NEWS FEATURE

# BACK TO THE THESIS

*Late nights, typos, self-doubt and despair. Three leading scientists dust off their theses, and reflect on what the PhD was like for them.*

BY KERRI SMITH & NOAH BAKER

CHRIS MADDALONI/*NATURE*

Francis Collins shakes his head in bewilderment as he flicks through the pages of his thesis. "At this point it looks very much like another language," he says, looking with puzzlement at page 71, which contains far more equations than text. The PhD was on theoretical quantum chemistry, and had "absolutely no practical application", Collins says. Looking at it now, "it does feel a little bit like this was another person".

Collins was in his early 20s when he was studying for his doctorate at Yale University in New Haven, Connecticut, modelling how small groups of atoms interact. "A lot of what I did was pencil on paper, trying to solve really complicated calculus equations. It was a little lonely at times," he says. Then, about halfway through his studies, he decided to quit his PhD and transfer to medical school. He ended up finishing the thesis in his spare time. "I spent many nights and many weekends trying to get this written out," he says, with something of a grimace. "I made myself a schedule and tried to stick to it, with my little electric typewriter, banging away."

The writing machines have changed, but the slog is the same. Completing a thesis is a huge undertaking for PhD students, and many struggle to get that far: only around 70% of UK students who embark on doctoral studies actually emerge with a PhD, and the rate is just 50% in the United States. Many of those who do finish move on to careers outside academia; even those who stay sometimes wish they'd spent more time writing papers — the currency of career progression — instead (see page 26).

So what value does the thesis retain, and what lessons does completing one impart? To find out, *Nature* asked three prominent scientists to dig out their theses, thumb through the pages and reflect on what they — and the world — gained from them. What did they learn that could be of value to students who are writing up today? Their reflections, sometimes surprising, are recorded in three short films that accompany this article online (see go.nature.com/297qrah).

Collins's PhD was the start of a stellar career: he famously moved into biological research, identified the gene that causes cystic fibrosis, led the Human Genome Project to completion and now, more than 40 years after writing his thesis, directs the US National Institutes of Health. But that doesn't mean that his PhD changed the world. "Did it really add significantly to the knowledge the Universe contains?" he says. "Well, it would be a rather small contribution, to be sure."

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Watch Collins, Seager and Frith talk about their theses at
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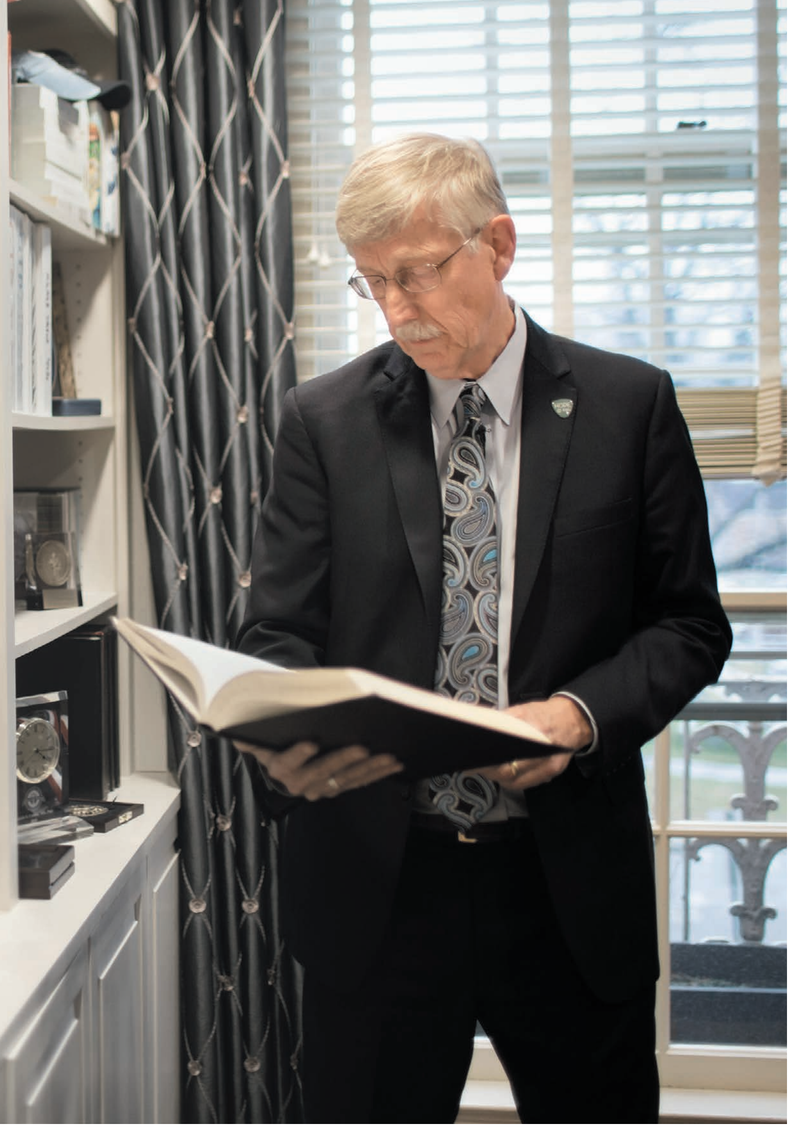
But like others who went 'back to the thesis' for *Nature*, he thinks that what matters was not so much the subject or results, but what he learnt about the process of research along the way. "I think the greatest beneficiary of my PhD was not the Universe," Collins says. "It was probably me."



# FRANCIS COLLINS

## SEMICLASSICAL THEORY OF VIBRATIONALLY INELASTIC SCATTERING, WITH APPLICATION TO $H^+$ AND $H_2$ (1974)

Collins keeps his PhD on a low shelf in his office, next to those from his past students. He pulls it out and places a paternal hand on the thick, leather-bound book. “I think it turned out pretty well. It’s quite a hefty document,” he says.

The road to that document started back in 1970, when Collins arrived in the lab of Jim Cross, a theoretical chemist at Yale. Cross remembers Collins as “a quiet, unassuming man, not particularly sophisticated culturally”. But, he says, “I quickly realized that he was one of the brightest and most broadly based students that I have ever met”.

Collins was tasked with developing theoretical models to explain what happens when a proton is fired at a hydrogen molecule: how does the energy of the two bodies dissipate, and could the hydrogen be coaxed into another state? Day after day, he sat at his basement desk, tackling calculus equations and writing corresponding computer programs in Fortran. He used a machine in the university computer centre to punch the programs onto cards, then waited until after 1 a.m., when electricity was cheaper, to feed the cards into the mainframe computer. “It did make me begin to wonder, OK, is this the right path for me?”

It wasn’t — something Collins came to realize during an all-nighter about halfway through his studies. He was talking to a fellow graduate student, Jay Gralla, who was examining how molecules of RNA fold up into secondary structures. The broader aim was to understand the rules by which genetic information in RNA and DNA is used to build biological systems. Collins was blown away. “I was astounded that I had missed this whole thing about biology — that it was digital, it was an information system, it did have principles,” he says. “It was a revelation.”

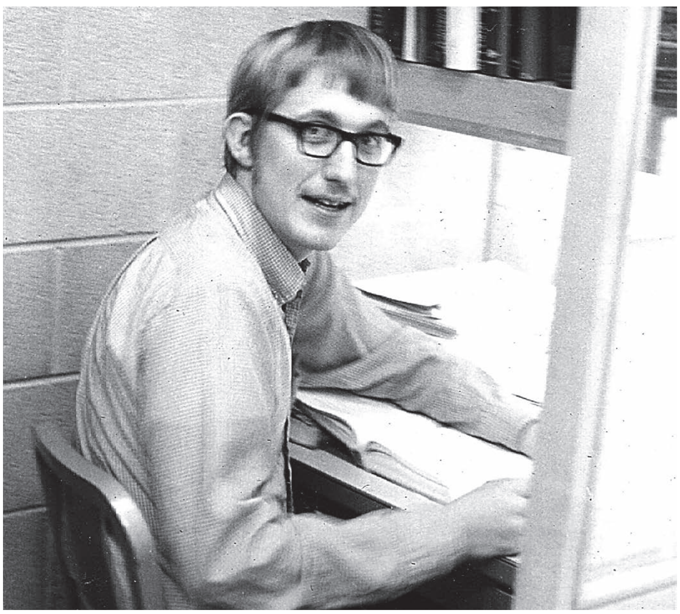
Shortly afterwards, Collins decided to switch to medical school. “That was a wrenching time,” he says. He was drawn to explore biology and medicine, but he also had a growing family, financial strains and “all kinds of self-doubts”. He also didn’t know if he’d actually done enough work to complete his PhD — but Cross told him to write it up anyway. Collins stayed behind in New Haven to write, while his wife and young daughter left for the family’s new home in North Carolina. He still couldn’t get it done before his medical studies started. By the time of his graduation ceremony, in May 1974, he was finishing his first year of medical school and expecting a second child. He didn’t attend.

Several years later, his medical training complete, Collins returned to Yale to work in a molecular-biology lab, and never looked back. The exactitude instilled in him by his PhD stayed with him. He had learned to assess a complex system, strip it down to its component parts and glean insights from it. “That’s something that I do now in my lab,” he says.

His thesis work isn’t in much demand. The model of colliding particles that Collins developed was a good match with others’ experimental findings, and made some useful approximations, but the work has been convincingly superseded by advances in processing power. “These days, a theoretical chemist wouldn’t dream of limiting themselves by doing these approximations,” he says.

Reflecting on it now, Collins is glad that he took the risk of switching fields, and would encourage today’s PhD students to take chances too. Transitions in a career are “when you grow the fastest; they’re when you’re really alive”. And think big, he urges. “If you’re going to study something, study something important. It might be risky, it might be hard, it might not work, but there are too many people spending their time on obvious next steps.”

**“IT DOES FEEL A LITTLE BIT LIKE THIS WAS ANOTHER PERSON.”**



COURTESY OF KATHERINE ALBEN

# SARA SEAGER

## EXTRASOLAR GIANT PLANETS UNDER STRONG STELLAR IRRADIATION (1999)

A flicker of embarrassment crosses Sara Seager's face when she is asked whether there are any mistakes in her thesis. "I definitely have at least one typo. I know where it is, unfortunately. I hate to talk about it." She thinks for a moment, her thesis unopened on the desk before her. "Now that you mention it, I should probably go back and correct it with a pen."

There is little else for Seager to regret about her thesis. She is now a planetary scientist at the Massachusetts Institute of Technology in Cambridge, and, unusually, her PhD helped to found a field. "It might have been one of the first — if not the first — PhD theses on exoplanets," she says.

In 1996, when Seager started her postgraduate studies at Harvard University in Cambridge, just half a dozen planets had been spotted orbiting distant suns. They could be detected only indirectly, mostly by capturing the 'wobble' that an orbiting planet caused in the movement of a star. And the signals were noisy — some astronomers didn't believe that exoplanets were real.

Seager was encouraged to enter the field by her supervisor at Harvard, Dimitar Sasselov, who was keen to take a different approach. Sasselov encouraged Seager to study the atmospheres of exoplanets to find ones that might harbour interesting chemistry or indicate life. This seemed unlikely to work when the planets themselves were so difficult to detect. "It was a big risk at the time: a non-tenured professor and a grad student. Despite the advice otherwise of colleagues in the department, we went ahead," Sasselov says.

Seager built a theoretical model suggesting that it should be possible to see starlight bouncing off a planet that was orbiting its star closely, and that analysing that light would reveal a fingerprint of the planet's chemical constituents, temperature and pressure[1]. Shortly afterwards, during her postdoc, she predicted that it should be possible to spot clouds in the atmosphere, and that one of the easiest elements to detect would be sodium[2].

It was tough going. She derived equations to represent the components of a planet's atmosphere and then, after teaching herself to code, plugged them into the computer models she was building. Her hours were long and isolated, and she would often hit programming bugs that threatened to derail her work. Meanwhile, ex-students from her department were calling from Silicon Valley: their companies were seeking people like her. "I was far from committed to a career in science. I often thought of leaving," she says.

Yet Seager "always expressed a certainty about what she was working on", recalls David Charbonneau, a contemporary of hers at Harvard who now leads an astronomy group there, and was using Seager's theoretical predictions to explain his observational results. He describes her as a


NOAH BAKER/NATURE

# UTA FRITH

## PATTERN DETECTION IN NORMAL AND AUTISTIC CHILDREN (1968)

"I have not looked at this in decades," declares Uta Frith as she retrieves her thesis from a study in her Victorian house in suburban London. The book, bound in sky-blue cloth, nestles on a low shelf, right next to a science-fiction encyclopaedia. She dusts it off with a cloth and opens it to the typewritten title page. "It looks very charming and childish. That's really my immediate impression. I did want a short and an interesting title."

The title is as brief as Frith's PhD was: she had only two years of funding, starting in September 1966, and at the end of 1968 she duly turned in the thesis: 205 pages, typed up by a secretary from her handwritten manuscript. The bibliography is concise, just 10 generously spaced pages. "So little was known about autism at the time that this was the extent of the references I found," she says. Today, the developmental disorder is the subject of several thousand publications each year.

Frith came to London from her native Germany in 1964 to attend a course in abnormal psychology at the Institute of Psychiatry. There, for the first time, she met children with autism, and was "completely fascinated. I still am," she says. She also met her future supervisors, psychologists Beate Hermelin and Neil O'Connor. At that time, autism spectrum disorders were poorly understood and carried a stigma. Those diagnosed were usually only the severe cases, children with profound intellectual and linguistic difficulties. The mainstream view in psychiatry was that autism was a product of a child's upbringing and environment and that distant, unloving parents — particularly mothers — were to blame.

Frith refused to subscribe to that view. "I was always struck, when I met the parents of these children, how little they corresponded to what was told about them in the literature," she says. The question that interested Frith was whether the children might process information differently from other kids. To investigate this, she showed children a simple box containing green and yellow counters that were arranged in a specific pattern. She then covered up the box and asked the child to build the sequence from memory.

She often travelled to hospitals to test children with autism, as well as to nurseries and schools to assess children in her control group. She plugged the data into mechanical calculators that were "very, very noisy" and then took the better part of a day to perform the statistical analysis.

Frith turns to the later pages of her thesis to remind herself of what she found, well aware of how dated — even naive — it might sound. "I'm a little bit afraid of this now. What nonsense can it be?" She

NOAH BAKER/NATURE

fierce intellectual and recalls how annoying she found any imperfection. "She would get frustrated if the data weren't as unambiguous as she would have liked."

Seager says that the day she got her computer code to work "was one of the defining moments of my entire life". And once her work was finished, she didn't have to wait long for her predictions to be tested: in 2002, astronomers including Charbonneau detected the first exo-atmosphere[3], and found that it contained the sodium signature, albeit at a slightly lower level than Seager had predicted. Since then, the field has flourished: 3,285 exoplanets have now been confirmed, and the study of their atmospheres has bloomed. The material in Seager's PhD has been used by astronomers to request time on the Hubble Space Telescope, Keck observatory and other instruments. And although Seager can't erase the sole typo from her thesis, she points out that the papers she published from it are free of mistakes.

Did Seager enjoy her PhD? "Unfortunately, I think the answer might be no." But she does have fond memories of the time she spent writing up her research. "I remember when I was finishing it, I didn't go to any other talks, I didn't really read the news, it was just put the blinkers on and get the job done." She found great satisfaction in devoting herself to a single task, and relished the clarity of thinking that afforded her. "The world goes away", she says. "And so when you're in that zone, actually you're happy."

Seager now tries to make sure that those in her lab have the space to think too. "I do let the students spin their wheels. They have to, or they won't find their own way." And if she could give advice to her younger self, it would be simply: "Hang in there."

As for the thesis itself — a slim, red volume with gold lettering — it's not something she feels sentimental about. "I've met people who, they cry when they give away their kids' baby clothes, but I was never one of those — and I think I felt the same way about the thesis." She's more inclined to look forward. "In exoplanets, the best planet, the best discovery, is the next discovery."

COURTESY OF UTA FRITH

**Uta Frith and her supervisor Neil O'Connor, in 1971.**

showed that children with and without autism both made errors in about 25% of the trials, but that they made different mistakes. Children in the control group tended to follow the pattern too strongly — perhaps placing three green counters together instead of two. Those with autism, however, placed the counters in their own simple pattern, such as green, yellow, green, yellow. Frith proposed that these children impose very strict patterns on the outside world, too, and this idea seemed to correlate with the behaviours that clinicians at the time considered characteristic of the condition — obsessions with particular objects, for example, or disliking change.

Frith saw logic in the children's responses, and felt that they were not necessarily inferior to those of others. "It is presumptuous to think that those patterns imposed by autistic children are any worse than the patterns I have imposed on the data," the concluding paragraph of her thesis reads. "Well, that's quite philosophical," she says, in modest delight.

Frith is aware that she was studying at a golden time. Psychology was thriving in the United Kingdom; she had the undivided attention of two supervisors; and, just as she was coming to the end of her PhD, she was offered a full-time job at a Medical Research Council (MRC) unit where one of her supervisors had just been appointed director. "I was just so fortunate," she says. The post led to a 50-year career with the MRC and University College London, during which Frith showed that children with autism have deficits in their 'theory of mind', the cognitive capacity to understand that others have their own beliefs and ideas. This was an important concept that was "just emerging in primate work" and that she adapted to studies of autism, says Ami Klin, who directs the Marcus Autism Centre at Emory University in Atlanta, Georgia, and whose 1998 PhD was co-supervised by Frith. "She was always extraordinarily open-minded, patient, supportive," he says.

Frith knows that today's PhD students have a much tougher time: funding is tight and academic jobs scarce. But she remains a fan of the PhD as an apprenticeship in research. She learned from scratch how to formulate hypotheses, design experiments and analyse data. "It does mean doing what we might call slave labour for some of the time, but you learn through that, and you can see what it feels like to be a scientist," she says.

"I'M QUITE SURE THAT IT WOULD NOT MEET REQUIREMENTS NOW."

She admits that her thesis is a product of a different era — "I'm quite sure it would not meet the requirements now" — and she is willing to bet that there are mistakes in the text. "But who knows? I haven't read it. Why should I? There's so much else more interesting to read." ■

**Kerri Smith** *and* **Noah Baker** *are multimedia editors for* Nature *in London.*

1. Seager, S. & Sasselov, D. D. *Astrophys. J.* **502,** L157–L161 (1998).
2. Seager, S. & Sasselov, D. D. *Astrophys. J.* **537,** 916–921 (2000).
3. Charbonneau, D., Brown, T. M., Noyes, R. W. & Gilliland, R. L. *Astrophys. J.* **568,** 377–384 (2002).