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An interview with Professor Gus Born

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Abstract

This article is taken from an interview with Professor Gustav Victor Rudolf Born (known as Gus), and focuses on his personal reflections and his distinguished career. Prof Born's innovative research led to the development of a pioneering device, the aggregometer, which opened up the field of platelet research. In this article, Prof Born gives his modest insight into the early stages of his career and the impact Hiroshima had on his decision to work on thrombosis and haemostasis. He details the key events that led to development of a machine which had a revolutionary effect on diagnosing platelet-related diseases and the development of antiplatelet agents, thereby making it a world-wide success and saving so many lives.

Gus Born: the early years

Gus was born in 1921 into a middle-class family in Göttingen, Germany, to Hedwig Born (née Ehrenberg) and Max Born. Gus's mother was a writer and poet and his father was renowned in the scientific community, as he was one of the founders of quantum mechanics (for which he received the Nobel Prize in Physics in 1954). In September 1933, when Gus was just twelve years old, due to the unrest in Germany, the Born family were forced to leave their home. Gus's father, who was a Jew, had sought guidance from his close friend, Albert Einstein, who advised Max to leave Germany at once.[1] Gus's father had a job offer at the University of Cambridge, which he accepted, and the family relocated to England.

"The Born family owes everything to Britain – our very lives when the British people first took us in, and again later when Churchill's courage and steadfastness prevented a German invasion, as well as everything else – livelihood, friendship and love. No wonder that the Born's love and cherish their adopted country!" [2]

Gus, had aspirations of becoming a historian of democratic institutions, he was very interested in Victorian times and was a self-confessed expert on Gladstone and Disraeli, however Gus's father foresaw the war and advised him to study medicine "*then you won't need to kill people and you are less likely to be killed yourself*". Gus thought it was sound advice; he therefore went on to study medicine in Edinburgh. Gus qualified in the height of the war in January 1943. The family had been naturalised before the war and so after six months residency Gus was called up into the army, upon which he served nearly four years in the Far East as a Medical Officer in the Royal Army Medical Corps. When the war ended, Gus was on the occupation force for Japan and was one of the first three medical doctors to attend Hiroshima after the atom bomb had been dropped; this was obviously a horrendous and very emotional time, Gus stated "*it's something that you never forget*". Gus saw first-hand the people who had been killed immediately by the bomb, but there were also thousands dying of bleeding, their bone marrow decimated by the radiation and their platelets not clotting. Horrifically there was nothing that could be done about it. That was the driving force for Gus's interest in platelets, to find a way to save future lives.

Family and inspirations

Throughout Gus's career, it was apparent that fellow prominent scientists influenced his work a great deal. However, family was hugely important to him; he spoke fondly

about his wife, Faith (née Maurice-Williams), a doctor, and Gus reminisced about his brilliant father, who was a warm and friendly person described as "*humble and brave".* His father had the choice of becoming a professional pianist but was given a maths PhD problem to solve, and solving this took him down an academic route instead. Nonetheless, alongside science, music has always been part of the Born family life; Gus himself was an accomplished flute player and played semi-professionally in Oxford, he even took his flute with him to war. Gus has five children, two of whom are prominent in their arts careers; Gus's daughter, Georgina Born, is a Professor of Music and Anthropology at the University of Oxford, and Gus's son, Sebastian Born, was an associate director of London's National Theatre.

Pioneering the way for platelet research

Gus's curiosity in platelets was piqued when after the war he became a DPhil student in the Pharmacology Department at the University of Oxford. As a postdoctoral researcher, Gus worked with a well-known biochemist, Hugh Blaschko, on the then recently discovered association of adrenaline with adenosine triphosphate (ATP) in adrenal granules.[3] It was during this time that Gus had an idea; he had heard that platelets had large amounts of amine (5-hydroxytryptamine [5-HT], also known as serotonin) and he wondered whether the storage in platelets was the same as the adrenal for adrenaline, and it turned out that his hypothesis was correct. Gus's first publications were on the storage of 5-HT in platelets.

Gus was interested in experimental pathology and so went on to work at the Sir William Dunn School, University of Oxford (he spent many years at Oxford, up until he was awarded a Chair position at the Royal College of Surgeons in 1960; for an appreciation of Gus's research path, see Fig 1 in Nurden et al.[4]) Initially at the Sir

William Dunn School of Pathology, Gus worked with Howard Florey, Professor of Pathology (who helped develop penicillin and was awarded a Nobel Prize for this work in 1945).

"Howard Florey to this day is my hero."

Gus talked fondly about Florey, recalling that he was very much a no nonsense man, with a wonderful sense of humour; Gus was in awe of the fact that Florey was responsible for penicillin around the world during the last half-century, when Florey took it from Fleming's discovery to developing the drug.

Florey mentored Gus and suggested to Gus that he should complete a year in London learning biochemistry. Gus gained the experience and went back to Florey who sent him to work with John Barnes at the Toxicology Unit of the Medical Research Council (MRC). At the MRC, Gus recalled one notable episode when Dr John Parker, who came from a very poor background and worked his way up, was offered a very lucrative position twice his salary at the Military Toxicology Unit in Porton Downs Science Park, but he turned it down as "*he didn't want anything to do with poisoning people*". Gus always remembered this and was impressed with John's ethos and stood by it in his life.

After 2½ years at the Toxicology Unit, Professor Geoffrey Dawes *FRS*, from the Nuffield Institute of Medical Research offered Gus a job with him in Oxford (Professor Dawes later went on to become the Director of the Nuffield Institute for nearly 40 years). For the next 3 years, Gus worked at the Nuffield Institute, helping out with Professor Dawes "*brilliant work*" on new-born lambs;[5] Gus's name is on many papers from that period of a mutually successful endeavour. Professor Dawes

was very generous with Gus's time, and allowed him to also carry out platelet research; thus in 1953, Gus started working on platelets.

The development of the aggregometer

Gus gained his DPhil in 1951 and during this time, in, what Gus describes as his "*very boring PhD*", he was measuring the effects of an extracellular enzyme (exoenzyme) on bacteria.[6] He had a suspension of bacteria which was turbid, and as he added the enzyme, the suspension cleared. Gus had an idea: "*wouldn't that be nice to follow the method with the platelet aggregation, because that's what platelets do as their function*". Gus then devised a "*simple, little device*", and it worked well; consequently, this was the first aggregometer.

In 1960, Gus was given his own department in the Royal College of Surgeon's in London; he took under his wing a "*brilliant and lovely*" Polish man called Zabikowszki, who was Gus's workshop technician. Together they built the very first aggregometer. The first paper, which detailed the use of an aggregometer, was in Nature in 1962 (Figure 1);[7] this has been cited over four thousand times.

Initial aggregometry traces were recorded as individual points at fixed time intervals, which Gus simply relayed by hand without any curve smoothing. This turned out to be ingenious; indeed it allowed Michael Oliver, Professor of Medicine from the University of Edinburgh, Gus's friend and co-worker, to notice an inflexion in the curve, a fact that was missed by Gus Born in his early work. This gave rise to the notion of the all-important secondary phase of aggregation, now vastly recognised as key in platelet response amplification, and the target of clinically-used antiplatelet therapy such as aspirin and ADP $P2Y_{12}$ receptor inhibitors. Gus discussed it good-

naturedly, as "*something he had completely missed*", and was delighted that Michael Oliver and his co-workers discovered it, described it, and that many people worked on it.

Gus initially thought the aggregometer was a "*toy*" just to use for platelet work, and then it became a major success. Gus was never tempted to patent the aggregometer, and does not regret it; Gus remembers as a student of Florey's, that Florey himself did not patent penicillin.

"*Florey said that you shouldn't patent anything in medicine*".

Life after the invention of the aggregometer

In many ways, the aggregometer opened up a field of research; prior to the aggregometer, researchers did not know how to work with platelets. There was a lot of industry interest in the instrument, at least twelve manufacturers followed suit and started making the machines. Companies would exhibit the machines at conferences all over the world; Gus would often attend these meetings and would visit the companies' stands. Once, Gus was even given one of the machines for free!

From the invention of the aggregometer, much of the basic information came from Gus's lab; most importantly, Gus and Michael Cross discovered the first inhibitors, they worked very well, particularly adenosine (Figure 2).[8] Gus went on to refine the aggregometer, for example, with the use of the firefly extract for ATP release from platelets; Gus was the first person in Britain to measure ATP with firefly extract. Tragically, Michael Cross was killed in a plane crash. This was a huge loss to Gus'ss team,[9] but the team had to continue and as a matter of course they looked at

anti-thrombotic/anti-platelet drugs. Gus carried out a lot of work *in vivo*, and the first anti-platelet effects he actually tried out on himself, taking aspirin![10]

For Gus, the aggregometer was a means to an end; he had scientific and medical questions to answer which he could do with his machine. He was happy to collaborate and contribute to scientific discoveries. Thus, when Helen Payling Wright, who was working on platelets and vitamin C, heard about the machine, Gus welcomed the collaboration and happily worked on platelets and scurvy. They discovered together that scorbutic platelets don't aggregate well and they went on to publish a paper on platelets and scurvy in The Lancet in 1967.[11]

Gus talked fondly of his close friend, Sir John Vane; in 1970 Vane (who, at the time was a Reader in Gus's department), came into Gus's office and declared, *"Gus, I know how aspirin works!"*. That day, he performed the experiment using the superfusion technique, and he showed that aspirin induces a formation of what had just been called prostaglandins, by the gut. By evening the discovery had been made, which played a key role in the award of the Nobel prize in 1982 with Sune Bergström and Bengt Samuelsson for "their discoveries concerning prostaglandins and related biologically active substances".

Vane also discovered prostacyclin and its inhibitory effects on platelets, which he described with the use of the Born aggregometer.[12] The whole discovery of prostaglandins and their biological effects Gus described as "*wonderful".* These are some of many examples where Gus lent his considerable intellect and expertise, with insatiable curiosity, good humour and humility.

Concluding remarks

The journey to the invention of the aggregometer came out of a strong desire to help people after seeing the horrors of war. Gus's flashes of perception and accomplishment bely the fact that Gus still referred to his invention as a "*hyper-simple machine*"; this machine, which has in fact saved so many people's lives through the discovery of antiplatelet drugs.

Acknowledgement

Professor Gus Born was a kind, thoughtful and generous man, and we are grateful to have been able to meet with him and for sharing his personal reflections and thoughts for discussion.

Declarations of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Figure legends

Figure 1: The first published platelet aggregation tracing in response to ADP, using the Born aggregometer

Reprinted by permission from Springer Nature; Born GVR. Aggregation of Blood Platelets by Adenosine Diphosphate and its Reversal. Copyright Nature (1962)

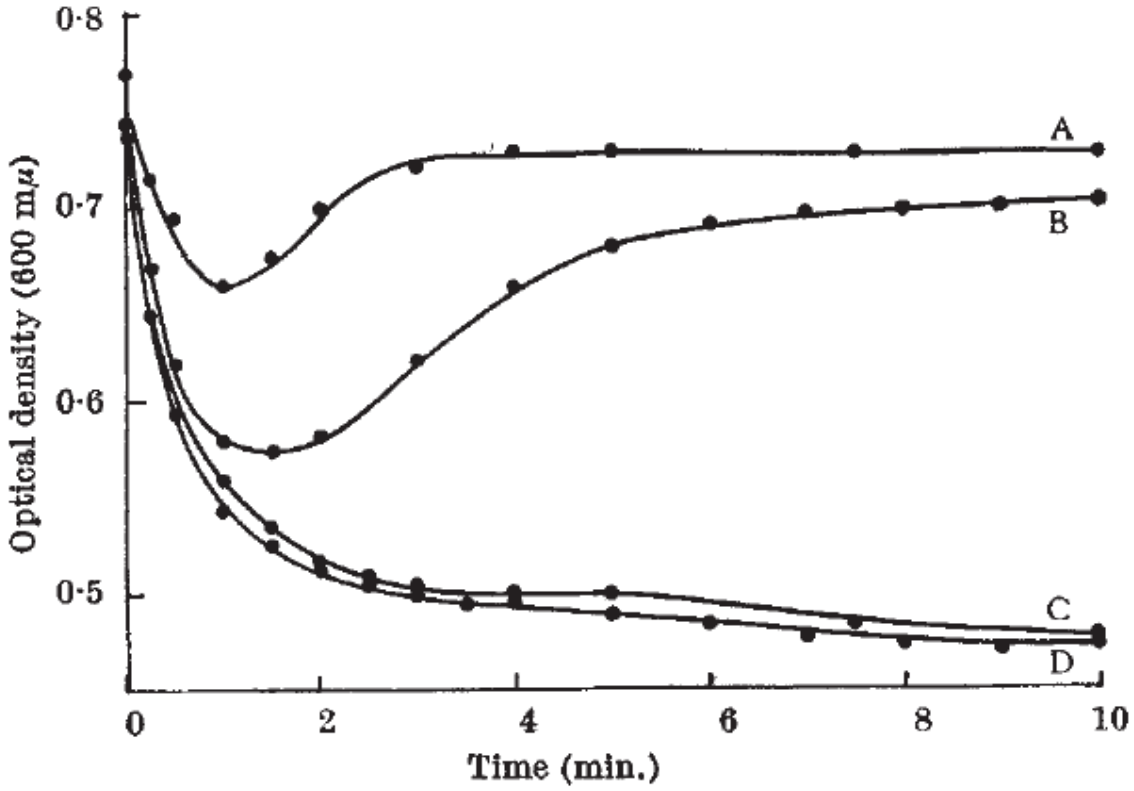


Fig. 2. Effect of adding ADP on the optical density of plasma containing $4 \cdot 75 \times 10^8$ platelets/ml. ADP was added at 0 min. to give the following concentrations: $2 \cdot 5 \times 10^{-7}$ *M* (curve *A*); 5×10^{-7} *M* (curve *B*); 1×10^{-6} *M* (curve *C*); and $2 \cdot 5 \times 10^{-6}$ *M* (curve *D*)

Figure 2: The effect of adenosine on ADP-induced platelet aggregation

Reprinted by permission from Proceedings of the Physiological Society; Born GVR & Cross MJ. Inhibition of the aggregation of blood platelets by substances related to adenosine diphosphate. Copyright The Physiological Society (1963)

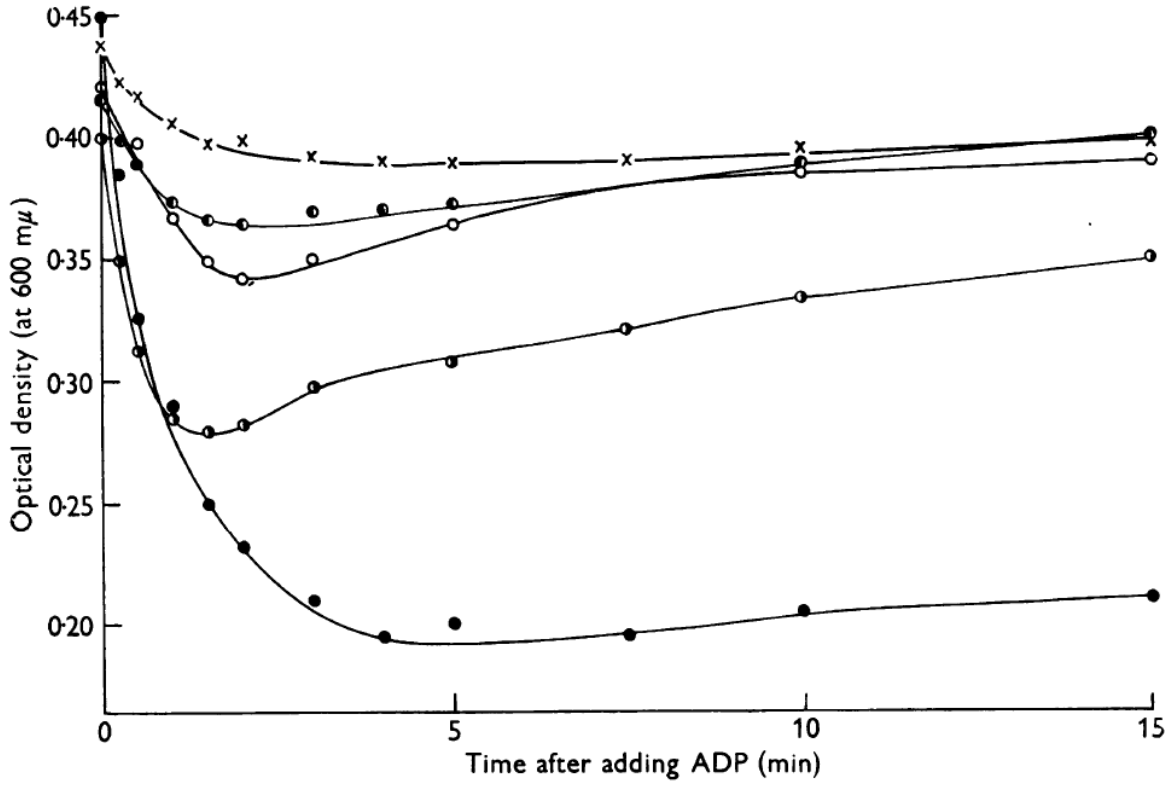
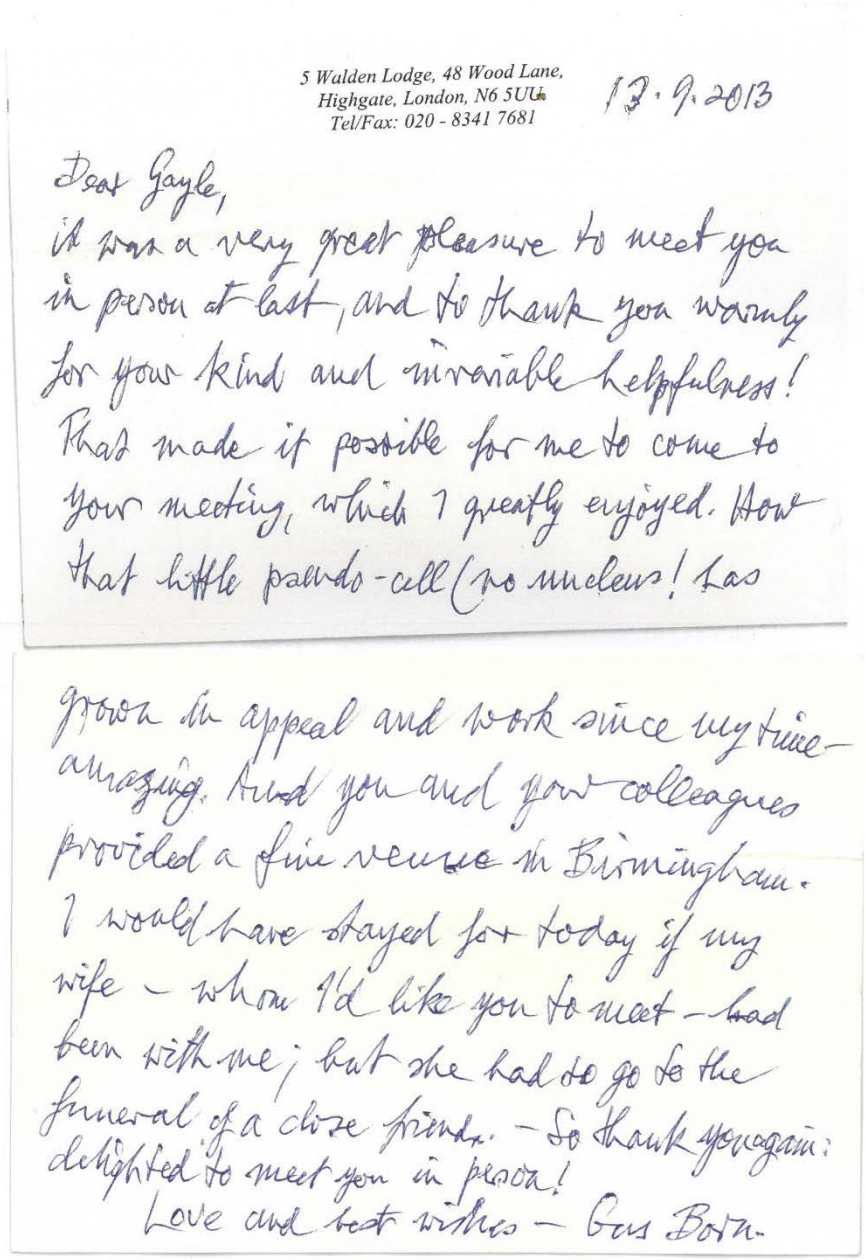


Fig. 1. Effect on the optical density of human plasma of adding adenosine (to a concentration of 1×10^{-5} M) at increasing intervals of time before adding ADP (2×10^{-6} M). The plasma contained sodium citrate (1×10^{-2} M) and $3{\cdot}4 \times 10^{8}$ platelets/ml. Control, i.e. no adenosine added, ●——●; adenosine added: 0·25 min ◑——◑, 2·5 min ○——○, 5 min ◐——◐, and 20 min ×——×, before the addition of ADP. The ADP was added at zero time.

Additional figures for the publication:

A photograph of Professor Gus Born during the interview in 2013



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13.9.2013

Dear Gayle,
it was a very great pleasure to meet you in person at last, and to thank you warmly for your kind and invariable helpfulness! That made it possible for me to come to your meeting, which I greatly enjoyed. How that little pseudo-cell (no nucleus! has grown in appeal and work since my time — amazing. And you and your colleagues provided a fine venue in Birmingham. I would have stayed for today if my wife — whom I'd like you to meet — had been with me; but she had to go to the funeral of a close friend. — So thank you again: delighted to meet you in person!
Love and best wishes — Gus Born.

A postcard to Gayle Halford from Gus after the 2013 UK Platelet Meeting held in Birmingham, UK.

15.9.2013

Vine Cottage, High Street
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Tel/Fax : 01993 830 492

Dear Gayle,

Just a few words of thanks for looking after me so well in connection with your very good platelet meeting. I enjoyed it very much: the science has moved on so far that some of it was beyond me. On the other hand, there was not very much of concern to doctors, and that is a great change from my time. You did your job brilliantly! You made me and I'm sure everyone else so welcome and involved. So I hope we can meet again sometime soon.

With warm thanks and best wishes, also to your family — Gus (Born).

Another postcard from Gus to Gayle Halford commenting on the science at the 2013 UK Platelet Meeting held in Birmingham, UK.