# The 2003 GSA Honors and Awards

The Genetics Society of America annually honors members who have made outstanding contributions to genetics. The Thomas Hunt Morgan Medal recognizes a lifetime contribution to the science of genetics. The Genetics Society of America Medal recognizes particularly outstanding contributions to the science of genetics within the past 15 years. The George W. Beadle Medal recognizes distinguished service to the field of genetics and the community of geneticists. We are pleased to announce the 2003 awards.

David Hogness and son, Peter

## The 2003 Thomas Hunt Morgan Medal

## David S. Hogness

At a time when genomics is adding new dimensions to the molecular characterization of life, it is fitting that David Swenson Hogness be recognized by the Genetics Society of America with the 2003 Thomas Hunt Morgan Medal, for a lifetime of contributions to the field of molecular genetics. Modern genome analysis was founded in 1972 by Hogness when, in anticipation of the first successful recombinant DNA cloning of eukaryotic DNA a year later, he proposed in a grant application the concepts and basic methodology for producing "libraries" of genomic DNA, for producing physical maps of overlapping clones covering entire chromosomes, and for isolating mutant genes solely on the basis of their position on chromosomes (a technique that later came to be known as "positional cloning"). Over the next decade, the Hogness lab successfully implemented his revolutionary proposals by producing the first random genomic clones from any organism, mapping the first cloned DNA segment to a specific chromosomal location, producing the first recombinant DNA clone library representing an entire genome, and screening that library for clones that carried specific sequences using a novel filter hybridization method called "colony hybridization." These achievements were followed by the first chromosomal "walk" and use of chromosomal rearrangements to achieve the first positional cloning of any gene. This was followed by the mapping of mutant alleles and transcripts on a genomic DNA map of over 300 kb, representing a first example of what we now call "functional genomics."

During his career, Hogness made important contributions using three model genetic organisms: *Escherichia coli*, bacteriophage λ, and *Drosophila melanogaster*. In Jacques Monod's laboratory, Hogness and Melvin Cohn showed for the first time that enzyme induction in bacteria results from an increase in the rate of the *de novo* synthesis of an enzyme from its constituent amino acids. This was fundamental groundwork for Monod's subsequent studies on inducible promoters that led to Jacob and Monod's operon model for gene regulation in bacteria. After moving to St. Louis, Hogness began his studies of the genetic organization of bacteriophage λ and its derivative λdg. With A. D. Kaiser, he invented a transformation assay for the activity of genes contained in purified phage DNAs and in terminal fragments containing either the "left" or "right" ends. Using this assay to determine the gene content of both left and right terminal fragments, Hogness and his colleagues generated the first physical maps of genes in DNA. Comparison of these physical maps with genetic recombination maps demonstrated their colinearity for the first time. Other experiments in the Hogness lab involving the isolation of each of the two strands of these phage DNAs provided a means of orienting the genes on the map according to the direction of their transcription.

In 1968 Hogness changed the focus of his research from the genome of λ to that of higher eukaryotes, and in particular that of *D. melanogaster*. He spent a sabbatical year in the laboratories of Edward B. Lewis (Caltech), James Peacock (CSIRO, Canberra), and Wolfgang Beerman (Max-Planck-Institut, Tübingen) learning about Drosophila and polytene chromosomes, with an aim of carrying out molecular genetic analyses of Drosophila and its development at the same level as he had for λ. During the early part of this transition, his laboratory solved the problem of how the long chromosomal DNAs

of Drosophila can replicate as fast as the shorter genome of λ. This was achieved by an electron microscopic determination of the distribution of replication origins in rapidly replicating Drosophila DNA.

In an NIH grant application in 1972 Hogness presented revolutionary plans for what is now called "genomics"—plans that included production of recombinant DNA libraries representing entire chromosomes or genomes, ordering of overlapping genomic clones to produce physical maps of entire chromosomes, the use of these chromosomal "walks" together with chromosome rearrangements to positionally clone genes identified solely on the basis of their mutant phenotype and genetic map position (positional cloning), and subsequent mapping of mutations and transcripts (what we now refer to as functional genomics).

This proposal was soon implemented in his laboratory. By 1973 small libraries of randomly cloned segments of Drosophila genomic DNA were obtained, the first such libraries for a higher eukaryote. The properties of some of these cloned DNA segments were reported in 1974, including their content of single-copy and repetitive sequences and the location of these sequences within the genome, work that led to the first molecular identification of transposable elements. The first clonal-hybridization method for identifying clones containing specific sequences, colony hybridization, was reported by the Hogness laboratory in 1975. This technique was first used in Hogness's laboratory for the analysis of rDNA and histone genes in Drosophila. Analysis of the first of these led to the discovery of interrupted eukaryotic genes. Analysis of the sequences immediately upstream of the histone genes carried out by Hogness while on sabbatical in Walter Gehring's laboratory resulted in discovery of the "Goldberg-Hogness box," now known as the TATA box. In 1978–1979, techniques were developed by Hogness and his colleagues to allow genes to be cloned solely on the basis of their position in the genome relative to sequences that had been isolated previously. At a truly seminal National Drosophila Meeting held in San Diego in 1987, Hogness shared a session with Ed Lewis in which Hogness described the application of this strategy in terms of his progress on cloning the *Ultrabithorax* gene. This approach, which was originally called "chromosome walking and jumping," is now better known as positional cloning, a method widely used in all genome mapping projects to clone genes that have been identified only by mutations that lie within them.

These methods were subsequently expanded by Hogness into what we now call functional genomics: the correlation of physical maps of chromosomes with genes, mutations, and transcribed regions (and, ultimately, the complete sequence of each region). To accomplish this, Hogness and colleagues studied the structure and function of the homeotic genes that specify the identity of cells in different body segments during Drosophila development. His positional cloning of the *Ultrabithorax* gene (*Ubx*) of the bithorax complex of *D. melanogaster* allowed Hogness and his colleagues to map mutations defining this gene and to identify its transcription unit, its mRNA sequences, and its large *cis*-regulatory regions. This revealed that, despite the complex phenotypes associated with mutations in this gene, *Ubx* comprises one long protein-encoding transcription unit and two large *cis*-regulatory regions rather than several protein-encoding genes as had been previously thought. Many of the complex phenotypes associated with mutations in the bithorax complex were shown to be due to changes affecting these regulatory regions rather than the protein-coding sequence. This is an important principle that is now known to apply to the other seven homeotic genes in the bithorax and Antennapedia complexes. The coding capacity of *Ubx* is also complex as alternative splicing of *Ubx* transcripts gives a set of protein isoforms expressed at different times and in different tissues and having different functions.

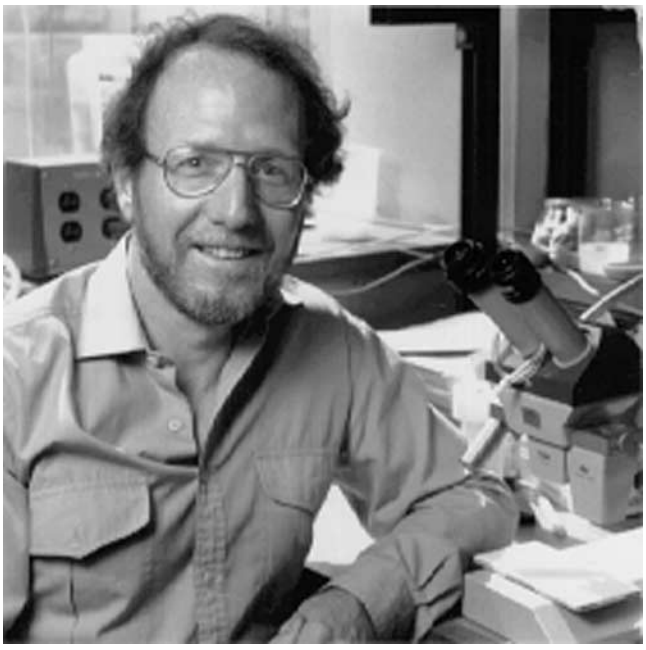
While the *Ubx* gene served as a model system for investigating the structure and function of regulatory genes, Hogness used a second model system to investigate the molecular nature of genetic regulatory hierarchies. The timing and process of metamorphosis in Drosophila is regulated by the steroid hormone ecdysone, which triggers a complex series of events that may differ from one tissue to another. Earlier work by M. Ashburner and others had suggested that these complex responses reflect hierarchies of genes whose expression is affected by ecdysone. Over a period spanning three decades, the Hogness lab isolated and studied genes encoding the ecdysone receptor, primary response genes whose transcription is directly regulated by the ecdysone-receptor complex, and secondary response genes whose expression is regulated by the transcription factors encoded by the primary response genes. The complex interactions between differentially expressed isoforms of the receptor, the diversity of the primary response genes, and the tissue-specific functions of the secondary response genes have provided an outstanding model for understanding the relationship between gene expression and the control of developmental processes.

A Festschrift held at Tomales Bay, California, in 1995 brought together for a few days almost all of the approximately 80 past and present members of the Hogness lab, as well as his colleagues from the Biochemistry Department at Stanford. The memories shared at that meeting captured many aspects of a remarkable person and career not immediately apparent from the above recitation of scientific accomplishments. The breadth of his vision was noted by S. Artavanis-Tsakonas, who noted that one was free to address almost any scientific problem in the Hogness lab, so long as you did it well and did it passionately. A remarkable illustration of this characteristic was Hogness's support of one of his graduate students, J. Nathans, who cloned the bovine rhodop-

sin and human rhodopsin and opsin genes, discovering the molecular basis of red-green color blindness. The breadth of Hogness's interests were described by P. Berg, who noted that he could likely have had as brilliant a career as an architect as he did in science, having designed not only the home he built at Stanford, but also the layout of the laboratories in the Department of Biochemistry. One well-known trait was pointed out by A. Kornberg, who described Hogness's "passionate reluctance to publish." There is indeed a remarkable body of work never published, including the first differential cDNA screens and the discovery of the TATA box. However, as noted by many, this did not in most cases interfere with the subsequent careers of the lab members doing the work, perhaps reflecting the eloquence of their mentor in writing letters. In any case, the relationship between David Hogness and his lab members was perhaps best captured in a quote attributed to a former postdoc, who said "Every time I think of Hogness, my heart warms up."

David S. Hogness was born on November 17, 1925, in Oakland, California, and obtained his B.S. (1949) and Ph.D. (1952) degrees from the California Institute of Technology, where he did his thesis research with Professor Herschel Mitchell in both the Chemistry and Biology Divisions. After postdoctoral studies in Jacques Monod's laboratory at the Institut Pasteur, Paris (1952–1954), Hogness was appointed in 1955 to a faculty position in the Microbiology Department chaired by Arthur Kornberg at Washington University, St. Louis. In 1959, the entire department moved to Stanford University where they created a new Department of Biochemistry. He chaired this department from 1986 to 1989, when he joined the new Department of Developmental Biology that he had done much to create, becoming Professor of Developmental Biology and Biochemistry. In 1991 he was named the Rudy J. and Daphne Donohue Munzer Professor of Developmental Biology and Biochemistry. He was elected to membership in the National Academy of Science (1976), the American Academy of Arts and Sciences (1976), Honorary Membership in the Japanese Biochemical Society (1987), and Associate Membership of EMBO (1992). He has received several awards including the Genetics Society of America Medal (1984), the Newcomb Cleveland Prize of the American Association for the Advancement of Science (1966 and 1988), the Ricketts Award, University of Chicago (1977), the Humboldt Research Award, Germany (1995), the Darwin Prize, University of Edinburgh (1995), the March of Dimes Prize in Developmental Biology (1997, shared with W. Gehring), and the Lifetime Achievement Award of the Society for Developmental Biology (2002). Hogness has been awarded honorary degrees by the University of Crete, Greece, and the University of Basel, Switzerland (both in 1986).

Kenneth C. Burtis
R. Scott Hawley
Howard D. Lipshitz



Jeff Hall in the lab.

# The 2003 Genetics Society of America Medal

## Jeffrey C. Hall

THIS year's GSA Medal is awarded to Jeffrey C. Hall for his seminal studies on the genetic and molecular bases of behavior in Drosophila. Over nearly 30 years, Hall has consolidated the field of Drosophila behavioral neurogenetics, which was initiated by his postdoctoral supervisor, Seymour Benzer, and elevated it to a level of molecular sophistication that would have hardly been thought possible when he began his work. He has focused his attention predominantly on two model systems of complex behavior, courtship and biological rhythms. Through all of this work, he has combined deep genetic insight and a firm belief in the power of mutant analysis with the broad biological perspective of placing the genes' actions into their proper anatomical and physiological context. In so doing, he has raised the entire field of animal behavior genetics to a new level and has set the standard for analytical rigor and power.

Prior to his entry into the field, Drosophila courtship genetics consisted principally of descriptive work on a small set of "classic" morphological mutants, selection experiments, and comparative evolutionary studies. Following his stint in Benzer's laboratory in the early 1970s, Hall transformed fly courtship into a mechanistic discipline through his genetic and behavioral studies of the functional neuroanatomy of sexual dimorphisms. Hall took the traditional approach of mosaic analysis and brought it to the cellular level through direct marking of neuronal genotype. This sophisticated use of genetics to define the neuroanatomical focus of a behavior laid the foundation for subsequent interpretations of all mutants affecting courtship. The first mutant he studied, *fruitless*, later became, through Hall's shepherding, the cornerstone of our current understanding of the genetic point of intersection between sex determination and sex-specific behavior. This work provided the first concrete molecular genetic account of how a gene controlled the sexual identity of the nervous system (rather than sex-specific morphology) and would not have been possible without Hall's foresighted and persistent genetic, behavioral, and anatomical work. Other lines of research on fly courtship launched in Hall's laboratory include the demonstration of a learning component to the otherwise innate courtship ritual, the functional demonstration of pheromonal differences between genetic variants, the genetic dissection of the sensory components of courtship behavior, and the molecular genetic analysis of courtship song.

One of Hall's studies of a gene affecting courtship song, the *period* gene, led him into his second major set of contributions. In 1979, the genetic study of circadian rhythms had ground to a virtual halt after the initial pioneering studies of Ron Konopka, which had also commenced Benzer's laboratory. After his postdoc Bambos Kyriacou noted that courtship songs from wild-type *Drosophila melanogaster* males have a rhythmic component with a period of about 1 min, Hall wondered whether Konopka's *period* mutants, which affected the circadian 24-hr oscillation of behavior, might affect these rhythmic oscillations. Their subsequent findings—that *period* short-day mutants also had a shorter song cycle, long-day mutants had a longer song cycle, and the song rhythm of arrhythmic mutants was obliterated—launched the extensive series of studies on the genetics of circadian rhythms from the Brandeis group that helped rejuvenate the field and led to the fundamental insights into circadian biology that are so well known today.

Jeff Hall in a less professional pose exhibiting some of his enthusiasms—dogs, beer, and Civil War scholarship (exemplified by the Confederate hat)—but omitting others: sports, rock (particularly "oldies"), motorcycles, and movies (specializing in Woody Allen and Inspector Clouseau). His unfettered (and, perhaps, unfetterable) sense of humor has enlivened interactions with his colleagues and his many friends.

Early on, Hall engaged another Brandeis biologist, Michael Rosbash, in the project, and together they inaugurated the molecular genetics of *period* (also independently undertaken by Michael Young at Rockefeller University). By focusing initially on the biology of the gene's action, these studies resulted in the key discoveries of the pacemaker cells in the fly's brain and the oscillation of *period*'s protein in them. Subsequent demonstration of *period*'s mRNA cycling established its role in the self-sustained autoregulatory feedback loop that provided the core of the circadian clock mechanism—an insight that broke open the problem. In his ongoing collaboration with Rosbash and others, Hall has continued to hammer away at the anatomy and physiology of the fly's pacemaker cells, using genetics as the key tool to dissecting the neurobiology of the clock. He has also sustained the hunt for new clock genes by means of forward genetic screens using a variety of methods such as luciferase reporting. These efforts have resulted in the identification of the pacemaker neurons and the neuropeptide that controls locomotor rhythms, the isolation of mutants identifying two genes, *cycle* and *dClock* (née *Jerk*) that encode transcription factors that control the expression of *period*, and the isolation of a mutation in the *cryptochrome* gene, identifying it as the fly's accessory circadian photoreceptor. Throughout this work, Hall has set the standard for care, rigor, completeness, and scholarliness that is unsurpassed in modern behavioral genetics.

Hall's original motivation for undertaking the molecular analysis of *period* was to test an idea on the genetic basis for evolutionary differences in behavior. He and Kyriacou had mapped a song rhythm difference between *D. simulans* and *D. melanogaster* to the X chromosome, where, coincidentally, the *period* locus resides. With the cloned gene in hand, the experiment that allowed a *period* gene from one species to "replace" that from the other became possible. The results were spectacular in that a *D. melanogaster* male host carrying a *D. simulans period* gene would now sing with the *D. simulans* song cycle. Similar interspecific transformation studies from the Brandeis group also showed that the species-specific differences between *D. melanogaster* and *D. pseudoobscura* locomotor rhythm patterns are also controlled in an all-or-none manner by *period*. The results from these two sets of studies demonstrated that interspecific differences in adaptive behavior can be transferred between species by means of a single gene, *period*. The implications for evolutionary mechanisms of Hall and his collaborators' experiments, although under-appreciated at present, may well turn out to be the most profound.

Aside from these scientific accomplishments, Hall occupies a unique position as the conscience of his discipline. He treats collaborators, colleagues, and competitors with a degree of integrity, honesty, openness, and generosity that is rare. He has extended himself to help younger scientists in their careers, whether or not they were his own students or postdocs, actively engaged in discussions, controversies, and arguments to get to the bottom of any issue, and fearlessly held all (whether junior, peer, or senior) to the highest standards of scientific behavior, sometimes to his own detriment. He is that rarity among scientists, in any era, who combines the strive for excellence with the penchant to do the right thing.

Ralph J. Greenspan

Gerald M. Rubin

Allan C. Spradling

# The 2003 George W. Beadle Medal

## Gerald M. Rubin and Allan C. Spradling

IN recognition of their innovative discoveries and outstanding leadership within the Drosophila research and general scientific communities, the 2003 George W. Beadle Medal is awarded to Gerald M. Rubin and Allan C. Spradling. Gerry and Allan developed seminal techniques that revolutionized molecular genetics in Drosophila and played crucial roles in advocating and implementing the Drosophila Genome Project. They are scientists of vision and creativity who have carried Drosophila research to new levels through their leadership, scientific generosity, outstanding individual research, and commitment to trainees.

Gerry and Allan's first stunning accomplishment marked the start of a remarkable scientific collaboration spanning two decades. While they were both staff members in the Department of Embryology of the Carnegie Institution of Washington they developed a germline transformation method for Drosophila using *P*-element transposons. This technology was born from the synergism of Gerry's expertise with Drosophila transposons and molecular biology and Allan's knowledge of embryogenesis and development. The ability to generate stable lines of Drosophila carrying a gene of interest revolutionized the field, suddenly permitting developmental control genes to be understood at a molecular level. The manner in which they made this technology freely and immediately available to everyone is a legend within the community, and it reflects their commitment to advancing Drosophila research that makes them so worthy of this award. Allan and Gerry presented the transformation technology at the 1982 National Drosophila Conference, and although the work was not yet in press, brought the plasmid reagents with them to the meeting and freely distributed them.

The success of the Drosophila Genome Project is in large part due to the combined and collaborative efforts

of these two scientists. Allan directed genetic screens to mutate the genome by *P* elements, generating invaluable mutant collections that were made available to the community. This ongoing project is well on its way to generating mutations in the majority of Drosophila genes. Gerry had moved to the University of California at Berkeley in 1983, and he subsequently established the Berkeley Drosophila Genome Project (BDGP) in 1991. The impact of BDGP cannot be overstated in that it produced a well-annotated genome and many resources. These include a versatile and accessible website, a physical map of genome contigs, EST library databases, and a Unigene set of cDNAs. Gerry was able to negotiate a collaboration that allowed the physical mapping and sequencing efforts of BDGP to be combined with the whole-genome shotgun sequencing efforts of Celera Genomics, leading to an initial sequence in 2000, at least 2 years ahead of schedule. He also had the vision and determination to ensure that work continued after this initial publication so that the community would have a high-quality, complete sequence of the Drosophila euchromatin. The information and reagents generated by BDGP have been freely available to the community at all stages of the project, with daily or weekly postings of data as they were being generated. Gerry faithfully kept the community abreast of progress and updates on the genome project at the annual national meeting. He also provided copies of the Unigene cDNA set to the community, permitting widespread development of microarrays and genomic technologies.

In addition to the significant technologies Allan and Gerry developed, their independent research programs produced seminal contributions to biology. Gerry's early work provided the foundation for our understanding of transposable elements in Drosophila. His lab deciphered the first tissue-specific transcriptional regulatory elements. In the 1990s, his research on the development of the Drosophila eye defined the role of signal transduction pathways in cell fate determination and differentiation. The methodologies he established for dominant genetic screens led to the discovery that the Ras oncogene is a key downstream effector of the evolutionarily conserved receptor tyrosine kinase signaling pathway. This finding not only helped to define a key signaling network, but also was crucial to our understanding of the molecular mechanisms underlying malignant transformation in mammals. Continued exploitation and improvement of these molecular genetic approaches led to the identification of other signal transduction components as well as genes involved in axon guidance, the cell cycle, and cell death.

Allan's research focused on oogenesis, and he used this as a developmental paradigm to elucidate fundamental concepts in chromosome biology and differentiation. Early in his career Allan found that the chorion genes were amplified in the follicle cells, and he developed this as a model metazoan replicon, identifying both DNA sequence elements necessary for amplification and *trans*-acting replication proteins. His lab has made important findings on the structure of metazoan chromosomes, on the properties of heterochromatin, and on the formation of polytene chromosomes. His lab carried out large-scale screens for enhancer-trap lines that permitted labeling, and thus identification, of several important cell types in oogenesis. These lines often served as the entry point for cloning genes involved in oogenic cell type interactions. By isolating and analyzing mutants defective in cystoblast divisions, oocyte specification, or nurse cell function, Allan has identified critical regulators for stem cells, a link between cell cycle control and oocyte specification, and provided crucial insights into nurse cell formation and function. This work is distinguished by the application of cell biology to problems in developmental biology or chromosome dynamics, and Allan's lab has always been at the forefront of this approach.

Gerry and Allan's laboratories have been dynamic and exciting, and both investigators provided superb training environments for their students and postdocs. The result is that they have a legacy in the large number of their trainees who are leaders in the Drosophila community. Gerry and Allan conveyed to their students and postdocs their fascination with Drosophila as a model organism and instilled the importance of posing biological questions and then answering them on a molecular level.

In the past few years Allan and Gerry have extended their scientific leadership roles beyond the Drosophila community, Gerry as a Vice President of the Howard Hughes Medical Institute and Allan as Director of the Department of Embryology of the Carnegie Institution of Washington. Although the wider biological research community is benefiting from their leadership, the Drosophila community remains particularly indebted to these two great scientists, and the Beadle Medal provides a measure of that gratitude.

Terry L. Orr-Weaver

# Previous Recipients of These Awards

| | Thomas Hunt Morgan Medal | Genetics Society of America Medal | George W. Beadle Medal |
|---|---|---|---|
| 1981 | Barbara McClintock and Marcus M. Rhoades | Beatrice Mintz | |
| 1982 | Sewall Wright | Gerald R. Fink | |
| 1983 | Edward B. Lewis | Charles Yanofsky | |
| 1984 | George W. Beadle and R. Alexander Brink | David S. Hogness | |
| 1985 | Herschel L. Roman | Philip Leder | |
| 1986 | Seymour Benzer | Gerald M. Rubin | |
| 1987 | James F. Crow | Sydney Brenner | |
| 1988 | Norman H. Giles | David Boststein and Ira Herskowitz | |
| 1989 | Dan L. Lindsley | Allan C. Spradling | |
| 1990 | Charles Yanofsky | Nancy Kleckner | |
| 1991 | Armin Dale Kaiser | Bruce S. Baker | |
| 1992 | Edward H. Coe, Jr. | Maynard V. Olson | |
| 1993 | Ray D. Owen | Jonathan R. Beckwith | |
| 1994 | David D. Perkins | Leland H. Hartwell | |
| 1995 | Matthew Meselson | Eric Wieschaus | |
| 1996 | Franklin W. Stahl | Elliot Meyerowitz | |
| 1997 | Oliver Evans Nelson, Jr. | Christine Guthrie | |
| 1998 | Norman H. Horowitz | Ronald W. Davis | |
| 1999 | Salome G. Waelsch | Charles H. Langley | Michael Ashburner |
| 2000 | Evelyn M. Witkin | Jack W. Szostak | John Sulston and Robert Waterston |
| 2001 | Yasuji Oshima | H. Robert Horvitz | Gerald R. Fink |
| 2002 | Ira Herskowitz | Andrew Fire | Robert Mortimer and André Goffeau |