## TABLE OF CONTENTS

| INTRODU  | CTION     |   | 1  |
|----------|-----------|---|----|
|          | 3         |   |    |
| CH APTER | I         | SIMULATION IN CELL POPULATIONS KINETICS | 5  |
| 1.1.     | General   | Features of Simulation Technique        | 5  |
| 1.2.     | Principa  | al Trends in the Development of         | ·  |
|          | Methods   | for Simulating Cell Proliferation       |    |
|          | Process   | es                                      | 7  |
| 1.3.     | Simulati  |   |    |
|          | Determin  | nistic Structure                        | 8  |
| 1.4.     | Stochast  |   |    |
|          | Kinetics  | 3                                       | 12 |
| 1.5.     | Simulati  | ion Modelling Software                  | 19 |
| 1.6.     |           | e Uses of Simulation Modelling          | 24 |
|          | Reference | ces                                     | 29 |
| CHAPTER  | II        | A SIMULATION MODEL FOR IN VITRO         |    |
|          |           | KINETICS OF NORMAL AND IRRADIATED       |    |
|          |           | CELLS                                   | 35 |
| 2.1.     | Introduc  | etion                                   | 35 |
|          |           | remises of Unirradiated Cell            | 33 |
|          | Populati  | on Model                                | 35 |
| 2.3.     | _         | rinciples of Simulating Cell            |    |
|          | Inactiva  | ation after Exposure to Ionizing        |    |
|          | Radiatio  | on                                      | 39 |
| 2.4.     | Process   | of Formation of Radiation Cell          |    |
|          | Damage    |   | 44 |
| 2.5.     | Radiatio  | n Blocking of Cells in the Mitotic      |    |
|          | Cycle     |   | 47 |
| 2.6.     | Repair o  | f Radiation Damage of Cells             | 49 |
| 2.7.     | Relation  | between Cell Radiosensitivity           |    |
|          |           | Position in Cell Cycle                  | 53 |
| 2.8.     | Criterio  | n of Radiation Effect                   | 54 |
| _        |           | ated Irradiation                        | 55 |
| 2.10.    |           | ion Available to Investigator in        |    |
|          |           | ng Simulation Experiments               | 57 |
|          | Referenc  | es                                      | 58 |

| CHAPTER  | III SIMULATION AND ANALYSIS OF            |     |
|----------|---|-----|
|          | RADIOBIOLOGICAL EFFECTS IN CELL           |     |
|          | CULTURES                                  | 63  |
| 3.1.     | Introduction                              | 63  |
| 3.2.     | Irradiation of the Synchronous Cell       |     |
|          | Population                                | 68  |
| 3.3.     | The Effect of Ionizing Radiation (single  |     |
|          | Irradiation) on a Cell Culture in the     |     |
|          | Exponential Phase of Growth               | 73  |
| 3,4,     | Stationary State of LICH Cell Cultures    | 78  |
| 3.5.     | Effects of Fractionated Irradiation       | 85  |
| 3.6.     | Factorial Variance Analysis of Simulation |     |
|          | Results                                   | 89  |
|          | References                                | 94  |
| CHAPTER  | IV SIMULATION OF CONTROLLED CELL          |     |
|          | Systems                                   | 97  |
| 4.1,     | Introduction                              | 97  |
| 4.2.     | Brief Description of the Model            | 98  |
| 4.3.     | The Dynamic and Stochastic Stability of   |     |
|          | the Model                                 | 102 |
| 4.4.     | Application of the Simulation Model.      |     |
|          | Simulation of Radiobiological Effects     | 109 |
|          | References                                | 112 |
| CHAPTER  | V THE PROPERTIES OF CELL KINETICS         |     |
|          | INDICATORS                                | 115 |
| 5.1.     | Introduction                              | 445 |
| •        | Integral Cell Flow into Transitive Popu-  | 115 |
| •        | lation                                    | 445 |
| 5.3.     | The Fraction of Labelled Mitoses Curve    | 115 |
|          | References                                | 127 |
|          |   | 129 |
| CONCLUSI | ON  | 131 |