Graeme Clark- CV Milestones and Achievements 2010

A description of the discovery and publications on which the nomination is based.

Graeme Milbourne Clark AC

Overview

Graeme Clark has discovered how to code speech with electrical stimulation of the auditory nerve and brain pathways to restore hearing to tens of thousands of severely-to-profoundly deaf people in more than 100 countries. This has been discovered by Clark using a multi-channel cochlear implant for people who are too deaf to benefit from a powerful hearing aid. It is generally considered one of the greatest advances in clinical neuroscience, the greatest advance in helping severely-to-profoundly deaf adults to hear, and for deaf children it is the greatest advance in enabling them to develop excellent spoken language.

Severe-to-profound deafness is a very common disability. Studies in Australia by Wilson et al 1999 and Mitchell 2002 indicate that 1.2% of the adult population are severely-to-profoundly deaf, and could benefit from a cochlear implant i.e. more than 200,000 people in Australia alone. It also affects more than four children in every 1,000 live births up to the age of 14 years. The multi-channel cochlear implant research, which Clark commenced in 1967, has been developed industrially by Cochlear Limited.

Nobel Laureate Professor Emeritus Sir Macfarlane Burnet wrote in 1985 “I feel it (the bionic ear) may represent a new benchmark in the understanding of neural and mental function in terms of their physical components. Perhaps the work will not reach a climax for centuries, but whatever may eventuate special credit will be made to Professor Clark and his colleagues for their pioneering and successful work”.

Clark has led all the key aspects of the research to create the multi-channel cochlear implant, due to his creative, innovative approach, wide training, and ability to interrelate the underlying different disciplines. These disciplines are: [1] surgical science, [2] auditory neurophysiology, [3] bio-engineering, [4] psychophysics and speech science, and [5] audiology.

Clark’s great contributions to the development of the cochlear implant have been his innovative and pioneering research, and his ability to interrelate the research in all the key underlying disciplines. He has been recognized for this internationally through being awarded prizes, fellowships and honorary degrees in the essential five disciplines. Clark’s international standing in: [1] surgical science is recognized by his being awarded the 2010 Lister medal and Oration, the most prestigious prize in surgical science in the UK as well as internationally (other winners of the Lister medal include: Howard Florey UK – Nobel prize for penicillin; Norman Shumway US pioneer of heart transplants; Harvey Cushing US – father of brain surgery; Peter Morris UK - pioneer renal transplants; John Charnley UK – hip replacement etc). He was also made an Honorary Fellow, Royal College of Surgeons, England, the (supreme single award of the College for outstanding achievement in medicine. [2] Clark has been honoured with the Züch prize from the Max Planck Institute in Germany, the highest award in

Germany in the Neurosciences. [3] Clark has been awarded the Otto Schmitt award, the highest accolade in Bio-engineering from the International Federation for Medical and Biological Engineering. [4] Clark has received the International Speech Communication Association Medal for significant contribution to the progress of speech science and technology. Finally [5] he pioneered the development of the field of Audiology in Australia and established its essential role in cochlear implantation internationally. For these contributions to Audiology he has received many awards including the A. Charles Holland Foundation International Prize for fundamental contribution to the progress of knowledge in the audiological/otological field. Graeme Clark has also received numerous and prestigious awards for his overall scientific and medical research in the development of the cochlea implant (bionic ear) and in understanding brain function and human consciousness. These awards include "The Australian Prime Minister's prize in science, Australia's premier award in science; fellow of the Australian Academy of Science, for outstanding contributions to science; Fellow of the Royal Society in London, for contribution to science, both in fundamental research resulting in greater understanding, and in leading and directing scientific and technological progress in industry and research establishments; Honorary Fellow, The Royal Society of Medicine, London, for exceptional distinction, and recipients drawn from across the world and from a wide range of endeavour, particularly from the medical sciences.

In addition, he established research not only for a bionic ear, but created a new field he has defined as Medical Bionics.

His contributions to medicine and science are monumental and are documented in over 1,000 scientific publications including a textbook, books, invited reviews, and scientific papers. A comprehensive list of publications is on his website Graeme@graemeclarkfoundation.org, through the National Library of Australia.,, and the University of Melbourne.

Not only did Clark lead the basic research in all these disciplines, undertake the surgery, establish audiology, in Australia, but he initiated and supported its industrial development of the cochlear implant (bionic ear) by the Australian company Cochlear Limited.

Clark was inspired to do research to restore hearing in profoundly deaf patients because of a childhood interest due to a deaf father. He became motivated in 1966 to leave a position as senior ear, nose, and throat surgeon at the Royal Victorian Eye and Ear Hospital to do research in auditory brain physiology to see if speech understanding could be achieved by fundamental and outcome focussed research. He commenced his research in 1967 in the Department of Physiology at the University of Sydney, chaired by Professor Peter Bishop. Clark faced considerable scepticism and later opposition. The general scientific view in the 1960s is typified by these written statements by Merle Lawrence, and Ed Fowler, two leading US auditory scientists. Lawrence wrote in 1964 "Direct simulation of the auditory nerve fibres with resultant perception of speech was not feasible"; and

Fowler wrote in 1968, “Direct stimulation of the cochlear nerve will from time to time be discovered. There is no indication that it will ever succeed in enabling a patient to readily hear speech”. This scepticism meant Clark had to overcome many scientific hurdles, and funding obstacles.

The following descriptions of Clark’s discoveries are based on information from Graeme Clark’s website: graeme@graemeclarkfoundation.org, gclark@unimelb.edu.au, and gclark@bionicear.org. They include Clark’s principal speaker address at the 37th Mini-Symposium - Frontiers in Medicine, Karolinska Institutet, Stockholm in 2006; his plenary address, at Interspeech 2005 – Eurospeech Conference, Lisbon in 2005; his address on receipt of the Otto Schmitt medal at the World Congress on Medical Physics and Biomedical Engineering in Munich, 2009; his address on receipt of an honorary doctorate from Zaragoza University in Spain, 2010; his opening plenary address at the International Congress on Acoustics, Sydney, 2010. The information is also available in his listed invited reviews and scientific papers, his autobiography (Sounds from Silence, Allen & Unwin 2000) and his textbook (Cochlear Implants: Fundamentals and Applications Springer 2003).

Normal hearing and deafness

To appreciate Clark’s achievements it is first necessary to review the physiology of normal hearing. With hearing, sound vibrations are transmitted along the ear canal to the ear drum and then via the small middle ear bones to the sense organ of hearing or organ of Corti, housed in the cochlea or inner ear (Figure 1). The cochlea spirals around a central axis and has three fluid filled compartments. The scala vestibuli is on the top, the scala media in the middle, and the scala tympani on the bottom. The organ of Corti lies in the scala media and rests on the basilar membrane. When it vibrates in response to sound it acts as a filter with high frequencies exciting the basal end and low frequencies the apical end of the cochlea (Figure 2).

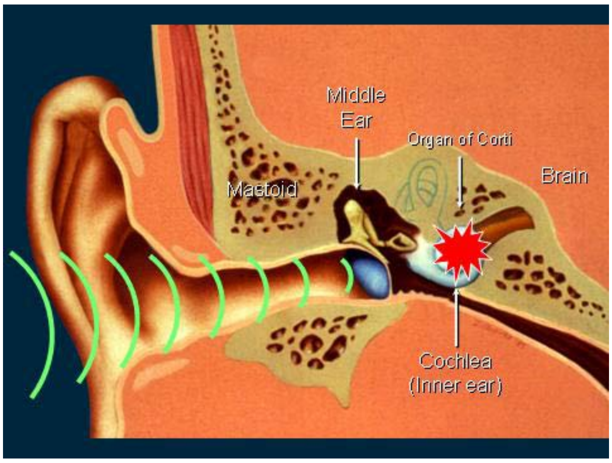


Figure 1: The outer, middle and inner ear (cochlea). Sound vibrations are transmitted along the ear canal, and via the middle ear to the cochlea, which houses the sense organ of hearing (organ of Corti).

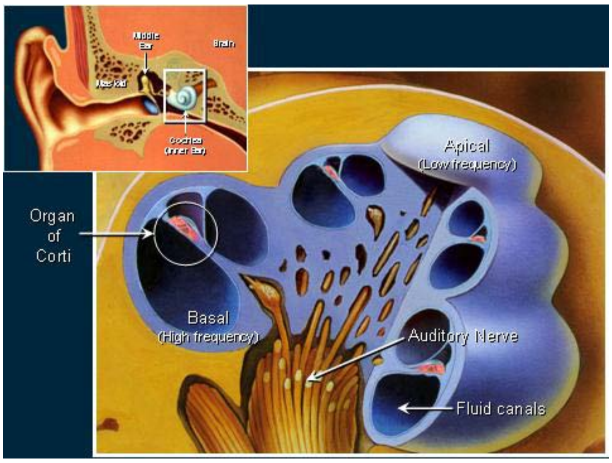


Figure 2: The sense organ of hearing (organ of Corti) rests on the basilar membrane that acts as a filter with high frequencies producing a maximal vibration at the basal end and low frequencies at the apical end.

The vibrations are converted into electrical signals by inner hair cells in the organ of Corti that excite the auditory nerve fibres (Figure 3). A detailed description of the basilar membrane travelling wave response to sound was made by von Békésy for which he received the Nobel prize in 1961. Von Helmholtz put forward an earlier theory that explained basilar membrane function as a series of resonators. The electrical responses generated in the nerve fibres by the organ of Corti pass up the central auditory pathways where they are coded as speech and other sounds. Clark's discoveries provide an important understanding of how the auditory brain functions, and how speech coding can be reproduced with electrical stimuli.

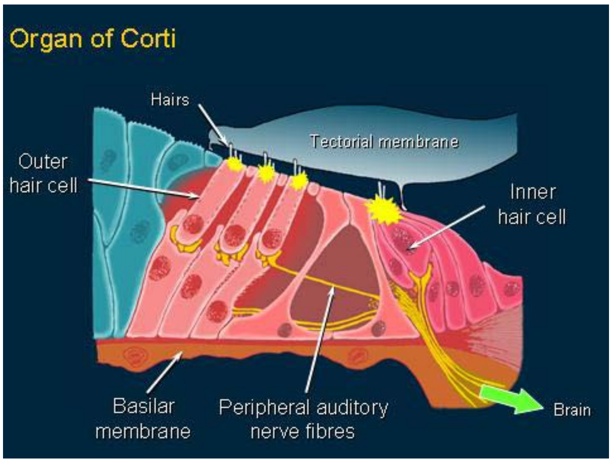


Figure 3: The sense organ of hearing or organ of Corti rests on the basilar membrane which vibrates to sound.

The encoding of sound frequencies occurs through a temporal and a place code. The relative importance of the temporal and place codes for different frequencies was not well understood when Clark commenced his research in the 1960s, but has been made clearer from Clark's research on electrical stimulation of the auditory nerve.

The combination of temporal and place excitation is illustrated in Figure 4. For the low frequency shown the sound wave travels along the basilar membrane to reach a point of maximal excitation (place theory), and the wave varies in time and phase (temporal theory).

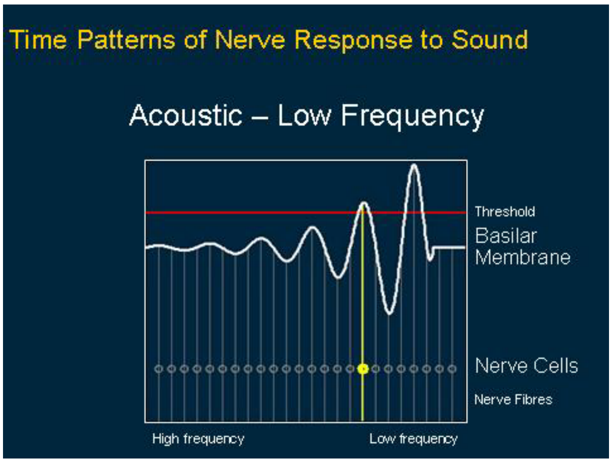


Figure 4: A model of the basilar membrane travelling wave showing a maximal displacement with temporal and phase responses.

The temporal code is illustrated in Figure 5. The sound waves at a frequency of 500Hz are in time or phase with the nerve spikes or action potentials. The intervals between the nerve action potentials are important for coding the frequency, as discussed in the reviews by Clark (2006 2008), and they relate to the pitch perceived.

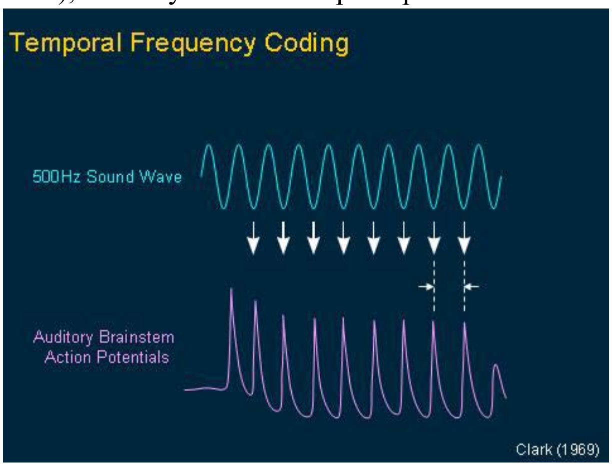


Figure 5: The temporal coding of sound.

With place coding the inner ear filters the frequencies, and high frequencies excite the basal end of the cochlea and low frequencies the apical end. The different frequency regions are connected spatially to all the centres in the brain so that a frequency scale is preserved. In other words, we recognize the pitch of a sound according to the site of stimulation in the brain.

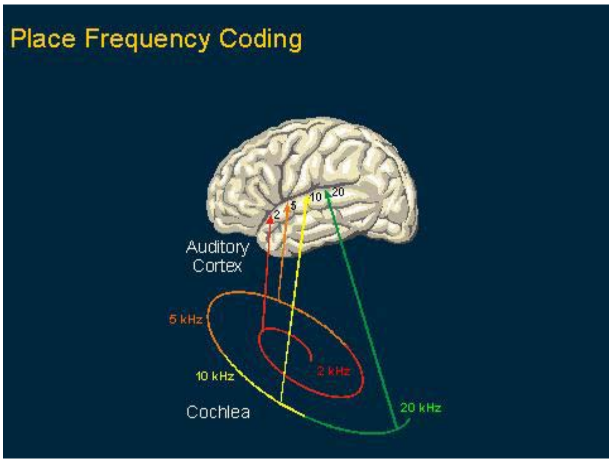


Figure 6: The place coding of frequency and tonotopic organization of the central auditory pathways.

With severe-to-profound deafness there is a marked loss of hair cells (Figure 7), and so amplifying sound with a hearing aid will not lead to speech comprehension. So the challenge for Clark was: could electrical stimulation of the auditory nerve achieve speech understanding?

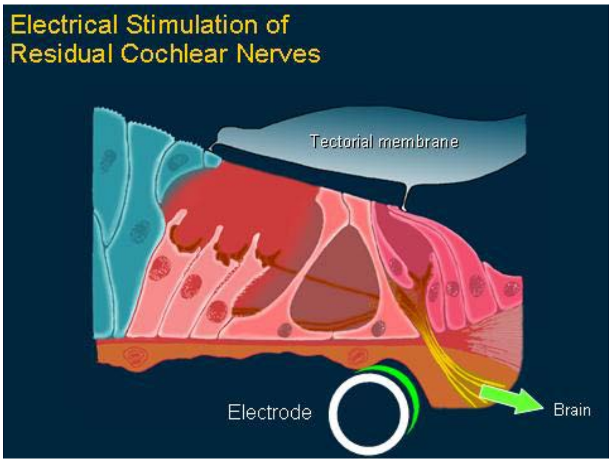


Figure 7: The deafened cochlea with the loss of the hair cells and idealized concept of direct electrical stimulation of remaining auditory nerve fibres.

Discoveries

Clark's fundamental discoveries in nine different disciplines are presented below. The key individual discoveries are discussed under the appropriate disciplines.

1. Auditory neurophysiology discoveries

Clark commenced auditory neurophysiological research in 1967 to study how direct electrical stimulation of residual auditory nerves in profoundly deaf people could bypass the inner ear or cochlea, and reproduce the coding of sound, to provide speech understanding.

Clark focussed his research initially on reproducing the coding of frequency, as it is of greater importance than intensity for speech understanding. As stated above, the relative importance of the two theories for frequency coding was not clear. With sound it is difficult to separate the temporal from the place code. However, with electrical stimuli the rate and place of stimulation can be varied independently to study their relative importance.

1.1 Reproduction of temporal code for low frequencies

Clark's first auditory neurophysiological discovery was: electrical stimulation could partially reproduce the low frequencies of speech, as shown by the auditory brain cells responding in time to the frequency of the electrical pulses.

If the temporal coding of speech frequencies were possible with electrical stimulation, only a simple single-channel implant would have been necessary to provide speech understanding for deaf people.

Clark's scientific paper in Experimental Neurology in 1969 is the first report in the literature of experimental physiological studies to examine the responses of brain cells to sound and electrical stimulation, with the specific intent of understanding how to electrically stimulate the auditory central nervous system for speech perception.

Clark first studied the responses of single cells. He found they could not follow stimulus rates above approximately 500 pulses/s, which is much less than the 4,000Hz required for speech perception. His data indicated this limitation was most likely due to the refractory properties of the neurons (absolute and relative refractory period), inhibitory mechanisms in the brain, and the underlying coding mechanisms of the brain which require convergent input from a localized population of neurons leading to co-incidence detection. He also discovered that the nerve cells responded much more precisely in time with the electrical pulses than is seen with sound, where there is less precision and more jitter. For the responses to become more like sound he used electrical sine waves to induce more asynchronous firing due to their slower rise time, but no difference was observed. To establish that the findings on individual cells applied to a wider population of neurons, field potentials were recorded as they are due to summed cellular activity. There was a reduction in the amplitude of the field potentials to near threshold for rates more than 300 pulses/s. An example of field potentials from the trapezoid body and superior olive in the cat brainstem is shown in Figure 8 for stimulus rates that varied from 1 pulse/s to 300 pulses/s. This confirmed the findings from cells, and showed there was an electro-neural "bottle neck" for the transmission of temporal information to the brain.

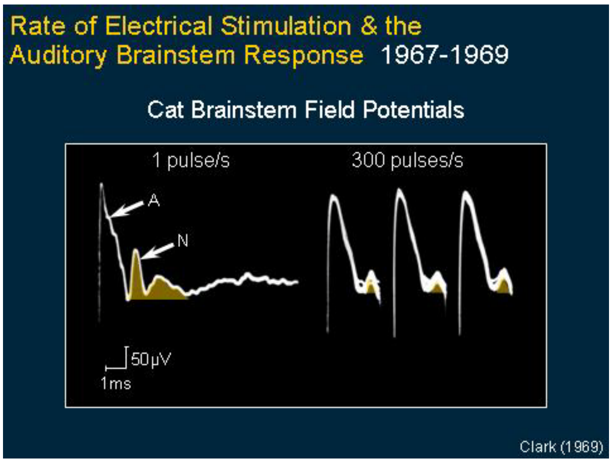


Figure 8: Field potentials from the brainstem of the cat to rate of electrical stimulation

From these initial studies from 1967 to 1969, Clark outlined in his Doctorate of Philosophy thesis his future research directions for speech understanding through electrical stimulation of the auditory nerve. These directions were as follows:

1) "The site and method of implantation are important as the neural pathways can be damaged and this would prevent the electrical signals being transmitted to the higher centres. Destruction of the cochlea can lead to trans-neuronal degeneration in the cochlear and superior olivary nuclei up to a year after the production of the lesions". 2) "A greater understanding of the encoding of sound is desirable. As emphasized by Lawrence (1964), the terminal auditory nerve fibres are connected to the hair cells in a complex manner, which could make it difficult for electrical stimulation to simulate sound". 3) "The relative importance of the volley (temporal) and place theories in frequency coding is also relevant to the problem. If the volley theory is of great importance in coding frequency, would it be possible for different nerve fibres, conducting the same frequency information, to be stimulated in such a way that they fired in phase at stimulus rates greater than 1,000 pulse/s? If this were possible, it would then have to be decided whether this could be done by stimulating the auditory nerve as a whole, or whether local stimulation of different groups of nerve fibres in the cochlea would be sufficient. On the other hand, if the place theory is of great importance in coding frequency, would it matter whether the electrical stimulus caused excitation of nerve fibres at the same rate as an auditory stimulus, or could the nerve fibres passing to a particular portion of the basilar membrane be stimulated without their need to fire in phase with the stimulus?" (4) "If the answers to these questions indicate that stimulation of the auditory nerve fibres near their terminations in the cochlea is important, then it will be necessary to know more about the internal resistances and lines of current flow in the cochlea, and whether the electrical responses normally recorded are a reflection of the transduction of sound into nerve discharges, or directly responsible for stimulating the nerve endings". (5) "The final criterion of success will be whether the patient can hear, and understand speech. If pure tone reproduction is not perfect, meaningful speech may still be perceived if speech can be analysed into its important components, and these used for electrical stimulation. More work is required, however, to decide which signals are of greatest importance in speech perception" [Clark, 1969, PhD thesis, and quoted from Clark's review in Plant and Spens, 1995].

However, before embarking on these studies Clark had to be sure that his acute discoveries from individual cells and field potentials were applicable to the patient, and therefore carried out a series of behavioural studies on alert experimental animals from 1971 to 1975 (Clark et al 1973, Williams et al 1976).

The studies showed that the cats perceived low rates of electrical stimulation at the basal or high frequency end of the cochlea as well as the apical or low frequency end, this suggested that the brain could process information for rate separately from that of place of stimulation. The upper limit on the rate that could be discriminated was found to be 600 – 800 pulses/s. This was consistent with Clark's cell studies on the experimental animal. In addition, the behavioural studies revealed that low rates of frequency modulated electrical stimuli or frequency glides, could be detected for similar rates as sound. At high rates responses to rate of change with electrical stimulation was much poorer than for sound stimuli. This suggested that place of stimulation rather than rate would be required to reproduce the rapid frequency transitions that are important for the coding of consonants. Clark's behavioural studies on electrical stimulation of the auditory central nervous system in the experimental animal were the first to be reported in the scientific literature.

As Clark's acute physiological and behavioural studies demonstrated the ability of the brain cells to follow in time with the electrical stimuli (temporal coding) was lost at mid-to-high frequencies, it indicated that single-channel stimulation, which would need to rely on temporal coding, would be inadequate for speech understanding. Single-channel stimulation was being considered elsewhere at the time. Clark's research demonstrated the need to explore how electrical stimuli could reproduce the place coding of frequency.

1.2 Reproduction of the place code with electrical stimulation

Clark's second auditory neurophysiological discovery was that electrical current could be localized to separate groups of auditory nerve fibres in the cochlea to allow the important mid-to-high speech frequencies to be coded as place or site of stimulation through bipolar, monopolar or common ground stimulation.

Clark initiated the research leading to this discovery in 1974-1975 with his doctoral student R.C. Black. Current localization seemed to be a major problem, as electrical current could short circuit through the fluid in the cochlear compartments. It was unclear where to place the electrodes, what electrode dimensions to use, what current path to facilitate, and how the growth of fibrous tissue around the electrode with long term implantation would affect the spread of current. Clark developed his research to best define the optimal conditions for the place coding of frequency. Furthermore, histopathological studies by Clark (1977) had also shown that an electrode in the scala tympani resulted in least damage to the nerve fibres, and this was therefore the best site for the electrode placement if the current could be localized to nerve fibres.

1.2.1 Bipolar stimulation

Black and Clark's first neurophysiological discovery was that current spread could be localized in the scala tympani of the cochlea for bipolar stimulation using electrodes with fine tips. Bipolar stimulation occurs with current passing between two neighbouring electrodes.

1.2.2 "Pseudo- bipolar" stimulation

Black and Clark discovered that current spread could be localized in the human cochlea for common ground stimulation (pseudo-bipolar) with banded electrodes. With common ground stimulation current flows from one electrode to all the others on the array. This mode of stimulation was used with the first speech processing strategy and was required in subsequent ones where more speech frequencies had to be coded near-simultaneously.

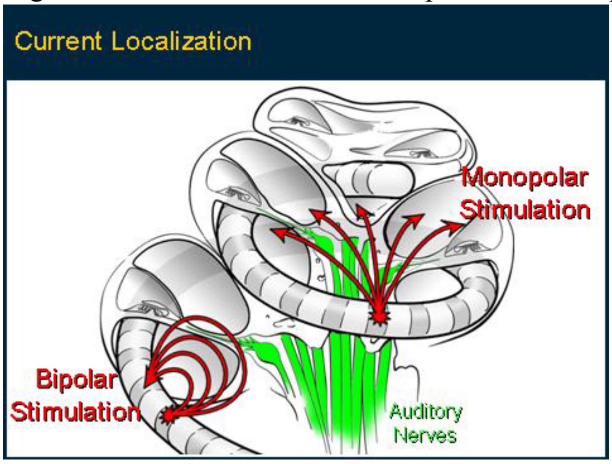
1.2.3 Half-band electrode stimulation

Clark and Black discovered in the experimental animal that localized stimulation of the auditory nerve could occur if his full-band electrode were divided in halves and current passed between them and across the cochlea. It was concluded that half- band electrodes were only an advantage when the placement and rotation of the half-band array could be closely controlled.

1.2.4 Monopolar stimulation

Busby and Clark then discovered that with monopolar stimulation and banded electrodes that were chronically implanted, good localization of current could be provided with monopolar stimulation (Busby et al, 1994). Monopolar stimulation (Figure 9) occurs between an electrode and a distant ground.

Figure 9: Current localization for bipolar and monopolar stimulation



2. Bio-mechanical discoveries

Clark made the bio-mechanical discoveries required for a multiple-electrode array for safe and effective insertion into the cochlea.

2.1 Bio-mechanical principles preventing cochlear damage

Clark discovered that if the array was round, soft and not directed at the basilar membrane then surgical trauma was minimal.

First with animal experimental studies from 1972 Clark discovered that if electrodes were inserted into the scala tympani through holes drilled in the overlying bone there was marked damage of all structures, and associated loss of the auditory nerve fibres [Clark 1977]. On the other hand, with an electrode passed along the scala tympani through an opening in the apical turn of the cochlea or along the scala tympani of the basal turn through the round window there were milder histopathological changes in the cochleae. The damage was least if the electrode was round, soft and not directed at the basilar membrane, and inserted from below upwards. This was the method of choice for inserting an electrode array. The study also emphasised that the inner ear needed to be protected from middle ear infection extending around the electrode.

2.2 Stiffness measurements for effective electrode insertion into the scala tympani of the human cochlea

Clark and Hallworth discovered on dissected human temporal bones and moulds of the cochleae that an optimal stiffness for electrodes to pass around the scala tympani was 2.4N Clark et al [1975].

With this stiffness the electrode carriers would pass easily downwards into the widening spiral of the cochlea through a hole drilled in the apical or middle turn. On the other hand, they would only pass 10mm upwards into the tightening spiral of scala tympani of the basal turn through the round window. In this case an electrode bundle lay at the periphery of the spiral, and its upward progress in the basal turn was impeded through frictional forces against the outer wall [Clark et al 1975] (Figure 10:).

2.3 Flexible tip and graded stiffness for insertion to the speech frequency region

Clark discovered that an electrode bundle with a flexible tip and graded stiffness could pass upwards around the inner ear cochlear spiral to safely lie opposite the auditory nerves transmitting the speech frequencies, especially those higher than 500Hz. Clark first discovered the importance of graded stiffness and a flexible tip on a sea shell in 1977. The flexible tip reduced resistance against the outer wall and the increasing stiffness allowed enough force to be applied to ensure its upward progress (Figure 11). This principle was applied to an electrode bundle for the human cochlea. This was achieved by the incremental addition of electrode wires that progressively stiffened the array from the tip to the base. This electrode with increasing stiffness could be passed around the basal turn to lie opposite the speech frequency region, as shown in Figure 12. These mechanical principles underlie all cochlear implant electrodes to this day.

Figure 10: A mould of the human cochlea illustrating the insertion of an electrode bundle into the scala tympani of the basal turn of the cochlea, showing limitation in its upward progress to the speech frequency region due to resistance against the outer wall of the cochlea.

Figure 11: Grass blade inserted into a turban shell with its passage around the first spiral due to its flexible tip reducing contact pressure against the outer wall and graded stiffness allowing a force to move it onwards.

Later in 2002 Clark instigated research with Chen using finite element analysis to measure the contact pressures at the tip and along the cochlear wall. This showed much lower contact pressures for an array with graded stiffness, rather than uniform stiffness or a flexible tip alone [Chen et al 2003].

2.4 Banded electrodes optimal design for deep, and safe insertion

Clark, Bailey and Patrick discovered in 1978 that circumferential platinum band electrodes had the required smooth surface to facilitate the insertion of a free-fitting array with graded stiffness [Clark et al, 1979] (Figure 12).

The patent and scientific paper [Clark et al 1978,1979] describe a banded array to pass around the scala tympani of the cochlea for localized stimulation of cochlear nerves transmitting speech frequencies. Because the bands were smooth there was no additional friction against the outer wall of the inner ear to restrict the depth of insertion. Being circumferential the array was tolerant of lateral displacement or rotation from insertion. The graded stiffness and smooth electrode bands allowed it to be inserted for a distance of 25mm in the first patient which was deep enough to provide localized stimulation for the place coding of the mid-to- high speech frequencies Figure 12).

Shepherd, Clark and colleagues [1985] discovered that the smooth, banded, free-fitting, tapered array with graded stiffness could be inserted into fresh human temporal bones with minimal damage to the cochlea, if the insertion was stopped when resistance was felt.

Clark with colleagues reported that the banded array could be easily withdrawn and replaced if required [1987]. His results in the experimental animal indicated the banded electrode array was not held tightly by a fibrous tissue sheath after long-term implantation. This meant that the future implantable receiver-stimulators did not require a connector, and this made them smaller and able to be implanted in young children.

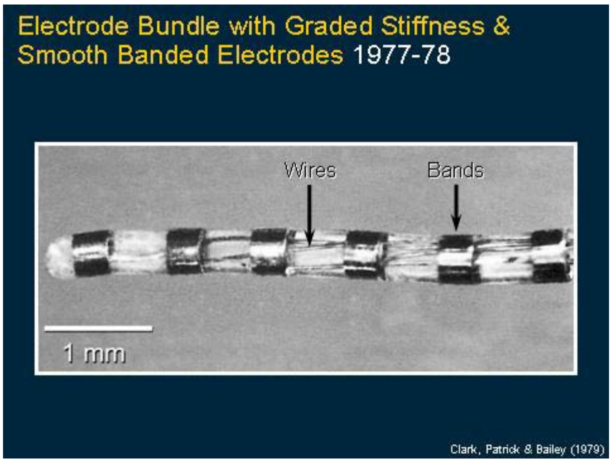


Figure 12: A banded electrode array with graded stiffness that was tapered and free-fitting for insertion into a human cochlea

2.5 Perimodiolar array

To better provide temporal and spatial coding of frequency Clark discovered in 1989 how design an electrode array to curl around the spiral of the cochlea and lie close to the central axis where the neural elements lie. This array was moulded to the spiral of the cochlea, then held straight prior to insertion, and then allowed to curl to the centre of the spiral as it was advanced along the cochlea. Clark also initiated the research on human temporal bones to ensure the perimodiolar array was safe. This discovery and it evaluation is outlined in detail in Clark's chapter on Bioengineering in his textbook "Cochlear Implants: Fundamentals and Applications". It was subsequently refined in the first CRC for Cochlear Implant Speech and Hearing Research under Clark as its first director.

3. Bio-materials discoveries

Clark's bio-materials discoveries showed that the candidate materials for an implant and electrode array were biologically safe and not toxic to the inner ear and auditory nerve. In the late 1970s there was a scarcity of data on the biocompatibility of materials for the electrode array and receiver-stimulator package. The procedures developed by Clark for the studies were appropriate modifications of those outlined in the US Pharmacopoeia [1980], and exceeded the recommendations. The assembled units were evaluated by implanting them intramuscularly for four weeks and examining the tissue response, as the manufacturing process and working of materials could change their biocompatibility [Clark 2008].

4. Bionic discoveries

Clark's bionic (bio-electronic) discoveries established the electrical stimulus parameters that would not damage the auditory nerve fibres.

4.1 Safe current and charge densities in the experimental animal

Clark first discovered with doctoral student R.K. Shepherd the safe electrical stimulus levels for chronic stimulation of the auditory nerve. This was carried out in the experimental animal and first reported in 1983 [Shepherd, Clark and Black, 1983]. They together with colleagues followed these discoveries with a series of more than 20 studies over the next 15 years to determine the safe stimulus levels for low and high rates of stimulation at different current levels and charge densities as well as DC levels. These were acute and chronic studies carried out on adult and immature animals that had normal hearing or were deafened. The studies are referenced and discussed in some detail by Clark in his textbook [2003].

They carried out long-term stimulation in the experimental animal with current levels and charge densities at the top of the range required to produce maximum loudness in patients. This was done to ensure the stimuli used in clinical practice would not have adverse effects on the auditory neurons. The charge per phase was balanced so there was no residual charge to produce a build up of damaging direct current. It can also be seen from Figure 13 the charge density will be low if the bands are wide and therefore safer, but a compromise was arrived at as the current would not be localized to separate groups of nerve fibres for place coding if the bands were too wide.

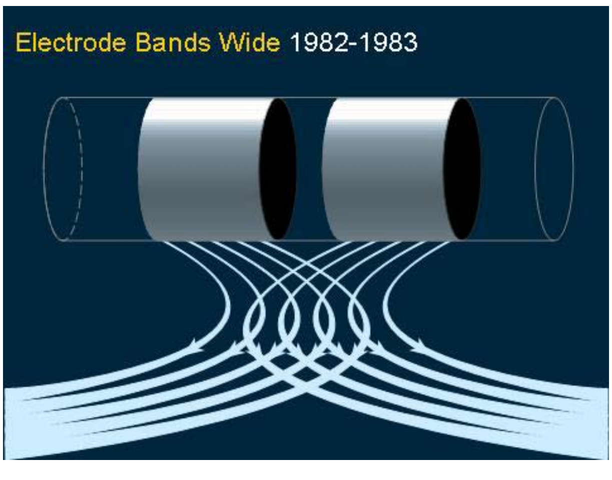


Figure 13: Banded electrodes and the electrical field density

4.2 Electrical stimulus parameters that are safe in the experimental animal are also safe for long term stimulation in the human

Clark discovered with his colleagues that long term stimulation with electrical stimulus parameters that are safe in the experimental animal, are also safe in patients. Clark studied in depth the temporal bone and brain of a person who had a cochlear implant and died from unrelated causes. Stimulation for 10,000 hours in this person did not lead to any observed adverse effect on the auditory spiral ganglion cells in the cochlea or the higher brain centres [Clark et al 1988].

5. Surgical pathology discoveries

Clark's surgical pathological discoveries showed that the spread of middle ear infection to the inner ear and thence to the meninges could be restricted by an autograft of tissue around the electrode entry point, by minimizing trauma to the inner ear, and by providing antibiotics and immunization against the pneumococcal bacteria. The aim of placing an autograft or gluing discs around the electrode at the opening into the cochlea was to encourage the in growth of fibrous tissue into the material, and so increase the path length for bacteria.

5.1 Spread of spontaneous middle ear infections to the inner ear

Clark discovered in 1973-75 in the experimental animal that spontaneous middle ear infections could spread around the implanted electrode to the inner ear. In some animals this resulted in severe infection of the inner ear with marked loss of the auditory neurons (spiral ganglion cells), with spread towards the meningeal lining of the brain.

In these experimental animals there had been no attempt to facilitate a seal at the point where the electrode entered the inner ear [Clark 1977, Clark et al 1975, Clark et al 1984]. As a result, in 1977 Clark commenced studies to determine how to seal the entry point.

5.2 A seal against the entry of infection at the electrode entry point to the cochlea

Clark discovered with his doctoral student R.K. Shepherd [1984] that a graft of tissue such as fascia from the animal's body or Teflon felt protected the inner ear from middle ear infection, but another foreign material such as Dacron mesh was associated with a severe infection. The seals were tested in the presence of experimentally induced Staphylococcus aureus and Streptococcus pyogenes infections of the middle ear. It was found that a muscle or fascia autograft around the electrode or a Teflon® felt disc prevented a Staphylococcus aureus or Streptococcus pyogenes infection in the middle ear extending to the cochlea (Figure 14). On the other hand, Dacron® mesh with an overlying fascial graft was associated with a strong inflammatory response and a high incidence of virulent infection in the inner ear. It was considered the bacteria found a home in the larger spaces in the Dacron® mesh in which to multiply, and the infection extended to the basal turn of the cochlea, and along the cochlear aqueduct towards the meninges. It was thus not recommended as a round window seal for patients.

The findings emphasized that care was needed in the choice of material, and its placement at the electrode entry point. But a graft of fascia around the electrode at its entry was effective in reducing the entry of infection.

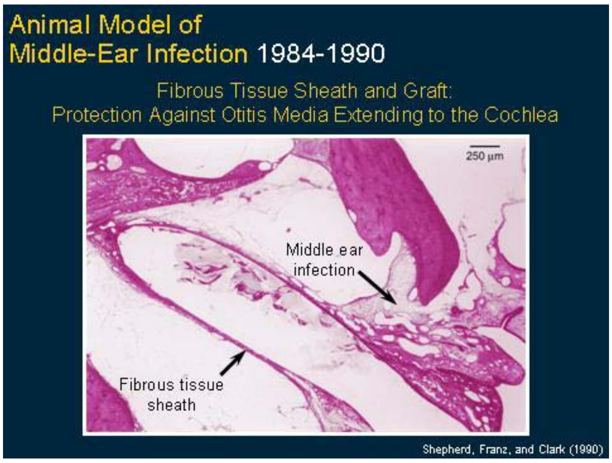


Figure 14: A seal at the electrode entry point and sheath for the electrode array which limit the entry of infection from the middle ear to the cochlea

5.3 How the seal at the electrode entry develops after surgery

Clark with his assistant: B.K-H. Franz discovered increased permeability of the tissue in the implant electrode seal and electrode sheath for at least two weeks after implantation which would make the inner ear vulnerable to spread of middle ear infection at this time, requiring prophylaxis with an aseptic surgical routine and antibiotics [Franz and Clark, 1984].

5.4 How the seal at the electrode entry and electrode sheath responded to infection

Clark and Franz discovered that with middle ear infection, the round window membrane demonstrated a marked proliferation of the connective tissue and the formation of protuberances of the mucous membrane, as well as mucous cell proliferation around the electrode [Franz, Clark and Bloom, 1987]. This was part of the body's first line of defense against bacteria, as the mucus is bacteriostatic and the cilia in the mucous membrane could sweep the bacteria away from the cochlea. In addition, Clark discovered that a fibrous tissue graft around the electrode bundle facilitated the formation of a sheath. With the formation of a sheath, capillaries brought phagocytic white cells to the tissue surrounding the electrode and the space between the electrode and sheath, to engulf the bacteria (second line of defense). It also allowed lymphocytes to penetrate the tissue and space next to the electrode, and provide antibodies against the invading organisms (third line of defense).

5.5 A well developed electrode entry seal and electrode sheath developed in a human temporal bone, and would have been effective in limiting the spread of infection to the inner ear

The response of the human cochlea to multi-electrode implantation and a fascial graft was first studied by Clark et al. [1988]. There was a good seal around the electrode at the entry through the round window and well developed fibrous sheath. Both would have been an effective barrier against the spread of infection from the middle ear. A similar sheath was later described by Clark with assistant M. Dahm in 14 implanted human bones, and is described in Clark's chapter on Surgical Pathology in Clark's textbook.

The above experimental results only apply to a single component free fitting array, but not a two-component array. A space between two components is a conduit for infection, a home to allow pathogens to multiply, as well as a site to increase the pathogenicity of the organisms and reduce the ingress of antibodies and antibiotics as discussed in [Clark 2008].

5.6 A fibrous tissue graft at the electrode entry point reduces the spread of pneumococcal middle ear infection to the inner ear.

Later, when it was discovered that cochlear implants should be best carried out on children less than two years of age, Clark initiated research to ensure that middle ear infections with Streptococcus pneumoniae, very common in this age group, could be prevented from extending to the inner ear and thus lead to meningitis. Clark considered that a separate study was required as the host agent responses vary for different bacteria. Clark with his group [Dahm et al 1994] discovered and showed a significant decrease in the incidence of inner ear infection if there was a graft around the electrode.

This discovery was confirmed by Imani completing his Master of Surgery degree under Clark. He stained the pneumococcal bacteria and examined their spread directly. He also discovered the bacteria entered the lymphatics and capillaries in the seal.

5.7 In an animal model of meningitis in the rat, a round window autograft seal and a ciprofloxin coated electrode reduced the incidence of meningitis.

Clark initiated research with one his doctoral students B. Wei and colleagues R. Robins-Brown, R.K. Shepherd and S.J. O'Leary to develop a rat model of meningitis to study whether a cochlear implant could lead to meningitis, and how it could be prevented.

They discovered that meningitis was likely to occur in association with an implant if blood born infection was induced through inoculation of the peritoneal cavity. This emphasized the need to immunize young children having a cochlear implant. They also confirmed the importance of a round window seal to prevent the spread of middle ear infection to the inner ear with the development of meningitis. They also discovered a ciprofloxacin coated array protected rats from meningitis via the haematogenous spread, but only delayed the onset following middle or inner ear inoculation.

6. Bio-engineering discoveries

Clark's discoveries in 1) auditory neurophysiology, 2) biomechanics, 3) biomaterials, 4) bionics, 5) surgical pathology and anatomy have been crucial for his bioengineering research to develop the first implantable cochlear implant receiver-stimulator. This was the most complex package of electronics to be implanted in a person.

Clark led the development of an implantable receiver-stimulator for multi-channel electrical stimulation to determine whether speech understanding was possible in severely-to- profoundly deaf patients (1974-1978). He commenced this development after he had shown the limitations of temporal coding, the possibility of place coding of frequency, and after he had commenced safety studies.

6.1 An implantable receiver-stimulator needed to be developed for power and data to be transmitted through the intact skin, rather than use a plug and socket.

As Clark had found infection occurred between a socket and the skin edges in his experimental animals, he initiated in 1974 the electronic engineering of a fully implantable receiver-stimulator, and provided the physiological design specifications from animal studies [Clark et al 1977].

6.2 Clark discovered with his anatomical dissections the size of the implant and its ideal location in the body.

It had to be small so that it could not use batteries but receive power from outside. Radio signals rather than infrared light or ultrasonic vibrations were the best alternative for the transmission.

At the time in the 1970s a number of placement sites were being considered, but Clark realized the importance of placing the implant close to the ear and making space in the mastoid bone. This is illustrated in this photograph of one of his original dissections of a human temporal bone (Figure 15). Clark realized this placement would also reduce the risk of fractures of the wire from head and other body movements, as he had seen with his animal behavioural work. It was also logical to site the microphone close to the ear as the head needs to be turned in the direction of the sound for attention.

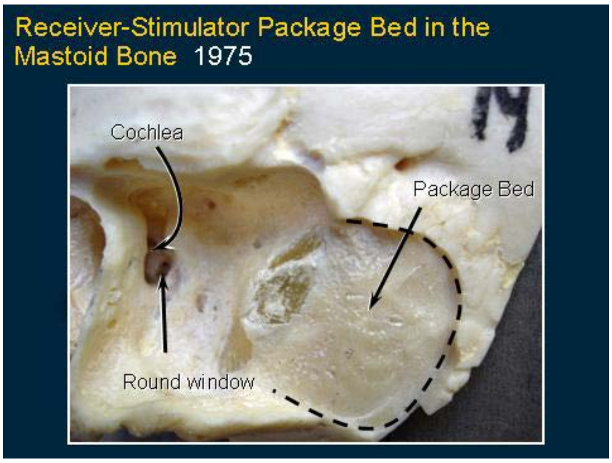


Figure 15: Human temporal bone with bed for the receiver-stimulator and dissected by Clark in 1975 prior to the implantation of the device by Clark at surgery

6.3 Specifications for the receiver-stimulator electronics.

Specifications for the design of the implantable receiver-stimulator were based on Clark's physiological studies. As the information needed to be transmitted through the intact skin as coded pulses on a radio wave, there would be less flexibility in the choice of test stimuli than with a percutaneous plug and socket. The latter was essentially the same as direct wiring with unlimited freedom in the choice of electrical pulses. For that reason the receiver-stimulator electronics had to be chosen carefully to provide enough flexibility for the right electrical stimuli to represent the speech signals. The data and power transmission levels were set to minimize biological damage from electromagnetic radiation. The principles underlying the electronic design were elaborated in the first scientific paper on a multiple-channel receiver-stimulator by Clark et al [1977].

The patent for this receiver-stimulator by [Clark et al] was filed in 1977 [Patent Nos.: Australia - 519,851 describes the transmission of multiple channel speech information and power to a fully implantable receiver-stimulator (Figure 16).

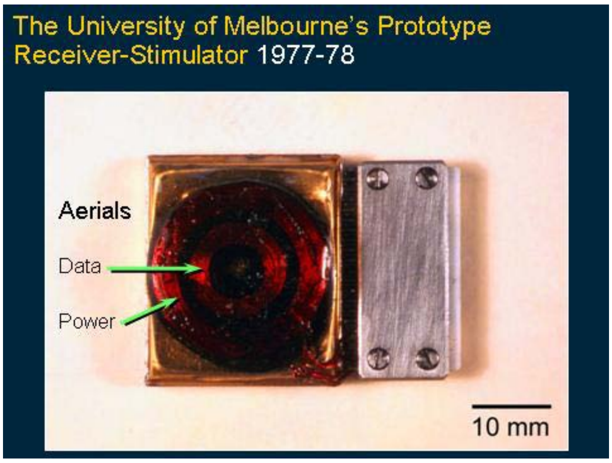


Figure 16: Receiver-stimulator for first implant operation. There are coils on the exterior for power and data and a connector at the front in case the electrodes failed and another had to be implanted. It was not known whether the electrodes would have to remain in the cochlea. Clark later discovered the electrode array could be removed. Clark Clark's contributions to biomedical engineering have been recognized with his election as a Fellow of the American Institute for Medical and Biological Engineering which is the highest honour of this institute, his being made an Honorary Doctor of Engineering from the CYC University in Taiwan which has an international reputation for biomedical engineering, and his award in 2009 of the Otto Schmitt Award from the International Federation for Medical and Biological Engineering at the 2009 World Congress on Medical Physics and Biomedical Engineering *(this is for exceptional contributions to the advancement of the field of medical and biological engineering presented every three years at the World Congress on Medical Physics and Biomedical Engineering)*.

EDIT

7. Pioneering Surgical Discoveries

Clark discovered the surgical and other clinical procedures required for the implantation of the first fully implantable multi-channel cochlear implant [Clark et al 1979].

7.1 Pioneering Surgery

In order to determine whether speech understanding could be achieved with electrical stimulation of the central auditory nervous system, Clark as head of the University Department of Otolaryngology, and head of the Royal Victorian Eye and Ear Hospital clinic, developed the pioneering surgery. He selected suitable patients, ensured the implantation of a foreign body did not significantly increase the incidence of infection, and discovered the surgical approach and instruments for the implantation, and was the chief surgeon for all crucial early operations on adults and then later children. Clark had prior training in both general surgery at the Royal College of Surgeons in Edinburgh, and in Ear, Nose and Throat surgery at the Royal College of Surgeons in England, and the Royal Australasian College of Surgeons.

His surgical achievements have been recognized in 2004 by being made Honorary Fellow of the Royal College of Surgeons, England, *(the supreme single award of the College for outstanding achievement in medicine);* receiving the Royal College of Surgeons of Edinburgh Medal, awarded in 2005 at the Quincentenary Celebrations of the College (*for outstanding contributions to medicine;* and in 2005 the

Excellence in Surgery Award, from the Royal Australasian College of Surgeons *(recognising the highest level of surgical achievement by world standards, advanced innovation in the field, continued quality and worth of the innovation, and the highest standard of ethics).* In 2010 he is to receive the Lister medal and deliver the Lister Oration. This honour is awarded 3-yearly by the Royal Society, The Royal College of Surgeons of England, The Royal College of Surgeons of Ireland, the University of Edinburgh, the University of Glasgow, and the Society of Academic and Research Surgery. (it is the most prestigious award in the surgical sciences in the UK and one of the most prestigious in the world).

7.2 Communication Science and Audiological Assessment of Implant Subjects

The first clinical routine to assess cochlear implant patients.

The clinical routine was based on Clark's experience as the chief examiner of the first school of audiology in Australia which he established, and his assessment of a group of prospective patients with severe sensori-neural deafness. With the early patients Clark coordinated research studies with the preoperative and postoperative assessment required.

7.2 Aseptic implantation of the receiver-stimulator and electrode array.

As Clark's initial animal experimental findings in the 1977 had shown that spontaneous middle ear infection could extend around the cochlear implant electrode into the inner ear and lead to inner ears infection,, he developed with B.C. Pyman procedures to minimize any risk of infection at the time of surgery [Clark et al 1979] (Figure 17).

Figure 17: Clark and the operating set-up for the initial surgical operations. The unit for the laminar flow of sterile air is shown.

7.3 Surgical procedures and special instruments for the multi-channel cochlear implant, and Clark undertook the first operations on adults and later children.

As surgeon-in-charge Clark undertook the surgery on the first and early adult patients, and then on the first children with his assistants B.C. Pyman and R.L. Webb. He saw it as his responsibility to ensure all his basic research was carried through to a good patient outcome. He has been a rare individual in combining high level of surgical clinical skills with outstanding interdisciplinary research.

Clark was the first to publish a comprehensive account of the surgical procedure required to implant a receiver-stimulator and electrode array for multi-channel electrical stimulation of the central auditory pathways [Clark et al 1979]. The surgical procedure evolved from Clark's bioengineering and anatomical studies showing how to place the electrode effectively and without trauma in the cochlea.

Clark has trained his surgical staff in the use of his procedure, and also run international workshops in Melbourne to train leading ear surgeons from overseas. He has continued to train surgeons for some years, and as part of the Graeme Clark surgical workshop held in the Bionic Ear Institute for Japanese surgeons. But once he had successfully operated on his first patients he concentrated on psychophysics and speech research.

Figure 18: Clark filmed implanting the first multi-channel cochlear implant on 1st August 1978.

8. Psychophysical Discoveries

Clark from 1978 discovered how multi-channel electrical stimulation of the brain reproduce frequency and intensity as pitch and loudness sensations in severely-to-profoundly deaf adults who originally had hearing before going deaf.

Clark was guided in this psychophysics research by the milieu in the Department of Physiology at the University of Sydney when he completed his doctorate of philosophy in 1969. The department under Professor Peter Bishop had a strong emphasis on visual physiology, and it was here that Clark learned the important relation between perception and brain cell coding. His later contributions to psychophysics have been recognized by being made a Fellow of the Australian Acoustics Society, and the many prizes, medals and awards he has received, including the Zülch prize from the Max Plank Society in 2007 (Germany's highest award in the neurosciences).

8.1 Clark discovered in 1978 with one of his postdoctoral students Y.C. Tong that low rates of stimulation were perceived as true pitch sensations. This was Clark's first key contribution to our understanding of how the brain codes sound.

Pitch at low rates of electrical stimulation e.g. at 50 pulses/s corresponded to the pitch for acoustic excitation at the same frequency, but at rates above 200 pulses/s the correspondence rose dramatically, and the discrimination was poor [Clark et al 1978, Tong et al 1979]. This discovery established that the timing of electrical stimuli was important for coding a low pitch. This had been difficult to determine with acoustic stimuli, as place and rate (timing) of excitation overlap, as illustrated in Figure 4.

However, the deterministic firing of the brain cells at low rates of electrical stimulation, but in time with the stimuli, has been hypothesized by Clark as the reason electrical stimulation was perceived as pitch, but more poorly discrimination than sound. Clark has discussed in his review for the Royal Society, his book and his specific papers, how he has shown that electrical stimulation has provided important knowledge on how the brain codes coarse and fine-temporal spatial patterns of excitation in brain cells for the coding of frequency and related pitch [Clark, 2003, Clark, 2006].

Above approximately 800 Hz the discrimination of pitch was lost, and Clark has demonstrated this is most likely due to the fact that the electrical stimuli produce a stronger inhibition of brain cell responses, than occurs with sound. As good discrimination of pitch up to 4000Hz was required for speech understanding, Clark emphasized early in the development of the cochlear implant that place coding through multi-channel stimulation would have to be used for the important mid-to-high speech frequencies.

8.2 Clark and Tong discovered that place of stimulation, resulted in the perception of the stimulus as timbre, but not as a strong pitch sensation [Clark et al 1978, Tong et al 1979].

One of the most important discoveries by Clark and Tong was that the patient described constant rate of stimuli on different electrodes as sharp or dull according to whether they stimulated the higher or lower regions of the cochlea respectively. This is discussed in more detail in Tong et al [1980, 1982], and in Clark's chapter on Psychophysics in his text book Cochlear Implants: Fundamentals and Applications.

Timbre relates to the quality of the sound, and is the auditory sensation that enables a listener to judge that two sounds similarly presented with the same loudness and pitch are dissimilar, e.g. different instruments. The pattern of sounds underlying timbre is complex, but does relate to the distribution of frequencies being coded on a place coding basis. This knowledge was becoming known at the time of Clark's discovery. Nevertheless, the discovery of Clark and Tong using electrical stimuli has provided fundamental knowledge showing how the pattern of neural excitation relates to timbre. This is discussed in Clark's textbook.

Furthermore, the patient could distinguish at least 10 sensations for timbre presented sequentially along the array. This demonstrated there would be at least ten separate place pitch sensations for the place coding of speech frequencies (Figure 19). Tong and Clark also discovered in 1985 the minimum overlap in stimulated neural populations for perceptual discrimination.

In addition, he then discovered if the pitch-like sensations from rate and place of stimulation were combined one could influence the other. Thus a lower rate of stimulation on a higher pitched electrode with sharp timbre corresponded to a higher rate on a lower pitched electrode with dull timbre.

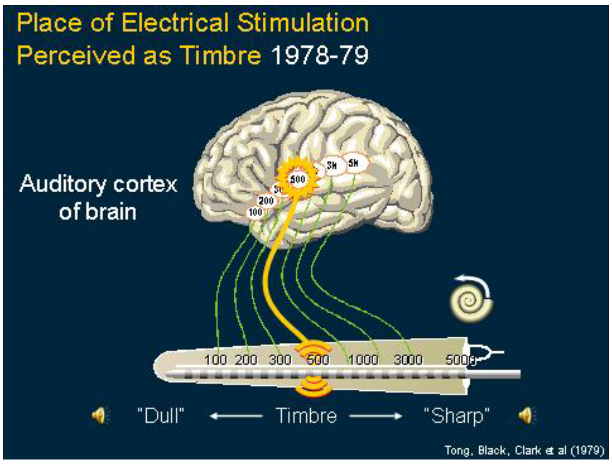


Figure 19: Place of electrical stimuli perceived as timbre (sharp to dull).

8.3 Clark and Tong made the very important discovery in 1978 that stimuli on each electrode were not only described as varying from sharp to dull, but were recognized as vowel-like.

It was noted that vowels were perceived when stimulating different electrodes (

Figure 20). The vowels corresponded to those that had second formant frequencies that would excite the same region as single speech formant in a normal hearing person. Formants are concentrations of frequency energy due to vocal tract resonances, and they are important for intelligibility iin both vowels and consonants as illustrated in (Figure 21). It was discovered that the vowel, could be changed by increasing or decreasing the duration of the stimuli, as seen for vowels presented to normal hearing subjects. If pairs of electrodes were stimulated together at a constant stimulus rate the vowel perceived was different from that perceived with single electrode stimuli. This depended on the relative amplitude of the two stimuli suggesting the central nervous system was using an averaging process for the two neural populations excited. When two electrodes were stimulated at different rates a consonant was perceived. The consonant was related to the difference in rate between the stimuli on the electrodes. It was considered by Clark and Tong that the consonant could have been coded by variations in summed intensities of the two stimuli or a phase difference induced in the nerve fibres from the two signals [Clark et al 1978, Tong et al 1979].

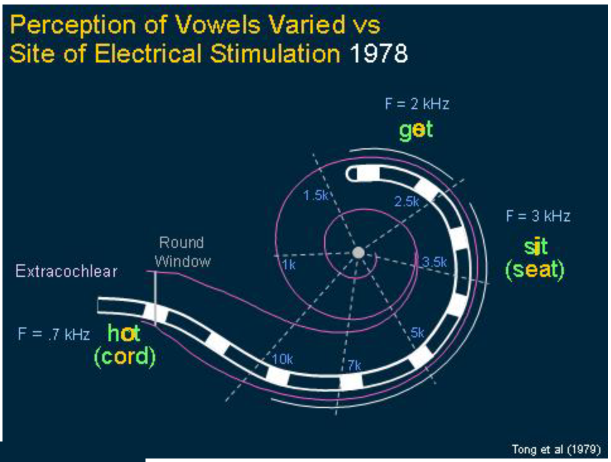


Figure 20: Vowel recognition versus site of stimulation showing vowels which have second formant frequencies corresponding in site of stimulation to those experienced by people with normal hearing and single formant excitation.

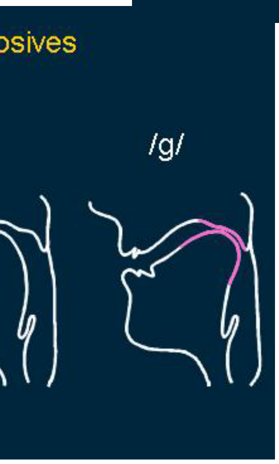


Figure 21: Resonant cavities in vocal tract that produce formant frequencies, in this case for consonants /b/d/g/, instead of vowels.

8.4 Clark and Tong discovered the range in loudness from threshold to maximum comfort level was much smaller for electrical stimulation than for sound.

Although there was a very restricted range in loudness with electrical stimulation of only 5 to 10 decibels compared to 120 decibels for sound the discriminable steps were smaller. There was thus an increase in the number of discriminable steps over the narrower dynamic range for electrical stimulation. Consequently, the

30dB speech signal would still have approximately half the number of steps normally available to transmit intensity changes.

9. Speech processing discoveries

Clark and Tong discovered in 1978 the first speech processing strategy to give open-set speech understanding using electrical stimulation alone, and in combination with lipreading.

In 1975 Clark foresaw the need to become well grounded in speech science prior to implanting a patient, as he reasoned from his physiological research that: “if pure tone reproduction is not perfect, meaningful speech may still be perceived if speech can be analysed into its important components, and these used for electrical stimulation. More work is required, however, to decide which signals are of greatest importance in speech perception”. He considered that speech research would provide the insights he needed to determine the signals of greatest importance.

For this reason, as outlined in his autobiography, Clark in 1976 spent four months with William Ainsworth at the University of Keel UK doing research with synthetic speech using a parallel formant synthesizer, and he visited John Holmes in London, and Gunnar Fant in Stockholm . For his pioneering research in speech Clark was awarded the 2005 International Speech Communication Association (ISCA) Medal, (The most prestigious award in speech science, previously awarded to pioneers in speech science).

9.1 Physiologically-based speech processor

Clark in 1976 initiated research with a master of engineering student R. K. Laird to develop and trial a physiologically-based speech processor that a) separated speech sounds into different frequency bands like the normal cochlea, b) introduced the time delays taken for each of these frequencies to reach their sites of maximum vibration along the basilar membrane, and c) produced a certain degree of jitter in the stimuli to mirror the way the brain cells respond to sound (Figure 22).

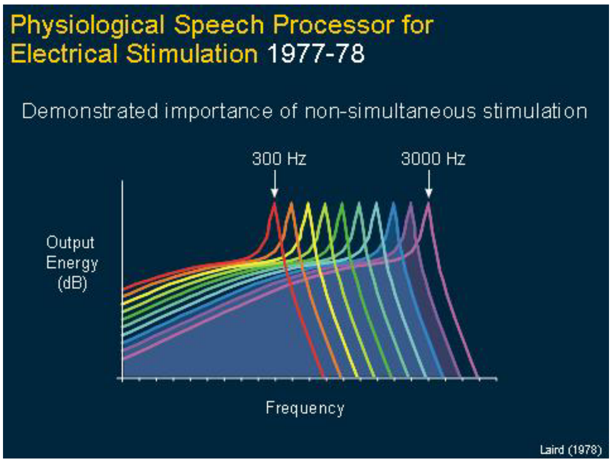


Figure 22: Filters for physiologically –based speech processor

Clark and colleagues found that speech understanding with this physiologically-based speech processor was very limited because the electrical currents representing the sound energy in each frequency band were overlapping, and this produced unpredictable variations in loudness. This discovery, that simultaneous stimulation produced unpredictable interactions of the electrical fields from each channel, led to the important principle for all advanced speech processing strategies that only non-simultaneous stimulation should be used. The stimuli on each channel should be separated by a short interval in time to avoid the interaction of the electrical fields on each electrode, and this would still allow neural integration over time to take place.

9.2 Clark and Tong made the crucial discovery that running speech could be understood in severely–to-profoundly people by coding the second formant as place of stimulation along the cochlear array, coding the amplitude of the second formant as current level, and coding the voicing frequency as pulse rate across the formant channels.

The discovery by Clark and Tong of the second formant/voicing speech processing strategy to give profoundly deaf patients running speech was made in December 1978, and established by Clark with objective audiological tests in 1979. It is reported by Clark and Tong in the following two publications in 1978 and 1979 (Clark et al 1978, Tong et al 1979).

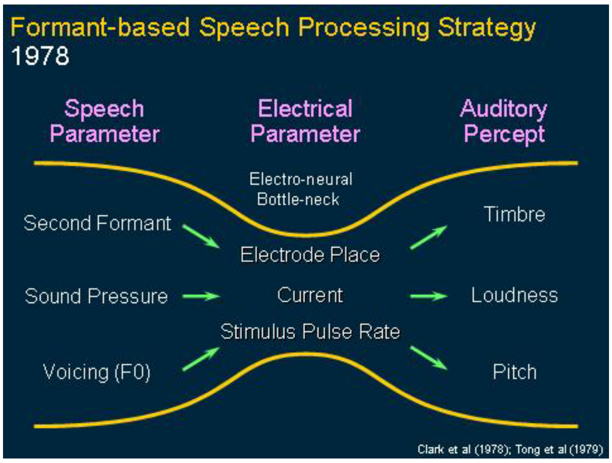


Figure 23: The inaugural formant-based multi-channel cochlear implant speech processor transmitting the second formant as place of stimulation, its amplitude as current level and voicing as rate of stimulation across the electrodes being stimulated. It transmitted an essential speech code through the electro-neural bottle neck between the world of sound and perception.

Clark and Tong extracted the second formant frequency as this is the formant that carries most information for speech intelligibility, and they presented it to separate electrodes, so there would no channel interaction. In addition, voicing which is low in frequency, was coded as changes in rate of stimulation. This code was used as Clark and Tong had discovered that only pitch at low rates of electrical stimulation could be discriminated. This was consistent with Clark's behavioural results on experimental animals for frequency discrimination and their ability to detect frequency modulated signals. Rate of stimulation, which coded voicing, was transmitted across the frequency sites as this had been shown by Clark to be how the brain coded rate and place stimulation.

Clark in December 1978 arranged that his audiologist present open-set words to his first patient, and the patient identified a few correctly. Clark realized then that this was the breakthrough in providing speech understanding that everyone had been hoping for. To quote from Clark's autobiography *"it was the moment I had been waiting for. I went into the adjoining room and cried for joy."*

This second formant/voicing strategy was shown to be successful on a second patient from the University of Melbourne Clinic at the Royal Victorian Eye and Ear Hospital, and thus indicated that it was not specific to one person's coding pattern in the brain.

The open-set speech test results on these two patients were the first time that speech recognition for electrical stimulation alone had been demonstrated, and under standardized conditions, and reported in the scientific literature. Previously single channel strategies had only shown a small improvement when electrical stimulation was used as a lip reading aid, but no speech understanding for electrical stimulation alone.

Clark then played the key role in facilitating the industrial development of the formant-based strategy through the pacemaker firm Telectronics and its soon to be formed subsidiary Nucleus/Cochlear Pty Ltd.

The industrial device had the same strategy incorporated as the one discovered by Clark, but it could sample the signal faster and had other features such as a better microphone response. When it was trialled on a large group of patients in the US the mean score for open-sets of words for electrical stimulation alone reached 40%, and is shown in Figure 24. This meant these patients could have a useful conversation on the telephone [Dowell et al 1986].

Furthermore, Clark was able to test a patient whose first language was Mandarin. This language depends on hearing changes in tone and not primarily formants, as occurs for other languages. Clark initiated this study, and together with his colleagues was the first to discover the marked benefits the second formant/voicing strategy provided in speech understanding for a tonal language [Xu et al 1987]. This means that the hundreds of thousands of severely-to-profoundly deaf Chinese can now benefit.

(In 1985 after a world trial, the second formant / voicing strategy and multi-channel cochlear implant, became the first multi-channel cochlear system to be approved as safe and effective by the US Food and Drug Administration or any health regulatory body for giving speech understanding both with lipreading and for electrical stimulation alone in people who had hearing before going deaf).

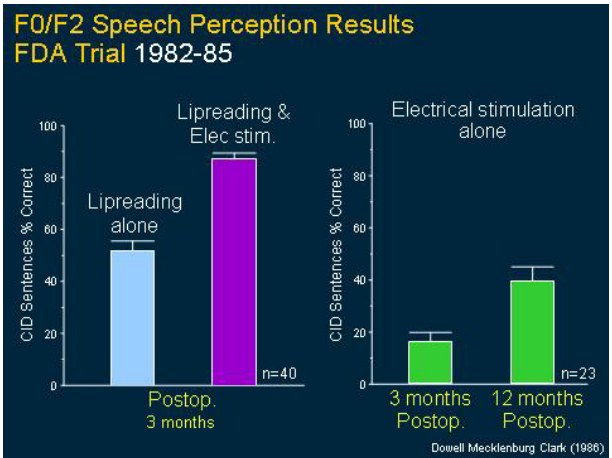


Figure 24: Speech perception results for the second formant/voicing processor for electrical stimulation with lipreading and electrical stimulation alone from the world trial for the US Food & Drug Administration In 1985 it

was the first multi-channel implant to be approved, as safe and effective for those with hearing before deafness.

9.3 Clark and Tong next discovered how the brain processed the information transmitted by the successful second formant / voicing speech processor.

Clark led the research to discover how the speech coding strategy was processed by the brain, and how he could improve the strategy so most deaf people could achieve near perfect speech perception, speech production, and language.

9.3.1 Clark and Tong discovered that frequency glides or transitions of great importance for speech intelligibility were best coded as transitions in place of stimulation rather than rate

Clark and Tong discovered that the frequency glides of importance for coding the plosive sounds in speech e.g. /b/, /d/, /g/, are best coded by changes in place of stimulation rather than rate of stimulation over the short durations required for these consonants.

The direction and extent of the frequency shifts in the second formant frequencies for the intelligibility of the consonants /b/, /d/, and /g/, referred to as plosives, are illustrated in Figure 25. The burst of noise that occurs after the closed vocal tract is opened and the sound released, is also an important cue. Figure 25 shows a rising second formant distinguishes /da/, a gentle fall /da/, and a rapid fall /ga/.

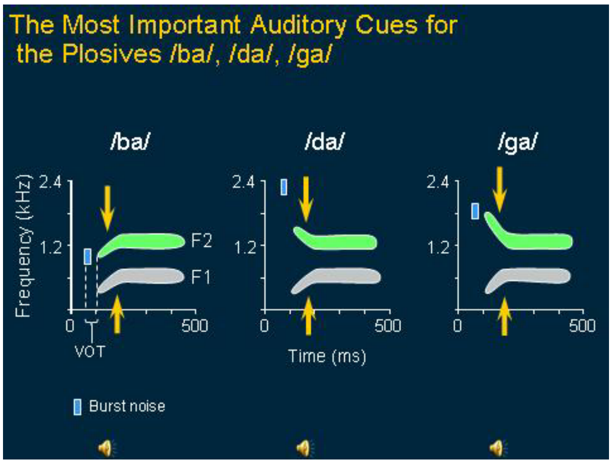


Figure 25: Frequency transitions in the second formant frequency distinguish the voiced plosives /ba/, /da/, /ga/.

The importance of place of electrical stimulation for the recognition of the plosive consonants is illustrated in Figure 26. This shows the percentage shifts in electrode place and rate of stimulation judged different for durations of 100, 50, and 25ms. The judgments of place of stimulation for all durations are on the left, and for rate of stimulation are on the right. The judgements fall off for rate of stimulation at durations of 25ms, but are maintained for place of stimulation [Tong et al, 1982].

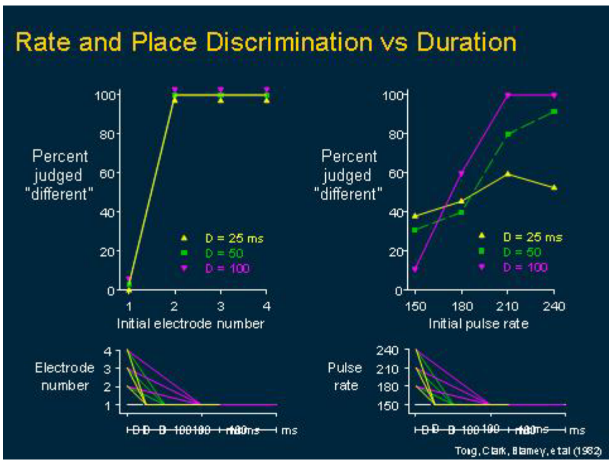


Figure 26: Place and rate discrimination vs. duration. Place is on the left and rate on the right. Discrimination of the glides is on the vertical axis and initial electrode in the transition on the horizontal axis.

9.3.2 Clark and Tong discovered that rate of stimulation was perceived as voicing

Clark, and Tong discovered that rate of stimulation was perceived as voicing in the appropriate speech context, and voicing was recognized for rate of stimulation across the spatial frequency channels.

This was consistent with Clark's previous physiological and psychophysical results, and is illustrated in Figure 27 from his keynote address to the International Speech Communication Association conference in Lisbon in 2005.

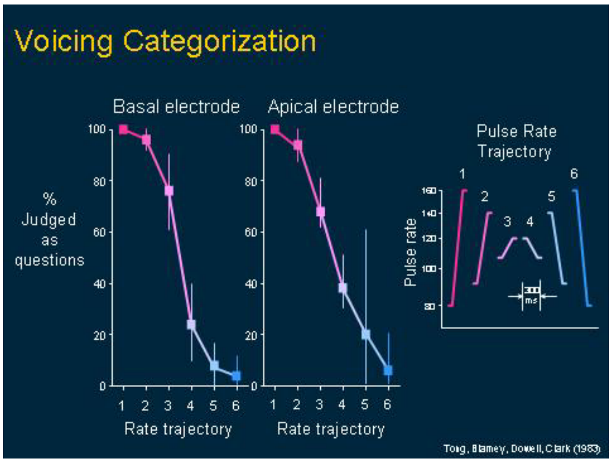


Figure 27: Rate of stimulation and the perception of voicing vs. site of stimulation of the apical and basal electrodes

9.3.3 Clark and Tong discovered that electrical stimuli presented along two spatial channels of excitation in the brain for the place coding of frequency were perceived as having two perceptual components.

Tong and Clark discovered that the perceptual space, as illustrated in Figure 28 for apical and basal stimulus pairs was a 2-dimensional perceptual space, indicating the two electrodes were perceived with two components. Furthermore, it was discovered that although place of stimulation gave two perceptual components, they were however fused into one speech percept (Tong et al 1983). This indicated that a speech processor that presented two formants instead on one should provide better speech perception.

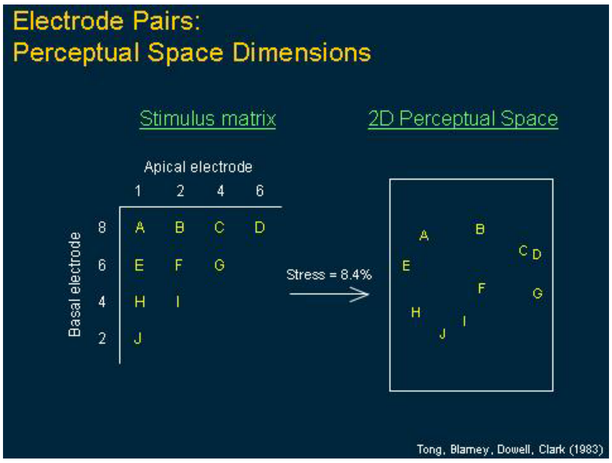


Figure 28: Perceptual space for two electrode pairs. The pairs of stimuli are on the left and the perceptual space on the right.

9.3.4 Clark and Blamey discovered an acoustic model of a first and second formant speech processing that predicted the results for speech processing codes using electrical stimulation

In view of the above findings on perception, Clark decided to determine to what extent a processor coding the first formant frequencies as well as the second formants would be effective for speech recognition. Before changing the design of the external hardware Clark led research to create an acoustic model of electrical stimulation. Filtered noise was used as it had the buzz-like qualities described by patients for electrical stimulation.

The model used seven bands of pseudo-random white noise with centre frequencies corresponding to the electrode sites, to represent different speech frequencies. Figure 29 shows the mean vowel and consonant scores for the second formant (F2) / voicing (F0) strategy as an acoustic model in bright green and electrical stimulation in bright pink. The results are similar suggesting the model provided a good representation of the electrical stimuli. The results for the acoustic model of adding the first formant or F1 to achieve the F0/F1/F2 processor are in lighter green and show an improvement in vowels and consonants. Later it was found that with an F0/F1/F2 processor for electrical stimulation there were similar improvements to those obtained with the acoustic model.

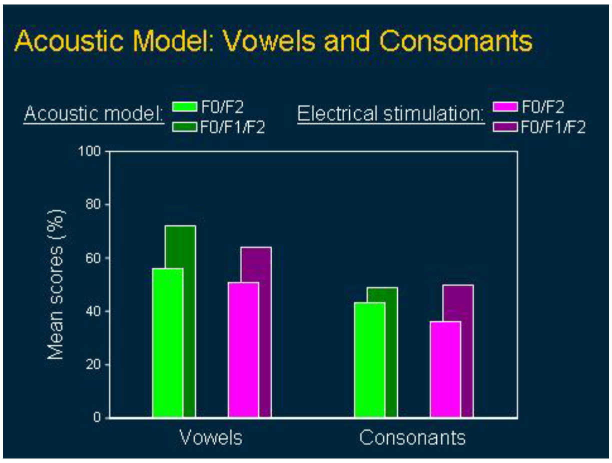


Figure 29: Acoustic model of formant speech processing vs. electrical stimulation coding the formants.

9.3.5 Clark and Blamey discovered an acoustic model for voicing that showed that electrical stimulation with the standard array does not transmit fine temporo-spatial pitch information

It was also of importance to know that the information transmission for voicing with rate of electrical stimulation and with the acoustic model of electrical stimulation were similar. This was seen when using the F0/F2 strategy as shown in Figure 30.. This demonstrated electrical timulation was not transmitting the fine temporo-spatial patterns for frequency coding. By using bands of noise with the model the sine waves for each frequency were removed, and the voicing was simply amplitude modulation of the noise at the modulation frequency.

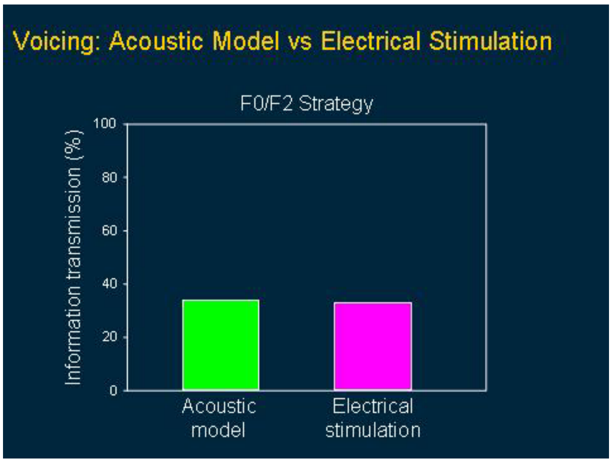


Figure 30: Voicing with the acoustic model and electrical stimulation. The voicing results for the acoustic model of electrical stimulation are shown in green and for electrical stimulation in pink.

9.3.6 Clark discovered that temporal and place information was processed by the brain along two different channels

So the above psychophysical and acoustic modelling studies of Clark's has shown that the brain effectively processes spatial and coarse temporal pitch information along separate channels (Figure 31). Fine temporo-spatial excitation was not evident. As a result Clark has guided further improvements in speech processing in the medium term by coding essential frequencies on a place coding basis. Improvements in speech processing in the long term will be expected by developing an improved interface with the nervous system for fine temporo-spatial processing of frequency.

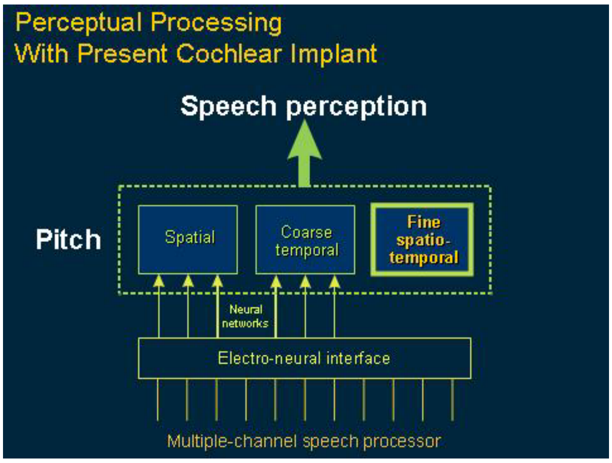


Figure 31: Perceptual processing be the brain with spatial, coarse temporal and fine-temporo- spatial frequency information.

9.4 Discovery that improvements in speech recognition were achieved with a processor coding second and first formants and high frequency spectral information

The next advance was made by Clark's doctoral student Dowell and Seligman who instead of extracting the third formant frequencies considered it desirable to extract the high frequency energy for the fricative or noise of the /t/ sound (Figure 32). For this reason the energy from three high frequency bands as well as the first and second formant were selected from high frequency filters and coded on a place basis (Figure 33). With this strategy the voicing frequency was still coded as rate of stimulation across all channels. It has been referred to as the "Multipeak" strategy, but this is a misnomer as it only picks two formant peaks, and the outputs of fixed filters. This strategy gave a further improvement in speech recognition and this improvement was most noticeable in noise.

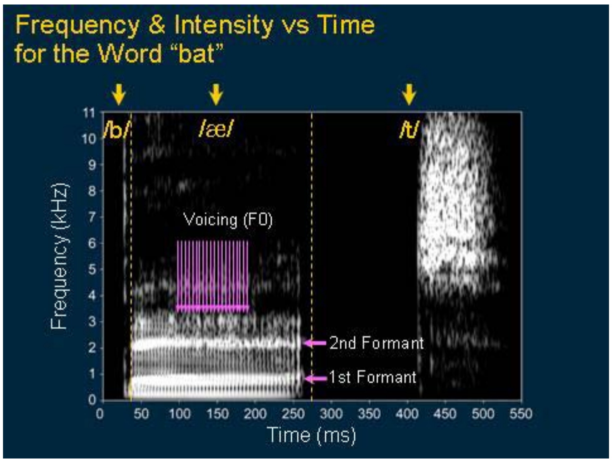


Figure 32: Spectrogram for the word /bat/. Intensity is the brightness of the trace showing the formants for the vowel in the word bat and the high frequency energy for the /t/ sound.

Dowell, together with his Clark discovered that the improvement in speech recognition with the "Multipeak" strategy was reflected in better representation of nasal and fricative sounds, and especially for high frequency noise (this is described in detail in Clark's chapter on Speech Processing in his textbook "Cochlear Implants").

The transmission of information on place of articulation was the lowest, and indicated the need to transmit more of the rapid frequency changes that occur with oral cavity movements with consonants (the work of Fant on resonant frequencies with place of articulation is referred to in Clarks' textbook).

Figure 33: Frequency filter characteristics for the second and first formant strategy with voicing across channels (F0/F1/F2) in yellow. The additional high frequency filters for the high energy noise, in particular for the Multipeak-MSP processor, are in purple.

At this point in time a comparison was made between the "Multipeak" strategy developed by Clark and team, and the Ineraid/Symbion strategies and reported by Cohen at al in 1993 in the New England Journal of Medicine. Both the Ineraid/Symbion strategies used the outputs from four to six frequency filters to stimulate the auditory nerves. The strategy underlying Ineraid was described by Eddington in 1980, and Symbion by Merzenich in 1984.

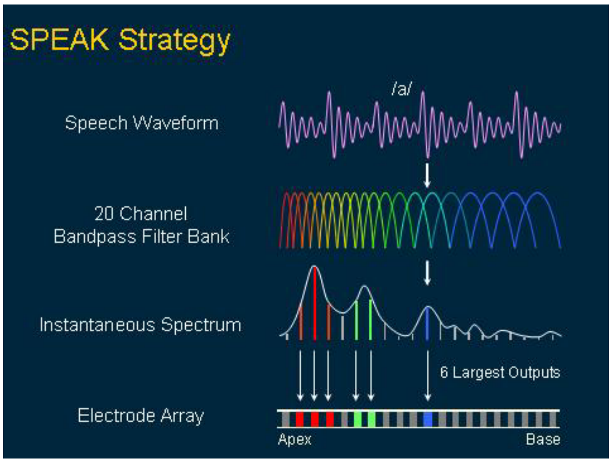


Figure 34: Selection of the six to eight maximal outputs from a bank of 16 to 20 band pass filters for place coding with amplitude of the speech wave coded across channels to convey voicing.

The results of this comparison by Cohen et al in 1993 showed "there was a significant difference between the Nucleus "Multipeak"-MSP and Symbion/Ineraid systems, particularly for the perception of open-set speech presented by electrical stimulation alone. There was a 75% score with the "Multipeak"-MSP system, and only a 42% with the Symbion/Ineraid system. Both speech-processing strategies presented information along approximately the same number of channels (five for "Multipeak" and six for Ineraid). Although the Ineraid strategy did not use a voicing decision the significantly better results with "Multipeak" would not have been due to that alone, but the selection of formants and presentation of the energy peaks over a range of frequency regions in the cochlea" (abstracted from Clark's text book Cochlear Implants.

9.5 It was discovered jointly by Tong and Clark and then McDermott and Vandalis that further improvements in speech recognition could be achieved with constant rate of stimulation and selecting the spectral maxima

Clark with Tong and other members of his group continued their research through Clark's US National Institutes of Health Speech Processor Contract. They found in 1989 and 1990 that if they extracted four to six frequency peaks from speech using a bank of band pass filters and coded this as place of stimulation, and then used a constant rate of stimulation to transmit the voicing amplitude across channels they achieved further improvements in speech recognition. This strategy provided the basis for an alternative strategy developed under Clark's supervision by McDermott and Vandali. This extracted the maximal outputs from a bank of six fixed filters rather than six frequency peaks. It resulted in a further improvement in results (Figure 34), and proved superior to another fixed filter and constant stimulus rate strategy reported by Wilson in 2000.

9.6 Clark with Vandali and Clark with Grayden discovered two further improvements in speech recognition could be achieved by selecting transients and processing differential rates respecitively

Further modifications to Clark's speech processing strategies have also been made by Clark and colleagues. These include the discovery by Clark with Vandali that if the frequency glides of consonants are emphasized then better speech recognition results. In addition, Clark and Grayden have found that using low rates of stimulation for speech features of place of articulation and high rates for manner of articulation leads to improvement.

As a result of the improvements in speech processing led by Clark after the initial ground breaking discovery by Clark and Tong, the mean open-set speech recognition scores have reached close to 60% for electrical stimulation alone. A score not dreamed possible when Clark first commenced his research.

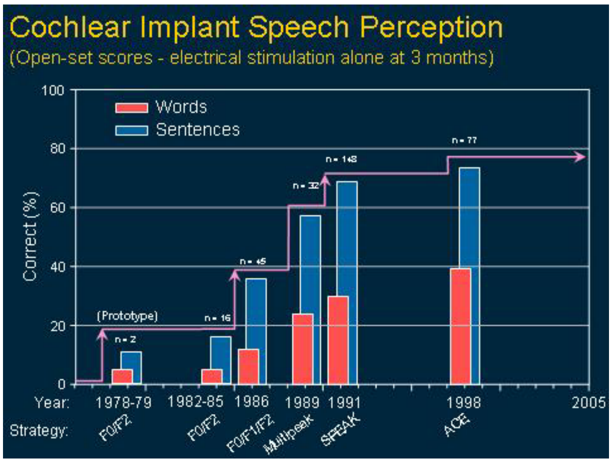


Figure 35: The improvements in the open-ser word and sentence scores for the speech processing advances led by Clark since the initial discovery of a formant based strategy that gave running speech.

10. Clark, van Hoesel and Tong were the first to discover how bilateral cochlear implants and bimodal hearing with a cochlear implant in one ear and a hearing aid in the other ear provided some of the benefits of hearing with two ears.

10.1 Bilateral cochlear implant

Once the benefit of a cochlear implant in one ear was established research commenced to determine the value of bilateral implants, particularly speech understanding in the presence of background noise. Furthermore, comparisons of speech perception for multi-electrode implants and hearing aids on children showed that a multi-channel implant for a profound hearing loss gave comparable results to that of a hearing aid in a child with a

severe hearing loss [van Hoesel and Clark, 1995]. This led to studies on adults and children with an implant in the worse ear, and a hearing aid in the better ear (bimodal hearing) [Blamey et al 1996].
With bilateral implants and bimodal hearing the aim was to reproduce the benefits of two ears. These benefits are: a) the ability to localize the direction of a sound (due to differences in the intensity as well as the time of arrival and phase of the sound at each ear); b) hearing speech in noise in each ear due to central neural mechanisms that partially remove the noise, but not the signal (squelch effect or binaural release from masking), c) hearing speech on one side with competing noise in the opposite ear (the head shadow effect) d) loudness summation.
Psychophysical studies on bilateral implant subjects using headphones showed that interaural intensity differences could be readily used for good sound localization, but not so for temporal differences. However, it was also important to ensure that equivalent sites in each ear were excited [van Hoesel and Clark, 1995]. Furthermore, when sound localization was tested with a series of free-field speakers the average detection was 15.5^0 compared to 1^0-2^0 for normal hearing. When the cues were isolated, the interaural temporal differences for electrical stimulation were similar for sound at 50 pulses/s (150 μs), but not at higher rates. The average interaural intensity difference perceived was 0.3 dB for electrical stimulation, and this was approximately three times that for normal hearing.
To investigate the head shadow as well as the "squelch" effect, it was necessary to present the noise separated in space from speech. The head acts as an acoustic barrier that attenuates the signal on the far side of the head compared to the near side. The effect is greater for high frequencies, and is approximately 7 dB in the speech frequency range. Firstly, the signal-to-noise ratio was determined for the reception of speech with the speech and noise presented from directly in front. The noise source was then separated and moved to say the left ear and the signal-to-noise ratio adjusted for speech reception. It would then be expected that on the left side the noise would have to be reduced when testing the left ear to achieve the same speech reception threshold (SRT). When testing the right side, the speech signal intensity could be reduced to achieve the same SRT. In the binaural case it could be reduced even further suggesting that not only was there a head shadow effect, but a "squelch" effect. When the data on four subjects were analyzed there was a very significant head shadow effect of 4-5 dB. A "squelch" effect was marginally significant at 1-2 dB.

10.2 Bimodal hearing

With bimodal stimulation a number of patients could fuse acoustic stimulation in one ear with electrical stimuli in the other ear with an overall improvement in speech understanding, both in quiet and noise. Loudness summation seen for acoustic stimulation in one ear and electrical in the other needed to be controlled in the bimodal presentation of speech. There were significant benefits also reported by Blamey, Clark and colleagues for sound localization and hearing speech in the presence of spatially separated noise.

11. Speech and spoken language discoveries

After Clark's cochlear implant research had been established by the US Food and Drug Administration as effective and safe for adults who had hearing before going deaf he was then prepared to implant children born deaf to see if they were be able to develop the right neural connections to be able to understand speech with electrical stimulation. Would they be able to use the strategies developed for adults who had hearing before going deaf?

11.1 The miniature receiver-stimulator for children

The implant was modified by Cochlear Limited in collaboration with The University of Melbourne Research team for use on children, in particular magnets were placed in the implant transmitting and receiving coils to allow ease of alignment.

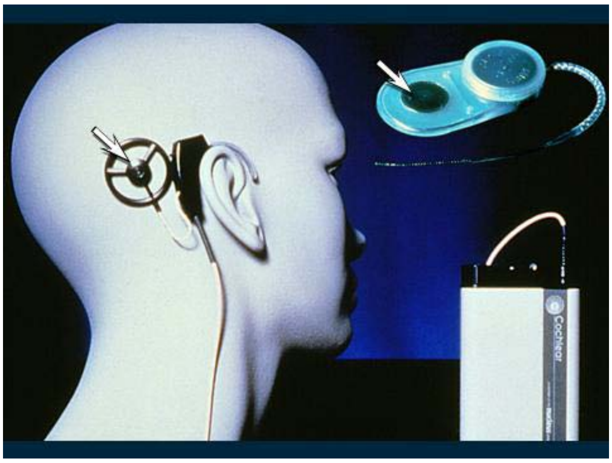
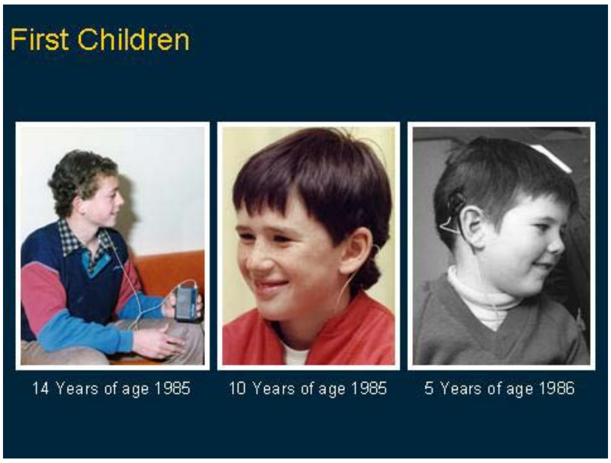


Figure 36: The miniature receiver-stimulator for children

11.2 The first three children to be operated on by Clark in 1985 and 1986

The first three children Peter aged 14, Scott 10 years and Bryn 5 years were operated on in 1985 and 1986 by Clark and his assistants at the Royal Victorian Eye and Ear Hospital. Following improved speech perception results on these children in Melbourne, a world trial was undertaken in 1987 for the US FDA using the F0/F1/F2 and "Multipeak" strategies. Up to 60% of children were able to reach open-set word recognition post-operatively. In 1990 the FDA announced that the 22-channel cochlear implant was safe and effective in enabling deaf children from ages two through 17 years to understand speech both with and without lipreading. It was the first cochlear implant to be approved by any world regulatory body for deaf children.

Figure 37:The first three children to have the University of Melbourne (Clark) implant in 1985 and 1986.

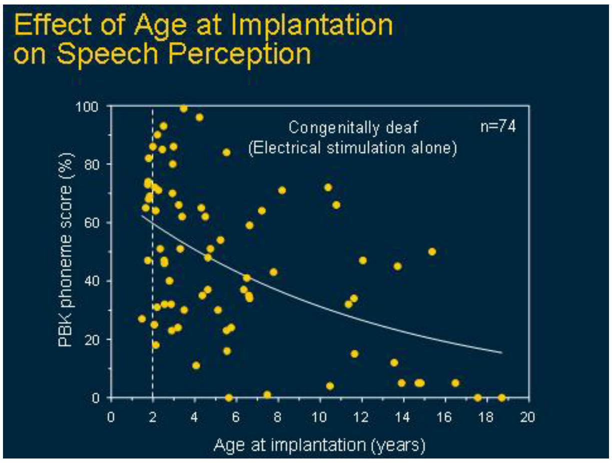


11.3 Clark and Dowell have discovered the effect of age and plasticity on speech results

It was next important to know whether electrical stimulation of the auditory nerve during the early plastic phase of brain development would lead to better speech perception in infants and young children. Clark's research showed there was a trend for better speech perception the younger the child.

For this reason Clark undertook further biological studies when he was awarded a 5 year contract to the US National Institutes of Health. He addressed important safety issues in this young age group, namely the effect of head growth, and prevention of a Pneumococcal middle ear infection spreading to the cochlea with the risk of meningitis. It was only after the safety studies were complete, and showed minimal risk that he carried out operations on young children.

Figure 38: The effect of age at implantation on speech perception results.



11.4 Clark, Dowell and colleagues discovered that children borne deaf can have speech results are comparable to those of adults with hearing before going deaf if they are operated on at a young age

Clark and Dowell and colleagues have discovered, as shown in (Figure 39), that children operated on under four have open-set phoneme, word and sentence scores shown in orange that are similar to those in the postlinguistically deaf adults who had hearing before going deaf shown in blue.

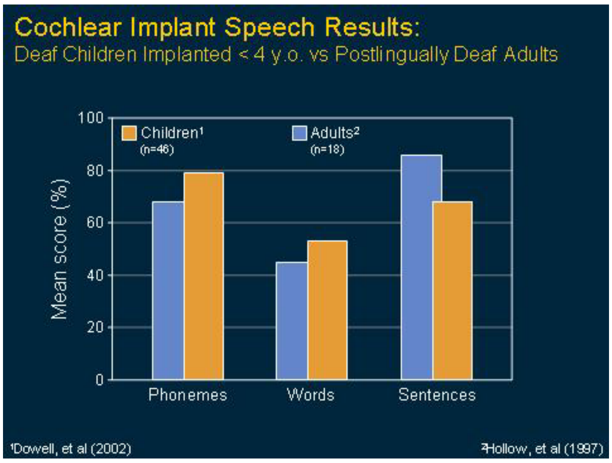


Figure 39: Cochlear implant speech results: deaf children implanted less than 4 years of age vs Postlingually deaf adults.

11.5 Clark with colleague Busby discovered the development of perceptual abilities for pitch and loudness perception in young children and how this leads to speech perception

Concurrent research was undertaken by Clark with Busby on early-deafened children to determine the development of perception skills of importance for speech understanding. It was shown by Busby and Clark [2000] in early-deafened children that the discrimination of electrode place was worse if there was a long period of hearing loss, or the child was implanted at an older age. The data suggested that exposure to sound or electrical stimulation during the “plastic” phase of brain development would be required for this perceptual skill to develop. In addition, the better the discrimination of electrode place in the apical turn the better the closed-set speech perception score.

The ability to discriminate place of stimulation varying over time was also an important skill for late-deafened adults (post-linguistically deaf) in understanding the dynamically changing speech signal, and for this reason it was also studied in children deafened early in life [Busby and Clark 2000]. The early-deafened children (pre-linguistically deaf) were less successful than late-deafened adults in discriminating electrode place trajectories, and this correlated with speech perception scores. It was also found that the discrimination of place trajectories had developed by the age of three years.

In addition it was considered that the ability of children to rank the pitch of electrodes monotonically with the electrode place of stimulation (rather than discriminate electrode place) would be an important determinant for speech perception. The speech scores in implanted children with and without the ability to rank the pitch of electrodes correctly, are shown in Figure 40. It can be seen that not all children who could rank electrode pitch (58%) had good speech perception results of 30% or more. This suggested that the development of neural connectivity for place discrimination or pitch ranking is not the only factor for learning speech. Other factors could be temporal processing or the development of language.

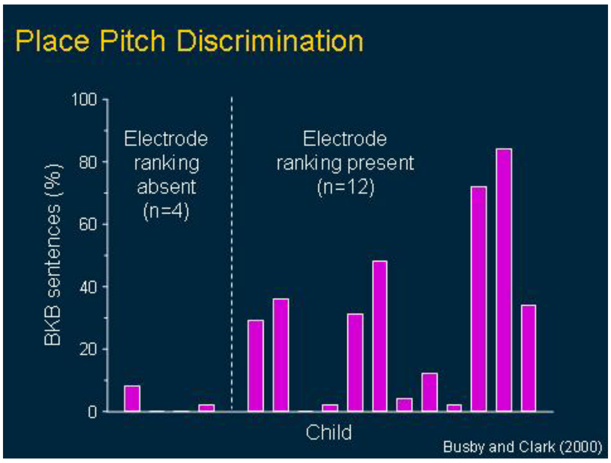


Figure 40: Pitch ranking according to whether pitch changes monotonically with electrode position.

Finally it has been established by Dettman and Dowell in the University of Melbourne’s Clinic at the Royal Victorian Eye and Ear Hospital that if children are operated on under 12 months of age, given an education that concentrates on developing listening skills the can achieve excellent spoken language and an observer would not know they had a severe-to-profound hearing loss. This ability is illustrated in Figure 41. This shows that for some implanted children their equivalent age increases at a rate faster than a child with good hearing. This is a result that Clark could not have dreamed of when he commenced his research let alone his sceptics and doubters.

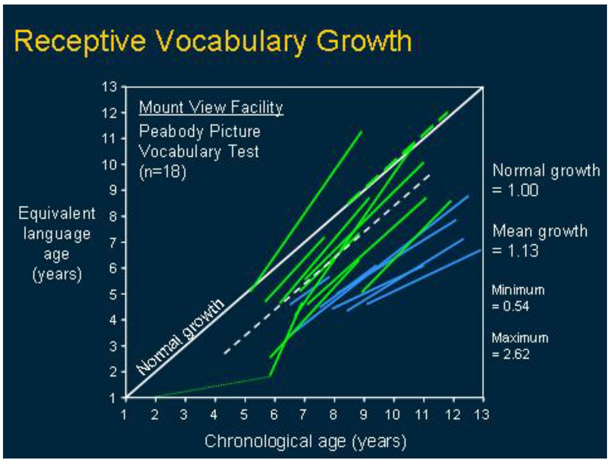


Figure 41: Growth in receptive vocabulary

A: Speech understanding with the multiple – channel cochlear implant: interfacing electronic technology to human consciousness. Plenary address, Interspeech 2005 – Eurospeech conference, Lisbon

B: The multiple – channel cochlear implant: The sensory interface between the world of sound and human consciousness. Graeme Clark, A principal speaker, Frontiers in Medicine at Nobel Forum: Cochlear Implants from Bench to Bedside, Karolinska Institutet.