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J.R. Carey, N.T. Papadopoulos, A.I. Yashin, A.I. Michalski

THE 1ST ROSTOCK EUROPEAN EXPLORATORY WORKSHOP ON AGING AND LONGEVITY IN WILD MEDFLY POPULATIONS

Max Planck Institute, Rostock, Germany. July 28–29, 2005; http://www.demogr.mpg.de/

Biodemography is a new approach to studying human population by integrating biological and demographic knowledge about birth, development, reproduction and aging in humans and laboratory animals. These studies are important for realization of synergetic potential of interdisciplinary research to better understand the driving forces and variability in population trends in health, functioning ability, and longevity. Important aspects of biodemography concerned with understanding the complementary biological and demographic determinants for and interactions between the birth and death processes (Carey and Tuljapurkar, 2003; Carey and Vaupel 2005; Wachter and Finch 1997). An exploratory 11/2 day workshop concerned with the biodemography of aging and longevity in medfly populations involving biologists from Greece, Israel, Italy, and the U.S. and mathematical modelers from Russia and Ukraine was held July 28–29, 2005 at the Max Planck Institute for Demographic Research in Rostock, Germany. The main objectives were to share information on current research involving fruit fly aging, discuss opportunities for conducting collaborative research related to the biodemography of aging, and identify possible funding sources. Whereas workshops involving mathematicians and biologists often have either modeling or biology as the dominant theme, this workshop was unique because the overarching theme was mutually complementary and synergistic. The mathematicians presented models based on data derived from several of the fruit fly researchers present at the workshop and the biologists offered new data and concepts that were of interest to the modelers.

The presentations by participating fruit fly biologists included the results of research on the relationship between medfly survival and both nutrition and reproductive success (B.Yuval, Israel), the nutritional status and energy budgets in developing and aging medflies (D.Nestel, Israel), assays of sperm use in wild medflies as a tool for investigating the field demography and aging in the medfly (A.Malacrida, Italy), on the medfly as a model system for examining demographic and behavioral aspects of aging in the wild (N.Papadopoulos, Greece), host selection in the medfly and its relevance for understanding aging in the field (N.Kouloussis, Greece), and the use of life tables constructed from wild-caught medflies to estimate the age structure and (with certain assumptions) survival of medflies in the wild (J.Carey, California).

The presentations by participating mathematical modelers included survival models of fruit flies in changing (stochasatic) environments (A.Michalski, Moscow), models on the effects of pulsed diets on medfly survival and reproduction (A.Romanyukha, Moscow), parameterization of an individual fecundity pattern in medflies (V.Novoseltsev, Moscow), modeling of links between aging, longevity, and supine behavior (A.Semenchenko, St.Petersburg), investigation of how seasons of birth affect longevity in different laboratory organisms (A.Semenchenko, St.Petersburg), model concerned with the connection between cancer and aging (A.Yashin, Duke), modeling perspectives on the role of insulin /IGF-1 signaling in reproduction and its relationship to longevity (V.Anisimov, St.Petersburg).

Workshops such as this one will increase understanding of aging in several ways. First, the concepts, principles, theories and ideas that emerge from the interdisciplinary exchanges will enhance coherence-seeking in aging science — the search for a higher unity of order and process. This higher unity cannot occur without viewing human aging in the context of other components or processes.

Biodemography has the potential for integrating biology into the pedagogical framework of classical demography and demography into gerontology in much the same way as basic biology is integrated into biomedicine. The focus on humans is retained but the epistemological foundations are strengthened, the biological scope is expanded, and the demographic perspectives are broadened. Second, many of the findings from both the empirical research on fruit flies and the modeling will provide better explanations for the life table patterns observed in human populations that are not evident in the absence of broader biological concepts. For example, biodemographic principles link senescence and sexual reproduction. The principles suggest explanations of sex differentials in life expectancies, why older individuals may grow old more slowly, whether life span limits exist,

whether post-reproductive life is common or rare, the relationship between sociality and life span, and if and how post-reproductive life spans in other species increase fitness. Third, the biodemographic principles derived from workshops such as this one on medfly modeling will provide a more secure foundation for making predictions about the trajectory of mortality at older ages, the nature of life span limits (or lack thereof), and the magnitude and sign of the gender gap. In general, every discipline including both demography and gerontology are faced with the perennial struggle to define and renew themselves and to ensure their relevance in an ever-changing world. These types of workshops on interdisciplinary topics such as the biodemography of aging will help both demography and gerontology maintain robust, energetic, and creative presences in modern science.

Carey J.R., Tuljapurkar S. (eds). (2003) Life Span: Evolutionary, Ecological and Demographic Perspectives. Population and Development Review 29, 1–320.

Carey J.R., Vaupel J.W. (2005) Biodemography. In: Handbook of Population (Poston, D, & Micklin, M, Eds.) pp in press, Kluwer Academic/Plenum Publishers, New York.

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- I -

Lead Speaker/Author: *James R. Carey*
Other Collaborators: *Nikos Papadopoulos, Nikos Koullousis, Byron Katsoyannos, Hans Müller, Jane-Ling Wang, Pablo Liedo, Lawrence Harshman*

Title of Presentation: **Aging in Wild Medfly Populations**

University Affiliation: University of California, Davis

Keywords: Ceratitis capitata, field ecology, life tables, age structure, life span

Abstract:

Despite its importance to gerontology, ecology and evolution, little research has been conducted on aging in wild populations of insects due to the inadequacy of available techniques used to determine the age of older adults as well as the various combinations of traits associated with this group of arthropods that make field research extraordinarily challenging — small size, cryptic coloration, secretive behaviors, inaccessible lifestyles, high mobility, and tendency to vanish without a trace once dead. We circumvented these obstacles for aging research on wild tephritid fruit flies by incorporating the remaining life spans in the laboratory of field-captured adults into a model that estimates the age structure and, in turn, the patterns of aging and longevity in the natural populations from which they were derived. The broad goal of this study was to test the hypothesis that the age composition of field populations of four species of tephritid fruit flies frequently consists of individuals that have survived for at least one month and sometimes two or more months. The underlying concept is that the age structure of the wild population from which flies are captured and subsequently monitored in the laboratory and, by extension, the ages of the longest-lived individuals at the time of their capture, can be deduced from their distribution of deaths in the laboratory. Biodemographic data (birth and death rates) were gathered in Chios, Greece on approximately 1,000 wild flies (captive cohorts) captured on 1-of-16 sampling dates during the 2003-04 field seasons and from a reference cohort of 134 medfly females reared from infested hosts. Analysis and modeling of these data combined with results of previous studies on the field ecology of the medfly contradicts the conventional wisdom that the survival of most insects is low and supports the hypothesis that medflies are long-lived in nature. Implications for demographic and gerontological research on aging in the wild regarding both the methodology and the empirical results are discussed.

Specific Aims:

Aim 1. **Biodemographic**: Develop a demography-based diagnostic system for estimating the physiological age of wild-captured medfly adults.

SubAim 1a. Measure lifetime rates of age-specific birth and death in the laboratory of individual flies derived from wild colonies and that are maintained under a variety of environmental conditions.

SubAim 1b. Determine rate of aging of individuals in the field relative to those maintained in the laboratory maintained under controlled, known conditions.

Aim 2. **Statistical:** Infer as much as possible about the demographic information that is unobserved (i.e. pre-capture traits and experience).

SubAim 2a. To infer the statistical age distribution and mortality schedule of flies that are captured in the wild based on the observed residual lifetimes, reproductive and behavioral profiles.

SubAim 2a. To infer properties of the population reproductive and behavioral schedules based on the observed residual reproductive and behavioral schedules.

Aim 3. **Field:** Assay life history patterns exhibited by wild populations of medflies in Greece.

SubAim 3a. Live-capture, record and analyze the birth and death rates of wild-caught individual medflies and worms at different times throughout the year and at multiple locations.

SubAim 3b. Analyze demography data from captive life of individuals using statistical models and biological information from techniques developed in Aim 1.

Aim 4. **Hypothesis testing:** Test the following hypotheses using information derived from wild populations of medflies.

SubAim 4a. H_0: Medflies age in the wild.

SubAim 4b. H_0: Old medflies are present in the wild.

SubAim 4c. H_0: Sex-specific aging rates and life spans differ in the wild.

SubAim 4d. H_0: High-quality adult food is scarce in nature.

References

1. Carey J.R. 2003. Longevity. The Biology and Demography of Life Span, Princeton University Press, Princeton.

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3. Müller H.G., Wang J.-L., Carey J. R. et al. 2004. Demographic window to aging in the wild: Constructing life tables and estimating survival functions from marked individuals of unknown age. Aging Cell 3, 125–131.

- II -

Lead Speaker/Author: *Nikos T. Papadopoulos*
Other Collaborators: *James Carey, Byron Katsoyannos, Nikos Kouloussis, Hans Müller, Jane-Ling Wang, Pablo Liedo*

Title of Presentation: Medfly as a model system for studies on field ecology, aging and behavioral demography

University/Affiliations: Department of Agriculture, Crop Production and Rural Environment, University of Thessaly

Keywords: Evolutionary biodemography, life time behavioral studies, behavioral demography, morbidity dynamics

Abstract:

The first part of the paper dealt with the importance of the life time behavioral studies to understand aging, morbidity dynamics and trade offs between life span and other life history traits. Special emphasis was place on the recently discovery of the "supine behavior" in the Mediterranean fruit fly (Medfly), which is a reliable behavioral biomarker of aging. The importance of appropriate model systems such as the Mediterranean fruit fly in these studies was highlighted.

In the second part, we presented empirical data and analyses regarding aspects of aging in the wild for medflies. The acquired data suggest temporal and spatial differences in age structure of wild of medfly populations. Data of a large base line life table for wild medflies were presented as well.

The evolution of life span and other life history traits of geographically isolated medfly population was the subject of the last part of the paper. Analyses of first data show big difference in life span between tropical and temperate strains of medflies.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To understand the demographic components of behavioral traits, and discover behavioral biomarkers of aging

2) To comprehend the evolution of life span and aging, and those factors affecting aging in the wild.

3) To study the morbidity dynamics in model systems such as the medfly.

4) To implement lifetime behavioral studies in understanding aging and the ecology of fruit flies.

References, as appropriate:

1. Papadopoulos N.T., Carey J.R., Katsoyannos B.I. et al. 2002. Supine behavior predicts time-to-death in male Mediterranean fruit flies. Proceedings: Biological Sciences: 1633-1637.

2. Papadopoulos N.T., Katsoyannos B.I., Kouloussis N.A. et al. 2004. High sexual calling rates predict extended life span in male Mediterranean fruit flies. Oecologia 138: 127–134.

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- III -

Lead Speaker/Author: *Romanyukha[1] A.A.*
Other Collaborators: *Carey[2] J.R., Karkach[1,3] A.S., Sannikova[1] T.E., Yashin[4] A.I.*

Title of Presentation: Effects of pulsed diet on medfly longevity and reproduction. Population heterogeneity and trade-offs detection

University/Affiliations: [1] Institute of Numerical Mathematics, Moscow, Russia
[2] Department of Entomology, University of California, Davis; Center for the Economics and Demography of Aging, University of California, Berkeley, USA
[3] Max-Planck Institute for Demographic Research, Rostock, Germany
[4] Center for Demographic Studies, Duke University, Durham, USA

Keywords: Trade-off, resource allocation, genetic correlation, reaction norms, fitness, adaptation, fertility, mortality, life-span

Abstract:

Understanding factors determining allocation and utilization of organism's resources provide insights into the mechanisms of adaptation, reproduction and ageing. Experiments with variable and pulsed feeding of female Mediterranean fruit flies (Ceratitis capitata) show that the feeding regime dramatically affects their lifespan, mortality and reproduction. Analysis of experimental data and nume-

rical experiments with mathematical model, relating mortality and reproduction, suggest that increase in fruit flies' life span, when females are switched from a sugar-only to a protein-containing diet, may be explained by a mechanism involving reallocation of available biological resources. We consider the reallocation of organism's resources in response to changes in dietary conditions as genetically controlled adaptive strategy, which "optimizes" organism's fitness in the new conditions. Our analysis shows that natural heterogeneity of female cohorts with respect to the amount of available resource and proportions of its allocation between maintenance and reproduction also make substantial contribution to the observed pattern of trade-offs between fertility and longevity. Analysis also reveals substantial (up to eight times) differences in the values of fitness traits — longevity and reproduction — between "strong" and "weak" quartiles of flies' population. This observation suggests that respective subpopulations may have genetic or phenotypic constructions appropriate for different environments.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To investigate the conditions of reproduction-longevity trade-off emergence.

2) To estimate parameters of reproduction/longevity trade-off phenomenon: cost of longevity, constrains and conditions necessary for initiation of resources reallocation process, optimal frequency and magnitude of such reallocation.

3) To clarify physiological mechanism of resources reallocation process.

References:

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2. Carey J.R., Liedo P., Harshman L. et al. 2002. Food pulses increase longevity and induce cyclical egg production in Mediterranean fruit flies. Functional Ecology.16, 313–325.

3. Romanyukha A., Carey J.R., Karkach A.S. and A. I. Yashin. 2004. The impact of diet switching on resource allocation to reproduction and longevity in Mediterranean fruitflies. Proc. R. Soc. Lond. B, 271, 1319–1324.

- IV -

Lead Speaker/Author: *Anatoli Yashin*[2]
Other Collaborators: *Golubovski*[2] *M.D., Weisman*[1] *N.Y., Arbeev*[2] *K.G. Ukraintseva*[2] *S.V.*

Title of Presentation: Experimental Confirmation of Connection Between Cancer and Aging

University/Affiliations: [1] Institute of Cytology and Genetics, Russian Academy of Sciences, Novosibirsk
[2] Duke University, Center for Demographic Studies, Durham, NC.

Keywords: Cancer and aging, tumor suppressor genes, hormesis, stress resistance

Abstract:

Recent studies of carcinogenesis in rodents reveal interesting connection between cancer and cellular aging mediated by tumor suppressor (TS) genes having homologues in humans. The effect of genetic loss of function mutations on aging and longevity, however, was not explicitly measured in adequate population study. The presence of homologues of human tumor suppressor genes in fruit fly Drosophila allows for further investigation of the effects of mutations in TS genes on aging and longevity in wide scale population experiments. It this paper we investigate the effect of the loss of function mutation in the TS *lgl* gene on survival population of Drosophila under different ambient temperature. We show that positive effects of such mutations on longevity become visible at high temperature and are mediated by maternal organism. These results provide additional support to the idea about connection between cancer and aging and elucidate the epigenetic mechanism by which such connection is realized.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To better understand the connection between aging, development of chronic pathologies and life span.

2) To better understand the role of genes in such a connection

3) To better understand what one can learn about mechanisms involved in regulation of aging and longevity in humans from animal studies.

References, as appropriate:

1. Ukraintseva S.V. & Yashin A.I. Individual aging and cancer risk: How are they related? Demographic Research 9, 163-196 (2003).

2. Peters G. & Vousden K.H. Oncogenes and Tumour Suppressors (Oxford Univ. Press Inc., NY, 1997).

3. Evan G.I. & Vousden K.H. Proliferation, cell cycle and apoptosis in cancer. Nature 411, 342-348 (2001).

4. Vousden K.H. Switching from life to death: the Miz-ing link between Myc and p53. Cancer Cell 5, 351-352 (2002).

5. Ukraintseva S.V. & Yashin A.I. Treating cancer with embryonic stem cells: Rationale comes from aging studies. Front. Biosci. 10: 588-595 (2005).

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9. Lim D.S. et al. Analysis of ku80-mutant mice and cells with deficient levels of p53. Mol. Cell. Biol. 20, 3772-3780 (2000).

10. van Heemst D. et al. Long Life study group. Variation in the human TP53 gene affects old age survival and cancer mortality. Exp. Gerontol. 40, 11-15 (2005).

- V -

Lead Speaker/Author: *Malacrida Anna R. / Giuliano Gasperi*
Other Collaborators: *M.Bonizzoni, L.M.Gomulski, S.Bertin, F.Scolari*

Title of Presentation: Sperm use in medfly: a tool for investigating the demography of this species

University/Affiliations: Università di Pavia, Dipartimento di Biologia Animale
Piazza Botta 9, I 27100 Pavia, Italy

Keywords: *Ceratitis capitata*, genetic variability, bio-invasion, remating, sperm use, demography

Abstract:

The medfly, *Ceratitis capitata*, is currently the most notorious tephritid species from an invasive perspective. A vast reservoir of genetic variability has been detected in the genome of this fly (Gasperi et al, 2002). This high genetic variability may contribute to the genetic plasticity of the fly, increasing its ability to colonise and survive in new habitats (Malacrida et al, 1996; Gomulski et al, 2004; Bonizzoni et al, 2004). In the field, medfly females can copulate more than once (Bonizzoni et al, 2002), thus creating the opportunity for sperm competition. An understanding of the frequency of remating and the factors that may influence it, together with an understanding of the extent and mechanisms that regulate sperm use, is of special interest in the analysis of the evolution and demography of this species.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) Sperm use during the female life span

2) Mating remating and fertility

3) Functional genomic approach to the analysis of reproduction.

References, as appropriate:

1. Bonizzoni M., Katsoyannos B.I., Marguerie De Rotrou R. et al. (2002) Microsatellite analysis reveals remating by wild Mediterranean fruit fly females, *Ceratitis capitata*. Molecular Ecology 11: 1915–1921.

2. Bonizzoni M., Guglielmino C.R., Smallridge C.J. et al. (2004) On the origin of medfly invasion and expansion in Australia. Molecular Ecology 13: 3845–3855.

3. Gasperi G., Bonizzoni M., Gomulski L.M. et al. (2002) Genetic differentiation, gene flow and the origin of infestation of the medfly, *Ceratitis capitata*. Genetica 116: 125–135.

4. Gomulski L.M., Torti C., Murelli V. et al. (2004) Medfly transposable elements: diversity, evolution, genomic impact and possible applications. Insect Biochemistry and Molecular Biology 34: 139–148.

5. Malacrida A.R., Guglielmino C.R., D'Adamo P. et al. (1996) Allozyme divergence and phylogenetic relationships among species of tephritid flies. Heredity 76: 592–602.

- VI -

Lead Speaker/Author: *Boaz Yuval*
Other Collaborators: *Adi Behar, Edouard Jurkevich, Karmit Levy & Todd Shelly**

Title of Presentation: Medfly nutrition- contribution of bacteria and effects on longevity

University/Affiliations: Hebrew University of Jerusalem, Israel.
* USDA-APHIS Hawaii, USA.

Keywords: *Ceratitis*, microbial ecology, nutrition, survival, nitrogen fixation

Abstract:

Our group studies the relationship between nutrition, reproductive success, and survival of fruit flies. Recently (Levy et al. 2005), we examined the effect of different diets on the ability of the medfly to withstand starvation. We maintained males on one of eight regimes combining a diet of either sugar, sugar and protein, a protein pulse or apricot, with or without the aroma of the sexual stimulant α-copaene. The apricot diet was associated with the lowest ability to resist starvation. The sugar-only diet was associated with the highest ability to resist starvation by sterile males. Exposure to α-copaene, in combination with the apricot diet, had a significant negative effect on the ability of males (from all strains) to resist starvation relative to other regimes examined. We conclude that the holding regimes that elicit the best sexual performance from males, paradoxically also hasten their demise, probably by initiating an irreversible metabolic cascade.

Another recent study deals with the bacteria associated with the medfly gut. We have shown (Behar et al., 2005), that species of the Enterobacteriacae are prominent in the bacterial communities extracted from the medfly digestive system. Since these species are known to fix atmospheric nitrogen, we hypothesized that they do so while living within the medfly. Accordingly, we showed that *Enterobacter* and *Klebsiella* species express dinotrogen reductase in the gut. Furthermore, nitrogen fixation was demonstrated in isolated guts and in live flies and may significantly contribute to the fly's nitrogen intake. The life history association between bacteria and fruit flies remains largely unexplored, and should prove a rewarding field for future research.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) Future work will continue to elaborate the link between nutrition, reproduction and longevity in the medfly.

2) We aim to determine the structure of diazotrophic bacterial communities at two scales: in the gut of C. capitata as a function of fly age, and in fly populations from different geographical areas. Furthermore, we will establish the contribution of these bacteria to fly fitness.

References:

1. Behar A., Yuval B. & Jurkevitch E. 2005. Enterobacteria-mediated nitrogen fixation in natural populations of the fruit fly Ceratitis capitata. Molecular Ecology, 14, 2637–2643.

2. Kaspi R. & Yuval B. 2000. Post-teneral protein feeding improves sexual competitiveness but reduces longevity of mass-reared sterile male mediterranean fruit flies (Diptera: Tephritidae). Annals of the Entomological Society of America, 93, 949–955.

3. Kaspi R., Mossinson S., Drezner T. et al. 2002. Effects of larval diet on development rates and reproductive maturation of male and female Mediterranean fruit flies. Physiological Entomology, 27, 29–38.

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- VII -

Lead Speaker/Author: *David Nestel*[1]
Other Collaborators: *Esther Nemny-Lavy*[1], *Nikos Papadopoulos*[2], *Pablo Liedo*[3], *James R. Carey*[4]

Title of Presentation: Nutritional Status and Energy Budget in Developing and Ageing Mediterranean fruit fly, *Ceratitis capitata*

University/Affiliations: [1] Institute of Plant Protection, Agricultural Research Organization, The Volcani Center, P.O. Box 6, Beit-Dagan 50250, Israel; nestel@agri.gov.il
[2] Department of Agricultural Crop Production and Rural Environment, University of Thessaly, Ionia Magnisias, Greece
[3] El Colegio de la Frontera Sur, Tapachula, Chiapas, Mexico
[4] Department of Entomology, University of California, Davis, USA

Keywords: Energy balance, lipids, proteins, nutrition, diet

Abstract:

Energy reserves (such as lipids and glycogen) in higher organisms are expected to reflect nutritional balances, other environmental effects upon the organism and endogenous metabolic processes (Downer, 1981). The Mediterranean fruit fly (Medfly) has serve as a model to investigate specific questions related to this relationship, specially concerning the effects of diet and development upon energy reserves (see for example, Kaspi et al, 2002; Nestel et al., 2003, 2004; Warburg and Yuval, 1996). Recently, we studied the effect of a restricted adult diet («no protein hydrolyzate») on patterns of lipid and protein contents, egg laying and mortality throughout adult life of male and female Medflies (Nestel et al., in press). As expected, protein fed females produced several fold more eggs than sucrose fed insects, while sucrose fed females tended to die early in life. Males showed similar mortality patterns in the two diets. Surprisingly, total lipid contents harmonically, and synchronously, oscillated with a periodicity of 10-days in males and females fed the protein restricted and the control («full») diet. Successive lipid crest tended to be smaller, with reduced lipid-reserve contents in advanced ages. Protein loads in flies fed a «full» diet stayed at a high level throughout life, while protein contents in flies maintained in a protein-restricted diet drastically drop during the first days of adult life, then stay stable at a low level until death. We suggest that an independent internal clock regulates the harmonic oscillation in lipid contents. Protein reserves are allocated according to access to protein food, and levels are closely associated with egg laying and mortality patterns.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) How nutritional balances affect survival and reproductive patterns of the Medfly?

2) Does the quantification of energy reserves throughout life reflect the interactions between the «income» and utilization of chemical energy?

3) How energy reserves are regulated throughout life in order to cope with the biological requirements of the organism and the restrictions imposed by the environment?

References, as appropriate:

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2. Kaspi R., Mossinson S., Drezner T. et al. (2002). Effect of larval diet on development rates and reproductive maturation of male and female Mediterranean fruit flies. Physiological Entomology, 27: 29–38.

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5. Nestel D., Papadopoulos N.T., Liedo P. (in press). Trends in lipid and protein contents during Medfly ageing: an harmonic path to death. Archives of Insect Biochemistry and Physiology, 60.

6. Warburg M.S. and Yuval B. (1996). Effect of diet and activity on lipid levels of adult Mediterranean fruit fly. Physiological Entomology, 21: 151–158.

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Lead Speaker/Author: *Nikos A. Kouloussis*[1]
Other Collaborators: *B.I.Katsoyannos*[1], *N.T.Papadopoulos*[2], *Ch.S.Ioannou*[1]

Title of Presentation: Host selection in *Ceratitis capitata*: a demographic/ ageing perspective

University/Affiliations: [1] Laboratory of Applied Zoology and Parasitology, School of Agriculture, Aristotle University of Thessaloniki, 54 124 Thessaloniki, Greece
[2] Laboratory of Entomology and Agricultural Zoology, Department of Agriculture Plant Production and Rural Environment

Keywords: Host-plant selection, chemical demography, life-time behavioral studies

Abstract:

Chemical stimuli emanating from host fruits are known to guide fruit flies during selection of oviposition sites (Prokopy and Roitberg 1984). Katsoyannos et al. (1997) found that odours from the juice of certain citrus fruits attract females of *Ceratitis capitata*. Other unpublished experiments conducted by our team showed that citrus juices also stimulate oviposition. The first part of my talk provided some preliminary evidence from laboratory experiments that this stimulation may vary with the age of the flies. In these experiments females oviposited in red plastic domes bearing small holes from which emanated volatiles from orange, mandarin, lemon, grapefruit or bitter orange juice. In a first set of two-choice experiments females of 18-20 days of age showed a significant preference to oviposit more in domes with lemon. However, in a subsequent no-choice experiment involving individuals that were monitored throughout their lives, females initially showed a preference for lemon but after day 20 this tendency shifted and females ended up laying most eggs in orange and mandarin.

These preliminary results are an indication that the whole process of host-plant selection in *C. capitata* and probably other insects might be viewed from a demographic/aging perspective. As with all living organisms ageing insects have different requirements from their environment, their physiology changes, their sensory receptors wear. All these alterations probably affect their responses to the chemicals that signal host finding and oviposition and perhaps also to other chemicals such as pheromones. This opens up a whole new avenue of research within the domains of chemical ecology and biodemography.

In the second part of my talk I described an experiment, which is underway and is aimed at studying under semi-natural conditions the response of wild *C. capitata* of different ages to plastic McPhail traps baited with the synthetic food attractants Ammonium acetate and Trimethylamine.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) Perception of host chemicals over the course of an insect's lifespan.

2) Manipulation of an insect's chemical environment to see if it affects lifespan.

3) Response of ageing insects to other chemicals such as pheromones.

References, as appropriate:

1. Katsoyannos B.I., Kouloussis N.A. & Papadopoulos N.T. 1997. Response of Ceratitis capitata to citrus chemicals under semi-natural conditions. Entomologia Experimentalis et Applicata: 82: 181–188.

2. Prokopy R.J. & Roitberg B.D. 1984. Foraging behaviour of true fruit flies. American Scientist 72: 41–49.

-IX -

Lead Speaker/Author: *Vladimir N. Anisimov*

Title of Presentation: Reproduction and longevity: the role of insulin/IGF-1 signaling

University/Affiliations: N.N.Petrov Research Institute of Oncology, St.Petersburg, Russia

Keywords: Aging, reproductive system, estrous cycle, antidiabetic drugs

Abstract:

Age-related increase of the hypothalamic threshold of sensitivity to feedback regulation by estrogens seems to be a key mechanism of switching-off reproductive function in mammals. The analysis of the results presented by J. Carey team at Aging Cell, 2004, has shown that this mechanism can explain the increase of life span by transplantation of ovaries to 11-month-old ovariectomized at the age of 3 weeks female mice. The administration of antidiabetic biguanides and diabenol, which increase the susceptibility of tissues to insulin, prolongs reproductive function and life span and inhibits spontaneous and induced carcinogenesis in rodents.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) The evaluation of the role of insulin/IGF-1 signaling in aging and cancer

2) The role of hypothalamus in mechanisms of aging

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- X -

Lead Speaker/Author: *A.I. Michalski*[1]
Other Collaborators: *J.R., Carey*[2], *A.I. Yashin*[3]

Title of Presentation: Surviving in Changing Environment

University/Affiliations: [1] Institute of Control Sciences, Moscow, Russia
[2] University of California, Davis, USA
[3] Duke University, Durham, USA

Keywords: Dietary restriction, stochastic feeding scheme, longevity, Markov chain model, hidden states, zero mortality, optimal treatment, reproduction projection

Abstract:

Effect of stochastic dietary restriction on a fly longevity was investigated using Markov chain model with states corresponding to protein diet, sugar diet and two additional hidden states corresponding to sugar-protein change and to protein-sugar change. Age specific mortalities at protein and sugar diets were estimated using Gompertz-Makeham model on survival data under corresponding treatments. Mortality and probabilities of transition from the change states were estimated on survival data under different treatments.

Estimates show than both in males and in females the change from sugar to protein diet leads to drop in mortality almost till zero. Later mortality increases as a result of transition to 'protein diet' state. Change from protein to sugar diet is associated with lowering mortality, which increases when transition to 'sugar diet' is made. The lowering of mortality in the result of the diet change explains experimentally observed increase in mean life span under stochastic feeding in comparison with fixed diet. The biological background for such mortality lowering is unclear. Figure 1 presents a chart for the resulting model.

The identified Markov chain model for survival in females was used to project age trajectory reproduction in females under different treatments. Reproductions at protein diet and at sugar diet were taken from the experiments. Age specific reproduction in the change states was estimated from reproduction data at different treatments using least square technique. At the present time satisfactory results were obtained only for high value of persistence probability q=0.8. The optimal reproduction in the change states was estimated as not depending on age and equals approximately 17 and 0.7 eggs/day per fly for sugar-protein and protein-sugar changes respectively. Figures 2–5 present observed and projected reproduction for different values of discovery probability «ρ» and fixed value of persistence probability. The model with reproduction depending on the time spent in the particular state probably will allow making reliable projections for reproduction in wide range of persistence probability.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) Investigate mechanisms involved in surviving under changing environment. Construct mathematical model for description and interpretation of observed data.

2) Propose a model for longevity in medflies under different feeding schemes, which demonstrates increase in longevity under changing feeding in comparison with fixed diets.

3) Apply the longevity model to predict reproduction trajectories in medflies under different treatments to identify the links between maintenance and reproduction.

References:

Carey J.R., Liedo P., Muller H.-G. et al. (2005) Stochastic dietary restriction using a Markov-chain feeding protocol elicits complex, life history response in medflies. Aging Cell, 4: 31–39.

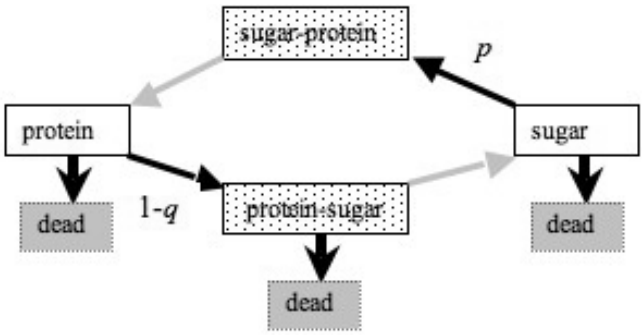

Figure 1. Chart for Markov chain model with two change states.

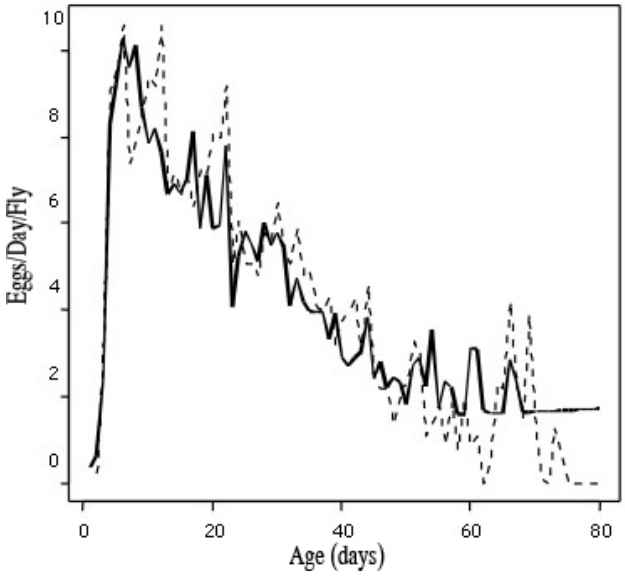

Fig. 2. Reproduction observed (dashed) and modeled (solid) for ρ=0.05, q=0.8.

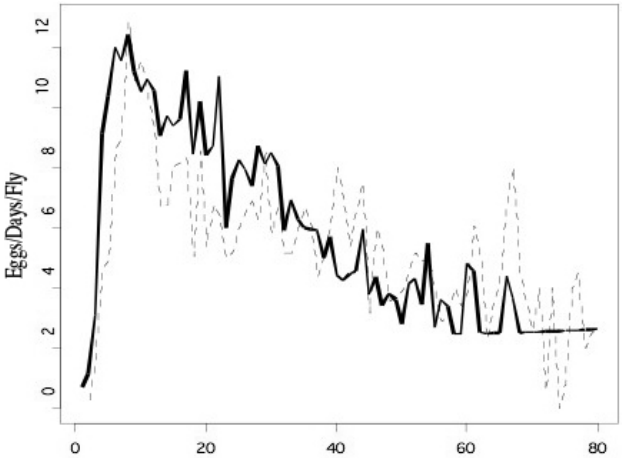

Fig. 3. Reproduction observed (dashed) and modeled (solid) for ρ=0.1, q=0.8.

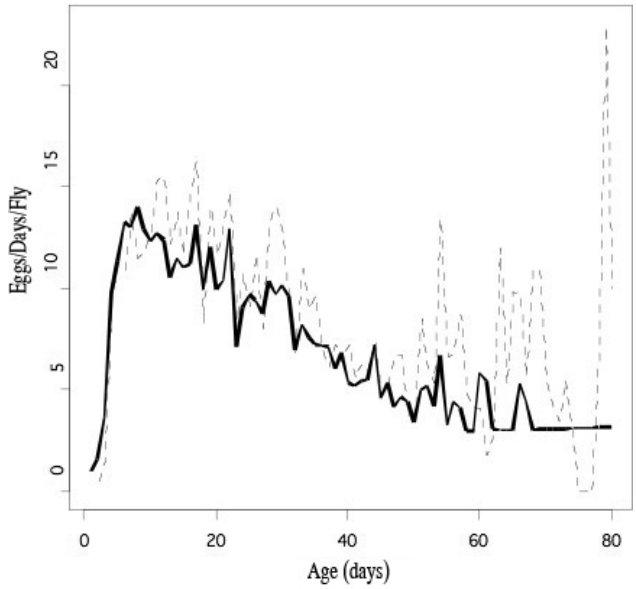

Fig. 4. Reproduction observed (dashed) and modeled (solid) for ρ=0.15, q=0.8.

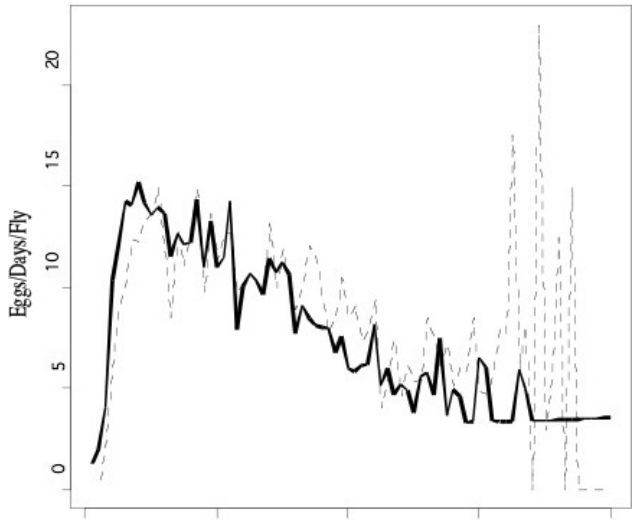

Fig. 5. Reproduction observed (dashed) and modeled (solid) for ρ=0.2, q=0.8.

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Lead Speaker/Author: *Novoseltsev[1,4] V.N.*
Other Collaborators: *Carey[2] J.R., Novoseltseva[1] J.A., Yashin[3, 4] A.I.*

Title of Presentation: Does a parameterization of an individual fecundity pattern in medflies allow for a prediction of remaining life expectancy?

University/Affiliations: [1] Institute of Control Sciences, ul. Profsoyuznaya, 65, Moscow, 117342, Russia;
[2] Department of Entomology, University of California, Davis; Center for the Economics and Demography of Aging, University of California, Berkeley;
[3] Center for Demographic Studies, 2117 Campus Drive, Duke University, Durham, NC 27708, USA;
[4] Max-Planck Institute for Demographic Research, Konrad Zusse Strasse, 1, Rostock; Germany

Keywords: Individual fecundity, reproduction, parameterization, resource allocation, trade-off, prediction, life expectancy

Abstract:

Strong associations of individual reproduction traits with longevity were found in medflies (Carey, Tuljapurkar, 2003). These findings assume that prediction of remaining expectancy of life in medflies can be detected basing on the individual scores of egg laying. In this presentation, to indi-

vidually predict a remaining life expectancy in a 1000-fly population of medflies we apply a parameterization of individual fecundity patterns. A prediction of longevity is based on the correlation existing between individual *LS* and the fecundity parameters. (Novoseltsev et al, 2003, 2004). In agreement with this parameterization, an individual fecundity pattern has three stages: maturation, maturity and senescence. The first stage (maturation) is defined as a period between eclosion and the first egg laid. It is described by a single parameter, t_{onset}. The maturity stage is described by two parameters, a duration *T* and 'reproductive capacity' *RC*, the height of the plateau of egg laying. The final part is an exponential decay of egg laying described by the time constant of the exponent, τ_{tail}.

To predict longevity in the *i*-th fly female, two values are essential. The first one is the period of the reproductive decline δ, and the second, its evaluation δ^*. The evaluation is made basing on the estimation of the exponent τ_{tail}: $\delta=LS-t_{onset}-T$. Correlation between δ and τ_{tail} is rather high, $r=0.69$. We define the regression function $\delta^*=a\cdot\tau_{tail}+b$, where the coefficients *a* and *b* are evaluated from the data.

We use this formula to estimate the general possibilities of the prediction, substituting for τ_{tail} its experimental value. Then we predict the expected life using the analogous expression $\delta^{i*}=a\cdot\tau^{i*}_{tail}+b$, where τ^{i*}_{tail} is the evaluated value of individual τ^{i}_{tail} at the moment of prediction. Only information available at that moment is used: $LS^{i*}=t^{i}_{onset}+T^{i}+\delta^{i*}$. In prediction we use the following technique.

To predict the life expectancy at days 20th, 25th, 30th and 35th we use only the information available, that is a current estimations of the time constant τ^{i*}_{tail} existing at these days. This means that the technique realizes so called 'online' prediction. To judge about the possibilities of this prediction we use the experimental exponents, τ^{i}_{tail}, which can be evaluated only at the day of the death of the fly.

Then we form the following groups of risk in life expectancy starting from the shortest predictions and finishing with the longest ones.

Group A consists of the flies predicted to die during 10 days after the prediction, group B — flies predicted to die during 10—20 days and group C — flies predicted to die 20+ days after the prediction.

The results are promising. For example, at the 25th day the «maximum possible» efficacy of prediction is as follows. The number of flies in a group A is 272 and 76% of them (206) really died. In a group B, from 446 flies only 23% (103 flies) dye, and 7 flies from 71 die in a group C. In 'online' prediction the figures are worse at this day: 55% of flies died in a group A (206 from 377), 28% (105 from 379) in a group B and 15% (5 from 33) in a group C. Similar results are observed at other days of prediction.

The only positive example of longevity prediction in Mediterranean fruit flies was presented in the paper by Müller et al. (2001). The authors choused 531 flies from a thousand and estimated their reproductive potentials. Then they predicted their mortality and divided the sample into the three groups (each of 177 flies) at day 26th basing on the fecundity data for the previous period. In the high-, medium- and low-risk groups the mortality during days 26—30 was 61, 26 and 14 flies respectively. Our prediction was better. Firstly, we did not choice any flies but analyze all the population living longer than 25 days. All 789 flies were divided by the predicted lifespan into the three equal-quantity groups of risk, 263 flies in the group.

Real mortality at the five-days period after the prediction is 147 flies. In the high-, medium- and small-risk groups 101, 27 and 19 flies really died.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To investigate the possibility of life expectancy prediction basing only on individual fecundity data thus making wider the area of application of parameterization of individual fecundity patterns.

2) To compare the results of hypothetical prediction based on 'full' information with the results of 'on-line' prediction of life expectancy based exclusively at information existing at the moment of prediction.

3) To compare the results of such a prediction with the existing results.

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- XII -

Lead Speaker/Author: *Anna Semenchenko*[1]
Other Collaborators: *Nikos Papadopoulos*[2], *James Carey*[3], *Anatoli Yashin*[4]

Title of Presentation: Aging, longevity, and supine behavior: New models and methods

University/Affiliations: [1] N. N.Petrov Research Institute of Oncology, St.Petersburg, Russia;
[2] Department of Agriculture, Crop Production and Rural Environment, University of Thessaly;

[3] Department of Entomology, University of California, Davis;
[4]Duke University, Center for Demographic Studies, Durham, NC

Keywords: Behavioral traits, frailty models, heterogeneity, survival patterns

Abstract:

Supine behavior (temporary upside-down orientation) has been reported in male Mediterranean fruit flies (medflies) *Ceratitis capitata* concerning its relationship to an individual's health and time-to-death. It was shown, that this remarkable behavior is unique to geriatric flies in general, but especially to individuals that are gradually approaching death. At the same time, the possibility that this behavior could, in fact, be adaptive should not be written off. If flies are becoming frail as they age, why not simply hang out upside-down to reduce stress?

In the present study we examined supine behavior of flies from a slightly different point of view. We performed survival analysis of the experimental data, using the model of heterogeneous mortality. The semi-parametric representation of this model allows us to avoid biologically unjustified assumptions of a parametric form of the baseline hazard and compare survival in different groups of medflies in terms of differences in the baseline hazard and parameters of the frailty distribution. It was shown that insects with the shortest inactive life duration are slightly debilitated, and debilitation is amplified with age. In addition, this subpopulation is frailer on average and slightly more heterogeneous than the group with an average duration of inactive life. Among flies with the longest inactive life duration, we observe a strong but vanishing adaptive effect. This population is less frail on average, and significantly more heterogeneous than the group with an average duration of inactive life.

Using the quadratic hazard model and the average behavioral trajectory (observed), we tested the assumption about existence of the 'optimal behavior' for different ages. The term optimal behavior means a strategy that increases chances of the flies for survival. It was shown that exponential increase of intensity of supine behavior with age minimizes the risk of dying for male medflies. The deviation of behavior from this pattern increases mortality.

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To investigate properties of supine behavior in medflies using sophisticated mathematical models and reveal relationship of such behavior to aging and longevity.

2) To understand whether an extreme deviation from the observed average duration of inactive life influences the life span and to study whether observed deviations were induced by an individual's characteristics such as robustness or frailty.

3) To study whether supine behavior can be adaptive (evolutionary evolved) or even optimal for longevity, in terms of minimal mortality.

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Lead Speaker/Author: *A. Semenchenko[1]*
Other Collaborators: *V.N. Anisimov[1], A.I. Yashin[2], J. Carey[3], G. Doblhammer[4]*

Title of Presentation: Seasons of birth affect longevity of Mediterranean fruit (Ceratitis capitata) and other laboratory animals

University/Affiliations: [1] N.N.Petrov Research Institute of Oncology, St.Petersburg, Russia;
[2] Duke University, Center for Demographic Studies, Durham, NC;
[3] Department of Entomology, University of California, Davis;
[4] Max Planck Institute for Demographic Research, Rostock, Germany

Keywords: Frailty model, laboratory animals, mortality, seasonality, survival patterns

Abstract:

Recent research shows that the month of birth influences life span and disease in humans. Nutrition of the mother during pregnancy and/or virus infections in-utero or in the first few months of life has been proposed as underlying causal mechanisms. In this study, we ask the question whether the season-of-birth effect in life span also exists in other species than humans and in particular, whether it exists in laboratory animals that are used as control groups in experiments.

We use data from large experiments on Mediterranean fruit flies with thousands of animals as well as smaller experiments on rats and mice. We find in all three species a significant season-of-birth pattern in life span that is not only consistent among the species but also shares similar characteristics with the pattern observed among humans.

In our study being born in winter is most favorable for the survival of laboratory animals. There is one exception, namely male flies: they experience slightly higher survival when they are born in autumn. The worst seasons for medflies are spring and summer, for female mice — summer and autumn, and for rats — summer. The analysis of the baseline hazard, average frailty and population heterogeneity reveals two common features. First, among all species those born in seasons less favorable for survival experience an increased baseline hazard and an amplification of mortality with age. Second, they are usually more robust on average, which may reflect the ability of the individual to adapt to less favorable environmental conditions. Among flies these two features coincide with larger population heterogeneity. Among rodents there is a tendency towards lower heterogeneity, however, the most heterogeneous female populations were born in the worst season (summer for mice, autumn for rats).

Specific Aims of Research & Linkages, as appropriate to understanding the biodemography of life span:

1) To check the data available from experiments on different laboratory animals for the presence of the season-of-birth effect on survival.

2) To study whether the observed seasonal patterns share some characteristics in terms of life expectancy, baseline hazard, average frailty and population heterogeneity.

3) To deepen our understanding of underlying biological mechanisms related to the season of birth/eclosion that can reveal themselves on the population level in the differences in survival patterns.

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