in William Kristan's group at the University of California, San Diego have demonstrated the feasibility of examining 'behavioral indeterminacy', analogous to what passes for 'choice' or 'free will' in human behavior, in terms of variations in the activity of individual neurons in the leech, a remarkable confluence of Gunther's passions for neurobiology and for philosophy of the mind.

During this period, Gunther also published what was to become one of his most cited and influential scientific papers, proposing a physiological basis for Hebb's postulate of synaptic plasticity during learning (1973). This work generated excitement and discussion among neurobiologists in much the same way that Schrödinger's book had stimulated molecular-biologists-to-be three decades earlier. Arguably, then, Stent's most important scientific contributions stem from his work in neurobiology.

After considerable arm-twisting by his Dean at Berkeley, who threatened to appoint an out-of-department 'enemy' if Gunther declined, he served with distinction, and an iron hand, as Chairman of the Department of Molecular Biology and later as the first Chairman of the present Department of Molecular and Cell Biology. During this period his research interests shifted for the last time, to developmental biology. He thus founded a new group, which established the leech as an organism for studies in evolutionary development and demonstrated the utility of microinjected cell lineage tracers for the analysis of complex embryos.

At Berkeley, life with Gunther revolved around heated discussions of experimental results and the theoretical models to which they gave rise (or vice versa), fine points of grammar, the paradoxes underlying anything worth considering and lunches at the Dynasty Chinese restaurant, punctuated by occasional trips across the Bay Bridge in his white 1963 Cadillac convertible with red leather upholstery, the top down, the road clear, and the sun shining. As Gunther would have said, in his best Chicago gangsterese, "Ya shoulda been there".

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Essay

Kinji Imanishi and 60 years of Japanese primatology

Tetsuro Matsuzawa[1] and William C. McGrew[2]

On December 3rd, 1948, only three years after the Second World War, Kinji Imanishi (1902–1992) went to Koshima island to study the wild Japanese monkeys. Imanishi was flanked by two young students, Jun'ichiro Itani (1926–2002) and Shunzo Kawamura (1924–2003). This year, 2008, is thus the 60th anniversary of the founding of primatology in Japan.

There are more than 200 living primate species. The Japanese monkey, also known as the snow monkey, lives at the northern limit of the global range of nonhuman primates. Over the past thousands of years, people in Japan have often encountered the monkeys in the wild — but before 1948, no one had dared to seek the details of their daily lives.

Imanishi, who was 46 years old in 1948, was an unpaid lecturer at Kyoto University. Some young zoology students preferred to follow Imanishi rather than the established professors of the prestigious university. Imanishi posed an interesting question: "Human society, where did it come from?" The students were attracted by his question and by his way of looking for the evolutionary basis of human society in the wild monkeys.

During the war, Imanishi was in Mongolia. He investigated the society of wild horses and the Mongolian people's way of life. Unusually, his research was based on the individual recognition of each horse. Upon returning to Japan after the war, in the 1948 survey, Imanishi and the two students first were engaged in the study of wild horses off the Toi-peninsula in Miyazaki prefecture. One day, they encountered a troop of wild Japanese monkeys, and this chance encounter led Imanishi to decide to study wild monkeys. So he went to Koshima island, which was close to the Toi-peninsula. Imanishi and his students applied their method of individual recognition of horses to the monkeys, giving a nickname to each monkey. Imanishi and his team, divided into several parties, went to 19 sites of wild monkeys, such as Koshima, Takasakiyama, Arashiyama and Yakushima, in the following 7 years. In total, they spent more than 1,500 days in the forest observing the monkeys in their natural habitat.

To know the details of the monkeys' behavior in close range, they started provisioning: that is, to habituate the monkeys to their presence by giving them food. They observed the monkeys for months, and then years, developing a unique style of field research consisting of individual recognition, habituation (provisioning), and long-term observation. This method of study remains a standard technique of fieldwork on nonhuman primates.

Frans de Waal gave a plenary talk in The First Imanishi-Itani Memorial Lecture on Primatology, held in Kyoto in February 18th 2002, celebrating the 100th anniversary of Imanishi's birth. In his talk, de Waal pointed out the influence of Imanishi's approach on Western science as a "silent invasion" [1]. If students of long-lived animals in the field routinely identify individuals and follow them over their lifespan, then they are employing techniques invented by Imanishi. No-one stops to think about who invented this method, but it has prevailed in the research community as the standard for doing fieldwork.

In the West, the study of monkeys and apes developed from work on captive populations, such as those in zoos, which contrasts with fieldwork in the natural habitat in Japan. This may be due partly to Japan's being the one country among the 'G8' countries that has indigenous monkeys. This natural coincidence may have provided the unique basis for the development of primatology in Japan.

Thanks to the efforts of Imanishi and his colleagues, we know much about wild monkeys. They recognized a breeding season: Japanese monkeys mate in the late autumn to winter and give birth in late spring to early summer. They found the matrilineal residence: solitary monkeys are always male, and they immigrate from the natal group to others. Females remain in the group to form a matrilineal society. They noted the dominance hierarchy: ranking in dominance across individuals is almost linear. They invented a simple test of ranking, in which a food item is thrown between two individuals; however, the

Figure 1. Sweet-potato washing by Koshima monkeys in 2008 (photo by T. Matsuzawa).

dominant–subordinate relationship, changes with the presence of a third individual. Itani [2] focused on monkey vocalizations and classified more than 30 types. Finally, they found evidence of proto-culture in the monkeys, illustrated by the famous sweet-potato washing.

On a hot day in September 1953, Ms Satsue Mito (1915–) saw a 1.5 year old young female monkey, later nicknamed 'Imo', which means sweet potato, wash a potato in a small stream. Mito was a primary school teacher living in a small village near Koshima island. Her family provided accommodation for Imanishi's team, and she took on the role of a local assistant. Mito recounted this interesting observation to the team, and Kawamura began observations of the behavior [3]. Long-running observations revealed that sweet-potato washing spread throughout the troop.

Not many people realise that sweet-potato washing began in a freshwater stream, near the sea shore. Later the monkeys started to wash the potatoes in the sea, presumably to add the salty taste. Sweet-potato washing clearly illustrated the three important aspects of cultural phenomena: emergence, transmission and modification. We know when and by whom the behavior was invented. We know that the behavioral pattern was socially transmitted and also modified in the process. By these criterion, sweet-potato washing is still one of the best examples of cultural phenomena in nonhuman animals [4–6].

Sixty years later, long-term observations of Koshima monkeys continues, following eight generations of wild monkeys and the descendants, which still practice sweet-potato washing (Figure 1). In the photograph, seagulls float nearby; the birds learned to scavenge the leftovers of the monkeys, so cultural behavior continues to evolve.

The study of chimpanzees in Africa

After 10 years' accumulation of knowledge and practice on wild monkeys, Imanishi and Itani went to Africa in February 1958 (Figure 2). They arrived in Africa two years before Jane Goodall began her famous study of wild chimpanzees at Gombe. Goodall began at Gombe in 1960, while the Japanese team began at Mahale in 1965. The idea of provisioning of wild chimpanzees accelerated the findings on behaviors such as tool making and use, hunting, and so on (for details, see [7,8]). The two studies, in Gombe and Mahale, have proceeded in parallel for decades, tracking both similar and different research topics [9].

Imanishi's focus was to seek the evolutionary origin of human society. For him the central issue was society, and society had its own reality: it cannot be reduced to its constituent individuals nor just relationships among individuals. The society exists as a whole. This belief was the primary force for Imanishi sending the expeditions to study the society of monkeys and the society of chimpanzees in the wild.

Imanishi retired from his professorship at Kyoto University in 1966, and handed the leadership of the scientific survey of African great apes, the genera *Pan* and *Gorilla*, to Itani, who had a different style of fieldwork. Imanishi organized large expedition teams, while Itani loved walking around

Figure 2. Imanishi (center) and Itani (left) in search of wild gorillas in Uganda on March 6th 1958. (Photo from Itani Jun'ichiro Archives at PRI, Kyoto University.)

the African continent in a small team or even solo.

Imanishi and Itani sent Toshisada Nishida (1941–), a graduate student at that time, to Mahale, where Nishida identified the social unit of chimpanzees, which now is called the unit-group or community. Japan's unique contribution of understanding chimpanzees is the recognition of a society in which we can see male philopatry (patrilineal lineage), fission–fusion of subgroups, and antagonistic relationships between communities.

Itani also encouraged Takayoshi Kano (1938–) to start his pioneering fieldwork on wild bonobos, *Pan paniscus,* in the Congo basin [10]. Itani also encouraged fieldwork on hunter-gatherers and other societies in Africa from the viewpoint of ecological anthropology. For example, Itani helped Jiro Tanaka's (1941–) fieldwork on the San hunter-gatherers of the Kalahari desert in Botswana [11].

A decade of monkey studies and a further decade of chimpanzee studies convinced the Japanese government of the importance of primatology. Primatology is the discipline that seeks to know the evolutionary origins of human nature. Thanks to the efforts by Imanishi, Itani and other colleagues, the Primate Research Institute of Kyoto University was founded in 1967 by the government. The Primate Research Institute from the beginning not only covered field science, such as sociology and ecology, but also various disciplines such as morphology, paleontology, physiology, neurophysiology, psychology, genetics, biochemistry, and so on.

The Primate Research Institute had two founding professors, Masao Kawai (1924–) and Kawamura, who continued to lead the fieldwork on nonhuman primates. They were succeeded by Kano and Yukimaru Sugiyama (1935–). Sugiyama first reported infanticide of hanuman langurs in India [12]: this finding of infanticide was followed in other species and became a hot topic in sociobiology and behavioral ecology [13]. Then, Sugiyama joined the chimpanzee field studies. He started the first long-running research site in West Africa, at Bossou, Guinea, where he observed the use of stone tools by wild chimpanzees.

The Primate Research Institute became the international center of primatological study in Japan. It has about 40 faculty members, 40 graduate students, and 20 postdoctoral researchers. Various kinds of primate studies have emerged from the institute over the past decades. For example, paternity discrimination by DNA finger printing was pioneered by Osamu Takenaka (1942–2005) and his colleagues [14]. Juichi Yamagiwa through his fieldwork compared the three species of gorillas in the wild: Mountain gorilla, Eastern lowland gorilla, and Western lowland gorilla [15]. Gen Suwa found fossils of *Australopithcus ramidus*, an extinct species close to the human-chimpanzee ancestor [16]. The Ai project [17], the 30-year study of chimpanzee cognition, is looking for the evolutionary basis of the human mind through both laboratory and field work [18,19].

The world of living things

Field work on nonhuman primates was already being carried out by Western scholars before the Second World War. One of the pioneers was Clarence Ray Carpenter (1906–1975). From 1931 to 1934, Carpenter did field research on the behavior of nonhuman primates, such as rhesus monkeys and gibbons, under the sponsorship of Professor Robert Yerkes (1876–1956) of Yale University. Carpenter [20] went to Thailand to study wild gibbons, and recorded their vocalizations and behavior. He was the first to recognize that gibbon society consisted of an adult pair, male and female, and their offspring, but also he killed the gibbons after his field work in order to examine their stomach contents and to bring back their bodies as specimens.

Imanishi and Itani visited Carpenter on the way back from Africa in 1958. Although Carpenter's first son had died in the war against the Japanese, he welcomed them. Imanishi, the founding editor, gave the first issue of the journal *Primates* to Carpenter (Figure 3). Imanishi wanted to publish the scientific discoveries in English in order to communicate with academia world-wide. Imanishi and Itani also visited many other primatologists in America and European countries during the 1958 journey. They met Kenyan archaeologist Louis Leakey (1902–1973), the Swiss morphologist Adolf Schluz, the American psychologist Harry Harlow, the American anthropologist Sherwood Washburn, and many other notable biologists.

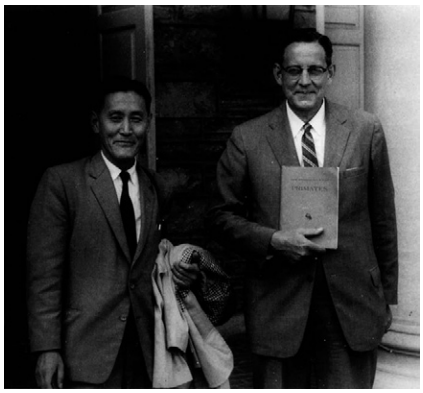

Figure 3. Imanishi (left) and Carpenter (right), who holds the first issue of the journal *Primates.*

(Photo from Itani Jun'ichiro Archives in PRI, Kyoto University.)

Imanishi was a student at Kyoto Imperial University, where lectures were often given by foreign scholars. Pamela Asquith and her colleagues have recently digitized his archives and opened them to the public on the internet: The Kinji Imanishi Digital Archive, http://tomcat.sunsite.ualberta.ca/Imanishi//team.html. Thanks to their efforts, many people can access and trace the thoughts of Imanishi. We can see that Imanishi took notes in German when he read German textbooks of entomology, and took notes in English when an English professor gave a lecture on biology. Imanishi read many books and articles on biological science before he went to the West, for example papers in *The Journal of Ecology* (UK) and *Ecology* (USA), key textbooks in ecology [21] and the works of Charles Darwin (1809–1882) — Darwin's theory of evolution was always on Imanishi's mind.

Imanishi started as an entomologist. His PhD thesis was on mayfly larvae, entitled 'Mayflies from Japanese Torrents' and was published in English in 1933. Based on the classification by morphology, he collected larvae and recognized that there were four species of mayfly larvae in the Kamo River in Kyoto. He discovered niche segregation: each species occupied a different niche, depending on the flow rate or speed of the river. One species preferred to stay in the relatively rapid flow in the centre of the river, while another preferred to stay in the slow flow near the river's bank.

Imanishi was struck by this niche segregation, and by the harmonious coexistence of the different species,

and he continued to ponder the relationships among sympatric species. Ecological theory at the time did not provide the answer to his questions. He wanted to know the social structure of whole, living organisms, based on his admiration for the findings of Darwin and his colleagues. All living organisms have diverged from common ancestry, yet Imanishi was not satisfied with the Darwinian explanation of the mechanism of evolution, that is, natural selection. At that time, natural selection was thought to be driven by environmental change. Imanishi, with his discovery of segregation, strongly believed that environmental selection was not the answer.

Imanishi's idea of the whole organism is clearly stated in his first book 'Seibutsu-no-sekai', which means 'The world of living things' [22,23]. He published this book at the age of 39, aware that the Second World War was approaching. In the foreword, he said that the book could be his note to posterity if he were to die in the war.

In short, Imanishi saw nature as inherently harmonious: species fit together in a large organic whole, with each species finding its own niche. There is no competition and mutual exploitation, as each species has a complementary role within the ecosystem. In his terminology, Imanishi looked at the living world as three essential layers: individual, specia, and holospecia. The key part is the specia, which means the society of a species. Each species has its own unique society, in which the individuals do not differ much from each other. In his belief, the specia is actual not just a concept. Many different specia coexist. The whole set of living things is then named as holospecia. In sum, Imanisi's view is a sort of holism, in which existence cannot be reduced to its parts; individuals have their life histories, as do specia, and holospecia too.

During the Second World War, Imanishi looked for the specia of horses in the wild by closely observing their behaviour. Although he carefully watched the behaviour of individuals, he wanted to know horse society, not individual behavior. This attitude led to his search for the origins of human society through observations on monkey and ape societies, and his outlook was shared by his Japanese followers. This holistic approach and its rejection of natural selection contrasted with Darwinism, and has been called Imanishiism by a Western scholar [24]. (The word Imanishiism became a subject index term in the journal *Nature* in 1985.) Although Imanishi read and wrote English well, he wrote few English articles, which left Imanishi and his ideas somewhat mysterious (but attractive) to western scholars.

Pioneer spirit and historical background

What is Imanishi's contribution to our understanding of the world of living things? Why was he so motivated to consider living things as a whole? To find answers to these questions, it is important to know the historical background of Imanishi and his era.

Imanishi was born in 1902, in the Meiji era in Japan. When Imanishi was being educated, Japan was striving to catch up with the advanced countries of the West. Before the Meiji revolution in 1868, in which the political power of the Shogun in the preceding Edo era was restored to the emperor, Japan had been closed to the outside world for about 270 years. In 1858, the British and French and then Americans put pressure on Japan to open up the country for trade. Western countries had already colonized India and parts of China and advanced to the Far East. America needed good ports, especially for whaling in the Pacific Ocean.

The Edo era shaped a unique cultural and ethical tradition among the people, called *Bushido* [25]. *Bushido* means the ethics of Samurai, which is somehow similar to '*noblesse oblige*' in the West. The modernization of Japan was promoted by young people, who had the ethics of Samurai and who learned a lot from the West. The Meiji government consisted of young revolutionists, who sought to advance the educational system in Japan. The government founded the first imperial university in Tokyo in 1877 and then in Kyoto in 1897. Japan quickly caught up with the West, winning two major wars in the Meiji era, against China in 1895 and then against Russia in 1905. In the first World War of 1914–1918, Japan was on the side of the winning countries.

By the 1920s, Japan was modernized and democratic. Suffrage for men more than 25 years old started in 1925. The era between the two world wars was quiet, with an atmosphere of freedom, and these were Imanishi's youthful days.

Imanishi became a student at Kyoto Imperial University in 1925. At the same time, Eizaburo Nishibori (1903–1989) and Takeo Kuwabara (1904–1988) entered the university. Nishobori was Imanishi's brother-in-law (married to Imanishi's sister). He later became a multi-talented scholar, inventing innovative electric components, creating the first nuclear-powered ship in Japan, and the front runner of quality control research. Kuwabara introduced French literature to Japan and became a leading opinion-maker of his time and received in 1987 the 'Order of Culture', the highest honor for scholars in Japan (Imanishi had received it in 1979).

Figure 4. Nishibori (left) and Einstein (right) in 1922 in Kyoto.

(Photo by Nishibori Memorial Explorer Museum).

When these three men were young, they loved mountain climbing. They were the pioneers who introduced alpinism to Japan. They founded in 1931 the Academic Alpine Club of Kyoto, in order to send an expedition to the Himalayan peaks over 8,000 m. At that time, no one had succeeded in climbing all 14 peaks of more than 8,000 m height. The first ascent of an 8,000 m peak was Annapurna (8,091 m) by the French in 1950; the highest peak, Mount Everest (8,848 m) was climbed by a Nepali and a New Zealander in 1953.

Imanishi was a biologist, but he also was a real mountaineer, who loved to wander in natural environments [26]. Imanishi led the first successful winter ascent of Mount Chángbáish (2,744 m) on the border of China and North Korea in 1935. In the following years, he continued to send out overseas expeditions and aimed to climb K2 (8,611 m) in Karakorum, the second highest peak in the world. K2 was actually first climbed by an

Italian in 1954, so Imanishi turned to the exploration of the unexplored wide range of Karakorum Himalayas, traversing the three major glaciers in 1955.

Then, in 1958, Imanishi and Itani went to Africa for the first time. In the same year, Nishibori led the all-Japanese team which succeeded in the first over-wintering stay in Antarctica. Kuwabara led the Himalayan expedition of AACK to the first ascent of Chogolisa (7,654 m) in Karakorum. Imanishi, Nishibori, and Kuwabara seem to have been triplets, sharing the same pioneering spirit, wanting to go to places where no one had been before. The year 2008 is the 50th anniversary of the exploration in Africa, Antarctic, and Himalaya for the field workers of Kyoto University.

Why were Imanishi and his comrades so strongly motivated to be such pioneers? History suggests that it was the atmosphere of freedom in the 1920s, and the silent invasion of the pioneering spirit from the West to the minds of the young people in the Far East. It may be due to Albert Einstein (1879–1955). He received the news of winning the Nobel Prize for Physics on his way to Japan for his first visit. Einstein and his wife arrived in Japan in November 17th 1922 and stayed for 43 days. He toured Japan and talked about how he came up with the general theory of relativity. When Einstein gave a plenary talk at the Kyoto Imperial University, Nishibori was given the role of his tour guide for three days (Figure 4). It is easy to imagine how the young person was powerfully influenced by the charismatic Nobel prize winner and how the excitement was shared by Imanishi, his closest friend.

Let us imagine an autumn day in 1922 in Kyoto. There were Imanishi, Nishibori and Kuwabara, living in a very small area less than a square kilometre. They were in their late teens, preparing to tackle the world outside Japan. Inspired by Einstein's pioneering work, they wanted to understand the world around them. The wind from the West may have triggered the young minds to look for their own intellectual niches.

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Primer

The spindle assembly checkpoint

Gianluca Varetti[1] and Andrea Musacchio[1,2]

Mitosis, the process of eukaryotic somatic cell division, consists of a series of consecutive, highly regulated events. It leads to the generation of two daughter cells containing identical complements of the genome. When mitosis fails, the daughter cells inherit an abnormal number of chromosomes (aneuploidy). This has dire consequences on cell physiology and might facilitate tumorigenesis. Here, we describe the organization of the spindle assembly checkpoint (SAC), a sophisticated surveillance mechanism that acts in mitosis to ensure the fidelity of chromosome segregation.

Mitosis and the SAC: general remarks

Classically, mitosis has been subdivided on the basis of the morphological features of its successive phases. In prophase, the replicated chromosomes (sister chromatids) begin to condense. Nuclear-envelope breakdown marks the beginning of prometaphase (in those organisms performing 'open' mitoses). In prometaphase, the sister chromatids individualize along the chromosome arms but remain associated at a visible constriction called the centromere that retains most of the cohesion between sister chromatids. Microtubule nucleation at the centrosomes increases, leading to the formation of a mirror-symmetrical, microtubule-based structure — the mitotic spindle — to which chromosomes attach. In metaphase, the chromosomes have completed congression to the equatorial plate of the spindle and are attached to robust microtubule fibers — the K-fibers. In anaphase, the sister chromatids have lost cohesion and physically segregate towards opposite poles of the spindle. In telophase, chromosomes decondense and a nuclear envelope reforms around the two masses of chromatin. The cleavage furrow ingresses and causes the physical