

THE SPETSES SUMMER SCHOOLS

Beginning and First Venues

The Spetses Summer Schools are well-known throughout the scientific community in Life Sciences, and anyone who ever attended one of these venues, will remember it enthusiastically.

It was *Marianne Grunberg-Manago*, professor at the Institut de Biologie Physicochimique in Paris, who started the International Summer Schools on Molecular Biology in 1966, and through her untiring initiative the Schools have been kept as a series of annual lecture courses, at least until 2006, when the School celebrated its 40th Anniversary.



Marianne Grunberg-Manago

Born January 6, 1921 in Petrograd
Deceased January 3, 2013 in Paris

1955 Detection of Polynucleotide-Phosphorylase in the Lab of Severo Ochoa in New York

Since 1967 Professor and Chef de service at Institut de Biologie physicochimique in Paris.

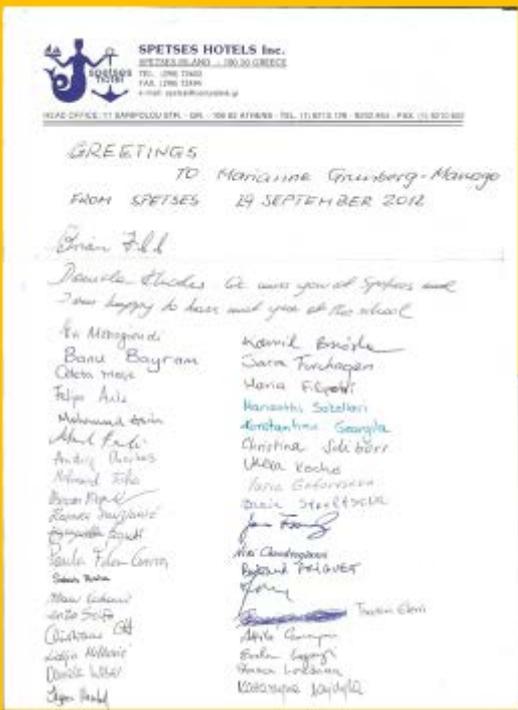
Research work on gene transcription processes and aspects of metabolism in bacteria

1977 Scientific Director of C.N.R.S.; Profesor at Université VII in Paris; Guest Professor at Harvard University

Member of Académie des Science; President of the Académie
Member of American Academy of Sciences

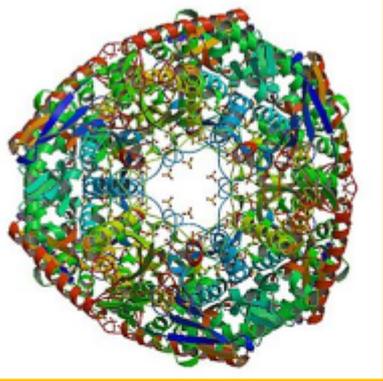
Member of Russian Academy of Sciences

Grand Officier de Légion d'Honneur



Greetings to Marianne
from an IUBMB Spetses Course in 2012

During this venue, the lecture hall
at Spetses Hotel was named
Brian Clark Lecture Hall



Structure of Polynucleotide Phosphorylase (PNPase)

This was the first enzyme for direct synthesis of RNA. RNA Polymerases known before needed DNA as a template. Shortly after its detection by Marianne, this enzyme was used in the Matthaei-Nirenberg experiments to synthesize Poly U for deciphering the Genetic Code.

Talking about Marianne at the above venue, Brian gave the following comment



In her preface to the Proceedings of the NATO/FEBS Advanced Research Workshop held in 1988 [1], Marianne gives an account of this enterprise: “....there were a number of different events that contributed to the origin of this Institute. In the middle of the 1960's, there was a shortage of Advanced Study Institutes in Molecular Biology and NATO representatives approached me to organize one. They were keen on holding it in a country where molecular biology was not taught at the University. I thought the time was appropriate for an Institute on Molecular Biology and that it would be nice to organize it on a Greek island. I believed that a pleasant location would contribute to a successful School and I felt that the environment would help to attract the best lecturers and encourage them to stay the whole time at the School, around two weeks. They would be relaxed and in a mood to interact socially and scientifically with the students. *Leslie Orgel* encouraged me to organize it the way I thought and promised to help me.” Marianne then met *Thanos Evangelopoulos*, a Greek postdoc working at MIT with *Alex Rich*. Soon returning home, he wanted to do something to help science in his country. *Efstathis Bricas*, another Greek working at that time in France, suggested the island of Spetses (Spetsai) as an ideal place. There was a boys' college (*Anargyrios* and *Korgialenios* School) large enough to accommodate students, and a nice hotel (*Kasteli* Hotel) at a short distance from it both of them adjacent to a good beach. The island was small enough to facilitate contacts between students and professors and it was large enough to provide peace and quiet. Marianne continues: “The first meeting (in 1966) was very successful: *Dr. Zervas* and *Dr. Pullman* (who previously organized two NATO Schools)..... acted as co-organizers. *Francis Crick* came on his boat as well as *Jacques Monod*, who introduced me to *Melina Mercouri*. The course immediately achieved a good reputation and should be organized from that time

on every year. Unfortunately, this endeavor had to be cancelled already in 1967 and in 1968, too, because of the “putsch of the colonels”.

In 1969, *Francis Crick*, **Brian Clark** and *Mark Bretscher* from Cambridge dared organize a fourth NATO Advanced Study Institute on Spetses. The school run very well.



Brian F.C. Clark

Born July 26, 1936 in Milford Haven (Wales)
Deceased October 6, 2014 in Aarhus

1961 PhD in Chemistry from Cambridge University, UK
1975 ScD in Molecular Biology from Cambridge University, UK
1961-1964 Postdoctoral research on cell-free protein synthesis at MIT and NIH
1964-1973 Scientific staff member at MRC in Cambridge
1966 discovery of the protein initiation code; 1968 first crystallization of a tRNA molecule

1974 Professor of Biostructural Chemistry in Aarhus, DK
Main areas of research: molecular mimicry and molecular mechanisms of protein synthesis as well as molecular and cellular mechanisms of ageing; beginning proteomics

2000-2003 President of IUBMB
2003 Chairman of FEBS, Vice Chairman of EMBO



Hans Georg Zachau

Born May 16, 1930 in Berlin

1948 Studies of Medicine and Chemistry in Frankfurt
1955 Dr. rer. at. in Chemistry at MPI Tübingen (with A. Butenandt)
1956-1957 Postdoc at MIT, Cambridge, MA (with J.C. Sheehan)
1957-1958 Postdoc at Rockefeller Univ. (with F. Lipmann)
1958-1961 Assistant at MPI for Biochemistry in Munich
1961-1967 Group Leader at Institute of Genetics, Cologne University
1967-1999 Professor of Physiological Chemistry, Munich Univ.
1967 Member German Academy Leopoldina
1976 Member Bavarian Academy of Sciences
1978 Honorary Member of American Society for Biochemistry and Molecular Biology
1978 Großes Bundesverdienstkreuz mit Stern
1981 Orden „Pour le mérite“; Chancellor 1992-2004
1985 Member Academia Europea
1989 Otto-Warburg Medal
1991 Bayerischer Maximiliansorden for Science and Arts
1994 Member Russian Academy of Sciences
Research: tRNA; Chromatin; Immunoglobulin genes in men/ mice

For the year 1970, *Hans Zachau* and I had been asked to organize the third Spetses Summer School in order to bring in the Germans as a third party and to make the School an annual

event. The directorship should from then on be rotated regularly between France, England and Germany. However, an obstacle was that the unclear political situation in Greece had not changed. In fact, it were the students of the 1969 Summer School, who opposed the initiative to organize the 1970 School in Spetses again in order to put pressure on the current government. I remember a long night discussion on the terrace of the main building of the school lead by a tall Italian student, *Alessandro Fantoni*, which resulted in a letter to Nature, containing a declaration that Summer Schools should not be organized in a country under a repressive political system. Also lecturers from Sweden, France and Switzerland refused to come to Spetses under such intolerable circumstances. A consequence was that the 1970 School had to be postponed, because no adequate place could easily be found in due time in Germany or elsewhere. Help came from Italian colleagues, mainly through *Alberto Monroy* from Naples: he suggested a priest's college in Erice (Sicily) as a location, which afforded the consent of *Antonio Zichichi*, who used this place for the meetings of the Italian nuclear physicists. So the 1971 (and also the 1974) School were run in this "exile". It was a nice place, located on top of a hill, some 900 m above sea level, but this location created some difficulty to reach the beach every day. Finally, in 1975, the School went back to Spetses. Between 1983 and 1990, the directorship of the Spetses Summer School for some years included *Tom Caskey* (Houston TX) and *John Hershey* (Davis CA) from the US as well as *John Mc Carthy* (Manchester UK) to reach a more or less four-yearly rotation. The Institute in 1991 had to be cancelled, since the proposed organizers failed to put in applications to the grant giving institutions; 2004 was completely exempted from any Spetses activity, since too much interference with the visitors of the Olympic Games in Athens had to be expected.

We should not forget about the merits of Thanos Evangelopoulos, who from the beginning until the year 1998 took care as the local organizer of the Spetses Summer Schools.



Athanasios E. Evangelopoulos

Deceased 2013

Studied Chemistry at Athens University

1960 Lecturer in Biochemistry Department of the University Hospital "Alexandra", PhD

1960-1965 Lecturer and Researcher at "Alexandra"

1967-1968 Associate Professor at MIT with I.W.Sizer

Mechanism of glutamic-aspartic glutaminase

1971 Laboratory Director at National Hellenic Research Foundation

1972 Founding Member of the Hellenic Society of Biochemistry and Molecular Biology, President and General Secretary for many years

Glycogen phosphorylase b: effects of

polymixins, prostaglandines, sphingolipids;

Protein kinases and phosphorylase kinase

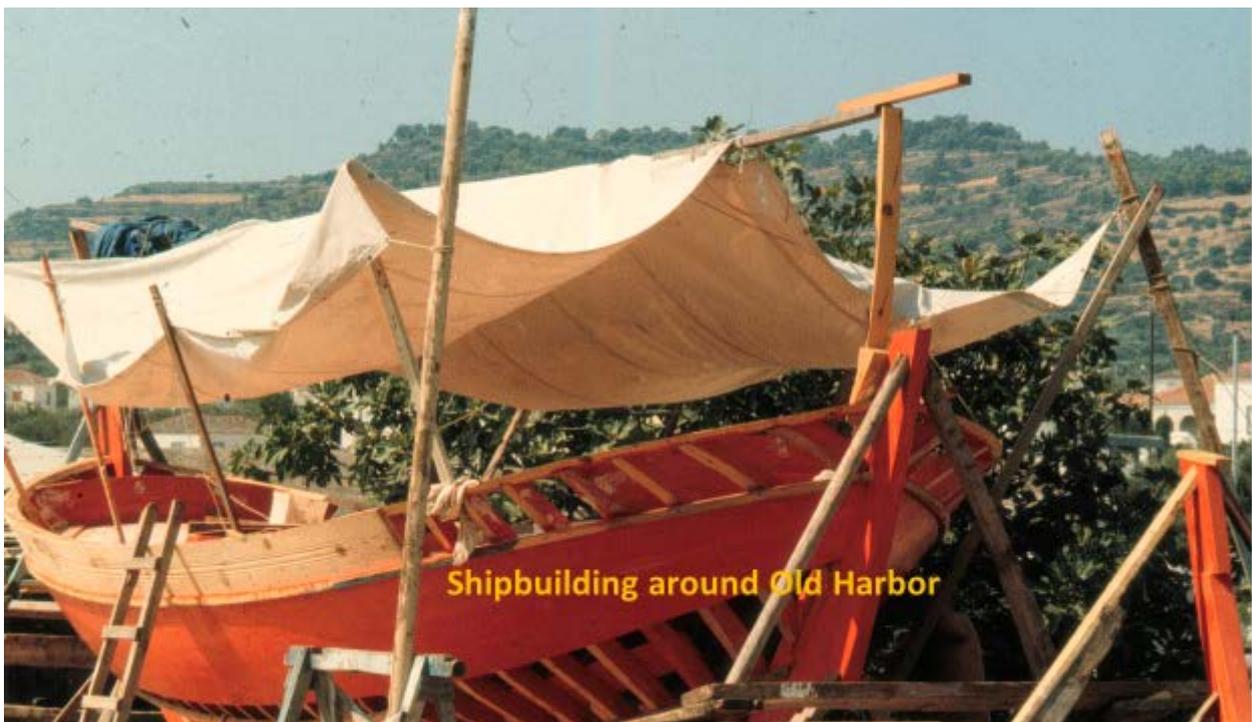
1992 Professor of Biochemistry at University of Thessaly

EMBO Member

1999 FEBS Diplôme d'Honneur

Some Geography and History of Spetses

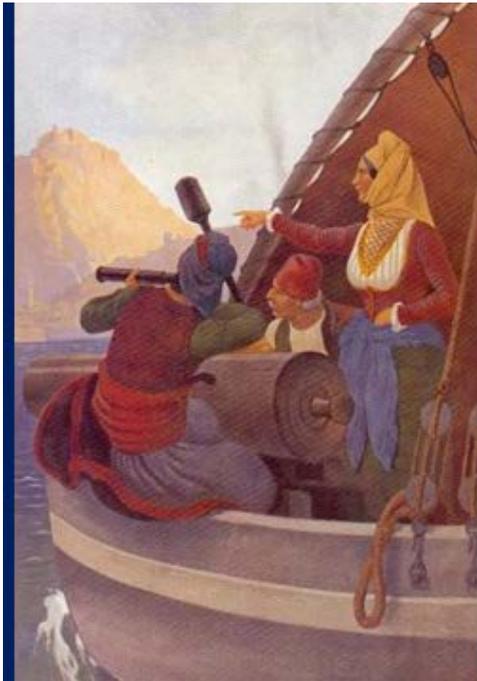
The island is largely built from limestone, thrust up from the sea about ten million years ago. Later in antiquity, the Mediterranean basin was flooded by the sea and the Aegean area sank by an estimated 3000 meters. The porous limestone has led to the formation of a number of caves, especially on the south side of the island. Two thirds of the island are covered with pine trees (an exception for Greek islands!). On the terraces up the hillside cereals, olive and almond trees are grown. Ship-building is still active in the Eastern part of Spetses.



Due to two terrible fires in 1990 and 2000, the once dense pine forests were heavily damaged, at *Anargyri* and near *Zogheria* bay; thus untouched areas severely diminished. Despite this, the island retains its natural beauty: the pine woods and the wide variety of wild flowers, but also the vast array of aromatic herbaceous plants which grow beneath low-shrub thickets, pine and gorse, are unique to Greek islands.



Spetses is already referred to by the 2nd century AD traveler *Pausanias* in his *Description of Greece*. According to *Pliny the Elder*, the island had a good harbor, wells, was suitable for the cultivation of trees and vines, so that it has been inhabited since ancient times. At the division of the Byzantine Empire, Spetses was given over to the rule of the Venetians, who were replaced by the Turks in 1460. Sometime later came the Arvanite refugees from Athens and the Peloponnesus, who settled at first in the Spetses' bays of *Anargyri* and *Zogheria*. The name Spetses, an Arvanite corruption of the Venetian "*Isola di Spezzi*", or "Isle of Spices", well befits the island that we know today.



Laskarina Bouboulina

Born May 11, 1771 in Constantinople (in prison)
Deceased May 22, 1825 in Spetses

In 1811, Bouboulina took over the fortune and trading business from her second husband, Dimitrios Bouboulis at Spetses, and built four ships, including one large warship *Agamemnon*, at her own expense. On 13 March 1821 Bouboulina sailed with eight ships to *Nafplion* and began a naval blockade. *Nafplion* fell, and she captured *Monemvasia* and *Pylos*.

After the War of Independence in 1824, Bouboulina was arrested and exiled back to Spetses. She lost all her fortune.

1832-1862 Otto I (son of King Ludwig I of Bavaria) became King of Greece, and under his successors Greece stayed a Monarchy until 1974.

During the 1821 Revolution, Spetses was the first of the Argo-Saronic islands to join the Greek War of Independence. The towns and villages of the Peloponnese had already taken to arms, and the elders sent out a call for support to their island neighbors. The reply came back without delay, though the Spetsiots did not suffer great hardships under Turkish rule. Nevertheless, on 3 April the people of Spetses revolted and later joined forces with a number of battle ships from other Greek islands like Hydra. A leading figure in this game was *Laskarina Bouboulina* (11 May 1771 - 22 May 1825), known as a Greek heroine [4]. *Bouboulina* was born in a prison in Constantinople. She was the daughter of captain *Stavrianos Pinotsis* who had been imprisoned because he had taken part in the revolution of 1769-1770 against the Ottoman rule. After her father had died soon afterwards, the mother and the child returned to the island of Hydra. Later, when *Laskarina* married again, the family moved to the island of Spetses. When her second husband, *Dimitrios Bouboulis* was killed in a battle against Algerian pirates in 1811, *Bouboulina* took over his fortune and trading business and built four ships, including one large warship *Agamemnon*, at her own expense. On 13 March 1821 *Bouboulina* sailed with eight ships to *Nafplion* and began a naval blockade. She led her own troops until the fall of the fort on 13 November 1822. Later she took part in the naval blockade and capture of *Monemvasia* and *Pylos*. After independence, which erupted into a civil war in 1824, the Greek government arrested *Bouboulina* and she was exiled back to Spetses, but all of her fortune was gone for the War of Independence. Every year in early September, the historic naval battle of Spetses (8 September 1821) is celebrated at the *ARMATA* festival, high-lighted by the burning of a Turkish battle ship at *Dapia*. After *Bouboulina's* death in 1825, the Spetses merchant fleet prospered for another twenty years, but then it fell into decline, taking with it the population of the island.



ARMATA

Every year, around September 8, the burning of the Turkish flagship during the naval battle 1821 at Dapia is celebrated as a historic event



A new chance for the island began with the return of *Sotirios Anargyrios* from the U.S. in the early 1920s. Realizing that the future for Spetses lie in tourism, he put his new-found wealth to the best possible use, constructing the road around the island, building the first hotel in the Greek islands (the *Possidonion*), and replacing the pine-forests of the island which had been depleted to facilitate the boat-building industry. Together with *Marinos Korgialenios* from *Cefhalonia*, he built the College which bears their names, and which for 60 years educated nobility from all over Greece.



Financing of the Spetses Summer Schools

Initially, the Spetses Summer Schools were sponsored exclusively by NATO (Scientific Affairs Division). The processes for application and accounting were extremely tedious for the organizers, but once an Institute had been accepted, support was always rather generous. One of NATO's demands, namely that the goals and achievements of every Institute should be documented in a book publication could successfully be circumvented. The way out for the organizers was to produce a booklet of abstracts, which was distributed to the participants and also half-heartedly accepted by NATO. The organizers felt that information available in most recent publications and monographies should not be repeated.

On the other hand, NATO's strict rules, to only finance lecturers and students coming from NATO countries soon caused the organizers to apply for further grants, from EMBO (sponsor since 1972), and from FEBS (sponsor since 1981), as to allow to invite and support lecturers and students from Non-NATO countries. In this respect, NATO accepted co-sponsorship. Within the years up to 1983, the number of students who came from universities of the Eastern block was modest, three or four each year. Mainly, these participants were resident in Poland, Hungary, former Yugoslavia, etc. It may well be that many more post-doctoral fellows from these countries were admitted, who had found a position in Western countries, since their names pointed to a provenience from an Eastern country. Russians who applied and were accepted mostly met difficulties to obtain their visa. During the time of German separation, students from the DDR (*Deutsche Demokratische Republik*) were never allowed by their authorities to apply. Due to political relaxation after 1989, increasing numbers of students from Eastern countries were accepted and supported through the FEBS Youth Travelling Fund. In 1998/99, a big change occurred in NATO's policy: contrary to former restrictions against Eastern countries, the rules now demanded to invite at minimum one co-organizer from an Eastern country and to admit some 40 percent of the students from these countries. As the organizers of the Summer School in 2000 felt this unacceptable, they decided from then on to give up NATO support and to rely on financial support from EMBO and FEBS only. Thanks to the co-operation and generosity of these latter organizations financing did not greatly suffer. Moreover, the organizers were able to again raise the number of students from Eastern countries.

In the early years, there were about four to five times more applicants than could be accommodated. Nearly everyone being accepted among the 120 or so student participants received a fellowship. Additionally, as a contribution to the general expenses, FEBS (after 1981) allocated fellowships to some 25 percent of the students, covering travel, accommodation and stay. According to FEBS rules, students from Eastern or developing countries were preferred. Over the years, due to the shortage of organizational income, the

organizers considered that ever more students coming from 'rich' countries should be asked to apply for financial support from their home institutions. None the less, the organizers kept two principles in selecting the participants: (i) a reasonable national and geographical proportion, (ii) a documented motivation and personal abilities of the student to follow the course successfully. To this end, a written application (in form of a questionnaire asking about training, personal interests, publications, future projects, etc.) and one or two letters of recommendation were obligatory.

How Spetses Summer Schools were run

The principles of organizing the Spetses Summer Schools have largely been maintained through many years. At the beginning, the Schools lasted for twelve days, but since the year 2000 the duration had to be cut down to some eight or nine days, as the supporting institutions felt that nearly two weeks were too much. One free afternoon was devoted to an extended boat-trip around the island. Thus anyone had a chance to see the marvelous shape of the island, to inspect the famous cave in *Anargyri* and to take a swim in the open sea. In former times, a highlight was always an excursion to the famous sites on Peloponnesus: the archaeological site of *Mycenae*, the ancient resort of *Epidaurus* with its huge amphitheatre, and *Nafplion*, the old Greek capital, with its strong fortification '*Palamidi* castle'. In the early years, the excursion ended in visiting a Greek play in the *Epidaurus* Amphitheatre performed at night by actors from Athens.

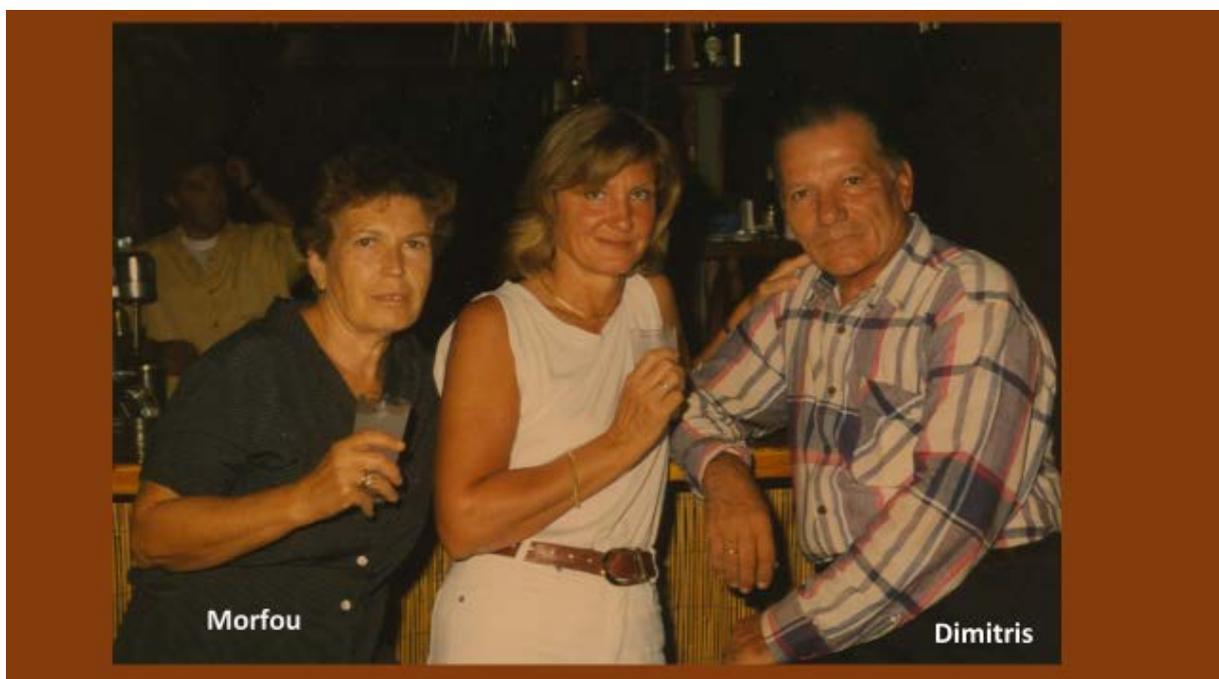
The student participants were accommodated in two buildings of the Anargyrios College, which had served to host the boys of the boarding school. Hence, these had a rather Spartan equipment without air-condition. Toilets and showers (run with brackish water) were in common rooms (male and female). Thus, the organizers always emphasized that accommodation was 'dormitory style'. Breakfast and lunches (the lecturers were expected to eat lunches together with the students) were served in the refectory of the main building; a small cafeteria with an open air sitting place was available. The lectures took place in an air-conditioned lecture hall in which some 130 people could be seated. The lecturers were put up in a nearby hotel. During the first years, it was *Kasteli* Hotel, which offered air-conditioned rooms at the main building as well as small bungalows up-hill on the same grounds. Over the years, the hotel was completely run down by the proprietor, as he never invested a penny for refurbishing it. Later the hotel was taken over by another company and restored but grew enormously expensive and finally had to be closed in 2006. Fortunately, a new hotel, Spetses Hotel, had opened close to the college, so that the lecturers from then on could be accommodated in much more comfortable surroundings. While this latter arrangement lasted for many years, a change occurred, when the Board of Trustees of the college and the Greek

government decided to apply to the EU for money that could be invested into the school's redevelopment. This measure was urgently required to improve the facilities, because the organizers wanted to meet the steady criticism of the participants. Also, the Board eventually grasped that the buildings remained empty most of the time of the year, and should be used for educational purposes other than the Spetses Summer Schools or similar courses. Apparently, this money was not enough to refurbish more than two of the five buildings. Among other improvements, the lecture hall received a new air conditioning, modern technical equipment and comfortable chairs (the old chairs suited for children had always been a torture to sit on). The sanitary installations of the main building and of two of the dormitories were improved as well as the refectory and the kitchen. None the less, the school facilities are still open for foreign courses during certain times of the year. In all, the students of the Summer Schools have continued to complain about many insufficiencies, but all of them tend to state that they would love to come back. Indeed, the place is still ideal because of its location in a huge park, near the shore, and its quietness. During recent years, the British and the French organizers preferred to hold the School at Spetses Hotel: the owner had built a lecture hall with sufficient technical equipment, and up to hundred participants can be accommodated in double rooms. Nowadays, the prices for rental are similar to those at the college. A drawback is that the lecture hall offers space for only ninety people. So, some 80 students at maximum can be accepted per course. As the students of each year had no chance to experience and compare both possibilities, they appreciate the 'hotel solution'. This became also true for courses organized by colleagues, who realized that this location offers an ideal place. Even the 'mixed solution' has been practiced through many years, for example, by Dutch organizers for courses in 'Membranes and signal transduction'.

Past and Future of the Spetses Summer Schools

From an overview of the Schools, which I developed over the years [3], one can infer that a broad palette of topical themes in the field of Molecular and Cell Biology could be covered thanks to the wide sight of the respective organizers, though finally not all relevant topics coming up in these fields could be covered, all the more as in later years appropriate time in the schedule was not available and the Schools had to be restricted to more specialized themes. The facts show [3] that over the years more than 500 (different !) renowned lecturers came to the island to teach more than 5000 young pre- and post-doctoral researchers. There is also no lack of illustrious names among the scientists who lectured at Spetses. Just to pick out the Nobel Prize winners: *D. Baltimore, P. Berg, M. Capecchi, A. Ciechanover, F.C.H.Crick, M. Eigen, W. Gilbert, T. Hunt, A. Klug, R. Kornberg, R. Levi-Montalcini, Venki Ramakrishnan, R.J. Roberts, F. Sanger, I. Sulston, and K. Wüthrich*. The aforementioned numbers

immediately disprove the steady criticism of discontent colleagues who blackened the Spetses Summer Schools to be a 'club'. Of course, some of the lecturers have been invited to come back several times for a number of reasons: they offered interesting subjects, presented good lectures, had excellent experience in interacting with the students, and were prepared to stay for the whole venue. Marianne, Brian and Thanos created the "*Bouboulina Prize*" that was yearly given to three lecturers (or organizers) who had most successfully supported the Spetses Summer Schools. An absolute devotion towards the aims of the Summer Schools was rather decisive, because I remember the many difficulties that arose, when lecturers would commit themselves for only a few days or even disappeared after a couple days of stay: the organizers as well as the students felt these attitudes incompatible with the aims of a Summer School. Moreover, the organizers ran into trouble with the grant-giving agencies. More satisfactorily then, one can realize that all participants to the courses until to date feel like a community, and that they keep a good reminiscence of these venues and of the island. Even there is still contact among some of the students who attended one of the Schools several years back. Remarkably, former students became lecturers once they had advanced in their own research. A further positive effect of the close interactions between students and lecturers was that many of the participants found a post-doctoral position in one or the other lecturer's lab under good conditions.



Most helpful in the organization were the secretaries mostly coming from the institutions of the respective organizers. For more than 30 years, *Morfo Houlis* (the former secretary of Professor *Zervas* from Athens), served the Schools as a Greek and English speaking secretary, facilitating the contacts with the personnel of the college. *Dimitris*, her husband, as well as their

children, *Liane* and *Elias*, also helped a lot with organizational matter. It was *Dimitris* who provided 200 chairs from Athens to equip the lecture hall with new furniture in 1996.

I think with the above arguments, the tradition kept in the Spetses Summer Schools is pretty clear: from its beginning, these venues were designed as teaching institutions, at the time giving young pre- and post-doctoral researchers a possibility of getting familiarized with new developments and novel ideas. Questions obvious to arise in the near future have to consider several challenging aspects, for example: "Is the format of the Summer Schools still valid? Should this type of educational activities for young researchers persist?" Developments during recent years indicate several problems potential organizers might have to cope with:

(1) Interest of potential student participants has decreased as they are aware that the Schools are designed in a way different from meetings or workshops; during the last years, the number of applications has been recessive. This is partly due to the fact that money from their home institutions is shorter and that they therefore prefer to apply for more specialized courses or meetings. None the less, these venues are still most helpful for young researchers who are just entering a particular field or for 'outsiders' who are interested in switching fields.

(2) Financial support from EMBO and FEBS has been limited or even suspended in particular cases, so that the organizers have to invite (additional) money from other grant giving institutions. Serious debates with EMBO and FEBS have uncovered that they have developed a critical attitude, so that it will need good arguments by the organizers and their restless engagement in organizing fruitful programs.

(3) The principal former organizers who strictly kept the format of the Summer Schools are deceased or have retired meanwhile; some of their successors obey a new format: shorter duration of the courses and invitation of lower numbers of lecturers and students. I have realized that during the last years many course organizers chose Spetses as a location for their courses - not only those who experienced the atmosphere of the Spetses Summer Schools and the attractiveness of the island. The 'older generation' of organizers had to respect the 'new' developments and had to call on younger colleagues to step in and keep the tradition of the Spetses Summer Schools, be it in a different format.

The next picture shows all senior organizers and lecturers together with selected students celebrating the 40th Anniversary in a three-day workshop in 2006.



We have to be extremely grateful to all of them. Special thanks should go to Pascale Cossart from Institut Pasteur, Alan Fersht from Cambridge and Brians colleagues from Aarhus, Peter Herrlich from Jena, Stathis Gonos from the Hellenic Research Foundation, as well as to the proprietors and all personal from Spetses Hotel, and finally to all staff from Anargyrios & Korgialenios School, who have hosted us so kindly through all these years.

I am convinced that their engagement will pay out for future training of young scientists. I am sure the people of Spetses will enthusiastically welcome any type of scientific clientele – as much as serious tourists. In summary, as a frequent ‘visitor’ to this wonderful island, I promise anyone coming to this place a pleasant stay and a long-lasting benefit from it. May Spetses prosper and flourish!



References

- [1] Evolutionary Tinkering in Gene Expression (Grunberg-Manago, M., Clark, B.F.C. and Zachau, H.G., eds.) NATO ASI Series, Series A: Life Sciences, Vol. 169, Plenum Press, New York and London, 1988.
- [2] Correspondence. Molecular Biology at Spetsai. Nature 223 (1969) 1186. (Reprint in ref. [1])
- [3] feldmann.userweb.mwn.de/Spetses

s; and human protein atlas.