the centers proceeds even when cytoplasmic cleavage is prevented by experimental means. Similarly it has been known that the chromosomes may continue to divide under the same circumstances (Wilson 1901, F. R. Lillie 1906) and this independence of chromosomes and cytoplasm has recently been emphasized once more by the differential effects of hydrostatic pressure (Pease 1941, 1946). Finally, the experiments of E. B. Harvey (1936) show that the complete absence of nuclear material does not necessarily make a cleavage of the cytoplasm impossible.

In short there is every likelihood that the behavior of several elements of the cell may be analyzed separately, and indeed it is because of this possibility that we may have hope of a final solution of the problem of mitosis. Without that the complexities of the process are so immense that one might well despair. It is this conviction which serves as a justification for treating here the mitotic behavior of the chromosomes as distinct from the division of the cytoplasm.

Although I have endeavored to be both reserved and fair in presenting the evidence, I have not refrained from expressing opinions wherever they might help to clarify the issue. It must be realized that in the present state of our knowledge of mitosis any opinion whatsoever will infallibly meet with some dissent, which in itself reflects the confusion in which the subject finds itself at the present time.

The word "mitosis" is used by most biologists as an inclusive term to cover any nuclear division that involves a spindle apparatus and the division of chromosomes. In recent years many geneticists have restricted the term to nonmeiotic cells, a usuage which though not correct is eminently practical from their point of view. That, however, leaves them without a general term, for "karyokinesis" is used by few workers. Since the present treatise is not solely concerned with the genetic point of view, "mitosis" will be used in the old, inclusive sense, and the term "meiotic mitosis" applied to the process in the maturing germ cells.

II. Structure

LIVING CELLS

IT APPEARS that division in living cells was observed by both botanists and zoologists early in the nineteenth century. However, the difficulties involved in the study of living cells are attested by the fact that a more or less exact conception of the mitotic spindle was not attained until the decade 1870-80, when observations on fixed cells were drawn upon for comparison (for instance by Schneider 1873, Strasburger 1875 and 1880, Bütschli 1876, and Flemming 1879).

A sweeping generalization concerning the appearance of the living spindle is hardly warranted. Even the chromosomes, which are perhaps more easily discernible than the other elements, are in some species almost invisible. In respect to visibility the difference that is to be observed in closely related species is remarkable. Thus Belar (1930) points out that the chromosomes of the acridid grasshoppers Chorthippus and Rhomaleum are easily seen, whereas in closely related members of the same family such as Trimerotropis they have practically the same index of refraction as the surrounding substances. If, as Belar suggests, this is due to a variation of water content in the chromosomes of different species, it is easily conceivable that other elements of the mitotic figure are subject to similar optical effects. The same may be said concerning the influence of variation in the pH (Yamaha 1935), and studies based on the optical properties of the live cells of a single species can have no general applicability.

Even in optically favorable cells the living spindle is discernible under the ordinary microscope primarily because the chondriosomes and other cytoplasmic elements do not usually enter into it. They thus roughly outline the extent of the spindle body, which itself is rather clear in appearance and, in the vast majority of cases, shows no internal structure (Fig. 1). This is not to deny that in

many instances the spindle substance does differ in its optical properties from other constituents of the cell. In the spermatocytes of some Coccidae the spindle as a whole is clearly visible before the nuclear wall has broken down (Hughes-Schrader and Ris 1941).

The living aster presents fewer such optical difficulties. Its rays are often rather conspicuous, perhaps chiefly because they are outlined by cytoplasmic granules, but sometimes even when the background of cytoplasm is comparatively clear. This differ-

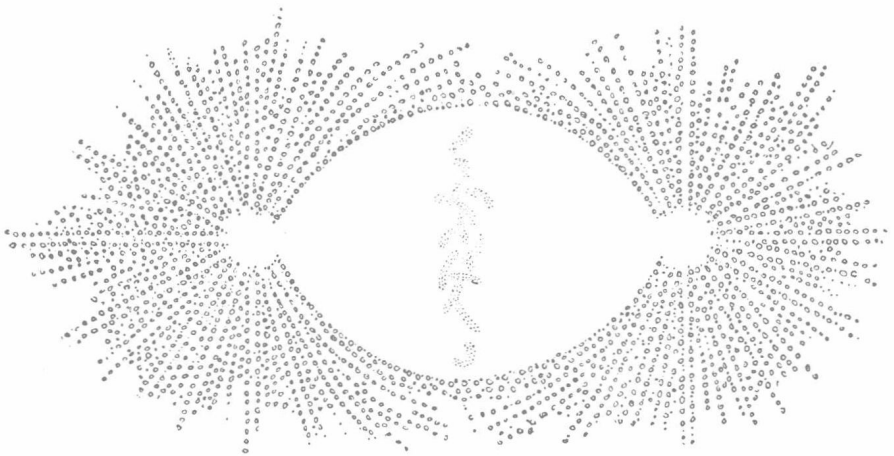

Fig. 1. Metaphase of an early cleavage in the living egg of Rhabditis, a nematode worm.

ence in the visible structure of the living spindle and aster is not without significance, as will appear further on.

Vital dyes that stain the spindle apparatus differentially would of course greatly aid the study of mitosis. But such dyes stain nuclear components only with difficulty and never without detriment to the living cell (Becker 1936, Ries 1938).

That the spindle possesses a certain rigidity has been demonstrated repeatedly. Thus as early as 1905 Foot and Strobell reported that spindles of Allolobophora maintained their form when eggs were punctured and their contents allowed to flow out. Recently, Carlson (1952) has shown that in the living cells of Chortophaga the metaphase spindle, including chromosomes and asters, consti-