Modelling the dynamics of the innovation process : a data-driven agent-based approach

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Appendix A

Supplementary information on Chapter 2

Summary

This appendix illustrates how we analyse an innovation process, namely identifying patterns from the large amounts of process data, using the Nylon innovation. Nylon is one type of synthetic plastic material composed of polyamides of high molecular weight, manufactured as a fibre. It was first produced in 1935 by DuPont, which created a revolution in the fibre industry. The products made of nylon range from civil applications (e.g., stocking, toothbrush, ropes) to military usages (e.g., parachutes, flak vests, and airplane tires). An interesting feature of Nylon case is the innovation of a technology gave rise to a new industrial sector. Besides, the many decades of development of Nylon are disturbed by strong events such as the Second World War or the world-wide oil crisis which clearly mark nonlinear dynamics of innovation.

This appendix consists of five parts: (1) the chronological list of events in Nylon innovation; (2) coding scheme; (3) coding Nylon innovation events into pre-defined categories (here we use Hekkert et al. (2007)'s seven system functions as a framework); (4) analyzing the interaction patterns between events; and (5) references.

AA.1 Chronological list of events in Nylon innovation

Time	By whom	Events[1]	References
1926/12/18	Stine, the director of Du Pont's Chemical (Central research) Department	Took the first step to nylon invention; submit a short memorandum entitles "Pure Science Work" to the company's executive committee.	(Hounshell & Smith, 1988a; Hounshell & Smith, 1988b)
1927	Stine	Stine received budget to start a fundamental research unit within Du Pont	(Hounshell & Smith, 1988a; The-Great-Idea-Finder, 2005)
1928	Stine	Hired Carothers	(Hounshell & Smith, 1988a)
1934/3/23	Carothers	Suggested to his assistant, that he attempt to prepare a fibre from an aminononanoic ester.	(Hounshell & Smith, 1988b)
1934/5/24	One assistants of Carothers	On the suggestion of Carothers, assistants drew a sample of synthetic fibre which overcoming the melting problem of earlier	(Hounshell & Smith, 1988a; Hounshell & Smith, 1988b)

[1] The events data are completely literal texts from the internet. We do not want to change the original texts when we analyse.

		attempts. This fibre was Nylon.	
1935/2/28		A "cousin" of this fibre, known technically as nylon 6.6, became Du Pont's most celebrated product.	(CHA; Nohria, 1996)
Summer, 1936	Du Pont's Rayon Department	Business model assessment: Nylon was evaluated as a high quality yarn superior to natural silk, and expected to bring huge market value to DuPont.	(Hounshell & Smith, 1988a)
Summer, 1936	Research Manager	On the basis of these optimistic forecasts, the research manager decided to expand the company's nylon-manufacturing capacity from two to one hundred pounds in order to improve the process and provide material for extensive testing.	(Hounshell & Smith, 1988a)
February,1937	Du Pont's development team	Du Pont's development team had made significant strides toward its goal of producing a standard and uniform product, but no yard had been knitted into stockings.	(Hounshell & Smith, 1988a)

	Everett Vernon Lewis, a Rayon department research chemist.	First knitting test in Union Manufacturing Company in Frederick, Maryland	(Hounshell & Smith, 1988b)
April, 1937		Further testing was done at the Van Raalte mill in Boonton, NJ, and the first experimental stockings were made.	(Hounshell & Smith, 1988b)
July, 1937		By July 1937 Van Raalte had knitted enough material to give Du Pont some definite feedback: the yarn performed quite well; the outstanding defect was the tendency of the stockings to wrinkle during dyeing and the other finishing operations.	(Hounshell & Smith, 1988b)
		A few months later it was discovered that these wrinkles could be eliminated by steam treating the stocking before dyeing.	(Hounshell & Smith, 1988a; Hounshell & Smith, 1988b)
		Thanksgiving and perhaps Christmas came early for DuPont in 1937. The Van	(Hounshell & Smith, 1988a; Hounshell &

		Raalte mills had started turning out "full-fashioned hosiery excellent in appearance and free from defects".	Smith, 1988b)
		The reaction of women to nylon: durable but easily wrinkled and too lustrous and slippery	(Hounshell & Smith, 1988b)
	Preston Hoff of the Rayon Department	Once skeptic, now found good future of the product.	(Betz; Hounshell & Smith, 1988a; Hounshell & Smith, 1988b)
1936, 1938	Two trial facilities: Semi-works (1936) and the pilot plant (1938)	Prototype machinery test	(McVie, 2006)
1937		The nylon polymer produced at the semi-works during equipment testing was not suitable for making yarn for hosiery.	(McVie, 2006)
1937		Nonetheless DuPont found a use for the nylon polymer	(Hounshell & Smith, 1988a;

		made at the semi-works--the amazing new Dr. West's toothbrushes hit the market.	Hounshell & Smith, 1988b; McVie, 2006)
1937		Nylon did not reveal the chemical nature of the new bristles. It simply referred to the material by the name "Exton".	(Hounshell & Smith, 1988b; McVie, 2006)
1938	Executive committee	Authorized a pilot plant of toughly one-tenth of expected production	(CHA)
1938	Du Pont plastics department	Began marketing nylon bristles under the trademark Exton. This offered an attractive entering wedge in the marketplace for nylon. Imperfect polymer produced in the pilot plant could be sold for toothbrush fibres.	(Klooster, 2009)
1938	Stine	Announced the invention of nylon.	(Hounshell & Smith, 1988a)
1939	Carothers	Unveiled nylon to three thousand women’s club members	(Hounshell & Smith, 1988a)

		Full-scale commercial production	(Bellis, retrieved in 2013)
1940		A second plant for nylon production was started in Martinsville, Virginia in 1940.	(Doyle & Stern, 2006)
1940		Nylon was an instant market and financial success when it became available in May of 1940. Production of $9 million sold out with a 33% profit.	(Doyle & Stern, 2006)
1941		$7 million profits on sales of $25 million.	(Doyle & Stern, 2006)
1941		Began pioneering research for the development of products of Orlon, Cardura and Dacron.	(CHA; Hounshell & Smith, 1988a)
1941-1942		All nylon was requisitioned by government and used for making parachutes, ropes, cords, instead of nylon stockings. Production was pushed.	(Hounshell & Smith, 1988a; Klooster, 2009)

1948		New plants in Chattanooga for Nylon. Increase investment in additional plant capacity, justified by new uses of Nylon.	(CHA; Doyle & Stern, 2006)
1951		Sensing that the demand for Nylon could be overwhelming, and perhaps volatile, DuPont licensed Nylon to Chemstrand by building them a 50 million pound per year plant for $110 million.	(Doyle & Stern, 2006)
1960-1980		Worldwide nylon market enjoyed a 10.5% compounded annual growth. Textile consumption grew at about 7.5% per annum, while carpet and industrial consumption grew at over 12%.	(CHA; Doyle & Stern, 2006; Nohria, 1996)
1973		The oil shortages of 1973 and 1979 hit nylon hard. Nylon made no profit in 1975.	(Anonymous; CHA; Doyle & Stern, 2006)
		In 1975, some nylon areas were directed to be cash generators and Fibre's	(CHA; Doyle & Stern, 2006)

		research was cut accordingly.	
1981	Du Pont	After the second oil shortage, DuPont acquired Conoco (as Continental Oil) for $7.6 billion.	(CHA)
1980s	Du Pont	During the 1980s, the amount of capital made available for upgrading DuPont's nylon plants was around 30% less than comparable companies such as 3M, Monsanto, Procotor and Kodak.	(CHA; Doyle & Stern, 2006; Nohria, 1996)

AA.2 Coding scheme

System functions	**Event category**
F1: Entrepreneurial activities	• New company entry, start-ups • Company quits • New technology or business expansion of current companies
F2: Knowledge development	• Technical trial • Experiment • Technical invention • Other R&D related events
F3: Knowledge diffusion	• Joint forces with other companies or institutions • Meetings • Workshops • Personal or informal relationships
F4: Guidance of the search	• Business assessment • Strategic decisions or strategic target • Technical or economic performance result • Entrepreneur's envision • Media report/announcement • Government policy and legislation • Debate
F5: Market formation	• Market stimulation program me (e.g., tax exemption measures, subsidy measures) • Niche market
F6: Resource mobilization	• Subsidy by government • Investments by venture capital • Expansion of manufacturing capacity • Hiring new people
F7: Support from advocacy coalitions	• Direct political lobbies • Indirect imposing pressure on government to issue a certain supporting policy

AA.3 Coding Nylon innovation events into pre-defined categories

Events[2]	Year	F1	F2	F3	F4	F5	F6	F7
Submitted a short memorandum entitles "Pure Science Work" to DuPont's executive committee.	1926	1						
Received budget to start a fundamental research unit within Du Pont.	1927						1	
Hired Wallace Hume Carothers, who later invented Nylon.	1928						1	
Attempted to prepare synthetic fibre	1934		1	1	1			
Invented Nylon, the first synthetic fibre	1934		1		1			
Nylon 6.6 became a market success.	1935				1	1		
Business model assessment: Nylon was evaluated as a high quality yarn superior to natural silk, and expected to bring huge market value to DuPont.	1936				1			

[2] The "Events" are the same events in AA.1. For references, please refer to AA.1.

Started process innovation in order to improve manufacture efficiency.	1936		1	1	1				
Manufacture process achieved a standard and uniform production.	1937				1				
Started application testing	1937		1	1					
Success in knitting Nylon into full-fashioned stockings free from defects	1937		1		1				
Built up two trial facilities	1937				1		1		
Nylon polymer which was not suitable for making yarn was used to make toothbrushes, and turned out a big market success.	1937	1	1		1	1			
Unveiled nylon to three thousand women's club members	1938			1	1				
Full-scale commercial production	1939				1		1		
A second plant for nylon production was started in Martinsville, Virginia in 1940.	1940						1		

Nylon was an instant market and financial success when it became available in May of 1940. Production of $9 million sold out with a 33% profit.	1940				1				
1941, $7 million profits on sales of $25 million.	1941				1				
1941, Began pioneering research for the development of products of Orlon, Cardura and Dacron.	1941	1	1		1				
All nylon DuPont was requisitioned by government and used for making parachutes, ropes, cords, instead of nylon stockings. Production was pushed.	1941				1				
New plants in Chattnooga for Nylon. Increase investment in additional plant capacity, justified by new uses of Nylon.	1948	1			1		1		
Sensing that the demand for nylon could be overwhelming, and perhaps volatile, DuPont licensed nylon to Chemstrand by building them a 50 million pound per year plant for $110 million.	1951			1			1		

Worldwide nylon market enjoyed a 10.5% compounded annual growth. Textile consumption grew at about 7.5% per annum, while carpet and industrial consumption grew at over 12%.	1960-1980				1			
The oil shortages of 1973 and 1979 hit nylon hard. Nylon made no profit in 1975.	1973, 1979				-1		-1	
Nylon made no profit in 1975.	1975				-1			
In 1975, some nylon areas were directed to be cash generators and Fibre’s research was cut accordingly.	1975				-1		-1	
After the second oil shortage, DuPont acquired Conoco (as Continental Oil) for $7.6 billion. This was done to insure a source of petroleum based feedstock.	1981				1		1	
During the 1980s, the amount of capital made available for upgrading DuPont's nylon plants was around 30% less than comparable companies such as 3M, Monsanto, Procotor and Kodak.	1980s				-1		-1	

AA.4 Analysing the interaction patterns between events

Nylon invention (1926-1934)

This period is characterized by a strategic shift of DuPont that leads to the invention of Nylon. In a situation where less resources were available for basic research in DuPont, on December 18, 1926, Charles Stine, the director of DuPont submitted a proposal to DuPont's executive committee entitled "Pure Science Work" (Hounshell & Smith, 1988a) [F1]. In this proposal, he convinced the executive committee to shift the strategy from applied research to fundamental research (Hounshell & Smith, 1988a) [F7]. Since April 1927, the DuPont executive committee decided to allocate $20,000 per month to fundamental research [F6] (Ament, 2005). Using part of this 1927 budget, Stine established a new laboratory for fundamental research [F1] (Ament, 2005; Hounshell & Smith, 1988a).

For DuPont, the technological development leading to the invention of Nylon begins in 1928 when Stine hired Dr. Wallace Hume Carothers from Harvard University [F6], who only agreed to work for DuPont on the promise of a fundamental research project in the pursuit of pure science (CHA). After studying large amounts of polymers cases [F2], in 1929, Carothers published a landmark paper proposing that "polymers were aggregates of small entities rather than true molecules" (Hounshell & Smith, 1988a) [F3]. This paper received favourable comments from numerous sources and increasing recognition in the scientific world (Hounshell & Smith, 1988a) [F4]. By 1929, Carothers had eight men working for him [F6] (Hounshell & Smith, 1988a). Carothers's group began to try an unusual compound [3](DVA) as an attempt to create a synthesized fibre [F2] but failed. In 1930, a new assistant director of the Chemical Department, Elmer K. Bolton, was assigned in Carothers's project (Hounshell & Smith, 1988a) [F6]. He asked Carothers to continue exploring the chemistry of DVA [F4]. In April 1930, Carothers's research group succeeded in producing neoprene synthetic rubber and the first laboratory-synthesized fibre (Hounshell & Smith, 1988a) [F2, F4]. The invention of neoprene, as a promising synthetic fibre, encouraged the fundamental research toward more clearly defined goals (Hounshell & Smith, 1988a) [F4]. But in June 1930, Elmer Bolton replaced Stine as the chemical director, and Stine was promoted to the corporate executive committee (Hounshell & Smith, 1988a;

[3] This unusual compound is a short polymer consisting of three acetylene molecules, divinylacetylene (DVA) (Hounshell, 1988), which later became the first laboratory-synthesized fibre.

Hounshell & Smith, 1988b). This brought a fundamental change in the research philosophy and style (Hounshell & Smith, 1988a). Different from Stine, Bolton emphasized practical applications. Therefore, he put the development of a new synthetic fibre at the top of his research priorities and pushed Carothers to renew efforts on synthetic fibres (Hounshell & Smith, 1988a) [F4]. Bolton was enthusiastic about this synthetic fibres and insisted on putting at least one man on this problem [F6]. In 1934, after some experimental difficulties and depressions, Carothers suggested his assistants to prepare a fibre from an aminononanoic ester [F2, F3, F4]. Under this suggestion and supervision, on May 24, 1934, one of the assistants drew a sample of synthetic fibre, which was Nylon [F2].

Interaction pattern analysis

In this period, the system functions of the Nylon innovation system were beginning to take shape. A careful examination of the relationships between the events in this period finds the following “lead-to” chains: “Carothers’s research group test synthetic rubbers” (F2, F3) lead to “success in producing the first laboratory-synthesized fibre”; the success leads to “high expectancy of scientific experiments” [F4]; the high expectancy leads to “the new chemical director, named Elmer Bolton, continued emphasizing and supporting application research of synthesized fibre” [F6], which further leads to “Carothers’s research group continued scientific experiments” [F2]. This chain of “lead-to” events constructs a self-reinforced reaction loop, initiating from knowledge development [F2], going through knowledge diffusion [F3], guidance of the search [F4], resource mobilization [F6], and finally going back to the initial knowledge development function [F2]. As such, they form a cycle, as illustrated in Figure AA.1. Because these activities contribute mainly to technological discovery and development, we call it technological cycle.

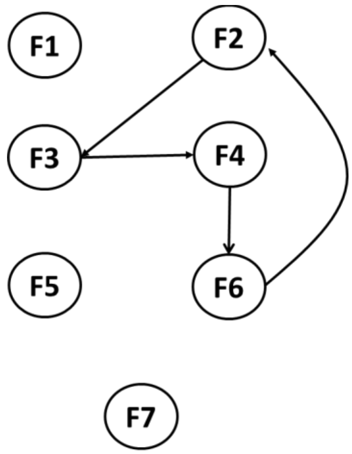

Figure AA.1 Technological cycle in Nylon innovation

Technological improvement (1935-1937)

This period focuses on technological improvement and application or exploitation of Nylon. After the invention of Nylon, the research team tried 81 possible variants of nylon [F1]. During these trials, a “cousin” of Nylon (technically called nylon 6.6) was first prepared on February 28, 1935 and became DuPont’s most famous product (CHA) [F2, F4]. By the summer 1936, DuPont had enough production of Nylon and was ready to develop Nylon production on a larger scale (Hounshell & Smith, 1988a)[F6]. DuPont’s Rayon Department did a business evaluation of Nylon [F2] and reported that the new fibre was “a high quality yarn superior to natural silk” with a huge market potential at two dollars a pound, roughly the price of silk (Hounshell & Smith, 1988a)[F4]. Encouraged by this high expectation, the research manager decided [F4] to expand the company’s Nylon-manufacturing capacity to improve the process and prepare enough material for extensive testing [F6] (Hounshell & Smith, 1988a). In February 1937, DuPont’s development team was successful in producing a standard and uniform product [F2], but still with knitting problems (Hounshell & Smith, 1988a) [F4]. Intensive testing was carried out in pilot plants[4] [F2] until April 1937 when the first experimental stockings were made (Hounshell & Smith, 1988a)[F2, F4] (F2→F4→F6→F2). By July 1937, there was enough material available for further step

[4] According to Hounshell (1988), the first test was in February 1937 in Union Manufacturing Company in Frederick; and the further testing was done at the Van Raalte mill in Boonton, NJ, and the first experimental stockings were made in April.

testing (Hounshell & Smith, 1988a)[F6] and to give DuPont some definite feedback on their investment in the new material. Nylon represented a well performing yarn but suffered from wrinkle problems during dyeing and other finishing operations [F4]. Focusing on solving these defects, the development team planned trial experimentations [F2] and succeeded in eliminating the wrinkles by steam treating the stocking before dyeing [F4]. Before Christmas in 1937, DuPont had developed "full-fashioned hosiery" with excellent appearance and free from defects [F2, F4].

Interaction pattern analysis

The dominant driver in this period is still the technological cycle, which was reflected in the "lead to" chain of events: F2→F4→F6→F2. The dynamics of this sequence of events involves positive scientific results [F2] feeding back on guidance of the search [F4], which lead to continuous resource investments [F6] to technological development [F2]. Obviously, this cycle mainly involves the following system functions: knowledge development [F2], guidance of the search [F4], and resource mobilization [F6]. A contrast with the previous technological cycle, it is interesting to notice that the knowledge diffusion function [F3] disappeared from the main activities, as shown in Figure AA.2. That's because DuPont wanted to enter the market first and therefore kept the material a secret for competitors. Just as Everett Vernon Lewis, a Rayon Department research chemist, later recalled that: the security precautions during his task of taking a few carefully measured skeins of yarn for a knitting test to the Union Manufacturing Company in Frederick, Maryland, were more stringent than those he encountered later in the Manhattan Project (Hounshell & Smith, 1988a). What is needed to be stressed is that the market formation function remains weak. Most attention was devoted to technological development and R&D [F2] yet no customers were involved in this development process [F5].

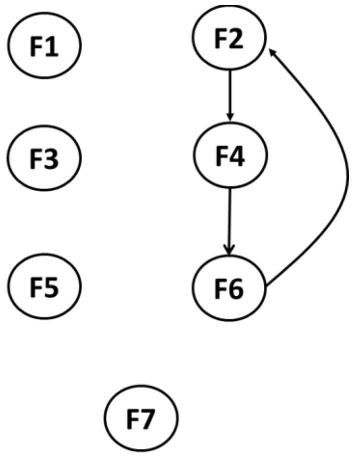

Figure AA.2 The second technological cycle in Nylon innovation

Market entry (1936-1940)

This period is characterized by the first market introduction of Nylon products. The initial market entry of Nylon can almost be considered an accident. During the testing of prototype machinery in semi-works in 1936 [F2], the nylon polymer produced was found not suitable for making yarn for hosiery [F4]. Nonetheless, DuPont found it useful as a material to make bristles [F2, F4]. In 1937, DuPont Plastics Department began marketing nylon bristles, under the brand name Exton in Dr. West's toothbrushes and it was a big market success [F4]. This created an attractive niche market for nylon [F5], where imperfect nylon polymer could be used to make toothbrush fibres. In 1938 January, DuPont's executive committee authorized a pilot plant to expand the production. But still DuPont didn't reveal what material was of these bristles [-F3].

On October 2, 1938, Charles Stine announced the invention of Nylon [F3]. And in the next year, he exposed Nylon to three thousand women's club members [F1, F5, F7]. After publication of Nylon, it became an instant market and financial success in 1940 [F4, F6]. Because the market success of Nylon, DuPont's Pioneering Research began developing other products made of Nylon [F1, F2]. At the same time, DuPont invested in additional plant capacity in South Carolina, Tennessee, and other places [F1, F6].

Interaction pattern analysis

The event sequences reveal two cycles in this period: (1) an entrepreneurial cycle and (2) a market cycle. The dominant cycles in this period have shifted from technical to entrepreneurial and market cycles. The dynamics within this period presents a self-reinforcing role of entrepreneurial activities, identified in the “lead-to” chain: F1→F5→F4→F6→F1, as shown in Figure AA.3. This event sequence was initiated by entrepreneurial activities, and went through market lobby/creation, resource mobilization and led to further more entrepreneurial activities, which shows a self-reinforcement cycle. We call it entrepreneurial cycle. As it shows, the most developed system functions in this period are entrepreneurial activities [F1], market formation [F5], guidance of the search [F4], resource mobilization [F6] and occasionally knowledge diffusion [F3] and support from advocacy coalitions [F7]. Therefore, the seven functions were all involved.

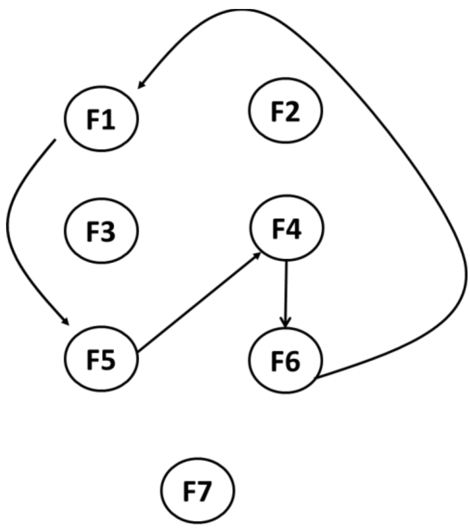

Figure AA.3 Entrepreneurial cycle in Nylon innovation

The first market introduction of nylon, namely using Nylon to make toothbrushes [F1], was a great success. The good market performance provided a guaranteed demand for Nylon [F5, F4] and resulted in DuPont’s further investments in Nylon application [F6], such as developing new products, investing in new pilot plants [F1]. Similarly, the activity that Charles Stine told three thousand women’s club about the invention of Nylon is classified as lobbying for potential customers [F5, F7]. It established an important niche market for Nylon, which is considered to be an essential step for Nylon’s commercialization. This publication of Nylon brought such great market success that it stimulates DuPont’s further investments in Nylon development and diverse products made of Nylon. At the same time, good market performance encouraged DuPont to explore new businesses and new markets of Nylon, which further led to a better market performance (F5→F4→F1→F5)., This sequence of event presents the driving power of market. We call it a market-driven cycle, as shown in Figure AA.4.

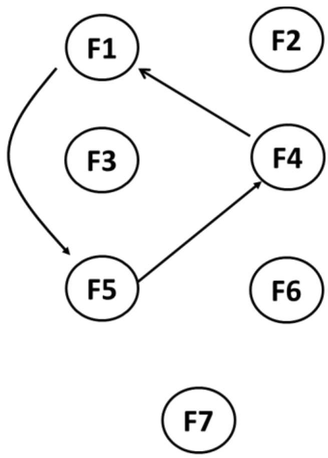

Figure AA.4 Market-driven cycle in Nylon innovation

It is interesting to note that (1) in this period all of the seven system functions have entered the Nylon innovation system; and (2) the cycles which dominate the development are significantly different from the previous ones. In this period, system functions F1, F5 and F6 play a central role to the Nylon development.

Market mature (1941-1970)

This period is characterized by a fast market growth. Nylon’s expansion in the market place was stopped by the Second World War between 1941 till 1945. During the Second World War, all Nylon products were requisitioned by government [F4]. In fact, in order to escape the monopoly of Japan in the silk market, the US government was eager to develop a substitute for silk [F4, F6]. Pushed and facilitated by US government, DuPont increased its Nylon production threefold [F6] and extended the application of nylon from civil into military uses, such as flak vests, parachutes, cords, instead of stockings [F1, F2, F5]. After the war, nylon uses expanded quickly, involving textiles, carpets, and industrial [F1, F5]. The huge demand and market of nylon guided DuPont's investment in additional plant capacity in Chattanooga, Tennessee (1948) and in Camden, South Carolina (1950) [F4, F6]. The worldwide nylon market enjoyed a fast growth with production going up to 1 billion pounds annually. The radical shift to continuous processing of nylon was delivering quality and profitability beyond all expectations. And it continues to do so for longer than could have been predicted.

Interaction pattern analysis

In this period the Second World War plays a critical role and serves as a catalyst. The war created new military demands of nylon [F5], stimulated DuPont to increase investment in Nylon production [F4, F6] as well as in technical research in terms of new products [F2]. After the war, the accumulated market demand [F5] triggers more resource allocation into nylon development [F6] in the purpose of nylon application exploitations and production expansion [F2]. A large diversity of nylon products, resulting from technical development, leads to much more market demand after the war [F5]. A self-reinforcing loop is identified, which starts from market stimulation [F5], leading to high expectations [F4] and increasing resource allocation [F6], followed by enhanced knowledge development [F2] and improved technological performance, thereby increasing market demand further [F5]. Given the centrality of market formation in this cycle, it makes sense to call it market-driven cycle, as illustrated in Figure AA.5. In this period, it is found that system functions F2, F4 and F6 play a central role again via the system function F5. Comparing with the first market-driven cycle shown in Figure AA.4, the second market-driven cycle in Figure AA.5 is triggered by environmental discontinuity, namely the Second World War, while the first market-driven cycle is triggered by DuPont's autonomous behaviour.

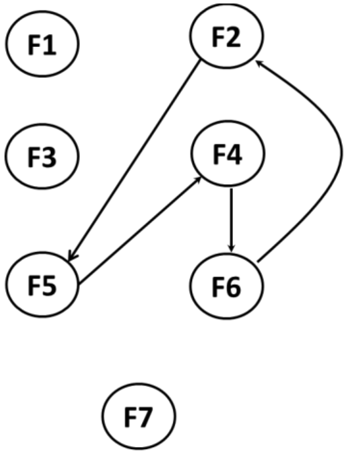

Figure AA.5 The second market-driven cycle in Nylon innovation

Decline (1971-1990)

The 1970s witness a hard time for Nylon after a long period of growth. The trigger of this crisis was an oil shortage in 1973 and 1979. The production of Nylon requires petroleum based material as input. In 1975, Nylon made no profit for the first time since it was commercialized [-F4]. In the same year, DuPont decided to reduce resources allocated to Nylon research and increased the budget for developing new materials that can substitute Nylon [-F6]. After the second oil shortage, in 1981 DuPont acquired Conoco (as Continental Oil) for $7.6 billion in order to insure a source of petroleum based feedstock for Nylon [F7, F6]. However, the huge investment contributed to a financial crisis for DuPont [-F6]. During the 1980s, DuPont reduced Nylon plants budgets to alleviate capital starvation [-F6, -F4]. The amount of capital allocated to upgrading Nylon plants was around 30% less than comparable companies such as 3M, Monsanto, and Kodak (Cook-Hauptman, 2013)[-F6].

Interaction pattern analysis

The cycle in this period is identified in the event sequence F6→F4→F6. Given the essential role of resource mobilization in this event sequence, we call it the resource cycle, as shown in Figure AA.6. This period is characterized by DuPont's continuous strategy adjustment in face of a resource crisis. The trigger event is the world-wide oil shortage which led to insufficient supplies to make Nylon and ultimately also made Nylons profits disappear [-F6]. As a remedy, DuPont invested in new substitutes of nylon, acquiring upper supply chain companies, decreasing nylon plant investments [F6], and so on. All these operations are through resource re-allocations. The two worldwide oil shortages influenced the Nylon innovation through changing the resource availability, namely through the system function F6.

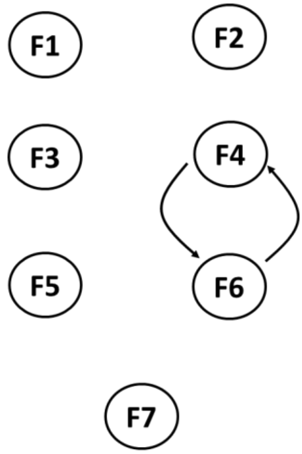

Figure AA.6 The resource cycle in Nylon innovation

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Appendix B

Supplementary information on Chapter 3

Summary

This appendix illustrates how we analyse the Selective Serotonin Reuptake Inhibitor (SSRI) innovation process. Serotonin Reuptake Inhibitors (SSRI) is a class of antidepressant drugs which are primarily used to treat depression. The development of SSRI is acknowledged as a breakthrough in psychotropic medications, because before the invention of SSRI all psychotropic medications were based on chance observation. SSRI were the first psychotropic medications that were purposefully designed. The complexity of the SSRI innovation is matched by tightly governmental regulations as well as unexpected contextual events. Dynamics were primarily driven by multiple waves of innovation activities by diverse pharmaceutical companies.

This appendix consists of five parts: (1) technological background of SSRI; (2) chronological list of events in SSRI innovation; (3) coding SSRI innovation events into pre-defined categories (here we use Hekkert et al. (2007)'s seven system functions as a framework); (4) analysing the interaction patterns between events; and (5) references.

AB.1 Technological background of SSRI

The SSRIs are the first rationally designed psychotropic drugs which are used to treat depression, anxiety disorders and other personality disorders (eMedExpert, 2011). Before SSRIs, all psychotropic medications (e.g., MAO-Is and Tricyclics) were discovered by chance observation (Preskorn). The rationality of the SSRIs lies in their selective effect on a specific neural site of action while avoiding effects on others instead of chance observations (eMedExpert, 2011; Wrobel, 2007). The discovery and development of the SSRIs opened up a new generation of antidepressants and rational drug designs (Carlsson, 1999).

The term SSRIs refer to a class of antidepressants instead of a single medicine. The first invented SSRI antidepressant was zimelidine by Astra, a Swiss pharmaceutical company (Carlsson, 1999), followed by Prozac (Fluoxetine) by Eli Lilly and Company, Zoloft (Sertraline) by Pfizer Inc, Paxil (Paroxetine) by GlaxoSmithKline, Celexa (Citalopram) and Lexapro (Escitalopram) by Forest Pharmaceuticals, Inc, respectively. The following five SSRIs were almost developed at the same time by different pharmaceutical companies.

All SSRIs work through the same mechanism. Research suggests that the special chemicals for brain communications, which are called neurotransmitters, play a significant role in affecting mood and behaviour. Low levels of neurotransmitters are proved to lead to depression, and on the other hand high levels of neurotransmitters are found to help improve mood. Serotonin and norepinephrine are two commonly known neurotransmitters. The SSRIs work through blocking the reuptake of serotonin, thereby increasing the level of serotonin and improving depressed people’s mood. And the SSRIs distinguish themselves by “selective”, which means they most significantly influence serotonin rather than other neurotransmitters.

Table AB.1 Commonly prescribed SSRIs (Source: eMedExpert.com)

Scientific name	Zimelidine	Fluoxetine	Sertraline	Paroxetine	Citalopram	Escitalopram
Trademarked name	Zelmid	Prozac	Zoloft	Paxil	Celexa	Lexapro
Country	Sweden	U.S.	U.S.	U.S.	U.S.	U.S.
Approval date	March 23, 1972	December 29, 1987	December 30, 1991	December 29, 1992	July 17, 1998	August 14, 2002
Pharmaceutical companies	Astra AB	Eli Lilly and Company	Pfizer Inc.	GlaxoSmith Kline	Forest Pharmaceuticals, Inc.	Forest Pharmaceuticals, Inc.

AB.2 Chronological list of events in SSRI innovation

Time	By whom	Events[1]	References
1953	John Gaddum and one of the founders of psycho-pharmacology in Britain	They speculated to a small but influential group of researchers, “It is possible that the 5-HT [serotonin] in our brains plays an essential part in keeping us sane.”	(Shorter, 1997)
1950s	A team in the United States and another team in Edinburgh, Scotland, led by Sir John H. Gaddum	A potential role of serotonin in brain function and consciousness was discovered	(Cozzi, 2013)
1953	John Gaddum	Through experimenting on himself, Gaddum discovered the existence of serotonin in certain parts of the brain and proposed its potential effect on mental performances	(Amin, Crawford, & Gaddum, 1954; Cozzi, 2013)
1954	Woolley and Shaw	Woolley and Shaw in New York proposed that the mental disorders may be caused by an the action of serotonin in the brain and the suppression of its action may result in a mental disorder	(Cozzi, 2013; Woolley & Shaw, 1954)
1957	Researchers in Bernard Brodie’s Laboratory of Chemical Pathology in the National Institutes of Health in Bethesda	The working mechanism of the role of serotonin was further proposed by Researchers in Bernard Brodie’s Laboratory of Chemical Pathology in the National Institutes of Health in Bethesda who discovered that amines in an antipsychotic drug may lead to behavioural changes through unlocking the body’s reuptake of serotonin	(Shorter, 1997)
Mid		By the mid-1960s, the MAOIs were	(Healy, 2004)

[1] The events data are completely literal texts from the internet. We do not want to change the original texts when we analyse.

1960s		rapidly disappearing from clinical practice because of worries about a dangerous interaction between them and cheese. Their demise left the TCAs on the market as the gold standard antidepressants.	
1963	Alec Coppen, a biochemist-psychiatrist of the Medical Research Council and staff member at St. Ebba's Hospital	Discovered that serotonin-equivalents were able to relieve depression.	(Shorter, 1997)
1967	Paul Kielholz	The origin of the SSRIs lies in 1967. Following early studies with imipramine, Paul Kielholz became the Professor of Psychiatry in Basel. Given the presence in Basel of the major Swiss chemical companies, Kielholz was well placed to become a leading figure in the world of psychopharmacology.	(Healy, 2004)
Late 1960s	Carlsson and his colleagues	Following Kielholz's lead, Carlsson, working with Hanns Corrodi and Peder Berndtsson at Astra's plant in Hässle in Sweden, took the anti-histamine chlorpheniramine and manipulating the molecule, came up with compound H102-09, later called zimeldine and finally given the brand name Zelmid.	(Healy, 2004)
1968	Carlsson, Fuxe and Ungerstedt	Reported that the reuptake of serotonin (or 5-HT) was also inhibited by a tricyclic antidepressant named imipramine	(Carlsson, 1999; Carlsson, Fuxe, & Ungerstedt, 1968)
1968	Clarsson	Went to Geigy to report their findings regards to the reuptake inhibition of serotonin by tricyclic antidepressants in order to persuade them to do the clinical	(Carlsson, 1999)

		trials of a potent inhibitor agent	
1968	Geigy	The agent selected by Geigy proved to possess some problem.	(Healy, 2004)
1968	Clarsson and his colleagues	Clarsson and his colleagues started to develop non-tricyclic agents which were able to selectively inhibit 5-HT (serotonin) reuptake inhibitor	(Carlsson, 1999)
Late 1960s	Arvid Carlsson	Arvid Carlsson reinforced the news that serotonin seemed to control mood	(Shorter, 1997)
Late 1960s		New alternative antidepressants drugs with minor side effects and low toxicity were extremely needed	(Healy, 2004)
Late 1960s		There was a backlash against over-prescription of anti-anxiety drugs because the side effects and addiction	(Lawlor, 2012)
Late 1960s	Carlsson together with Hanns Corrodi in Astra	Developed the first SSRIs called zimeldine and known as the brand name Zelmid	(Healy, 2004)
1970	Barr Labs	Barr Labs was founded in Pomona, N.Y., as a maker of generic antibiotics.	(McLean, 2001)
Early 1970s	Eli Lilly	SSRIs research also became fashion in Eli Lilly Company.	(Shorter, 1997)
1971	Ray Fuller	Persuade Lilly to start develop an antidepressant using serotonin in particular	(Shorter, 1997)
Early 1970s	Ray Fully and David Wong	Organized a serotonin depression team in Lilly.	(Shorter, 1997)
1971	Carlsson	Applied for a patent on Zelmid in Sweden, Belgium and Great Britain as a	(Healy, 2004)

		selective serotonin uptake inhibitor	
1971	Lilly	Fluoxetine (LY110141) - the compound that became Prozac - was developed	(The-Observer, 2007)
1971	Astra	A phase I clinical development of zimelidine was carried out at Hassle	(Carlsson, 1999)
1972	Lilly	The lab experiments with fluoxetine were carried out by David Wong.	(Carlsson, 1999)
1972	Wong	Hoping to find a derivative inhibiting only serotonin reuptake, Wong proposed to re-test the series for the in-vitro reuptake of serotonin, norepinephrine and dopamine.	(Wikipedia)
1972	Jong-Sir Horng	Showed the compound later named fluoxetine to be the most potent and selective inhibitor of serotonin reuptake of the series	(Wikipedia)
1973	DuPhar Laboratories in Weesp	Developed fluvoxamine	(Healy, 2004)
1973	Lilly	Applied for a patent for fluoxetine	(Carlsson, 1999)
1974	Lilly	Prozac was patented	(Healy, 2004)
1975	DuPhar Laboratories in Weesp	Applied for a patent on fluvoxamine	(Healy, 2004)
1976	Lilly	Clinical trial of fluoxetine was carried out in healthy volunteers	(Carlsson, 1999)
1976	Astra	Testing of zimelidine in patients who were suffering from depression	(Carlsson, 1999)
1977	Pharmacologist Le Fur and Uzan at Pharmuka	Discovered Indalpine	(Healy, 2004)

1978	Lilly	Clinical trials of fluoxetine were being carried out in Indianapolis and Chicago	(Shorter, 1997)
Late 1970s	US government	At the end of the 1970s, due to several factors (the financial burden of the Vietnam war, escalation of healthcare costs and other issues), the Nixon administration was not very keen on approving new drugs. This intention was manifested by changing the head of the FDA and introduction of harder and more costly drug approval procedures	(Shorter, 1997)
1980	Lilly	Decided to cooperate with John Feighner, a famous biological psychiatrist	(Shorter, 1997)
1980	Astra	At a symposium of depression treatment zimelidine was commented as effective as existing antidepressants in treating depressions, but with less side-effects	(Carlsson, 1999)
1980	Astra	Zelmid trials published	(Healy, 2004)
1982	Astra	Zimelidine was approved as antidepressant agent in Sweden and several other countries	(Carlsson, 1999)
1982	Astra	Zimelidine was trade marked as Zelmid by Astra in Europe	(Carlsson, 1999)
1982	Astra	Submitted its application to FAD	(Carlsson, 1999)
1982	Astra	Some patients with zimelidine treatment were found to subject to GuillainBarre syndrome	(Carlsson, 1999)
1983	Lilly	1983 clinical trials in clinic found fluoxetine was as effective as tricyclic agent	(Shorter, 1997)

1983	Astra	Withdraw all zimelidine drugs from market in all countries	(Carlsson, 1999)
1983	Astra	Derivative of Zelmid, called alaproclat, was also found to cause serious side effect (aplastic anaemia) and was withdrawn from the market	(Healy, 1997)
1984	US government	The landmark Hatch-Waxman Act of 1984 was aimed almost entirely at making low-priced generics available more quickly	(McLean, 2001)
1985	Lilly	The weight loss effect of fluoxetine, was published in Lilly's annual report, thereby leading to stock rising of Lilly	(Shorter, 1997)
1985	Lilly	Prozac trials published	(Healy, 2004)
1986	Lilly	Fluoxetine made its appearance on the Belgian market	(Wikipedia)
1987	Lilly	Fluoxetine was approved for use by the FDA in the United States.	(FDA)
1987	Lilly	Fluoxetine was handed to Interbrand, the world's leading branding company for an identity, and the name Prozac was chosen	(The-Observer, 2007)
1987	Lilly	Market introduction of Prozac	(Wong, Perry, & Bymaster, 2005)
1987	Lilly	Lilly carried out large scale promotion campaigns for Prozac	(The-Observer, 2007)
1988	Lilly	Prozac was brought onto the market	(Healy, 1997, 2004; The-Observer, 2007)
1990	Researchers at McLean	Published an article suggesting that	(Shorter, 1997)

	Hospital	Prozac was effective for a range of disorders such as panic and drop attacks	
1990	Lilly	Prozac became the number one drug prescribed by psychiatrists.	(Shorter, 1997)
Early 1990s	Astra	Astra contemplated withdrawing from the research-based pharmaceutical market, in favour of a focus on over-the counter medicines.	(Healy, 2004)
1990s		Prozac, Zoloft and Paxil became household names	(Healy, 2004)
1990s		The acronym SSRI came into general use	(Shorter, 1997)
1992	Royal College of Psychiatrists	Launched its Defeat Depression campaign in the 1992, it surveyed the population using professional polling organizations and found that most people thought the antidepressants were likely to be addictive.	(Pill, Prior, & Wood, 2001)
1993	Fuller, Bryan Molloy and David Wong in Lilly	Fuller was posthumously awarded the Pharmaceutical Discoverer's Award. Bryan Molloy and David Wong were also awarded.	(Bellis)
1994	Lilly	Prozac had become the number two best-selling drug in the world.	(Shorter, 1997)
1995	Barr Labs	Filed its application to market a 20-milligram capsule of fluoxetine, charging that two Lilly patents - one set to expire in 2001 and the other in 2003 - weren't valid	(McLean, 2001)
1997	David Healy	Wrote *The Anti-Depressant Era* (1997) and *Let Them Eat Prozac (2004)*, in which he alleged that the use of Prozac increases the risk of suicide in younger	(Healy, 1997; Lawlor, 2012)

		patients especially	
1997	FDA	Approved direct marketing to consumers	(Lawlor, 2012)
End of 1990s		The threshold of what people were defined as illness was reduced.	(Shorter, 1997)
2000	Lilly	A three-judge appeals court panel annulled the Lilly's 2001 patent	(McLean, 2001)
2001	Barr Labs	The first generic fluoxetine was released in August 2001 in America by Barr Laboratories	(Druss, Marcus, Olfson, & Pincus, 2004)
2001		There was a long-running campaign waged by Scientologist against Lilly's Prozac	(McLean, 2001)
2001	Lilly	All the security checks at Eli Lilly's main headquarters are partly the result of a long-running campaign waged by Scientologists.	(McLean, 2001)
2001	Lilly	Eli Lilly lost $35m of its market value in one day - and 90 per cent of its Prozac prescriptions in a single year.	(The-Observer, 2007)
2001		In the wake of the traumatic events of September 11, pharmaceutical companies drastically increased their expenditures for television advertising of antidepressants and prescription sleep aids.	(Rosack, 2002)
2001	GlaxoSmithKline	Spent a whopping $16.5 million on television ads promoting the drug during the month of October of last year, nearly twice as much as it did during the same month in 2000.	(Rosack, 2002)

2001	Pfizer	spent $5.6 million promoting the benefits of Zoloft (sertraline) in treating posttraumatic stress disorder during October 2001	(Rosack, 2002)
2001		Total sales of the three brand-name SSRIs amounted to $499.6 million during the month of October 2001—an increase of 19 percent over a year earlier	(Rosack, 2002)
2002		Generic fluoxetine represented 69.6 percent of all fluoxetine prescriptions. There was a corresponding decline in prescriptions for brand-name fluoxetine (Prozac).	(Druss et al., 2004)
2005	Tom Cruise	Tom Cruise fired for suggesting using vitamins instead of Prozac….. In May 2005, Tom Cruise was promoting War of the Worlds and Shields was promoting Down Came the Rain. Scientologists are vehemently opposed to all forms of psychiatry.	(The-Observer, 2007)
2009	Irving Kirsch	Wrote book "*The Emperor's New Drugs: Exploding the Antidepressant Myth*" to question the effectiveness of antidepressants.	(Kirsch, 2011; Lawlor, 2012)
2010	Gary Greenberg	*Wrote book "Manufacturing Depression: The Secret History of a Modern Disease"* to question the effectiveness of antidepressants.	(Greenberg, 2010; Lawlor, 2012)

AB.3 Coding SSRI innovation events into pre-defined categories[2]

Events[3]	Year	F1	F2	F3	F4	F5	F6	F7
They speculated to a small but influential group of researchers, "It is possible that the 5-HT [serotonin] in our brains plays an essential part in keeping us sane."	1953				1			
A potential role of serotonin in brain function and consciousness was discovered	1950s		1		1			
Through experimenting on himself, Gaddum discovered the existence of serotonin in certain parts of the brain and proposed its potential effect on mental performances	1953		1		1			
Woolley and Shaw in New York proposed that the mental disorders may be caused by an the action of serotonin in the brain and the suppression of its action may result in a mental disorder	1954		1		1			
The working mechanism of the role of serotonin was further proposed by researchers in Bernard Brodie's Laboratory of Chemical Pathology in the National Institutes of Health in Bethesda who discovered that amines in an antipsychotic drug may lead to behavioural changes through unlocking the body's reuptake of serotonin	1957		1		1			
By the mid-1960s, the MAOIs were rapidly disappearing from clinical practice because of worries about a dangerous interaction between them and cheese. Their demise left the TCAs on the market as the gold standard	Mid 1960s				1			

[2] The coding scheme can be found in AA.2.
[3] The "Events" are the same events in AB.2. For references, please refer to AB.2.

antidepressants.								
Discovered that serotonin-equivalents were able to relieve depression.	1963		1		1			
The origin of the SSRIs lies in 1967. Following early studies with imipramine, Paul Kielholz became the Professor of Psychiatry in Basel. Given the presence in Basel of the major Swiss chemical companies, Kielholz was well placed to become a leading figure in the world of psychopharmacology.	1967		1		1		1	
Following Kielholz's lead, Carlsson, working with Hanns Corrodi and Peder Berndtsson at Astra's plant in Hässle in Sweden, took the anti-histamine chlorpheniramine and manipulating the molecule, came up with compound H102-09, later called zimeldine and finally given the brand name Zelmid.	Late 1960s		1		1			
Reported that the reuptake of serotonin (or 5-HT) was also inhibited by a tricyclic antidepressant named imipramine	1968		1		1			
went to Geigy to report their findings regards to the reuptake inhibition of serotonin by tricyclic antidepressants in order to persuade them to do the clinical trials of a potent inhibitor agent	1968	1	1					1
The agent selected by Geigy proved to possess some problem.	1968				1		1	
Clarsson and his colleagues started to develop non-tricyclic agents which were able to selectively inhibit 5-HT (serotonin) reuptake inhibitor	1968		1					
Arvid Carlsson reinforced the news that	Late		1		1			

serotonin seemed to control mood	1960s							
New alternative antidepressants drugs with minor side effects and low toxicity were extremely needed	Late 1960s				1	1		
There was a backlash against over-prescription of anti-anxiety drugs because the side effects and addiction	Late 1960s				1			
Developed the first SSRIs called zimeldine and known as the brand name Zelmid	Late 1960s		1		1			
Barr Labs was founded in Pomona, N.Y., as a maker of generic antibiotics.	1970	1						
SSRIs research also became fashion in Eli Lilly Company.	Early 1970s	1			1		1	
Persuade Lilly to start develop an antidepressant using serotonin in particular	1971	1						1
Organized a serotonin depression team in Lilly.	Early 1970s	1					1	
Applied for a patent on Zelmid in Sweden, Belgium and Great Britain as a selective serotonin uptake inhibitor	1971				1		1	
Fluoxetine (LY110141) - the compound that became Prozac - was developed	1971	1						
A phase I clinical development of zimelidine was carried out at Hassle	1971		1				1	
The lab experiments with fluoxetine were carried out by David Wong.	1972		1					
Hoping to find a derivative inhibiting only serotonin reuptake, Wong proposed to re-test the series for the in-vitro reuptake of serotonin,	1972		1		1			

norepinephrine and dopamine.								
Showed the compound later named fluoxetine to be the most potent and selective inhibitor of serotonin reuptake of the series	1972		1		1			
Developed fluvoxamine	1973		1					
Applied for a patent for fluoxetine	1973				1		1	
Prozac was patented	1974						1	
Applied for a patent on fluvoxamine	1975		1				1	
Clinical trial of fluoxetine was carried out in healthy volunteers	1976		1				1	
Testing of zimelidine in patients who were suffering from depression	1976		1				1	
Discovered Indalpine	1977		1					
Clinical trials of fluoxetine were being carried out in Indianapolis and Chicago	1978		1				1	
At the end of the 1970s, due to several factors (the financial burden of the Vietnam war, escalation of healthcare costs and other issues), the Nixon administration was not very keen on approving new drugs. This intention was manifested by changing the head of the FDA and introduction of harder and more costly drug approval procedures	Late 1970s				1			
Decided to cooperate with John Feighner, a famous biological psychiatrist	1980		1		1		1	
At a symposium of depression treatment zimelidine was commented as effective as existing antidepressants in treating depressions,	1980				1			

but with less side-effects								
Zelmid trials published	1980			1				
Zimelidine was approved as antidepressant agent in Sweden and several other countries	1982				1			
Zimelidine was trade marked as Zelmid by Astra in Europe	1982					1		
Submitted its application to FAD	1982				1		1	
Some patients with zimelidine treatment were found to subject to erious risk called GuillainBarre syndrome	1982				-1			
1983 clinical trials in clinic found fluoxetine was as effective as tricyclic agent	1983				1			
Withdraw all zimelidine drugs from market in all countries	1983					-1		
Derivative of Zelmid, called alaproclat, was also found to cause serious side effect (aplastic anaemia) and was withdrawn from the market	1983				-1			
The landmark Hatch-Waxman Act of 1984 was aimed almost entirely at making low-priced generics available more quickly	1984				1			
The weight loss effect of fluoxetine, was published in Lilly's annual report, thereby leading to stock rising of Lilly	1985					1		
Prozac trials published	1985			1				
Fluoxetine made its appearance on the Belgian market	1986					1		
Fluoxetine was approved for use by the FDA in the United States.	1987				1			

Fluoxetine was handed to Interbrand, the world's leading branding company for an identity, and the name Prozac was chosen	1987					1	1	
Market introduction of Prozac	1987					1		
Lilly carried out large scale promotion campaigns for Prozac	1987					1	1	
Prozac was brought onto the market	1988					1		
Published an article suggesting that Prozac was effective for a range of disorders such as panic and drop attacks	1990				1			
Prozac became the number one drug prescribed by psychiatrists.	1990				1			
Astra contemplated withdrawing from the research-based pharmaceutical market, in favour of a focus on over-the counter medicines.	Early 1990s	-1				-1		
Prozac, Zoloft and Paxil became household names	1990s				1			
The acronym SSRI came into general use	1990s				1			
Launched its Defeat Depression campaign in the 1992, it surveyed the population using professional polling organizations and found that most people thought the antidepressants were likely to be addictive.	1992				-1			
Fuller was posthumously awarded the Pharmaceutical Discoverer's Award. Bryan Molloy and David Wong were also awarded.	1993				1			
Prozac had become the number two best-selling drug in the world, following, …, an ulcer drug	1994				1			

named Zantac.								
Filed its application to market a 20-milligram capsule of fluoxetine, charging that two Lilly patents--one set to expire in 2001 and the other in 2003--weren't valid	1995	1			1			1
Wrote *The Anti-Depressant Era* (1997) and *Let Them Eat Prozac (2004)*, in which he alleged that the use of Prozac increases the risk of suicide in younger patients especially	1997				-1			
Approved direct marketing to consumers	1997				1	1		
The threshold of what people were defined as illness was reduced.	End of 1990s				1	1		
A three-judge appeals court panel annulled the Lilly's 2001 patent	2000				1		-1	
The first generic fluoxetine was released in August 2001 in America by Barr Laboratories	2001	1			1	1		
There was a long-running campaign waged by Scientologist against Lilly's Prozac	2001				-1			
This paranoia is partly the result of a long-running campaign waged by Scientologists.	2001				1		1	
Eli Lilly lost $35m of its market value in one day - and 90 per cent of its Prozac prescriptions in a single year.	2001				-1	-1		
In the wake of the traumatic events of September 11, pharmaceutical companies drastically increased their expenditures for television advertising of antidepressants and prescription sleep aids.	2001				1	1	1	
Spent a whopping $16.5 million on television ads promoting the drug during the month of	2001					1	1	

October of last year, nearly twice as much as it did during the same month in 2000.								
Spent $5.6 million promoting the benefits of Zoloft (sertraline) in treating posttraumatic stress disorder during October 2001	2001					1	1	
Total sales of the three brand-name SSRIs amounted to $499.6 million during the month of October 2001—an increase of 19 percent over a year earlier	2001				1			
Generic fluoxetine represented 69.6 percent of all fluoxetine prescriptions. There was a corresponding decline in prescriptions for brand-name fluoxetine (Prozac).	2002				1			
Tom Cruise fired for suggesting using vitamins instead of Prozac….. In May 2005, Tom Cruise was promoting War of the Worlds and Shields was promoting Down Came the Rain. Scientologists are vehemently opposed to all forms of psychiatry.	2005				-1			
Wrote book “*The Emperor's New Drugs: Exploding the Antidepressant Myth*” to question the effectiveness of antidepressants.	2009				-1			
Wrote book “Manufacturing Depression: The Secret History of a Modern Disease” to question the effectiveness of antidepressants.	2010				-1			

AB.4 Analysing the interaction patterns between events

The time period during which the development of SSRI is analysed starts in the early 1950s and ends in the early 2000s. The section is structured in a story-telling way consisting of four periods: (1) the scientific discovery ranging from the early 1950s till the late 1960s; (2) the product development phase ranging from late 1960s till late 1980s, which was characterized by pharmaceutical companies' starting developing SSRIs; (3) Prozac's marketing phase in 1990s, which was characterized by a fast growth of Prozac; and (4) Prozac's maturity phase in 2001 due to the expiration of Prozac's patent. It needs to say that the term "period" is not referred to a predefined and predictable sequential process but a representation of continuity in activities. Just as Langley (1999) pointed out that this is only a way of structuring the events rather than any particular theoretical significance.

The analysis of the SSRIs innovation process is based on historical events. The database came from various sources, such as journal papers, scientific books, interviews with professionals in relative field, as well as rich information on the internet. In particular, the earlier development phase of the SSRI (1950s-1960s) was based on the accounts from Shorter (1997) and Stanford et al. (1999); the later phase of SSRI development was referred to Healy (2004), the influence of institutional changes was referred to Lawlor (2012).These professional publications about the discovery and development of the SSRIs provided us with valuable information about the evolutionary history of the SSRIs medicines. A contribution of our study is a representation of the SSRIs innovation history using the system function framework and analysing in term of cycles. The storyline of how SSRI evolved over time has been given in Chapter 3. Below we focus on analysing the cycles underlying each developmental phase of SSRI.

The scientific discovery phase (1950s - 1960s)

Cycle analysis

This period is characterized by scientific discoveries which paved way for the further research of the SSRIs. They provided a knowledge base for SSRI research through identifying the function mechanism of serotonin in brains and opened up a new direction of antidepressant research through blocking the reuptake of serotonin in brains. The most developed functions in this period are knowledge development [F2], knowledge diffusion [F3], guidance of the search [F4], resource mobilization [F6], and accidently the support from advocacy coalitions [F7]. Other functions, such as entrepreneurial activities [F1], market formation [F5], etc. haven't entered the system. It needs to point out that here the "support from advocacy coalitions" mainly focusses on forming scientific alliance in new generation of antidepressants – the SSRIs.

A cycle is observed to dominate the development of the SSRIs research in this period, which can be identified through the event sequence F2→F3→F4→F6→F2, as shown in Figure AB.1. Given the significance of knowledge development, it is reasonable to call it a technological cycle. This cycle is characterized by continuous scientific discoveries [F2], starting from the discovery of the role of serotonin in brains, to the existence of serotonin in tricyclic antidepressants, then to the working mechanism of blocking reuptake of serotonin to treat depression, and to the beginning of research on non-tricyclic agents for inhibiting serotonin reuptake, which was later called selective serotonin reuptake inhibitor. The dynamics involve an event sequence consisting of positive experimental outcomes spreading out [F3], creating positive expectations [F4], leading to more research projects [F6] which directly contribute to the knowledge development of the SSRI (selective serotonin reuptake inhibitors) field [F2].

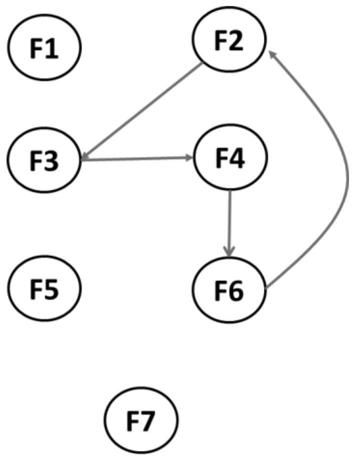

Figure AB.1 The technological cycle in SSRI development

Product development phase (late 1960s - late 1980s)

Cycle analysis

This period was characterized by the involvement of pharmaceutical companies in SSRI commercialization. Science advance achieved in the previous phase as well as great market demand helped facilitating the emergence of SSRI research. Previous antidepressants were found to have side effects and the market needs new alternative antidepressants with same effect but less side effects. All of these factors together attract researchers into SSRI development.

One entrepreneurial cycle is identified in this period, indicated in event sequence: F1 →F5→F4→F6→F1. Since the entrepreneurial cycle happens mainly within established pharmaceutical companies, we call it 'corporate entrepreneurial cycle'. It is a direct result from the positive outcome of knowledge development. Positive research outcomes provide high expectancies and promises for pharmaceutical companies, which push them embark on entrepreneurial activities in terms of new business development [F1]. In order to promote the new drugs, both Astra and Eli Lilly had increased their expenditure on marketing [F6, F5]. The feedbacks from the market (either positively or negatively) affect the next step resource allocation strategies [F4], which would in turn increase or constrain the range of pharmaceutical companies' business activities [F1] (F1→F5→F4→F6→F1). The visual presentation of this cycle is shown in Figure AB.2.

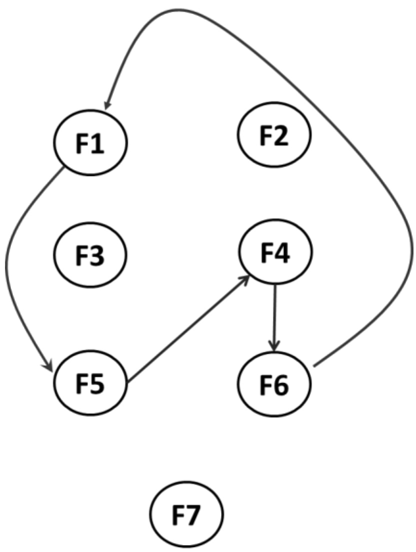

Figure AB.2 The corporate entrepreneurial cycle in SSRI development

What need to be noticed is that the entrepreneurial cycle in Zelmid's later phase presented a vicious circle, triggered by a negative feedback [-F4] that some patients with zimelidine treatment were found to exhibit GuillainBarre syndrome [-F5]. This event forced Astra to withdraw all zelmid drugs from its market [-F5] and stopped its original plan into American market [-F1] (-F5→-F4→-F1). The vicious circle led to quit of Astra from the Zelmid antidepressant market. Prozac quickly superseded Zelmid and became dominant in the market.

Prozac's marketing phase (1990s)

Cycle analysis:

This period is characterized by the establishment of a stable market environment as a result of previous entrepreneurial activities. The most developed system functions are entrepreneurial activities [F1], knowledge development [F2], knowledge diffusion [F3], guidance of the search [F4], market formation [F5] and resource mobilization [F6]. It is obvious that all the system functions have been developed except the support from advocacy coalitions [F7]. Prozac became the dominant SSRI drugs that were prescribed by psychiatrists. The rapid diffusion of SSRI was driven by a Rogers (2010) adoption cycle: the effective of SSRI in treating depression was broadcasted by mass media [F3], leading to more people know and start to use Prozac drugs [F5] (F5→F3→F4→F5). In light of the pivot position of market formation in this event sequence, it is defined as a market-driven cycle, illustrated in Figure AB.3.

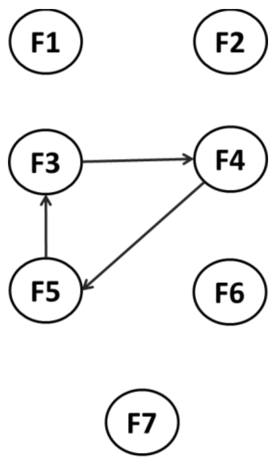

Figure AB.3 The adoption cycle in SSRI development

Two external events were found to play an important role in Prozac's take-off: (1) at the end of 1970s, the Nixon administration changed the head of FAD and required harder and more costly drug approval procedures. "Around 1990, it was estimated that new FDA regulations and other hurdles to drug development meant that the cost of bringing a drug to market had rocketed to $300 million" (Healy, 2004). The effect was that it became harder for a new drug to enter the market. As a result, for a long time, there was no new drug brought out onto the market, and Prozac was exactly one of the drugs to enter the market after many years (Pla & Ortt, 2008). The market thirst for new medications was dramatically fulfilled by Prozac, leading to Prozac's fast diffusion. (2) The second critical external event was the reduced threshold to diagnose people as illness in the end of 1990s. As a result, previous non-illness who suffered from pressure and life problems was also defined with illness. This had created a stunning increase of market demand for antidepressant drugs, including Prozac.

It is needed to point out that during the new antidepressant development process both Astra and Lilly pharmaceutical company chose to keep the clinical and lab experimental trials secret. It is obvious that both were using a patent protection strategy to protect their innovation benefits.

Prozac maturity phase (2001 -)

Cycle analysis

Two cycles became dominant in this period: (1) entrepreneurial cycle indicated from event sequence F1 →F5→F4→F1 and (2) market-driven cycle, which is indicated from event sequence: F5→ F6 →F5. The most developed system functions in this period are market formation [F5], resource mobilization [F6], entrepreneurial activities [F1] and the guidance of the search [F4].

The entrepreneurial cycle, shown in Figure AB.4, is initiated by the entrepreneurial activities of generic pharmaceutical companies, represented by Barr's launching of the first generic fluoxetine [F1]. The quick market diffusion of Barr's generic fluoxetine [F5] sent a promising signal to other companies [F4], which previously were not in generic fluoxetine market, to enter this market [F1] (F1 →F5→F4→F1).

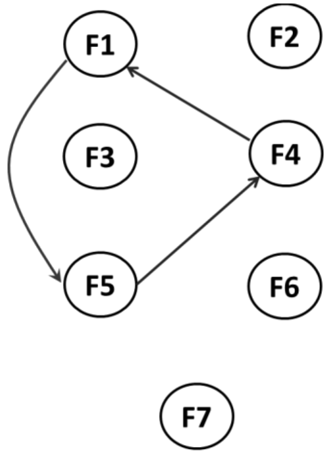

Figure AB.4 The entrepreneurial cycle in SSRI development

The market-driven cycle is triggered by the September 11 traumatic event, after which increasing people were suffered from depression [F5]. The increased market demand attracted existing pharmaceutical companies to enhance marketing their own anti-depressant drugs [F6], which in turn reinforce the formation of market demand [F5] (F5→F6→F5). The visual presentation of the market-driven cycle can be referred to Figure AB.5.

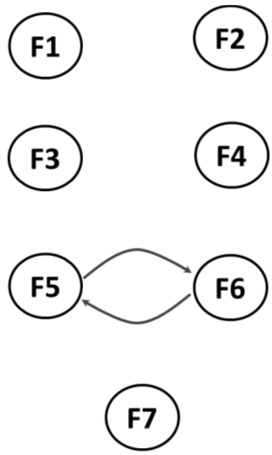

Figure AB.5 The market-driven cycle in SSRI development

Three external events have disturbed the development of SSRIs TIS in this period. (1) The 1984 Hatch Waxman act decreased the entry obstacles for generic companies to enter SSRIs market, which re-shaped the matured market environment and competition order, providing stimulus for entrepreneurial activities from generic companies. (2) The September 11 event created a bigger market for antidepressants drugs. (3) The long-running campaign waged by Scientologist against Lilly's Prozac induced higher production cost for Prozac.

AB.5 References

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Appendix C

Supplementary information on Chapter 4

Summary

This appendix illustrates how we analyse the Teflon innovation process. Teflon, technically called polytetrafluoroethylene (PTFE), is the plastic with slippery, inert, non-corrosive and heat-resistant characteristics, and is commonly used for non-stick coating for pans and other cookware. Teflon was discovered by accident, instead of purposefully planned results, which provides a good representation of the emergent process. In 1930 when DuPont and General Motors decided to cooperate in developing new refrigerant, nobody would have known a by-product material with slippery, non-stick and heat-resistant characteristics would be discovered. Even, nobody would have said, “Let’s coat our cooking pans with this material and make a non-sticky cookware industry”. Yet, this is what Teflon technology exactly grew into: commonly used for non-stick coating for cookware and contributing to one of the world’s most slippery materials. Therefore, the Teflon case provides an excellent setting for examining the emergence of a technological innovation. Besides, the long history of Teflon provides a time range that enables the examination of how the process evolved over time. The historical data can be obtained from the internet.

This appendix consists of four parts: (1) the chronological list of events in Teflon innovation; (2) coding Teflon innovation events into pre-defined categories (here we use Hekkert et al. (2007)’s seven system functions as a framework); (3) analysing the interaction patterns between events, and (4) references.

AC.1 Chronological list of events in Teflon innovation

Time	**By whom**	**Events**[1]	**References**
Early 1930s	General Motors chemists, A.L.Henne and Thomas Midgley	Brought samples of two compounds to the Jackson Laboratory at Du Ponts Chambers Works in Deepwater, New Jersey.	(Funderburg, 2000)
1930	GM, Du Pont, Kinetic Chemicals.	GM and Du Pont formed a joint venture called Kinetic Chemicals. GM wants to make use of Du Pont's expertise in manufacturing and research and development.	(Funderburg, 2000)
Mid-1930s	Kinetic Chemicals	Isolated and tested a lot of CFCs and put the most promising ones (Freon 114) into mass production.	(Funderburg, 2000)
	Kinetic Chemicals	Kinetic had agreed to reserve its entire output of Freon 114 for Frigidaire.	(Funderburg, 2000)
Late 1930s	Du Pont	Du Pont was looking for an equally effective refrigerant that it could sell to other manufacturers.	(Friedel, 1996; Funderburg, 2000)
1936	Plunkett	Plunkett was hired and assigned to this project.	(MIT, 2000)
1936	Plunkett	Plunkett worked on a new CFC that he hoped would be a good refrigerant. He synthesized it by reacting TFE with hydrochloric acid.	(Funderburg, 2000)
1936	Plunkett and his assistant, Jack Rebok	Prepared 100 pounds of TFE and stored it in pressure cylinders. To prevent an explosion or rupture of the cylinder, they kept the canisters in dry ice.	(Funderburg, 2000)
1938	Plunkett	He discovered PTFE accidently. And he found very interesting characteristics of this substance.	(Funderburg, 2000)

[1] The events data are completely literal texts from the internet. We do not want to change the original texts when we analyse.

1939	Plunkett	He applied for a patent, which he assigned to Kinetic Chemicals on PTFE.	(Funderburg, 2000; Myers, 2007; Wikepedia)
1940		WWII gave a large boost to the development of PTFE.	(Funderburg, 2000; Smith, 1988)
1940	Manhattan project	Faced a problem of separating the isotope U-235 from U-238.	(Funderburg, 2000; McKeen, 2006)
	Gen. Leslie Groves, director of the Manhattan project	Chose Du Pont to design the separation plant. To make it work, the designers needed equipment that would stand up to the highly corrosive starting material, uranium hexafluoride gas. PTFE was just what they needed.	(Funderburg, 2000)
	Du Pont	Du Pont agreed to reserve its entire output for government use.	(Funderburg, 2000)
		For security reasons PTFE was referred to by a code name, K416.	(McKeen, 2006)
1941		The patent was granted.	(Funderburg, 2000)
	Du Pont's organic chemical's department	For about three years, Du Pont's organic chemicals department experimented with ways to produce IFE, which is also known as TFE monomer, the raw material for PTFE.	(Funderburg, 2000)
	Du Pont	Plunkett and Rebok had produced small batches for laboratory use, but if PTFE was ever going to find a practical use and be produced commercially, the company would have to find a way to turn out TFE monomer in industrial quantities.	(Funderburg, 2000)

	Organic group and Du Pont's central R&D department	When the organic group came up with a promising method, Du Pont's central R&D department began looking into possible polymerization processes.	(Funderburg, 2000)
	Chemist Rober M. Joyce	Found a feasible but costly procedure for spontaneous polymerization of TFE	(Funderburg, 2000)
	Du Pont's applications group	Began identifying the properties of PTFE that would be useful in industry.	(Funderburg, 2000)
1944		The Arlington production unit was wrecked by an explosion one night in 1944.	(Funderburg, 2000)
	Army, FBI, Du Pont chemists	they found that the explosion had been caused by uncontrolled, spontaneous polymerization	(Funderburg, 2000)
	Manhattan project	Consumed about two-thirds of Arlington's PTFE output, and the remainder was used for other military applications. Such as nose cones of proximity bombs, airplane engines and in explosive manufacturing.	(Funderburg, 2000)
		When the Army needed tape two-thousandths of an inch thick to wrap copper wires in the radar systems of night bombers, it was painstakingly shaved off a solid block of PTFE at a cost of $100 per pound. The high cost was justified because PTFE did a job nothing else could do.	(Funderburg, 2000)
1945	Du Pont	Go ahead with commercializing PTFE, since its manifold military uses had shown its great industrial potential.	(Funderburg, 2000)
1945	Du Pont	Registered the trademark Teflon, TFE. The new substance was an ideal fit for Du Pont's traditional marketing strategy, which was to shun the manufacture of commodity plastics and specialize in sophisticated materials that could command premium prices.	(Wikipedia)

	DuPont	Other materials with some of Teflon's properties were available, but none were as comprehensively resistant to corrosion, and none of the lubricants or low-friction materials then in use was anywhere near as durable or maintenance-free.	(Funderburg, 2000)
1946	DuPont	The Teflon® trademark was coined by DuPont and registered in 1945; the first products were sold commercially under the trademark beginning in 1946	(Deshpande, 2012)
	Du Pont	Faced significant obstacles before it could produce large amounts of Teflon uniformly and economically. The properties of the product varied significantly from batch to batch. And nearly every step of the manufacturing process raised problems that no chemical manufacturer had faced before.	(Funderburg, 2000)
	Du Pont	After the synthesis was completed, fabricating Teflon into useful articles raised another set of difficulties. Its melting point was so high that it could not be moulded or extruded by conventional methods. Another problem was how you make the greatest non-stick substance ever invented bond to another surface.	(Funderburg, 2000)
	DuPont	Du Pont chemists also developed fluorocarbon resins that would stick to both Teflon and metal surfaces. And of course, sheets of Teflon could be attached to other items with screws, bolts, clamps, and other mechanical fasteners.	(Paucka, 2006)
By 1948	DuPont	By 1948 Du Pont had made enough progress to prepare for full-scale production.	(Funderburg, 2000)
1950	DuPont	First commercial Teflon plant, designed to produce a million pounds a year, went on line at the Washington Works.	(Funderburg, 2000)
1950	Du Pont	Du Pont stepped up its efforts to market Teflon for	(Funderburg,

		industrial applications.	2000)
1950	Du Pont	To help users understand the polymer's unusual properties and tricky fabrication requirements, Du Pont sent out a team of scientists to advise customers on integrating Teflon into their production processes. Members of the research, manufacturing, and sales staff met regularly to compare notes.	(Funderburg, 2000)
1951	DuPont	Teflon was also being used in commercial food processing, like bread manufacturing, in candy factories.	(Funderburg, 2000)
1951	DuPont	Teflon-lined bread pans and muffin tins became standard equipment in many bakeries.	(Funderburg, 2000)
1951	DuPont	Du Pont saw the potential for expansion in this field but decided to proceed slowly.	(Funderburg, 2000)
1953	DuPont	Du Pont television commercial advertisement.	(Funderburg, 2000)
As late as 1960s	Du Pont	Du Pont sold less than 10 million pounds of Teflon per year, with receipts of a piddling $28 million, because some toxic fumes will be given off by overheated Teflon pans. Expanding consumer uses would be the key to boosting sales, but Du Pont had to convince itself that Teflon was harmless before selling it to the housewives of America	(Funderburg, 2000)
1954	Marc Gregoire	Heard about Teflon from a colleague, who had devised a way to affix a thin layer of it to aluminium for industrial applications.	(Funderburg, 2000; Pegg, 2012)
1954	Marc Gregoire	Decided to coat his fishing gear with Teflon to prevent tangles.	(Pegg, 2012; Pinterest, 2013)
1954	His wife, Colette	Had an idea, why not coat her cooking pans? Gregoire agreed to try it, and he was successful	(Funderburg,

		enough to be granted a patent in 1954.	2000)
1955	Gregoires couple	They set up a business in their home.	(Funderburg, 2000)
1956	Gregoires couple	Encourages by this reception, the couple formed the Tefal corporation in May 1956 and opened a factory.	(Funderburg, 2000)
1956	DuPont	DuPont recognizes the potential of Teflon® for cookware as well, and begins the process of gaining approval from the U.S. Food and Drug Administration (FDA) for its use in consumer cooking and food processing.	(United Steelworkers International Union, 2005)
1956	Du Pont	Tested frying pans and other cooking surfaces under conditions even more rigorous than those used in France. Du Pont's researchers concluded that utensils coated with Teflon were unquestionably safe for both domestic and commercial cooking.	(Funderburg, 2000)
1956	France's Conseil Superieur de I'Hygiene publique	Officially cleared Teflon for use on frying pans.	(Funderburg, 2000)
1956	The Laboratoire Municipale de Paris and the École Sup érieur de Physique et Chimie	Also declared that Teflon-coated cookware presented no health hazard.	(Funderburg, 2000)
1958	The French ministry of agriculture	Approved the use of Teflon in food processing.	(Funderburg, 2000)
1958	Gregoires	Sold one million items from their factory.	(Funderburg, 2000)
1958	Bill Gore	Decided to commit himself to his own innovations and left DuPont. On January 1958, he and his wife Gore founded a small PTFE company out of the basement of his home, called W.L.GORE &	(Motion System Design)

		Associates.	
1958	Gore	In the company's early years, Gore discovered how to apply PTFE tape to insulate wire and cable. These products were in high demand by the mainframe manufacturers of a fledgling computer industry.	(Gore & Associates)
1957	Thomas G. Hardie	Trip to France, met Marc Gregoire at a party. The Frenchman enthusiastically told Hardie about his business and the factory he was building in a Paris suburb. Hardie was intrigued by Gregoire's tale of the fast-selling cookware.	(Funderburg, 2000)
	Thomas G. Hardie	He decided that the popular French pans would sell in the US too.	(Funderburg, 2000)
	Thomas G. Hardie	Went back to Paris to meet with Gregoire, who was reluctant to do business with an American because he didn't trust Yankees. But Hardie was very persuasive and eventually won Gregoire's confidence.	(Funderburg, 2000)
	Thomas G. Hardie	With visions of quick success, he went back to US with the rights to manufacture non-stick cookware using Tefal's process.	(Funderburg, 2000)
1958-1959	Thomas G. Hardie	Called on many American cookware manufacturers, trying to persuade them to make Teflon-coated pans. He had no success because the idea of non-stick pans was simply too new.	(Funderburg, 2000)
	Thomas G. Hardie	He asked the French factory to ship him 3,000 Tefal pans, which he warehoused in a barn on his sheep farm in Mary land.	(Funderburg, 2000)
	Thomas G. Hardie	He sent free sample pans, along with promotional literature, to housewares buyers at 200 department stores. Not one of them placed an order.	(Funderburg, 2000)
	Thomas G. Hardie ,	Hardie met with an executive at Du Pont in Wilmington, Delaware. He was able to convince the	(Funderburg,

	Du Pont executive	executive that cookware could be a valuable new market.	2000)
	Du Pont executive	Refused the name Tefal, because it was too close to Teflon.	(Funderburg, 2000)
	Thomas G. Hardie	Agreed to market his imported French pans under the name T-fal.	(Funderburg, 2000)
	Du Pont	A salesman was assigned to accompany Hardie on a visit to Macy's in New York City	(Funderburg, 2000)
	George Edelstein	A buyer named George Edelstein placed a small order.	(Funderburg, 2000)
1960	Gregoires	The sales approached the three million mark.	(Funderburg, 2000)
1960	Du Pont	Gave the FDA four volumes of data, collected over nine years, on the effects of Teflon resins in food handling.	(Funderburg, 2000)
1960	FDA	FDA decided that the resins did not present any problems under the food additives amendment.	(Funderburg, 2000)
1960	Du Pont	Despite the favourable FDA decision, Du Pont continued to move slowly, since marketing Teflon-coated cookware was not a high priority.	(Funderburg, 2000)
1960	Macy's Herald Square store	A severe snowstorm, the T-fal "Satisfy" skillets went on sale for $6.94. The pans quickly sold out.	(Funderburg, 2000)
1960	Hardie, Horchow	Made his second sale when he telephoned Roger Horchow, a buyer for the Dallas department store Neiman Marcus.	(Funderburg, 2000)
	Horchow	Agreed to test a sample skillet even though his store didn't have a housewares department.	(Funderburg, 2000)
	Horchow, Helen Corbit, a cookbook	Gave the skillet to Helen Corbitt, a cookbook editor	(Funderburg,

	editor.	who ran a popular cooking school in Dallas.	2000)
	Corbitt	He loved it, prompting Neiman Marcus to place a large order and run a half-page newspaper advertisement. The store sold 2,000 skillets in a week.	(Funderburg, 2000)
	Hardie	The news spread to other department, buyers jumped on the non-stick bandwagon, and Hardie was swamped with orders.	(Funderburg, 2000)
	Hardie	The inventory in Hardie's barn was quickly exhausted. He phoned France daily to ask for more pans, but the French plant couldn't work fast enough to supply both sides of the Atlantic.	(Funderburg, 2000)
	Hardie	Flew to France to press his case with Gregoire. He even lent Tefal $50,000 to expand its facilities, but it still could not meet the American demand.	(Funderburg, 2000)
1960	DuPont	FEP (the family of Teflon® fluoropolymers) was introduced	(Anonymous)
1961	A magazine	In New York, a magazine publishes a photo of a "rich and famous" lady buying a Tefal frying pan at Macy's. American orders soar to 7,500 pans a week.	(Tafal, 2011)
Mid 1961	Hardie	To cope with the avalanche of orders, which reached a million pans per month in mid-1961, Hardie built his own factory in Timonium, Maryland.	(Funderburg, 2000)
1961	Competitors: American companies	Several major American cookware companies decided to start making Teflon pans. The market was saturated with non-stick cookware.	(Funderburg, 2000)
1961	American companies	Because they had no experience with Teflon coatings, much of it was inferior to the French product, and non-stick pans soon acquired a bad name.	(Funderburg, 2000)

1961		Just as quickly as the U.S. demand for non-stick pans had soared, it plummeted and warehouses were filled with unsold stock.	(Funderburg, 2000)
1961	Hardie	Sold his factory and focused on his family's business.	(Funderburg, 2000)
1961	Du Pont's managers	Despite the problems with early Teflon cookware, DuPont's managers still believed that it had enormous potential. So the company commissioned some research.	(Funderburg, 2000)
1961	Du Pont, consumers, professionals in the cookware business	Six thousand consumers, along with professionals in the cookware business, were asked what was wrong with Teflon products.	(Funderburg, 2000)
1961	Du Pont	Du Pont knew that cookware could be more than just a way to sell lots of Teflon. It could also be an invaluable marketing tool, a vehicle to familiarize vast numbers of consumers with Teflon and its properties. Conversely, low-quality merchandise could only harm the product's reputation.	(Funderburg, 2000)
1968	Du Pont	As a result the company established coating standards for manufacturers and initiated a certification program, complete with an official seal of approval for Teflon kitchenware. To verify compliance with its standards, Du Pont performed more than 500 tests per month on cookware at its Marshall Laboratories in Philadelphia.	(Funderburg, 2000)
mid-1960s	Du Pont, customers	The Du Pont certification program was so successful that a marketing survey in the mid-1960s found that 81 percent of homemakers who had purchased non-stick pans were pleased with them.	(Funderburg, 2000)
1968	Du Pont	By 1968 Du Pont had developed Teflon II, which not only prevented food from sticking to the pans but was also (supposedly) scratch-resistant.	(Funderburg, 2000)

1968	French	Tefal is France's No. 1 manufacturer of cookware with sales of FF59 MILLION. It is acquired by the French domestic appliances company, SEB.	(Tefal)
1960-70s		As Teflon became better known to consumers, rumours began to circulate that it was unsafe	(Funderburg, 2000)
1960-70s	Du Pont	Whenever one of these false reports came to Du Pont's attention, the company demanded a published retraction. It also published a booklet called The Anatomy of a Rumour that summarized the results of research carried out at Du Pont and elsewhere.	(Funderburg, 2000)
1970	National magazines	Many national magazines printed articles about the new products. Most discussed the safety issue, and several mentioned the rumours, but none gave any credence to the gossip.	(Funderburg, 2000)
1970	Du Pont	DuPont introduces two new melt processable fluoropolymers.	(Teng, 2012)
1970	Du Pont	Tefzel, ETFE	(DuPont)
1972	Du Pont	PFA	(DuPont)
1973	Consumer Reports	Still receive mails on old bugaboo about non-stick, prompting the editors to publish yet another article emphasizing that they knew of no consumer illnesses resulting from non-stick cookware in ordinary home use.	(Funderburg, 2000)
1976	Du Pont	DuPont sought fluorocarbon polymers that would provide even greater non-stick performance and scratch resistance, achieving success in 1976 with the introduction of Silverstone®, a three-coat system that set a new standard for durability and performance.	(Funderburg, 2000)
1978	Du Pont	Patent new fluoropolymer technology for very high-speed data communications cables	(Drobny, 2008)

1979	Du Pont	DuPont also develops two- and three-coat reinforced non-stick coating systems that provide improved scratch and abrasion resistance on cookware	(Whitford, 2010)
1984	Du Pont	"Another improvement in non-stick coatings occurred in 1984 with the development of Silverstone® SUPRA"	(Funderburg, 2000)
1985	Du Pont	"Du Pont registered another variant of Teflon in 1985, Teflon AF, which is soluble in special solvents."	(Made How)
1985	Plunkett	Dr. Plunkett was inducted into the Plastics Hall of Fame in 1973, and in 1985, the National Inventors Hall of Fame."	(Funderburg, 2000)
1986	Du Pont	Silverstone Supra was introduced to the cookware market in 1986	(Coy, 1986)
1988	Du Pont	DuPont has presented the Plunkett Award each year since 1988 to innovative customers and partners who develop unique, sustainable applications for fluoropolymers	(Funderburg, 2000)
1989	W. L. Gore & Associates	"GORE-TEX® is a registered trademark and the best-known product of W. L. Gore & Associates, Inc. The trademarked product was introduced in 1989."	(Wikepedia)
1990	U.S. National Medal of Technology	DuPont receives the U.S. National Medal of Technology from President George H.W. Bush in 1990 for the company's role in the development and commercialization of high-performance, man-made polymers, including fluoropolymers."	(Wikepedia)
2004	DuPont	DuPont settled for $300 million in a 2004 lawsuit filed by residents near its manufacturing plant in Ohio and West Virginia based on groundwater pollution from this chemical.	(Anonymous; Van de Poel & Royakkers, 2011)

2005	United States Environmental Protection Agency's	Found in 2005 that perfluorooctanoic acid (PFOA), a chemical compound used to make Teflon, is a "likely carcinogen	(Van de Poel & Royakkers, 2011)

AC.2 Coding Teflon innovation events into pre-defined categories[2]

Events[3]	Year	F1	F2	F3	F4	F5	F6	F7
Brought samples of two compounds to the Jackson Laboratory at Du Pont's Chambers Works in Deepwater, New Jersey.	Early 1930s			1				
GM and Du Pont formed a joint venture called Kinetic Chemicals. GM wants to make use of Du Pont's expertise in manufacturing and research and development.	1930	1		1				1
Isolated and tested a lot of CFCs and put the most promising ones (Freon 114) into mass production.	Mid-1930s		1					
Kinetic had agreed to reserve its entire output of Freon 114 for Frigidaire.					1		1	
Du Pont was looking for an equally effective refrigerant that it could sell to other manufacturers.	Late 1930s		1					
Plunkett was hired and assigned to this project.	1936						1	
Plunkett worked on a new CFC that he hoped would be a good refrigerant. He synthesised it by reacting TFE with hydrochloric acid.	1936		1					
Prepared 100 pounds of TFE and stored it in pressure cylinders. To prevent an explosion or rupture of the cylinder, they kept the canisters in dry ice.	1936		1					
Plunkett discovered PTFE accidently. And he found very interesting characteristics of this substance	1938		1		1			
He applied for a patent, which he assigned to Kinetic Chemicals on PTFE.	1939		1				1	
WWII gave a large boost to the development of PTFE.	1940				1			
Faced a problem of separating the isotope U-235 from U-238.	1940				1			

[2] The coding scheme can be found in AA.2.
[3] The "Events" are the same events in AC.1. For references, please refer to AC.1.

Chose Du Pont to design the separation plant. To make it work, the designers needed equipment that would stand up to the highly corrosive starting material, uranium hexafluoride gas. PTFE was just what they needed.	1940	1			1			
Du Pont agreed to reserve its entire output for government use.					1		1	
For security reasons PTFE was referred to by a code name, K416.				-1				
The patent was granted.	1941				1		1	
For about three years, Du Pont's organic chemicals department experimented with ways to produce IFE, which is also known as TFE monomer, the raw material for PTFE.			1					
Plunkett and Rebok had produced small batches for laboratory use, but if PTFE was ever going to find a practical use and be produced commercially, the company would have to find a way to turn out TFE monomer in industrial quantities.			1					
When the organic group came up with a promising method, Du Pont's central R&D department began looking into possible polymerization processes.			1	1				
Chemist Rober M. Joyce found a feasible but costly procedure for spontaneous polymerization of TFE			1					
Began identifying the properties of PTFE that would be useful in industry.			1		1			
The Arlington production unit was wrecked by an explosion one night in 1944.	1944						-1	
they found that the explosion had been caused by uncontrolled, spontaneous polymerization			1		1			
Consumed about two-thirds of Arlington's PTFE output, and the remainder was used for other military applications. Such as nose cones of proximity bombs, airplane engines and in explosive manufacturing.					1			
When the Army needed tape two-thousandths of an inch thick to wrap copper wires in the radar systems of night					1	1		

bombers, it was painstakingly shaved off a solid block of PTFE at a cost of $100 per pound. The high cost was justified because PTFE did a job nothing else could do.								
Go ahead with commercializing PTFE, since its manifold military uses had shown its great industrial potential.	1945				1	1		
Registered the trademark Teflon, TFE.	1945					1		
The Teflon® trademark was coined by DuPont and registered in 1945; the first products were sold commercially under the trademark beginning in 1946	1946					1	1	
Faced significant obstacles before it could produce large amounts of Teflon uniformly and economically.			1					
After the synthesis was completed, fabricating Teflon into useful articles raised another set of difficulties.			1					
Du Pont chemists also developed fluorocarbon resins that would stick to both Teflon and metal surfaces. And of course, sheets of Teflon could be attached to other items with screws, bolts, clamps, and other mechanical fasteners.			1					
By 1948 Du Pont had made enough progress to prepare for full-scale production.	By 1948					1		
First commercial Teflon plant, designed to produce a million pounds a year, went on line at the Washington Works.	1950					1		
Du Pont stepped up its efforts to market Teflon for industrial applications.	1950					1	1	
To help users understand the polymer's unusual properties and tricky fabrication requirements, Du Pont sent out a team of scientists to advise customers on integrating Teflon into their production processes. Members of the research, manufacturing, and sales staff met regularly to compare notes.	1950			1		1		
Teflon was also being used in commercial food processing, like bread manufacturing, in candy factories.	1951		1			1		
Teflon-lined bread pans and muffin tins became standard	1951				1	1		

equipment in many bakeries.								
Du Pont saw the potential for expansion in this field but decided to proceed slowly.	1951				1			
Du Pont television commercial advertisement.	1953					1		
Du Pont sold less than 10 million pounds of Teflon per year, with receipts of a piddling $28 million, because some toxic fumes will be given off by overheated Teflon pans. Expanding consumer uses would be the key to boosting sales, but Du Pont had to convince itself that Teflon was harmless before selling it to the housewives of America	As late as 1960s				1	1		
Heard about Teflon from a colleague, who had devised a way to affix a thin layer of it to aluminium for industrial applications.	1954			1				
Decided to coat his fishing gear with Teflon to prevent tangles.	1954	1	1					
Had an idea, why not coat her cooking pans? Gregoire agreed to try it, and he was successful enough to be granted a patent in 1954.	1954	1						
They set up a business in their home.	1955	1				1		
Encourages by this reception, the couple formed the Tefal corporation in May 1956 and opened a factory.	1956	1						
DuPont recognizes the potential of Teflon® for cookware as well, and begins the process of gaining approval from the U.S. Food and Drug Administration (FDA) for its use in consumer cooking and food processing.	1956			1	1			
Tested frying pans and other cooking surfaces under conditions even more rigorous than those used in France. Du Pont's researchers concluded that utensils coated with Teflon were unquestionably safe for both domestic and commercial cooking.	1956		1					
Officially cleared Teflon for use on frying pans.	1956				1			
Also declared that Teflon-coated cookware presented no health hazard.	1956				1			

Approved the use of Teflon in food processing.	1958				1			
Sold one million items from their factory.	1958					1		
Decided to commit himself to his own innovations and left DuPont. On January 1958, he and his wife Gore founded a small PTFE company out of the basement of his home, called W.L.GORE & Associates.	1958	1						
In the company's early years, Gore discovered how to apply PTFE tape to insulate wire and cable.	1958		1					
Trip to France, met Marc Gregoire at a party on the Left Bank. The Frenchman enthusiastically told Hardie about his business and the factory he was building in a Paris suburb. Hardie was intrigued by Gregoire's tale of the fast-selling cookware.	1957	1		1				
He decided that the popular French pans would sell in the US too.		1						
Went back to Paris to meet with Gregoire, who was reluctant to do business with an American because he didn't trust Yankees. But Hardie was very persuasive and eventually won Gregoire's confidence.				1				1
With visions of quick success, he went back to US with the rights to manufacture non-stick cookware using Tefal's process.				1				
Called on many American cookware manufacturers, trying to persuade them to make Teflon-coated pans. He had no success because the idea of non-stick pans was simply too new.	1958-1959							1
He cabled the French factory to ship him 3,000 Tefal pans, which he warehoused in a barn on his sheep farm in Mary land.				1				
He sent free sample pans, along with promotional literature, to housewares buyers at 200 department stores. Not one of them placed an order.					-1	1		
Hardie met with an executive at Du Pont in Wilmington, Delaware. He was able to convince the executive that cookware could be a valuable new market.		1		1				1

Refused the name Tefal, because it was too close to Teflon.					1			
Agreed to market his imported French pans under the name T-fal.				1	1			1
A salesman was assigned to accompany Hardie on a visit to Macy's in New York City				1				1
A buyer named George Edelstein placed a small order. Hardie was so excited that he sent a victory cable to the French factory.					1	1		
The sales approached the three million mark.	1960				1			
Gave the FDA four volumes of data, collected over nine years, on the effects of Teflon resins in food handling.	1960		1				1	
FDA decided that the resins did not present any problems under the food additives amendment.	1960				1			
Despite the favourable FDA decision, Du Pont continued to move slowly, since marketing Teflon-coated cookware was not a high priority.	1960				1			
A severe snowstorm, the T-fal "Satisfy" skillets went on sale for $6.94. The pans quickly sold out.	1960				1	1		
Made his second sale when he telephoned Roger Horchow, a buyer for the Dallas department store Neiman Marcus.	1960			1		1		1
Agreed to test a sample skillet even though his store didn't have a housewares department.						1		
Gave the skillet to Helen Corbitt, a cookbook editor who ran a popular cooking school in Dallas.				1				
He loved it, prompting Neiman Marcus to place a large order and run a half-page newspaper advertisement. The store sold 2,000 skillets in a week.					1	1		
The news spread to other department, buyers jumped on the non-stick bandwagon, and Hardie was swamped with orders.				1	1			

The inventory in Hardie's barn was quickly exhausted. He phoned France daily to ask for more pans, but the French plant couldn't work fast enough to supply both sides of the Atlantic.					-1			
Flew to France to press his case with Gregoire. He even lent Tefal $50,000 to expand its facilities, but it still could not meet the American demand.					-1		1	
FEP (the family of Teflon® fluoropolymers) was introduced	1960		1					
In New York, a magazine publishes a photo of a "rich and famous" lady buying a Tefal frying pan at Macy's. American orders soar to 7,500 pans a week.	1961			1	1	1		
To cope with the avalanche of orders, which reached a million pans per month in mid-1961, Hardie built his own factory in Timonium, Maryland.	Mid 1961	1						
Several major American cookware companies decided to start making Teflon pans. The market was saturated with non-stick cookware.	1961	1						
Because they had no experience with Teflon coatings, much of it was inferior to the French product, and non-stick pans soon acquired a bad name.	1961		-1					
Just as quickly as the U.S. demand for non-stick pans had soared, it plummeted and warehouses were filled with unsold stock.	1961				-1			
Sold his factory and focused on his family's business.	1961	-1						
Despite the problems with early Teflon cookware, DuPont's managers still believed that it had enormous potential. So the company commissioned some research.	1961				1			
Six thousand consumers, along with professionals in the cookware business, were asked what was wrong with Teflon products.	1961					1		
Du Pont knew that cookware could be more than just a way to sell lots of Teflon. It could also be an invaluable marketing tool, a vehicle to familiarize vast numbers of consumers with Teflon and its properties. Conversely, low-quality merchandise could only harm the product's	1961				1			

reputation.								
As a result the company established coating standards for manufacturers and initiated a certification program, complete with an official seal of approval for Teflon kitchenware. To verify compliance with its standards, Du Pont performed more than 500 tests per month on cookware at its Marshall Laboratories in Philadelphia.	1968		1		1			
The Du Pont certification program was so successful that a marketing survey in the mid-1960s found that 81 percent of homemakers who had purchased non-stick pans were pleased with them.	mid-1960s				1			
By 1968 Du Pont had developed Teflon II, which not only prevented food from sticking to the pans but was also (supposedly) scratch-resistant.	1968		1					
Tefal is France's No. 1 manufacturer of cookware with sales of FF59 MILLION. It is acquired by the French domestic appliances company, SEB.	1968				1			
As Teflon became better known to consumers, rumours began to circulate that it was unsafe	1960-70s				-1			
Whenever one of these false reports came to Du Pont's attention, the company demanded a published retraction. It also published a booklet called The Anatomy of a Rumour that summarized the results of research carried out at Du Pont and elsewhere.	1960-70s					1	1	
Many national magazines printed articles about the new products. Most discussed the safety issue, and several mentioned the rumours, but none gave any credence to the gossip.	1970				-1			
DuPont introduces two new melt processable fluoropolymers.	1970		1					
Tefzel, ETFE	1970		1					
PFA	1972		1					
Still receive mails on old bugaboo about non-stick, prompting the editors to publish yet another article emphasizing that they knew of no consumer illnesses resulting from non-stick cookware in ordinary home use.	1973				-1			

DuPont sought fluorocarbon polymers that would provide even greater non-stick performance and scratch resistance, achieving success in 1976 with the introduction of Silverstone®, a three-coat system that set a new standard for durability and performance.	1976		1						
Patent new fluoropolymer technology for very high-speed data communications cables	1978		1						
DuPont also develops two- and three-coat reinforced non-stick coating systems that provide improved scratch and abrasion resistance on cookware	1979		1						
"Another improvement in non-stick coatings occurred in 1984 with the development of Silverstone® SUPRA"	1984		1						
"Du Pont registered another variant of Teflon in 1985, Teflon AF, which is soluble in special solvents."	1985		1						
Dr. Plunkett was inducted into the Plastics Hall of Fame in 1973, and in 1985, the National Inventors Hall of Fame."	1985				1				
Silverstone Supra was introduced to the cookware market in 1986	1986	1	1			1			
DuPont has presented the Plunkett Award each year since 1988 to innovative customers and partners who develop unique, sustainable applications for fluoroplymers	1988				1		1		
"GORE-TEX® is a registered trademark and the best-known product of W. L. Gore & Associates, Inc. The trademarked product was introduced in 1989."	1989	1			1				
DuPont receives the U.S. National Medal of Technology from President George H.W. Bush in 1990 for the company's role in the development and commercialization of high-performance, man-made polymers, including fluoropolymers."	1990				1		1		
DuPont settled for $300 million in a 2004 lawsuit filed by residents near its manufacturing plant in Ohio and West Virginia based on groundwater pollution from this chemical.	2004				-1		1		
perfluorooctanoic acid is a likely carcinogen	2005				-1				

AC.3 Analysing the interaction patterns between events

The time period during which the development of Teflon is analysed starts in the late 1930s and ends by 1990. The history of Teflon technology development can be divided into five discrete periods: (1) invention (1930s-1938); (2) military application (1939-1944); (3) industrial application (1944-1953); (4) household application (1954-1968) and (5) market maturity (1969-1980s). Figure AC.1 visualizes the timeline of Teflon innovation process, where the pentagon refers to milestone events in Teflon innovation, and the whole process was divided into five phases as illustrated at the top of the figure. The red pentagon represents critical crisis which postponed or deviated Teflon innovation from the main trajectory, while the green one indicates the events which help push Teflon innovation into the next developmental phase.

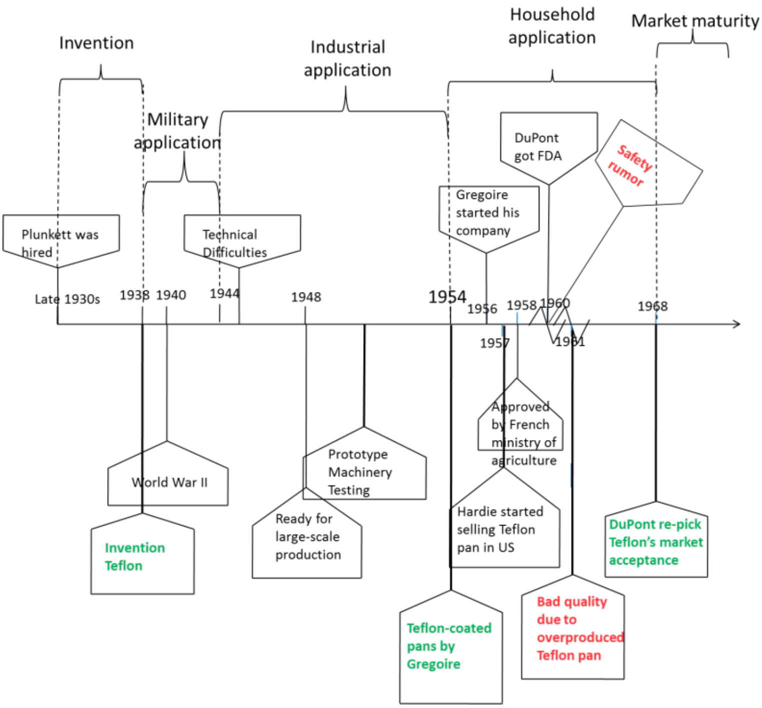

Figure AC.1. Timeline of Teflon innovation process

Phase I: Invention (1930 - 1938)

The reciprocal conditioning between scientific research and positive research outcomes helped drive the emergence of a scientific group focusing on the exploration of the chemical properties of the new material. This feedback loop involves continuous research activities [F2] leading to positive experimental results, which provide high expectancy for the new technology [F4], leading to continuous resource allocation [F6] to further knowledge development [F2]. The re-enforcing cycle that starts from knowledge development [F2], going through guidance of the search [F4], resource mobilization [F6], and finally goes back to enhance further knowledge development [F2] indicates a positive feedback loop which amplifies the accident discovery of Teflon, as shown in Figure AC.2.

In this period, the majority of activities were focusing on scientific research and development of the newly discovered material. The knowledge development function then dominated the system. Given the significance of knowledge development function, it is reasonable to call the cycle a technological cycle.

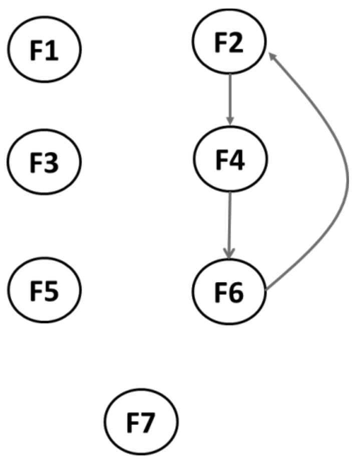

Figure AC.2. Technological cycle in phase I

Phase II: Military application in war time (1939 - 1944)

The main source of dynamics in this period is the Second World War. The feedback loop involves "mutual causation" (Chiles, Meyer, & Hench, 2004, p.509)between system functions of market formation [F5], entrepreneurial activities [F1], resource allocation [F6], knowledge development [F2], and guidance of the search [F4]

(F5→F1→F6→F2→F4 →F5, as shown in Figure AC.3). The World War II served as the first niche market for PTFE in terms of military application as anti-corrosive material in Manhattan project [F5]. The government supported programmes were established with DuPont [F1]. The financial resources were granted by the government in the form of project findings [F6]. Using these findings, technological development activities were carried out to fulfil the requirements of military use [F2]. Successful fulfilment of these programmes created positive expectations and promises [F4] and led to the expansion of PTFE into other military uses [F5]. This self-reinforcing cycle brought wide range of technological developments and applications in the military market, which matches complexity theory arguments that "positive feedback processes drive system toward increasing diversity" (cf., Chiles et al., 2004, p 510).

Given the significant role of market formation function in initiating and stimulating the re-enforcing cycle, it is reasonable to call it a market-driven cycle. The activities in this period are attracted around market formation in military field.

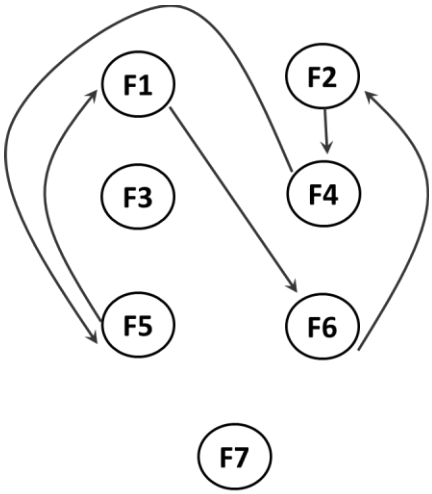

Figure AC.3. Market-driven cycle in Phase II

Phase C: Industrial application after war (1944 - 1953)

The positive feedback loop involves mutual causations between entrepreneurial activities and market formation; and between entrepreneurial activities and technological development. Considering Teflon's satisfactory performance in the military market, DuPont decided to continue with the industrial market [F1]. Following this decision, technological improvement and adjustment to catering industrial requirements were carried out [F2]. At the same time, marketing activities were enhanced by DuPont to persuade industrial customers to accept the new material [F5]. All of these led to market growth [F4], which in turn reinforced the entrepreneurial activities [F1] in terms of new market applications. Therefore, the feedback loops are two parallel ones: F1→F2→F4→F1 and F1→F5→F4→F1, as shown in Figure AC.4. It is interesting to note that the activities were no longer supported by government programmes, but by DuPont itself.

The dominant behaviour regime in this period is characterized by active initiations by firms from the supply-side of the innovation system, in contrast with the foregoing market-driven cycle. The underlying cycle is formed by the entrepreneurial decisions of DuPont. Therefore, we call it entrepreneurial regime; and the cycle as entrepreneurial cycle.

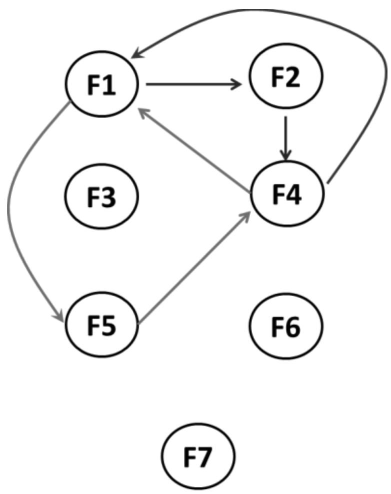

Figure AC.4. Entrepreneurial cycle in phase III

Phase IV: Household application (1954 - 1968)

There are two positive feedback loops: the re-enforcing relationship between the entrepreneurial activities and market formation and between entrepreneurial activities and resource allocation played an important role in the emergence of Teflon's cookware market. The main enactors in this period were individual entrepreneurs, e.g., Gregoire who established the first Teflon pan Company, and Hardie who introduced

Teflon-coated pans from Europe in the U.S. market. The pivot is looking for cooperation and required resources [F6] through continuous lobbying (to government or to potential business partners) [F7] (F1→F7→F6→F1). On the other side, with resources, entrepreneurs are able to market and diffuse the Teflon pan [F5], thereby providing positive expectations [F4] and attracting companies, many of which were previously outsiders to the Teflon-coated pan business. By entering this market, these companies boosted entrepreneurial activities [F1] (F1→F5→F4→F1). These feedback loops are shown in Figure AC.5. These self-reinforcing cycles drive a quick expansion of Teflon in the cooking pan market.

Given the centrality of the entrepreneurial activities in the cyclical pattern, it is reasonable to name the cycle in this period the "entrepreneurial cycle". The difference between this entrepreneurial cycle and the one in the previous phase is that small entrepreneurial companies became the dominant actors in the later period, instead of the big company DuPont. Due to different actors, the system functions within the feedback loops also differ. Entrepreneurial cycles by DuPont were supported by a mechanism of top-down resource allocation. But entrepreneurial cycles were initiated by small firms that have to follow a resource searching event sequence constructed by support from advocacy coalitions and resource mobilization. Besides, there are different forms of reinforced entrepreneurial activities. DuPont's entrepreneurial cycle boosted DuPont's new business expansion. But the small firms' entrepreneurial cycle attracted new entries of firms that were previously outsider in this market.

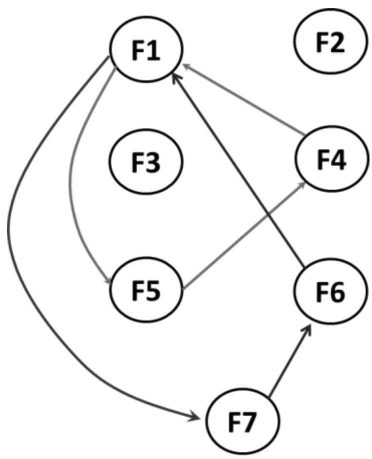

Figure AC.5. Positive feedback loops in phase IV

Phase IV: Market maturity (1954 - 1968)

There is one positive feedback loop in this phase: market responses [F5] leading to high expectations [F4], which directly fed back on continuous financial support [F6] for developing new generations of Teflon [F2]. This further improved performance and increased market demand [F5]. This positive feedback loop is visualized in Figure AC.6. This self-reinforcing cycle drives the emergence of an established institutional structure.

Notably, positive feedback loops do not always lead to positive results. When Teflon was plagued by a safety rumor, the system function F4 became a negative signal which led to a negative outcome of system function F6 in terms of decreasing market demand (-F4→-F6). The set of activities carried out by DuPont, such as public retraction, publishing research results, aimed at re-gaining a positive guidance function [F4], which would reverse the effect of the loop.

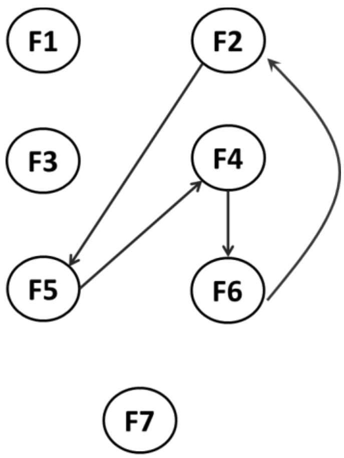

Figure AC.6. Positive feedback loop in phase V

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