SPYROS PAPAGEORGIOU

CURRICULUM VITAE

1934: Born in Arcadia, Greece

1951: Graduated from Varvakeion Standard High School (Classics)

1951-1956: Studied Physics, University of Athens, Greece, fellowship of the National Scholarship Foundation

1956: Graduated in Physics, University of Athens

1957-1958: Served in the Greek Army

1959-1960: Studied Theoretical Physics, University of Goettingen, scholarship of The German Academic Office DAAD

1961-1964: Continued graduate studies in Theoretical Physics, Oxford and Sussex Universities, scholarship of the Greek Atomic Energy Agency

1964: Ph.D. in Theoretical Physics (Nuclear Physics), University of Sussex

1964: Appointed junior research scientist, Nuclear Research Centre 'Demokritos', Athens

1968-1970: Appointed Research Fellow at CERN, Geneva, Switzerland

1971-1973: Appointed Corresponding Fellow at CERN and NRC 'Demokritos'

1975: Visited the Max-Planck-Institut fuer Virusforschung, Tuebingen, Germany, started working on Theoretical Developmental Biology

1976-1979: Organised a 2 term Physics Course and Laboratory, Medical School, University of Athens

1981-1982: Visited on sabbatical leave the Developmental Biology Laboratory, Kings' College London

1985: Organised and headed the Theoretical Biology Group, NRC 'Demokritos'

1988: Research Director, Institute of Biology, NRC 'Demokritos'

1992-1994: Headed the Biology Graduate School, NRC 'Demokritos'

1995-1996: Visited on sabbatical leave the Developmental Biology Research Centre, Kings' College London

1999: With a grant of The Royal Society (London) collaborated with the Developmental Biology Group, University of Dundee

1999- present: As emeritus research scientist collaborates with the Theoretical Biology Group, Institute of Biology, NCSR 'Demokritos'

Teaching activity

For several years S.P. taught different courses:

1. Physics for medical students: two term course (University of Athens)
2. Quantum Mechanics, Statistical Physics and High Energy Phenomenology (NRC 'Demokritos', Physics Graduate School)
3. Topics in Developmental Biology and Mathematical Methods in Biology (NRC 'Demokritos', Biology Graduate School)

Supervised: Master and PhD Theses on Theoretical Biology (University of Patras) and Developmental Biology (University of Athens)

Invited speaker in numerous Conferences, presented several posters in International Meetings and Conferences, gave seminars and lectures (see e.g. the lecture in **Embryogenesis Explained** (2012) organized by Richard Gordon: http://hoxgenecollinearitycomparisonofmodels.blogspot.com/)

Textbooks by S.P.

1. *Lecture Notes on Quantum Mechanics* (edited by ΚΑΦΣ&ΦΕ, Demokritos, 1966)
2. *Theory of Lie Groups* (with **P. Deliyannis**, edited by ΚΑΦΣ&ΦΕ, Demokritos, 1967)
3. *Physics for Biology and Medical students* (with **S. Alivisatos, A. Angelopoulos** and **D. Sotiriou**) 3 Volumes adapted and translated in Greek from **L.H. Greenberg,** W.B. Saunders 1975).
4. *HOX Gene Expression* (Editor), Springer & Landes Bioscience 2007.

Short List of Publications in Peer-Reviewed Journals

1. R.J. Blin-Stoyle and S. Papageorgiou (1965). The β-decay process in one, two and three-nucleon systems. *Nucl. Phys.* **64,** 1-7.
2. R.J. Blin-Stoyle and S. Papageorgiou (1965). Mesonic exchange effects and the effective coupling constant G_A in β-decay. *Phys. Lett.* **14,** 343-344.
3. R.J. Blin-Stoyle, S.C.K. Nair and S. Papageorgiou (1965). ft-values of $0^+ \rightarrow 0^+$, $\Delta T = 0$, β- decays: implications for the conserved Vector Current Theory. *Proc. Phys. Soc.* **85,** 477.
4. S. Papageorgiou and A. Verganelakis (1967). Phenomenological study of the photodisintegration of the deuteron by polarized photons. *Nuovo Cimento* **51A,** 820.
5. G.V. Dass and S. Papageorgiou (1969). $A_1 \rightarrow 3\pi$ decay. *Nuovo Cimento* **64A,** 36.

6. G.V. Dass, M. Jacob and S. Papageorgiou (1970). Duality and unnatural-parity trajectories. *Nuovo Cimento* **67A,** 429-436.

7. K. Kajantie and S. Papageorgiou (1970). Dual + Pomeron analysis of $K^{\pm} p \rightarrow K^{\pm} \pi^{o} p$. *Nucl. Phys.* **B22,** 31-44.

8. S. Papageorgiou (1972). A phenomenological dual description of the reactions $K^{+} p \rightarrow K^{*o} \pi^{+} p$ and $K^{-} p \rightarrow \acute{K}^{*o} \pi^{-} p$. *Nuovo Cimento* **8A,** 635.

9. S. Papageorgiou (1973). Isospin invariance constraints, Factorization and Exchange degeneracy in inclusive processes. *Nuovo Cimento* **13A,** 210-216.

10. H.K. MacWilliams and S. Papageorgiou (1978). A model of gradient interpretation based on morphogen binding. *J. theor. Biol.* **72,** 385-411.

11. S. Papageorgiou (1980). A morphogen gradient model for pattern regulation. I. Formation of non-repetitive and repetitive structures. *Biophys. Chem.* **11,** 183-190.

12. S. Papageorgiou (1980). A morphogen gradient model for pattern regulation. II. Time description of global morphogen formation and field compartmentalization. *Biophys. Chem.* **11,** 191-198.

13. S. Papageorgiou and D. Venieratos (1983). A reaction-diffusion theory of Morphogenesis with inherent pattern invariance under scale variations. *J. theor. Biol.* **100,** 57-79.

14. S. Papageorgiou and N. Holder (1983). The structure of supernumerary limbs formed after 180^{o} blastemal rotation in the newt *Triturus cristatus. J. Embryol. Exp. Morph.* **74,** 143-158.

15. S. Papageorgiou (1984). A hierarchical polar coordinate model for epimorphic regeneration. *J. theor. Biol.* **109,** 533-554.

16. P. Costaridis, C. Zafeiratos, V. Kiortsis and S. Papageorgiou (1989). Diverse supernumerary structures develop after inverting the anteroposterior limb axis of the Anuran. *Dev. Biol.* **132,** 502-511.

17. S. Papageorgiou (1989). Cartesian or Polar co-ordinates in pattern formation? *J. theor. Biol.* **141,** 281-283.

18. P. Costaridis, S. Papageorgiou, V. Kiortsis and C. Zafeiratos (1991). Types of supernumerary outgrowths produced after inverting the dorsoventral limb axis of the anuran *Bufo bufo. Roux's Arch. Dev. Biol.* **200,** 104-107.

19. S. Papageorgiou and Y. Almirantis (1992). Diffusion or Autocatalysis of Retinoic Acid cannot explain pattern formation in the Chick Wing bud. *Dev. Dyn.* **194,** 282-288.

20. S. Papageorgiou & Y. Almirantis. Autocatalytic action of retinoic acid cannot explain pattern duplications in the chick wing bud. Progress in Clinical and Biological Research (1993) **383**, 725-733.

21. S. Papageorgiou (1996). Distalization in insects and amphibians *Bioessays* **17,** 1089
22. S. Papageorgiou and Y. Almirantis (1996). Gradient model describes the spatial-temporal expression pattern of *Hoxa* genes in the developing vertebrate limb. *Dev. Dyn.* **207,** 461-469.
23. S. Papageorgiou (1998). Cooperating morphogens control *Hoxd* gene expression in the developing vertebrate limb. *J. theor. Biol.* **192,** 43-53.
24. Y. Almirantis and S. Papageorgiou (1999). Modes of morphogen cooperation for limb formation in Vertebrates and Insects. *J. theor. Biol.* **199,** 235-242.
25. N. Vargesson, K. Kostakopoulou, G. Drossopoulou, S. Papageorgiou and C. Tickle (2001). Characterisation of *Hoxa* gene expression in the chick limb bud in response to FGF. *Dev. Dyn.* **220,** 87-90.
26. S. Papageorgiou (2001). A physical force may expose *Hox* genes to express in a morphogenetic density gradient. *Bull. Math. Biol.* **63,** 185-200.
27. S. Papageorgiou (2004). A cluster translocation model may explain the collinearity of *Hox* gene expressions. *BioEssays* **26,** 189-195.
28. Papageorgiou, S. Pulling forces acting on *Hox* gene clusters cause expression collinearity. *Int. J. Dev. Biol.,* **2006**, *50*, 301-308.
29. Papageorgiou, S. A biophysical mechanism may control the collinearity of *Hoxd* genes during the early phase of limb development. *Hum. Genomics,* **2009**, *3*, 275-280.
30. Papageorgiou, S. Physical forces may cause *Hox* gene collinearity in the primary and secondary axes of the developing vertebrates. *Develop. Growth & Differ.,* **2011**, *53*, 1-8.
31. Papageorgiou, S. Comparison of models for the collinearity of *Hox* genes in the developmental axes of vertebrates. *Current Genomics,* **2012**, *13*, 245-251.
32. Almirantis, Y.; Provata, A.; Papageorgiou, S. Evolutionary constraints favor a biophysical model explaining *Hox* gene collinearity. *Current Genomics*, **2013,** *14*, 279-288.
33. Papageorgiou S. Biophysics precedes Biochemistry in HOX gene collinearity. (submitted).

Research Activity

Spyros Papageorgiou started his research career in Oxford in 1961 under the supervision of Professor Roger J. Blin-Stoyle FRS. The first problem he faced was related to the reaction

proton + proton → deuteron + positron + neutrino

a fundamental 'hydrogen burning' process –the first step of the chain reaction responsible for the energy released in the stars. The modification of the β-decay coupling constant was

calculated due to mesonic exchange effects. His D. Phil. Thesis (University of Sussex) was entitled '**Mesonic exchange effects in allowed β-decays'**. Then he studied the β-decay process in light nuclei [1,2,3].

On his appointment at the Nuclear Research Centre 'Demokritos' in 1964 he started working on High Energy Phenomenology and continued his research in this field when he moved to CERN as a Research Fellow in 1968. In particular he worked on several problems of Strong and Electromagnetic Interactions. In 1970-1973 he served as Corresponding Fellow between CERN and 'Demokritos'[4-9].

In 1975 after a major switch in his research, he got involved in problems of Developmental Biology and formulated several mathematical models based on Turing's theory of Morphogenesis. Among other problems, he worked out a mechanism that generates pattern regulation. This scale invariance property is a fundamental feature of early Embryogenesis that the reaction-diffusion models fail to reproduce. The model he proposed achieves pattern regulation in a satisfactory approximation [10-13, 19-21].

He formulated a hierarchical polar coordinate model which can successfully explain the supernumerary outgrowths observed after 180° blastemal rotations. The polar coordinate model itself cannot explain the structure of these outgrowths. He proposed experiments for the verification of his model. The subsequent experiments were in agreement with the model predictions [14-18].

During a sabbatical leave at King's College (London) in 1995 he got involved in the study of *Hox* gene expressions [22-25]. After his retirement, he has being working as an emeritus scientist at 'Demokritos' and he is mainly involved in the collinearity enigma of *Hox* gene expressions [26-33]. This phenomenon has been intensively studied since it was first observed by E.B. Lewis in 1978. The last decade or so some genetic engineering experiments on mouse embryos have revealed many fascinating features of collinearity. Several models, based on these experiments, have been formulated in order to explain this collinearity. These models make use of the familiar action of enhancers, repressors and the other elements of the biomolecular machinery. Such biomolecular models are endorsed by the scientific community although they cannot reproduce or anticipate all existing data.

In contrast to the above biomolecular approach S. P. has proposed a 'biophysical model' since 2001 which is based on the hypothesis that physical forces cause the surprising collinearity phenomenon. The motivation for this hypothesis is based on the multiscale nature of collinearity which results from the involvement of various mechanisms from different disciplines (a characteristic feature of Systems Biology). According to the biophysical model, a physical force pulls the *Hox* genes one after the other (*Hox1, Hox2, ...*) from the sequestered region where the *Hox* cluster is inactive toward the transcription

factory domain where the genes are activated. Admittedly this hypothesis was beyond the established ideas that biochemical processes govern almost exclusively the pathways of development and evolution. As a result the biophysical model was not well accepted (to put it mildly) by the experts in the field. The exact nature of the force acting on the DNA thread has to be further investigated. It may be electrostatic, or a secondary intermolecular force acting either locally or as a result of the overall architecture of the molecular surroundings of the *Hox* cluster. An explicit model based on forces resembling the Coulomb forces has been worked out. This particular model can satisfactorily explain the existing collinearity data [28-31].

It has been only recently confirmed that during activation, the *Hox* genes are sequentially translocated in agreement with the biophysical model prediction. Although these gene translocations were explicitly observed and described they were not attributed to physical forces as it should be proper for reasons of scientific exactness and academic correctness. Instead it was vaguely stated that the *Hox* genes move and 'it remains to be demonstrated whether such a process underlies collinear activation or is consequence of it'. According to the biophysical model this is a pseudo-dilemma since collinearity and gene translocations are inseparable and they constitute indispensable elements of a single integral mechanism for *Hox* gene activation.

The ultimate verification of any theory is impossible, therefore it is necessary to invent ever- new tests challenging the validity of the theory. Such tests for the biophysical model have been proposed and the experimental outcome is still eagerly awaited [31].