Networks Against Time: From Food to Pharma

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Acknowledgments

Thanks to the Organizing Committee for organizing this workshop.

Special acknowledgments and thanks to my students and collaborators who have made research and teaching always stimulating and rewarding.

Support for Our Research Has Been Provided by:



Outline

- Background and Motivation
- Representation of Supply Chains as Networks
- Why User Behavior Must be Captured in Supply Chain Network Analysis and Design
- Time as a Challenge and Competitive Advantage
- Methodology The Variational Inequality Problem
- Supply Chain Networks Optimization Models
 - Blood and Medical Nuclear Supply Chains
- Supply Chain Networks Game Theory Models
 - Electric Power and Food Supply Chains
- ▶ The Pharmaceutical Industry, Issues, and a Full Model
- Some Other Issues in Supply Chain Networks that We Have Explored from Mergers & Acquisitions to Design for Critical Needs Products
- Summary, Conclusions, and Suggestions for Future Research

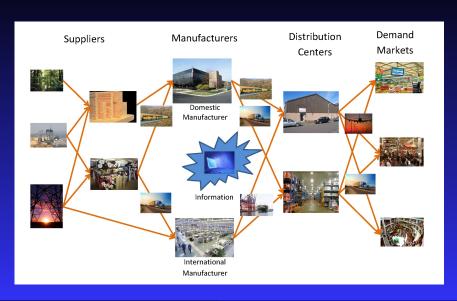
Background and Motivation

Supply chains are the *critical infrastructure and backbones* for the production, distribution, and consumption of goods as well as services in our globalized *Network Economy*.

Supply chains, in their most fundamental realization, consist of manufacturers and suppliers, distributors, retailers, and consumers at the demand markets.

Today, supply chains may span thousands of miles across the globe, involve numerous suppliers, retailers, and consumers, and be underpinned by multimodal transportation and telecommunication networks.

A General Supply Chain



Examples of Supply Chains

- ► food and food products
- high tech products
- automotive
- ► energy (oil, electric power, etc.)
- clothing and toys
- healthcare supply chains
- ▶ humanitarian relief
- supply chains in nature.

Examples of Supply Chains



Characteristics of Supply Chains and Networks Today

- ► *large-scale nature* and complexity of network topology;
- congestion, which leads to nonlinearities;
- alternative behavior of users of the networks, which may lead to paradoxical phenomena;
- possibly conflicting criteria associated with optimization;
- ➤ interactions among the underlying networks themselves, such as the Internet with electric power networks, financial networks, and transportation and logistical networks;
- ► recognition of *their fragility and vulnerability*;
- policies surrounding networks today may have major impacts not only economically, but also socially, politically, and security-wise.

Supply Chains Are Network Systems

Supply chains are, in fact, Complex Network Systems.

Hence, any formalism that seeks to model supply chains and to provide quantifiable insights and measures must be a system-wide one and network-based.

Such crucial issues as the stability and resiliency of supply chains, as well as their adaptability and responsiveness to events in a global environment of increasing risk and uncertainty can only be rigorously examined from the view of supply chains as network systems.

Supply chains may be characterized by *decentralized decision-making* associated with the different economic agents or by *centralized* decision-making.



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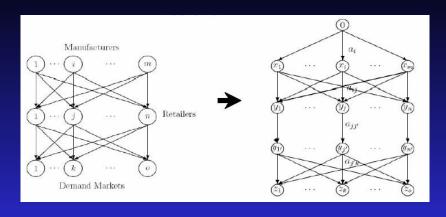
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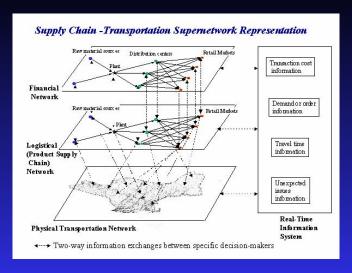
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- build meaningful extensions using the graphical/network conceptualization.



The equivalence between supply chains and transportation networks established in Nagurney, *Transportation Research E* **42** (2006), 293-316.



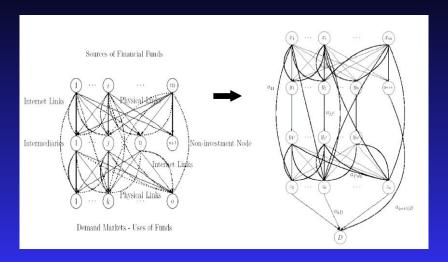
Multilevel supply chain established by Nagurney, Ke, Cruz, Hancock, and Southworth in *Environment & Planning B* **29** (2002), 795-818.

In 1952, Copeland in his book, *A Study of Moneyflows in the United States*, NBER, NY, asked whether money flows like water or electricity?

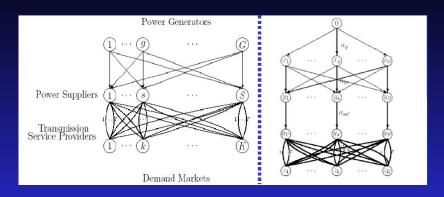
In 1956, Beckmann, McGuire, and Winsten in their classic book, *Studies in the Economics of Transportation*, Yale University Press, hypothesized that electric power generation and distribution networks could be transformed into transportation network equilibrium problems.



Transportation Network Equilibrium Reformulation of the Financial Network Equilibrium Model with Intermediation



Liu and Nagurney, Computational Management Science (2007).



The transportation network equilibrium reformulation of electric power supply chain networks by Nagurney, Liu, Cojocaru, and Daniele, *Transportation Research E* **43** (2007), 624-646.

Hence, we have shown that both electricity as well as money flow like transportation flows.

Some of Our Books Related to Supply Chain Network Analysis and Design



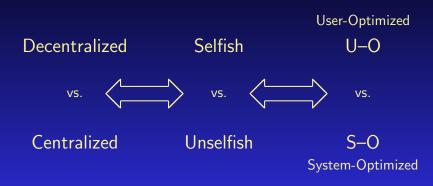
Why User Behavior Must be Captured in Supply Chain Network Analysis and Design

Supply Chain Network Design Must Capture the Behavior of Users



Behavior on Congested Networks

Decision-makers select their cost-minimizing routes.



Flows are routed so as to minimize the total cost to society.

Two fundamental principles of travel behavior, due to Wardrop (1952), with terms coined by Dafermos and Sparrow (1969).

User-optimized (U-O) (network equilibrium) Problem – each user determines his/her cost minimizing route of travel between an origin/destination, until an equilibrium is reached, in which no user can decrease his/her cost of travel by unilateral action (in the sense of Nash).

System-optimized (S-O) Problem – users are allocated among the routes so as to minimize the total cost in the system, where the total cost is equal to the sum over all the links of the link's user cost times its flow.

The U-O problems, under certain simplifying assumptions, possess optimization reformulations. But now we can handle cost asymmetries, multiple modes of transport, and different classes of travelers, without such assumptions.



The U-O and S-O Conditions

Definition: U-O or Network Equilibrium - Fixed Demands

A path flow pattern x^* , with nonnegative path flows and O/D pair demand satisfaction, is said to be U-O or in equilibrium, if the following condition holds for each O/D pair $w \in W$ and each path $p \in P_w$:

$$C_p(x^*)$$
 $\begin{cases} = \lambda_w, & \text{if } x_p^* > 0, \\ \ge \lambda_w, & \text{if } x_p^* = 0. \end{cases}$

Definition: S-O Conditions

A path flow pattern x with nonnegative path flows and O/D pair demand satisfaction, is said to be S-O, if for each O/D pair $w \in W$ and each path $p \in P_w$:

$$\hat{C}'_p(x)$$
 $\begin{cases} = \mu_w, & \text{if } x_p > 0, \\ > \mu_w, & \text{if } x_p = 0, \end{cases}$

where $\hat{C}_p'(x) = \sum_{a \in \mathcal{L}} \frac{\partial \hat{c}_a(f_a)}{\partial f_a} \delta_{ap}$, and μ_w is a Lagrange multiplier.

The importance of behavior will now be illustrated through a famous example known as the Braess paradox which demonstrates what can happen under *U-O* as opposed to *S-O* behavior.

Although the paradox was presented in the context of transportation networks, it is relevant to other network systems in which decision-makers act in a noncooperative (competitive) manner.

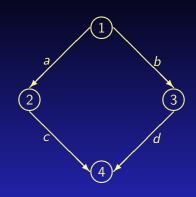
The Braess (1968) Paradox

Assume a network with a single O/D pair (1,4). There are 2 paths available to travelers: $p_1 = (a, c)$ and $p_2 = (b, d)$.

For a travel demand of **6**, the equilibrium path flows are $x_{p_1}^* = x_{p_2}^* = 3$ and

The equilibrium path travel cost is

$$C_{p_1} = C_{p_2} = 83.$$



$$c_a(f_a) = 10f_a, \quad c_b(f_b) = f_b + 50,$$

 $c_c(f_c) = f_c + 50, \quad c_d(f_d) = 10f_d.$

Adding a Link Increases Travel Cost for All!

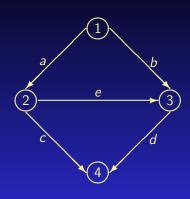
Adding a new link creates a new path $p_3 = (a, e, d)$.

The original flow distribution pattern is no longer an equilibrium pattern, since at this level of flow the cost on path p_3 , $C_{p_3} = 70$.

The new equilibrium flow pattern network is

$$x_{p_1}^* = x_{p_2}^* = x_{p_3}^* = 2.$$

The equilibrium path travel cost: $C_{\infty} = C_{\infty} = C_{\infty} = 92$.



$$c_e(f_e) = f_e + 10$$

The 1968 Braess article has been translated from German to English and appears as:

"On a Paradox of Traffic Planning,"

D. Braess, A. Nagurney, and T. Wakolbinger (2005) Transportation Science **39**, 446-450.







The Braess Paradox Around the World



1969 - Stuttgart, Germany - The traffic worsened until a newly built road was closed.

1990 - Earth Day - New York City - 42nd Street was closed and traffic flow improved.





2002 - Seoul, Korea - A 6 lane road built over the Cheonggyecheon River that carried 160,000 cars per day and was perpetually jammed was torn down to improve traffic flow.



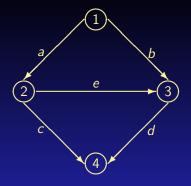


Interview on Broadway for *America Revealed* on March 15, 2011



Under S-O behavior, the total cost in the network is minimized, and the new route p_3 , under the same demand, would not be used.

The Braess paradox never occurs in S-O networks.



Recall the Braess network with the added link e.

What happens as the demand increases?

For Networks with Time-Dependent Demands
We Use Evolutionary Variational Inequalities

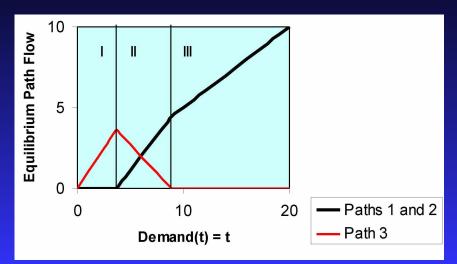
Radcliffe Institute for Advanced Study – Harvard University 2005-2006





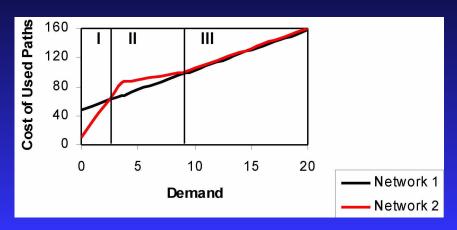
Research with Professor David Parkes of Harvard University and Professor Patrizia Daniele of the University of Catania, Italy

The U-O Solution of the Braess Network with Added Link (Path) and Time-Varying Demands Solved as an *Evolutionary Variational Inequality* (Nagurney, Daniele, and Parkes, *Computational Management Science* (2007)).



In Demand Regime I, Only the New Path is Used.
In Demand Regime II, the travel demand lies in the range [2.58, 8.89], and the Addition of a New Link (Path) Makes Everyone Worse Off!

In Demand Regime III, when the travel demand exceeds 8.89, *Only the Original Paths are Used!*



The new path is never used, under U-O behavior, when the demand exceeds 8.89, even when the demand goes out to infinity!

Other Networks that Behave like Traffic Networks



The Internet and electric power networks and even supply chains!



• More knowledgeable (and demanding) consumers are expecting timely deliveries, despite, paradoxically, the great distances that may be involved from the producers to the consumers.



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- Delivery times are becoming a strategy, as important as productivity, quality, and even innovation.
- Practitioners realize that **speed** and consistency of delivery time are two essential components of customer satisfaction, along with price.

Stalk, Jr., in his *Harvard Business Review* 1988 article, "Time - The next source of competitive advantage," utilized the term *time-based competition*, to single out time as the major factor for sustained competitive advantage.

Today, time-based competition has emerged as a paradigm for strategizing about and operationalizing supply chain networks in which efficiency and timeliness matter.

Added challenges arise in the case of *Perishable Products*, which, by definition, are time-sensitive.

Benjamin Franklin wrote in 1748 in his "Advice to a Young Tradesman," *Remember that Time is Money*.

It may also be said that *time is life*, since time-sensitive products, such as vaccines and medicines, as well as, at the most fundamental level, food and water, are of a life-sustaining, if not, life-saving, nature,

Classical examples of perishable goods include fresh produce in the form of fruits and vegetables, meat and dairy products, medicines and vaccines, radioisotopes, cut flowers, and even human blood.

We take the broader perspective of products being perishable not only in terms of their characteristics (such as their chemistry and the underlying physics) and *supply* (that is, the manner of procurement/production/processing, storage, transportation, etc.) aspects, but also in terms of the *demand* for the products.

We include, under the *perishable product* umbrella, products that are *discarded* (or replaced) relatively quickly after purchase, because of changing consumer tastes, such as *fast* fashion apparel, or those that become obsolete (as in certain high technology products).

Such an approach follows from Whitin (1957), who considered the deterioration of fashion goods at the end of a prescribed shortage period.

Supply chain management of perishable products at the strategic, tactical, and operational levels of the decision-making hierarchy is faced with such challenges as:

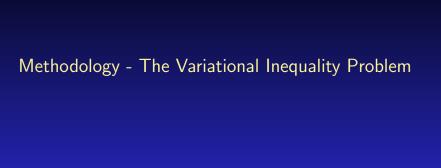
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- ➤ Safety and environmental impact: Perished products and the associated waste may be hazardous and may pollute.
- ➤ Demand management: Demand may be uncertain or known (as in scheduled treatments) and fixed. It may be price-sensitive (fashion apparel, consumer goods and pharma).



Methodology - The Variational Inequality Problem

We utilize the theory of variational inequalities for the formulation, analysis, and solution of both centralized and decentralized supply chain network problems.

Definition: The Variational Inequality Problem

The finite-dimensional variational inequality problem, VI(F, K), is to determine a vector $X^* \in K$, such that:

$$\langle F(X^*), X - X^* \rangle \ge 0, \quad \forall X \in \mathcal{K},$$

where F is a given continuous function from K to R^N , K is a given closed convex set, and $\langle \cdot, \cdot \rangle$ denotes the inner product in R^N .

Methodology - The Variational Inequality Problem

The vector X consists of the decision variables – typically, the flows (products, prices, etc.).

 ${\cal K}$ is the feasible set representing how the decision variables are constrained – for example, the flows may have to be nonnegative; budget constraints may have to be satisfied; similarly, quality and/or time constraints may have to be satisfied.

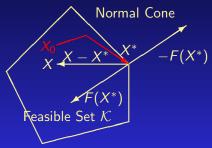
The function F that enters the variational inequality represents functions that capture the behavior in the form of the functions such as costs, profits, risk, etc.

The variational inequality problem contains, as special cases, such mathematical programming problems as:

- systems of equations,
- optimization problems,
- complementarity problems,
- game theory problems, operating under Nash equilibrium,
- and is related to the fixed point problem.

Hence, it is a natural methodology for a spectrum of supply chain network problems from centralized to decentralized ones as well as to design problems. Geometric Interpretation of VI(F, K) and a Projected Dynamical System (Dupuis and Nagurney, Nagurney and Zhang)

In particular, $F(X^*)$ is "orthogonal" to the feasible set K at the point X^* .



Associated with a VI is a Projected Dynamical System, which provides natural underlying dynamics associated with travel (and other) behavior to the equilibrium.

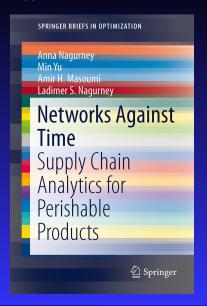
To model the *dynamic behavior of complex networks*, including supply chains, we utilize *projected dynamical systems* (PDSs) advanced by Dupuis and Nagurney (1993) in *Annals of Operations Research* and by Nagurney and Zhang (1996) in our book *Projected Dynamical Systems and Variational Inequalities with Applications*.

Such nonclassical dynamical systems are now being used in evolutionary games (Sandholm (2005, 2011)), ecological predator-prey networks (Nagurney and Nagurney (2011a, b)), and even neuroscience (Girard et al. (2008)).

A Multidiscipinary Perspective for Perishable Product Supply Chains

In our research on perishable and time-sensitive product supply chains, we utilize results from physics, chemistry, biology, and medicine in order to capture the perishability of various products over time from food to healthcare products such as blood, medical nucleotides, and pharmaceuticals.

A variety of perishable product supply chain models, computational procedures, and applications can be found in our new book:





A. Nagurney, A. H. Masoumi, and M. Yu, "Supply Chain Network Operations Management of a Blood Banking System with Cost and Risk Minimization," *Computational Management Science* **9(2)** (2012), pp 205-231.





- ► The shelf life of platelets is 5 days and of red blood cells is 42.
- ▶ Over 39,000 donations are needed everyday in the US, and the blood supply is frequently reported to be just 2 days away from running out (American Red Cross (2010)).
- ➤ Some hospitals have delayed surgeries due to blood shortages on 120 days in a year (Whitaker et al. (2007)).
- ➤ The national estimate for the number of units blood products outdated by blood centers and hospitals was 1,276,000 out of 15,688,000 units (Whitaker et al. (2007)).

The American Red Cross is the major supplier of blood products to hospitals and medical centers satisfying over 45% of the demand for blood components nationally (Walker (2010)).

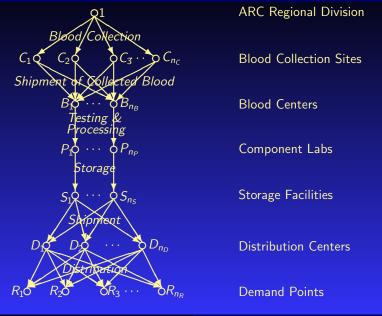


The hospital cost of a unit of red blood cells in the US had a 6.4% increase from 2005 to 2007.

In the US, this criticality has become more of an issue in the Northeastern and Southwestern states since this cost is meaningfully higher compared to that of the Southeastern and Central states.



Supply Chain Network Topology for a Regionalized Blood Bank



We developed a supply chain network optimization model for the management of the procurement, testing and processing, and distribution of a perishable product – that of human blood.

Novel features of the model include:

- ▶ It captures *perishability of this life-saving product* through the use of arc multipliers;
- ▶ It contains *discarding costs* associated with waste/disposal;
- ▶ It handles uncertainty associated with demand points;
- ► It assesses costs associated with shortages/surpluses at the demand points, and
- ▶ It quantifies the *supply-side risk* associated with procurement.

We developed a medical nuclear supply chain network design model which captures the decay of the radioisotope molybdenum.

"Medical Nuclear Supply Chain Design: A Tractable Network Model and Computational Approach," A. Nagurney and L. S. Nagurney, *International Journal of Production Economics* **140(2)** (2012), pp 865-874.



In our medical nuclear supply chain models we capture the radioactive decay through the use of arc multipliers.

Hence, the framework for both our blood supply chain work and medical nuclear work is that of *generalized* networks.

We will highlight how this is done in a full developed game theory model for pharmaceuticals later in this presentation.

Medical nuclear supply chains are essential supply chains in healthcare and provide the conduits for products used in nuclear medical imaging, which is routinely utilized by physicians for diagnostic analysis for both cancer and cardiac problems.

Such supply chains have unique features and characteristics due to the products' time-sensitivity, along with their hazardous nature.

Salient Features

- complexity
- economic aspects
- underlying physics of radioactive decay
- ► importance of considering both waste management and risk management.

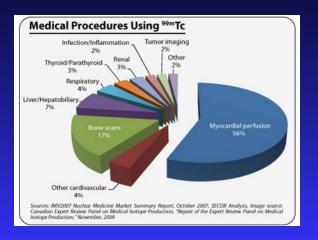
Over 100,000 hospitals in the world use radioisotopes (World Nuclear Association (2011)).

Technetium, ^{99m} Tc, which is a decay product of Molybdenum-99, ⁹⁹ Mo, is the most commonly used medical radioisotope, used in more than 80% of the radioisotope injections, with more than 30 million procedures worldwide each year.

The half-life of Molybdenum-99 is 66 hours.

Each day, 41,000 nuclear medical procedures are performed in the United States using Technetium-99m.

A radioactive isotope is bound to a pharmaceutical that is injected into the patient and travels to the site or organ of interest in order to construct an image for medical diagnostic purposes.



For over two decades, all of the Molybdenum necessary for US-based nuclear medical diagnostic procedures has come from foreign sources.



⁹⁹Mo Supply Chain Challenges:

➤ The majority of the reactors are between 40 and 50 years old. Several of the reactors currently used are due to be retired by the end of this decade(Seeverens (2010) and OECD Nuclear Energy Agency (2010a)).

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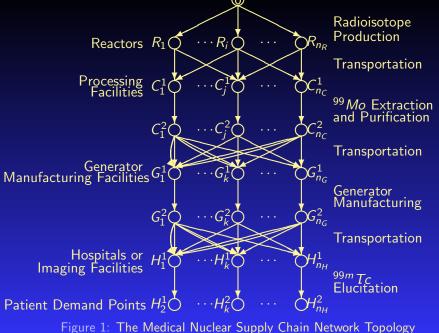
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- ► Limitations in processing capabilities make the world critically vulnerable to Molybdenum supply chain disruptions.
- ► The number of generator manufacturers is under a dozen (OECD Nuclear Energy Agency (2010b)).
- ► Long-distance transportation of the product raises safety and security risks, and also results in greater decay of the product.





Electric Power Supply Chains

We developed an empirical, large-scale electric supply chain network equilibrium model, formulated it as a VI problem, and were able to solve it by exploiting the connection between electric power supply chain networks and transportation networks using our proof of a hypothesis posed in the classic book, Studies in the Economics of Transportation, by Beckmann, McGuire, and Winsten (1956).

The paper, "An Integrated Electric Power Supply Chain and Fuel Market Network Framework: Theoretical Modeling with Empirical Analysis for New England," by Zugang Liu and Anna Nagurney was published in *Naval Research Logistics* **56** (2009), pp 600-624.

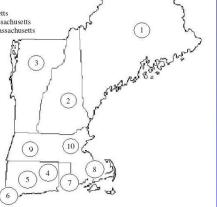
An Empirical Example of an Electric Power Supply Chain for New England

There are 82 generating companies who own and operate 573 generating units. We considered 5 types of fuels: natural gas, residual fuel oil, distillate fuel oil, jet fuel, and coal. The whole area was divided into 10 regions:

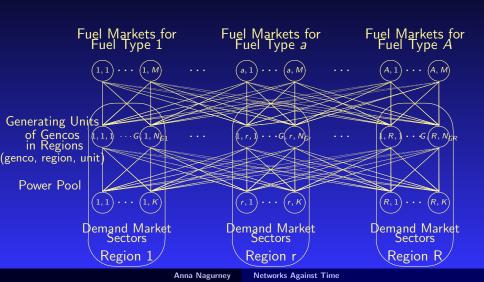
- 1. Maine,
- 2. New Hampshire,
- 3. Vermont,
- 4. Connecticut (excluding Southwest Connecticut),
- 5. Southwestern Connecticut (excluding the Norwalk-Stamford area),
- 6. Norwalk-Stamford area,
- 7. Rhode Island,
- 8. Southeastern Massachusetts,
- 9. Western and Central Massachusetts,
- 10. Boston/Northeast Massachusetts.

Graphic of New England

- 1. Maine
- 2. New Hampshire
- 3. Vermont
- Connecticut (excluding Southwestern Connecticut)
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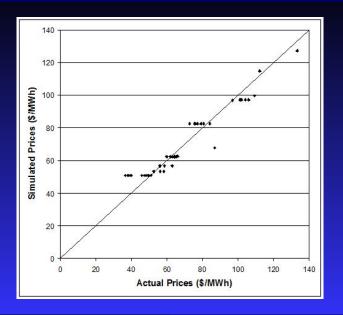
The Electric Power Supply Chain Network with Fuel Supply Markets



We tested the model on the data of July 2006 which included $24 \times 31 = 744$ hourly demand/price scenarios. We sorted the scenarios based on the total hourly demand, and constructed the load duration curve. We divided the duration curve into 6 blocks ($L_1 = 94$ hours, and $L_w = 130$ hours; w = 2, ..., 6) and calculated the average regional demands and the average weighted regional prices for each block.

The empirical model had on the order of 20,000 variables.

Actual Prices Vs. Simulated Prices (\$/Mwh)



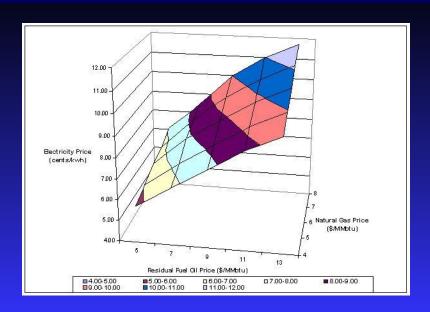
Sensitivity Analysis

We used the same demand data, and then varied the prices of natural gas and residual fuel oil. We assumed that the percentage change of distillate fuel oil and jet fuel prices were the same as that of the residual fuel oil price.

The next figure presents the average electricity price for the two peak blocks under oil/gas price variations.

The surface in the figure represents the average peak electricity prices under different natural gas and oil price combinations.

Sensitivity Analysis



Food Supply Chains

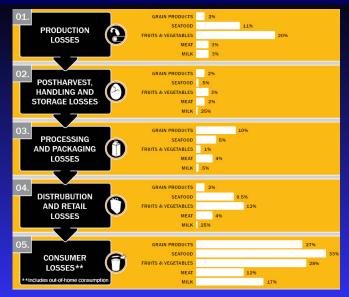
Food is something anyone can relate to.



Fascinating Facts About Food Perishability



Fascinating Facts About Food Perishability



Source: Food and Agriculture Organization 2011

Fascinating Facts About Food Perishability

ABOUT 10 PERCENT OF THE U.S. ENERGY BUDGET GOES TO BRINGING FOOD TO OUR TABLES.

Source: Webber, Michael, "How to Make the Food System More Energy Efficient," Scientific American, December 29, 2011.



ONE INDUSTRY CONSULTANT
ESTIMATES THAT UP TO ONE
IN SEVEN TRUCKLOADS OF
PERISHABLES DELIVERED TO
SUPERMARKETS IS THROWN AWAY.

Source: Beswick, P. et al, "A Retailer's Recipe for Fresher Food and Far Less Shrink," Oliver Wyman, Boston. ergoeditorial.biz/ worksamples/OW%20grocery%20shrinkage.pdf.

FOR THE AVERAGE U.S. HOUSEHOLD OF FOUR, FOOD WASTE TRANSLATES INTO AN ESTIMATED \$1,350 TO \$2,275 IN ANNUAL LOSSES.



Source: Food and Agriculture Organization 2011

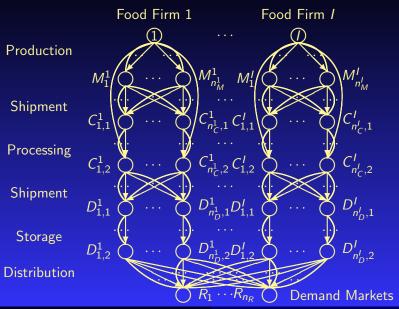
Fresh Produce Food Supply Chains

We developed a fresh produce supply chain network oligopoly model that

- 1. captures the deterioration of fresh food along the entire supply chain from a network perspective;
- 2. handles the exponential time decay through the introduction of arc multipliers;
- formulates oligopolistic competition with product differentiation;
- 4. includes the disposal of the spoiled food products, along with the associated costs;
- 5. allows for the assessment of alternative technologies involved in each supply chain activity.

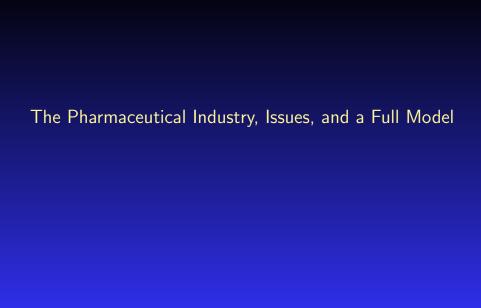
Reference: "Competitive Food Supply Chain Networks with Application to Fresh Produce," Min Yu and Anna Nagurney, European Journal of Operational Research 224(2), (2013), pp 273-282.

Fresh Produce Food Supply Chains



Anna Nagurney

Networks Against Time



The Pharmaceutical Industry

Pharmaceutical, that is, medicinal drug, manufacturing is an immense global industry.

In 2003, worldwide pharmaceutical industry sales were at \$491.8 billion, an increase in sales volume of 9% over the preceding year with *US being the largest national market, accounting for 44% of global industry sales.*

In 2011, the global pharmaceutical industry experienced approximately a growth of 5-7% on sales of approximately \$880 billion (Zacks Equity Research (2011)).

The Pharmaceutical Industry

Although pharmaceutical supply chains have begun to be coupled with sophisticated technologies in order to improve both the quantity and the quality of their associated products, despite all the advances in manufacturing, storage, and distribution methods, pharmaceutical drug companies are far from effectively satisfying market demands on a consistent basis.

In fact, it has been argued that pharmaceutical drug supply chains are in urgent need of efficient optimization techniques in order to reduce costs and to increase productivity and responsiveness (Shah (2004) and Papageorgiou (2009)).

Pharmaceutical Product Perishability

Product perishability is another critical issue in pharmaceutical / drug supply chains.

- In a 2003 survey, the estimated loss incurred *due to the* expiration of branded products in supermarkets and drug stores was over 500 million dollars.
- In 2007, in a warehouse belonging to the Health Department of Chicago, over one million dollars in drugs, vaccines, and other medical supplies were found spoiled, stolen, or unaccounted for.
- In 2009, CVS pharmacies in California, as a result of a settlement of a lawsuit filed against the company, had to offer promotional coupons to customers who had identified expired drugs, including expired baby formula and children's medicines, in more than 42 percent of the stores surveyed the year before.

Pharmaceutical Product Perishability

Other instances of medications sold more than a year past their expiration dates have occurred in other pharmacies across the US.

According to the Harvard Medical School (2003), since a law was passed in the US in 1979, drug manufacturers are required to stamp an expiration date on their products. This is the date at which the manufacturer can still guarantee the full, that is, 100%, potency and safety of the drug, assuming, of course, that proper storage procedures have been followed.

For example, certain medications, including insulin, must be stored under appropriate environmental conditions, and exposure to water, heat, humidity or other factors can adversely affect how certain drugs perform in the human body.

Product Shortages

Ironically, whereas some drugs may be unsold and unused and / or past their expiration dates, the number of drugs that were reported in short supply in the US in the first half of 2011 had risen to 211 — close to an all-time record — with only 58 in short supply in 2004. Currently, more than 300 medicines crucial to treating cancer, infections, cardiac arrest, premature infants, pain, and more are in short supply in the U.S.

H1N1 (Swine) Flu

As of May 2, 2010, worldwide, more than 214 countries and overseas territories or communities reported laboratory confirmed cases of pandemic influenza H1N1 2009, including over 18,001 deaths (www.who.int).

Parts of the globe experienced serious flu vaccine shortages, both seasonal and H1N1 (swine) ones, in late 2009.



An Example of a Critical Medicine Shortage – Cytarabine

In the past year, the US experienced shortages of *critical drug*, *cytarabine*, *due to manufacturer production problems*.



Due to the severity of this medical crisis for leukemia patients, Food and Drug Administration is exploring the possibility of importing this medical product (Larkin (2011)).

Hospira re-entered the market in March 2011 and has made the manufacture of cytarabine a priority ahead of other products.

Some Possible Causes of Shortages

While the causes of many shortages are complex, most cases appear to be related to manufacturers' decisions to cease production in the presence of financial challenges.

It is interesting to note that, among curative cancer drugs, only the older generic, yet, less expensive, ones, have experienced shortages.

As noted by Shah (2004), pharmaceutical companies secure notable returns solely in the early lifetime of a successful drug, before competition takes place. This competition-free time-span, however, has been observed to be shortening, from 5 years to only 1-2 years.

Economic and Financial Pressures

Pharmaceutical companies are expected to suffer a significant decrease in their revenues as a result of losing patent protection for ten of the best-selling drugs by the end of 2012 (De la Garza (2011)).

These include Lipitor and Plavix, that, in 2011, generated more than \$142 billion in sales, and are expected, over the next five years, to be faced with generic competition.

In 2011, pharmaceutical products valued at more than \$30 billion lost patent protection, with such products generating more than \$15 billion in sales in 2010.

Safety Issues

- More than 80% of the ingredients of drugs sold in the US are made overseas, mostly in remote facilities located in China and India that are rarely if not ever visited by government inspectors.
- Supply chains of generic drugs, which account for 75 percent of the prescription medicines sold in the US, are, typically, more susceptible to falsification with the supply chains of some of the over-the-counter products, such as vitamins or aspirins, also vulnerable to adulteration.
- The amount of counterfeit drugs in the European pharmaceutical supply chains has considerably increased.

In the past, product recalls were mainly related to local errors in design, manufacturing, or labeling, a single product safety issue may result in huge global consequences.



The supply chain generalized network oligopoly model has the following novel features:

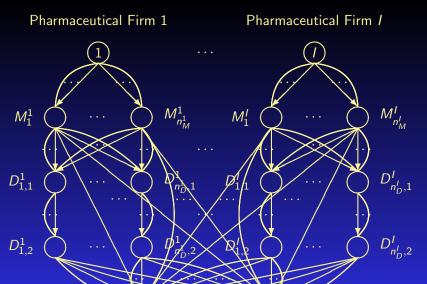
- 1. it handles the perishability of the pharmaceutical product through the introduction of arc multipliers;
- 2. it allows each firm to minimize the discarding cost of waste / perished medicine;
- 3. it captures product differentiation under oligopolistic competition through the branding of drugs, which can also include generics as distinct brands.

References can be found in our paper, "A Supply Chain Generalized Network Oligopoly Model for Pharmaceuticals Under Brand Differentiation and Perishability," A. H. Masoumi, M. Yu, and A. Nagurney, *Transportation Research E* **48** (2012), 762-780.

We consider I pharmaceutical firms, with a typical firm denoted by i.

The firms compete non-cooperatively, in an oligopolistic manner, and the consumers can differentiate among the products of the pharmaceutical firms through their individual product brands.

The supply chain network activities include manufacturing, shipment, storage, and, ultimately, the distribution of the brand name drugs to the demand markets.



 $R_1 \cdots R_{n_R}$ Demand Markets
Figure 3: The Pharmaceutical Supply Chain Network Topology

Each pharmaceutical firm i; $i=1,\ldots,I$, utilizes n_M^i manufacturing plants and n_D^i distribution / storage facilities, and the goal is to serve n_R demand markets consisting of pharmacies, retail stores, hospitals, and other medical centers.

 L^i denotes the set of directed links corresponding to the sequence of activities associated with firm i. Also, G = [N, L] denotes the graph composed of the set of nodes N, and the set of links L, where L contains all sets of L_i s: $L \equiv \bigcup_{i=1,...,I} L^i$.

In the Figure, the first set of links connecting the top two tiers of nodes corresponds to the process of production of the drugs at each of the manufacturing units of firm $i; i = 1, \ldots, I$. Such facilities are denoted by $M_1^i, \ldots, M_{n_M^i}^i$, respectively, for firm i.

We emphasize that the manufacturing facilities may be located not only in different regions of the same country but also in different countries.

The next set of nodes represents the distribution centers, and, thus, the links connecting the manufacturing nodes to the distribution centers are shipment-type links. Such distribution nodes associated with firm $i; i = 1, \ldots, I$ are denoted by $D_{1,1}^i, \ldots, D_{n_D^i,1}^i$ and represent the distribution centers that the produced drugs are shipped to, and stored at, before being delivered to the demand markets.

There are alternative shipment links to denote different possible modes of transportation. In the shipment of pharmaceuticals that are perishable, one may wish, for example, to ship by air, but at a higher cost.

The next set of links connecting nodes $D^i_{1,1},\ldots,D^i_{n^i_D,1}$ to $D^i_{1,2},\ldots,D^i_{n^i_D,2}$; $i=1,\ldots,I$ represents the process of storage.

Since drugs may require different storage conditions / technologies before being ultimately shipped to the demand markets, we represent these alternatives through multiple links at this tier.

The last set of links connecting the two bottom tiers of the supply chain network corresponds to distribution links over which the stored products are shipped from the distribution / storage facilities to the demand markets. Here we also allow for multiple modes of shipment / transportation.

There are direct links connecting manufacturing units with various demand markets in order to capture the possibility of direct mail shipments from manufacturers and the costs should be adjusted (see below) accordingly.

While representing a small percentage of the total filled prescriptions (about 6.1 percent in 2004), mail-order pharmacy sales remained the fastest-growing sector of the US prescription drug retail market in 2004, increasing by 18 percent over the preceding year (The Health Strategies Consultancy LLC (2005)).

Although pharmaceutical products may have different life-times, we can assign a multiplier to each activity / link of the supply chain to represent the fraction of the product that may perish / be wasted / be lost over the course of that activity.

The fraction of lost product depends on the type of the activity since various processes of manufacturing, shipment, storage, and distribution may result in dissimilar amounts of losses.

In addition, this fraction need not be the same among various links of the same tier in the supply chain network since different firms and even different units of the same firm may experience non-identical amounts of waste, depending on the brand of drug, the efficiency of the utilized technology, and the experience of the staff, etc.

Also, such multipliers can capture pilferage / theft, a significant issue in drug supply chains.

We associate with every link a in the supply chain network, a multiplier α_a , which lies in the range of (0,1]. The parameter α_a may be interpreted as a throughput factor corresponding to link a meaning that $\alpha_a \times 100\%$ of the initial flow of product on link a reaches the successor node of that link.

Let f_a denote the (initial) flow of product on link a with f_a' denoting the final flow on link a; i.e., the flow that reaches the successor node of the link after wastage has taken place. Therefore, we have:

$$f_a' = \alpha_a f_a, \qquad \forall a \in L.$$
 (1)

Consequently, the waste / loss on link a, denoted by w_a , which is the difference between the initial and the final flow, can be derived as:

$$w_a = f_a - f_a' = (1 - \alpha_a)f_a, \qquad \forall a \in L.$$
 (2)

The parameter α_a is assumed to be constant and known a priori. We can construct a total discarding cost function, \hat{z}_a , associated with discarding the medical waste, which is a function of the flow, f_a , and is assumed to be convex and continuously differentiable:

$$\hat{z}_a = \hat{z}_a(f_a), \qquad \forall a \in L.$$
 (3)

Let x_p represent the (initial) flow of product on path p joining an origin node, i, with a destination node, R_k . The path flows must be nonnegative, that is,

$$x_p \ge 0, \qquad \forall p \in P_k^i; i = 1, \dots, I; k = 1, \dots, n_R,$$
 (4)

where P_k^i is the set of all paths joining the origin node i; i = 1, ..., I with destination node R_k .

Also, μ_p denotes the multiplier corresponding to the throughput on path p, defined as the product of all link multipliers on links comprising that path, that is,

$$\mu_p \equiv \prod_{\mathbf{a} \in p} \alpha_{\mathbf{a}}, \qquad \forall p \in P_k^i; \ i = 1, \dots, I; k = 1, \dots, n_R.$$
(5)



We define the multiplier, α_{ap} , which is the product of the multipliers of the links on path p that precede link a in that path, as follows:

$$\alpha_{ap} \equiv \begin{cases} \delta_{ap} \prod_{a' < a} \alpha_{a'}, & \text{if } \{a' < a\} \neq \emptyset, \\ \delta_{ap}, & \text{if } \{a' < a\} = \emptyset, \end{cases}$$

$$(6)$$

where $\{a' < a\}$ denotes the set of the links preceding link a in path p, and \emptyset denotes the null set. In addition, δ_{ap} is defined as equal to 1 if link a is contained in path p, and 0, otherwise. As a result, α_{ap} is equal to the product of all link multipliers preceding link a in path p. If link a is not contained in path p, then α_{ap} is set to zero. If a belongs to the first set of links; i.e., the manufacturing links, this multiplier is equal to 1.

Hence, the relationship between the link flow, f_a , and the path flows can be expressed as:

$$f_a = \sum_{i=1}^{I} \sum_{k=1}^{n_R} \sum_{p \in P_L^i} x_p \ \alpha_{ap}, \qquad \forall a \in L.$$
 (7)

Note that the arc multipliers may be obtained from historical and statistical data.

They may also, in the case of certain perishable products, be related to an exponential time decay function where the time, in our framework, is associated with each specific link activity (see, for instance, Blackburn and Scudder (2009) and Bai and Kendall (2009)).

For example, Nagurney and Nagurney (2011) constructed explicit arc multipliers for molybdenum, which is used in nuclear medicine, which were based on the physics of time decay for this pharmaceutical product used in cancer and cardiac diagnostics, among other procedures.

Let d_{ik} denote the demand for pharmaceutical firm i's brand drug; $i=1,\ldots,I$, at demand market R_k ; $k=1,\ldots,n_R$. The consumers differentiate the products by their brands.

The following equation reveals the relationship between the path flows and the demands in the supply chain network:

$$\sum_{p \in P_k^i} x_p \mu_p = d_{ik}, \quad i = 1, \dots, I; k = 1, \dots, n_R,$$
 (8)

that is, the demand for a brand drug at the demand market R_k is equal to the sum of all the final flows – subject to perishability – on paths joining (i, R_k) . We group the demands d_{ik} ; $i = 1, \ldots, I$; $k = 1, \ldots, n_R$ into the $n_R \times I$ -dimensional vector d.

The Demand Price Functions

A demand price function is associated with each firm's pharmaceutical drug at each demand market. We denote the demand price of firm i's product at demand market R_k by ρ_{ik} and assume that

$$\rho_{ik} = \rho_{ik}(d), \quad i = 1, \dots, I; k = 1, \dots, n_R.$$
(9)

The Total Cost Functions

The total operational cost on link a may, in general, depend upon the product flows on all the links, that is,

$$\hat{c}_a = \hat{c}_a(f), \quad \forall a \in L,$$
 (10)

where f is the vector of all the link flows. The total cost on each link is assumed to be convex and continuously differentiable.

 X_i denotes the vector of path flows associated with firm i; $i=1,\ldots,I$, where $X_i\equiv\{\{x_p\}|p\in P^i\}\}\in R_+^{n_{p^i}}$, and $P^i\equiv \cup_{k=1,\ldots,n_R}P_k^i$. In turn, n_{P^i} , denotes the number of paths from firm i to the demand markets. Thus, X is the vector of all the firms' strategies, that is, $X\equiv\{\{X_i\}|i=1,\ldots,I\}$.

The Profit Function

The profit function of firm i, denoted by U_i , is expressed as:

$$U_{i} = \sum_{k=1}^{n_{R}} \rho_{ik}(d) \sum_{p \in P_{k}^{i}} \mu_{p} x_{p} - \sum_{a \in L^{i}} \hat{c}_{a}(f) - \sum_{a \in L^{i}} \hat{z}_{a}(f_{a}).$$
 (11)

In lieu of the conservation of flow expressions (7) and (8), and the functional expressions (3), (9), and (10), we may define $\hat{U}_i(X) = U_i$ for all firms i; i = 1, ..., I, with the I-dimensional vector \hat{U} being the vector of the profits of all the firms:

$$\hat{U} = \hat{U}(X). \tag{12}$$

Supply Chain Generalized Network Cournot-Nash Equilibrium

In the Cournot-Nash oligopolistic market framework, each firm selects its product path flows in a noncooperative manner, seeking to maximize its own profit, until an equilibrium is achieved, according to the definition below.

Definition 1: Supply Chain Generalized Network Cournot-Nash Equilibrium

A path flow pattern $X^* \in K = \prod_{i=1}^{I} K_i$ constitutes a supply chain generalized network Cournot-Nash equilibrium if for each firm i; i = 1, ..., I:

$$\hat{U}_i(X_i^*, \hat{X}_i^*) \ge \hat{U}_i(X_i, \hat{X}_i^*), \quad \forall X_i \in K_i,$$
(13)

where
$$\hat{X}_i^* \equiv (X_1^*, \dots, X_{i-1}^*, X_{i+1}^*, \dots, X_l^*)$$
 and $K_i \equiv \{X_i | X_i \in R_+^{n_{pi}}\}.$

Anna Nagurney

An equilibrium is established if no firm can unilaterally improve its profit by changing its production path flows, given the production path flow decisions of the other firms.

Next, we present the variational inequality formulations of the Cournot-Nash equilibrium for the pharmaceutical supply chain network under oligopolistic competition satisfying Definition 1, in terms of both path flows and link flows (see Cournot (1838), Nash (1950, 1951), Gabay and Moulin (1980), and Nagurney (2006)).

Theorem 1

Assume that, for each pharmaceutical firm i; i = 1, ..., I, the profit function $\hat{U}_i(X)$ is concave with respect to the variables in X_i , and is continuously differentiable. Then $X^* \in K$ is a supply chain generalized network Cournot-Nash equilibrium according to Definition 1 if and only if it satisfies the variational inequality:

$$-\sum_{i=1}^{I}\langle\nabla_{X_i}\hat{U}_i(X^*),X_i-X_i^*\rangle\geq 0,\quad\forall X\in\mathcal{K},$$
 (14)

where $\langle \cdot, \cdot \rangle$ denotes the inner product in the corresponding Euclidean space and $\nabla_{X_i} \hat{U}_i(X)$ denotes the gradient of $\hat{U}_i(X)$ with respect to X_i .

Variational inequality (14), in turn, for our model, is equivalent to the variational inequality: determine $x^* \in K^1$ such that:

$$\sum_{i=1}^{I} \sum_{k=1}^{n_R} \sum_{p \in P_i^i} \left[\frac{\partial \hat{C}_p(x^*)}{\partial x_p} + \frac{\partial \hat{Z}_p(x^*)}{\partial x_p} - \rho_{ik}(x^*) \mu_p - \right]$$

$$\sum_{l=1}^{n_R} \frac{\partial \rho_{il}(x^*)}{\partial d_{ik}} \mu_p \sum_{p \in P_i^l} \mu_p x_p^* \bigg] \times [x_p - x_p^*] \ge 0, \quad \forall x \in K^1, \quad (15)$$

where $K^1 \equiv \{x | x \in R_+^{n_P}\}$, and, for notational convenience, we denote:

$$\frac{\partial \hat{C}_{p}(x)}{\partial x_{p}} \equiv \sum_{b \in L^{i}} \sum_{a \in L^{i}} \frac{\partial \hat{c}_{b}(f)}{\partial f_{a}} \alpha_{ap} \text{ and } \frac{\partial \hat{Z}_{p}(x)}{\partial x_{p}} \equiv \sum_{a \in L^{i}} \frac{\partial \hat{z}_{a}(f_{a})}{\partial f_{a}} \alpha_{ap}.$$
(16)

Variational inequality (15) can also be re-expressed in terms of link flows as: determine the vector of equilibrium link flows and the vector of equilibrium demands $(f^*, d^*) \in K^2$, such that:

$$\sum_{i=1}^{I} \sum_{a \in L^{i}} \left[\sum_{b \in L^{i}} \frac{\partial \hat{c}_{b}(f^{*})}{\partial f_{a}} + \frac{\partial \hat{z}_{a}(f^{*}_{a})}{\partial f_{a}} \right] \times [f_{a} - f^{*}_{a}]$$

$$+\sum_{i=1}^{I}\sum_{k=1}^{n_{R}}\left[-\rho_{ik}(d^{*})-\sum_{l=1}^{n_{R}}\frac{\partial\rho_{il}(d^{*})}{\partial d_{ik}}d_{il}^{*}\right]\times[d_{ik}-d_{ik}^{*}]\geq0,\quad\forall(f,d)\in\mathcal{K}^{2},$$
(17)

where $K^2 \equiv \{(f, d) | x \ge 0, \text{ and } (7) \text{ and } (8) \text{ hold} \}.$

Variational inequalities (15) and (17) can be put into standard form (see Nagurney (1999)): determine $X^* \in \mathcal{K}$ such that:

$$\langle F(X^*), X - X^* \rangle \ge 0, \quad \forall X \in \mathcal{K},$$
 (18)

where $\langle \cdot, \cdot \rangle$ denotes the inner product in *n*-dimensional Euclidean space. Let: $X \equiv x$ and

$$F(X) \equiv \left[\frac{\partial \hat{C}_{p}(x)}{\partial x_{p}} + \frac{\partial \hat{Z}_{p}(x)}{\partial x_{p}} - \rho_{ik}(x)\mu_{p} - \sum_{l=1}^{n_{R}} \frac{\partial \rho_{il}(x)}{\partial d_{ik}} \mu_{p} \sum_{p \in P_{l}^{i}} \mu_{p} x_{p}; \ p \in P_{k}^{i}; \ n \in P_{k}^{i$$

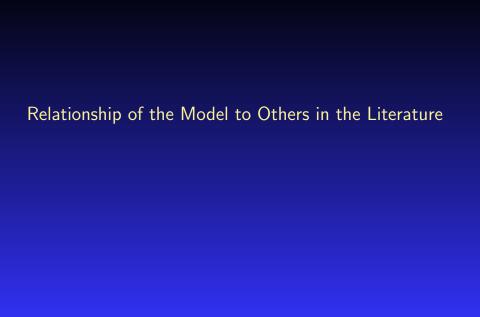
and $\mathcal{K} \equiv K^1$.

Similarly, for the variational inequality in terms of link flows, if we define the column vectors: $X \equiv (f, d)$ and $F(X) \equiv (F_1(X), F_2(X))$:

$$F_1(X) = \left[\sum_{b \in L^i} \frac{\partial \hat{c}_b(f)}{\partial f_a} + \frac{\partial \hat{z}_a(f_a)}{\partial f_a}; \ a \in L^i; \ i = 1, \dots, I \right],$$

$$F_2(X) = \left[-\rho_{ik}(d) - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d)}{\partial d_{ik}} d_{il}; i = 1, \ldots, l; k = 1, \ldots, n_R\right],$$

and let $\mathcal{K} \equiv K^2$.



The above model is now related to several models in the literature.

If the arc multipliers are all equal to 1, in which case the product is not perishable, then the model is related to the sustainable fashion supply chain network model of Nagurney and Yu in the *International Journal of Production Economics* **135** (2012), 532-540. In that model, however, the other criterion, in addition to the profit maximization one, was emission minimization, rather than waste cost minimization, as in the model in this paper.





If the demands are fixed, and there is a single organization, but there are additional processing tiers, as well as capacity investments as variables, the model is the medical nuclear supply chain design model of Nagurney and Nagurney, *International Journal of Production Economics* (2012).

If the demands are fixed, and there is a single organization, but there are additional processing tiers, as well as capacity investments as variables, the model is the medical nuclear supply chain design model of Nagurney and Nagurney, *International Journal of Production Economics* (2012).

If there is only a single organization / firm, and the demands are subject to uncertainty, with the inclusion of expected costs due to shortages or excess supplies, the total operational cost functions are separable, and a criterion of risk is added, then the model above is related to the blood supply chain network operations management model of Nagurney, Masoumi, and Yu, Computational Management Science (2012).

If the product is homogeneous, and all the arc multipliers are, again, assumed to be equal to 1, and the total costs are assumed to be separable, then the above model collapses to the supply chain network oligopoly model of Nagurney (2010) in which synergies associated with mergers and acquisitions were assessed.



The Original Supply Chain Network Oligopoly Model

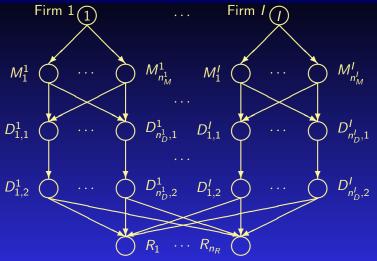


Figure 4: Supply Chain Network Structure of the Oligopoly Without Perishability; Nagurney, *Computational Management Science* **7**(2010), 377-401.

Mergers Through Coalition Formation

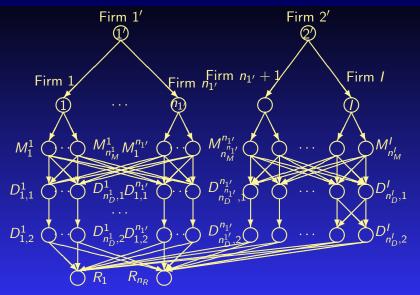


Figure 5: Mergers of the First $n_{1'}$ Firms and the Next $n_{2'}$ Firms



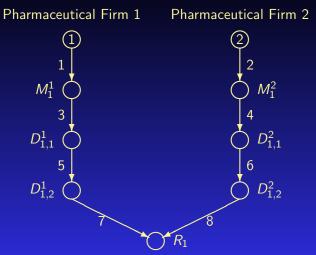


Figure 6: Supply Chain Network Topology for the Pharmaceutical Duopoly in the Illustrative Example

In this example, two pharmaceutical firms compete in a duopoly with a single demand market (See Figure). The two firms produce differentiated, but substitutable, brand drugs 1 and 2, corresponding to Firm 1 and Firm 2, respectively.

The total cost functions on the various links of manufacturing, shipment, storage, and distribution are:

$$\hat{c}_1(f_1) = 5f_1^2 + 8f_1, \ \hat{c}_2(f_2) = 7f_2^2 + 3f_2, \ \hat{c}_3(f_3) = 2f_3^2 + f_3,$$

$$\hat{c}_4(f_4) = 2f_4^2 + 2f_4,$$

$$\hat{c}_5(f_5) = 3f_5^2 + 4f_5, \ \hat{c}_6(f_6) = 3.5f_6^2 + f_6, \ \hat{c}_7(f_7) = 2f_7^2 + 5f_7,$$

$$\hat{c}_8(f_8) = 1.5f_8^2 + 4f_8.$$

The arc multipliers are given by:

$$\alpha_1 = .95, \ \alpha_2 = .98, \ \alpha_3 = .99, \ \alpha_4 = 1.00, \ \alpha_5 = .99, \ \alpha_6 = .97,$$

$$\alpha_7 = 1.00, \ \alpha_8 = 1.00.$$

The total discarding cost functions on the links are assumed identical, that is,

$$\hat{z}_a(f_a) = .5f_a^2, \quad \forall a.$$

The firms compete in the demand market R_1 , and the consumers reveal their preferences for the two products through the following nonseparable demand price functions:

$$\rho_{11}(d) = -3d_{11} - d_{21} + 200, \quad \rho_{21}(d) = -4d_{21} - 1.5d_{11} + 300.$$

In this supply chain network, there exists one path corresponding to each firm, denoted by p_1 and p_2 .

Thus, variational inequality (15), here takes the form:

$$\left[\frac{\partial \hat{C}_{p_{1}}(x^{*})}{\partial x_{p_{1}}} + \frac{\partial \hat{Z}_{p_{1}}(x^{*})}{\partial x_{p_{1}}} - \rho_{11}(x^{*})\mu_{p_{1}} - \frac{\partial \rho_{11}(x^{*})}{\partial d_{11}}\mu_{p_{1}} \times \mu_{p_{1}}x_{p_{1}}^{*} \right] \\
\times [x_{p_{1}} - x_{p_{1}}^{*}] \\
+ \left[\frac{\partial \hat{C}_{p_{2}}(x^{*})}{\partial x_{p_{2}}} + \frac{\partial \hat{Z}_{p_{2}}(x^{*})}{\partial x_{p_{2}}} - \rho_{21}(x^{*})\mu_{p_{2}} - \frac{\partial \rho_{21}(x^{*})}{\partial d_{21}}\mu_{p_{2}} \times \mu_{p_{2}}x_{p_{2}}^{*} \right] \\
\times [x_{p_{2}} - x_{p_{2}}^{*}] \ge 0, \ \forall x \in K^{1}.$$

Under the assumption that $x_{p_1}^* > 0$ and $x_{p_2}^* > 0$, the two expressions on the left-hand side of inequality (27) must be equal to zero, that is:

$$\left[\frac{\partial \hat{C}_{\rho_{1}}(x^{*})}{\partial x_{\rho_{1}}} + \frac{\partial \hat{Z}_{\rho_{1}}(x^{*})}{\partial x_{\rho_{1}}} - \rho_{11}(x^{*})\mu_{\rho_{1}} - \frac{\partial \rho_{11}(x^{*})}{\partial d_{11}}\mu_{\rho_{1}} \times \mu_{\rho_{1}}x_{\rho_{1}}^{*} \right] \times [x_{\rho_{1}} - x_{\rho_{1}}^{*}] = 0,$$

and

$$\left[\frac{\partial \hat{C}_{p_{2}}(x^{*})}{\partial x_{p_{2}}} + \frac{\partial \hat{Z}_{p_{2}}(x^{*})}{\partial x_{p_{2}}} - \rho_{21}(x^{*})\mu_{p_{2}} - \frac{\partial \rho_{21}(x^{*})}{\partial d_{21}}\mu_{p_{2}} \times \mu_{p_{2}}x_{p_{2}}^{*} \right] \times [x_{p_{2}} - x_{p_{2}}^{*}] = 0.$$

Since each of the paths flows must be nonnegative, we know that the term preceding the multiplication sign in both of the above must be equal to zero.

Calculating the values of the multipliers from (6), and then, substituting those values, as well as, the given functions into (16), we can determine the partial derivatives of the total operational cost and the total discarding cost functions. Furthermore, the partial derivatives of the given demand price functions can be calculated and substituted into the above. Applying (5), the path multipliers are equal to:

$$\mu_{p_1} = \alpha_1 \times \alpha_3 \times \alpha_5 \times \alpha_7 = .95 \times .99 \times .99 \times 1 = .93,$$

$$\mu_{p_2} = \alpha_2 \times \alpha_4 \times \alpha_6 \times \alpha_8 = .98 \times 1 \times .97 \times 1 = .95.$$

Simple arithmetic calculations, with the above substitutions, yield the below system of equations:

$$\begin{cases} 31.24x_{p_1}^* + 0.89x_{p_2}^* = 168.85, \\ 1.33x_{p_1}^* + 38.33x_{p_2}^* = 274.46. \end{cases}$$

Thus, the equilibrium solution corresponding to the path flow of brand drugs produced by firms 1 and 2 is:

$$x_{p_1}^* = 5.21, \quad x_{p_2}^* = 6.98.$$

Using (7), the equilibrium link flows can be calculated as:

$$f_1^* = 5.21$$
, $f_3^* = 4.95$, $f_5^* = 4.90$, $f_7^* = 4.85$, $f_2^* = 6.98$, $f_4^* = 6.84$, $f_6^* = 6.84$, $f_8^* = 6.64$.

From (8), the equilibrium values of demand for products of the two pharmaceutical firms are equal to:

$$d_{11}^* = 4.85, \quad d_{21}^* = 6.64.$$

Finally, the equilibrium prices of the two branded drugs are:

$$\rho_{11} = 178.82, \quad \rho_{21} = 266.19.$$

Note that, even though the price of Firm 2's product is observed to be higher, the market has a slightly stronger tendency toward this product as opposed to the product of Firm 1.

This is due to the willingness of the consumers to spend more on one product which can be a consequence of the reputation, or the perceived quality, of Firm 2's brand drug.

The Algorithm with Explicit Formulae

The Algorithm

We recall the Euler method, which is induced by the general iterative scheme of Dupuis and Nagurney (1993). Its realization for the solution of the supply chain generalized network oligopoly model with brand differentiation governed by variational inequality (15) induces subproblems that can be solved explicitly and in closed form.

Specifically, iteration τ of the Euler method (see also Nagurney and Zhang (1996)) is given by:

$$X^{\tau+1} = P_{\mathcal{K}}(X^{\tau} - \mathsf{a}_{\tau} \mathsf{F}(X^{\tau})),$$

where $P_{\mathcal{K}}$ is the projection on the feasible set \mathcal{K} and F is the function that enters the variational inequality problem (18).

The Algorithm

As shown in Dupuis and Nagurney (1993) and Nagurney and Zhang (1996), for convergence of the general iterative scheme, which induces the Euler method, the sequence $\{a_{\tau}\}$ must satisfy: $\sum_{\tau=0}^{\infty} a_{\tau} = \infty$, $a_{\tau} > 0$, $a_{\tau} \to 0$, as $\tau \to \infty$.

Conditions for convergence of this scheme as well as various applications to the solutions of network oligopolies can be found in Nagurney and Zhang (1996), Nagurney, Dupuis, and Zhang (1994), Nagurney (2010a), and Nagurney and Yu (2011).

The Algorithm

Explicit Formulae for the Euler Method Applied to the Supply Chain Generalized Network Oligopoly Variational Inequality (15)

The elegance of this procedure for the computation of solutions to our supply chain generalized network oligopoly model with product differentiation can be seen in the following explicit formulae. We have the following closed form expressions for all the path flows $p \in P_{\nu}^{i}, \forall i, k$:

$$x_p^{\tau+1} = \max$$

$$\{0, x_p^{\tau} + a_{\tau}(\rho_{ik}(x^{\tau})\mu_p + \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(x^{\tau})}{\partial d_{ik}}\mu_p \sum_{p \in P_l^i} \mu_p x_p^{\tau} - \frac{\partial \hat{C}_p(x^{\tau})}{\partial x_p} - \frac{\partial \hat{Z}_p(x^{\tau})}{\partial x_p})\}.$$

Numerical Cases



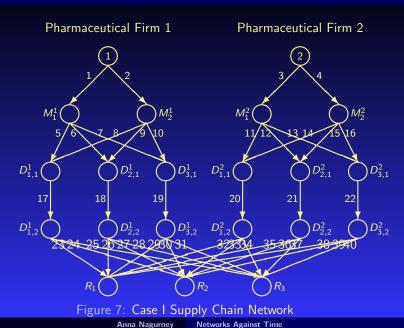
Case I

This case is assumed to have occurred in the third quarter of 2011 prior to the expiration of the patent for Lipitor.

Firm 1 represents a multinational pharmaceutical giant, hypothetically, Pfizer, Inc., which still possesses the patent for Lipitor, the most popular brand of cholesterol-lowering drug.

Firm 2, on the other hand, which might represent, for example, Merck & Co., Inc., has been producing Zocor, another cholesterol regulating brand, whose patent expired in 2006.

The Pharmaceutical Supply Chain Network Topology for Case I



Case I (cont'd)

The demand price functions were as follows:

$$\rho_{11}(d) = -1.1d_{11} - 0.9d_{21} + 275; \ \rho_{21}(d) = -1.2d_{21} - 0.7d_{11} + 210;$$

$$\rho_{12}(d) = -0.9d_{12} - 0.8d_{22} + 255; \ \rho_{22}(d) = -1.0d_{22} - 0.5d_{12} + 200;$$

$$\rho_{13}(d) = -1.4d_{13} - 1.0d_{23} + 265; \ \rho_{23}(d) = -1.5d_{23} - 0.4d_{13} + 186.$$

The Euler method for the solution of variational inequality was implemented in Matlab. The results can be seen in the following tables.

Link Multipliers, Total Cost Functions and Link Flow Solution for Case I

Link a	α_{a}	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	13.73
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	10.77
3	.96	$6.5f_3^2 + 4f_3$	$.3f_3^2$	8.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	10.55
5	1.00	$.7f_5^2 + f_5$	$.5f_5^2$	5.21
6	.99	$.9f_6^{2} + 2f_6$	$.5f_6^2$	3.36
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	4.47
8	.99	$f_8^2 + 2f_8$	$.6f_8^2$	3.02
9	1.00	$.7f_9^2 + 3f_9$	$.6f_9^2$	3.92
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^2$	3.50
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	3.10
12	.99	$.8f_{12}^2 + 5f_{12}$	$.4f_{12}^2$	2.36
13	.98	$.9f_{13}^2 + 4f_{13}$	$.4f_{13}^2$	2.63
14	1.00	$.8f_{14}^2 + 2f_{14}$	$.5f_{14}^2$	3.79
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	3.12
16	1.00	$1.1f_{16}^2 + 3f_{16}$	$.6f_{16}^2$	3.43
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	8.20
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^{\overline{2}}$	7.25
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^2$	7.97
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^{2}$	6.85

Link Multipliers, Total Cost Functions and Solution for Case I (cont'd)

Link a	$lpha_{a}$	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f _a *
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	5.42
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	6.00
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	3.56
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.66
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	2.82
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	3.34
27	.99	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^{2}$	1.24
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	2.59
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	3.45
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.28
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	3.09
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.54
33	.99	$.4f_{33}^2 + 3f_{33}$	$.3f_{33}^2$	3.43
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^2$	0.75
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^2$	1.72
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	2.64
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^2$	0.95
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^{\bar{2}}$	3.47
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^2$	2.47
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^{2}$	0.00

Case I: Result Analysis

The computed equilibrium demands for each of the two brands were:

$$d_{11}^* = 10.32, d_{21}^* = 7.66,$$

 $d_{12}^* = 4.17, d_{22}^* = 8.46,$
 $d_{13}^* = 8.41, d_{23}^* = 1.69.$

The incurred equilibrium prices associated with the branded drugs at each demand market were as follows:

$$ho_{11}(d^*) = 256.75, \
ho_{21}(d^*) = 193.58,$$

$$ho_{12}(d^*) = 244.48, \
ho_{22}(d^*) = 189.46,$$

$$ho_{13}(d^*) = 251.52, \
ho_{23}(d^*) = 180.09.$$

Case I: Result Analysis

Firm 1, which produces the top-selling product, captures the majority of the market share at demand markets 1 and 3, despite the higher price. In fact, it has almost entirely seized demand market 3 forcing several links connecting Firm 2 to demand market 3 to have insignificant flows including link 40 with a flow equal to zero.

Firm 2 dominates demand market 2, due to the consumers' willingness to lean towards this product there, perhaps as a consequence of the lower price, or the perception of quality, etc.

The profits of the two firms are:

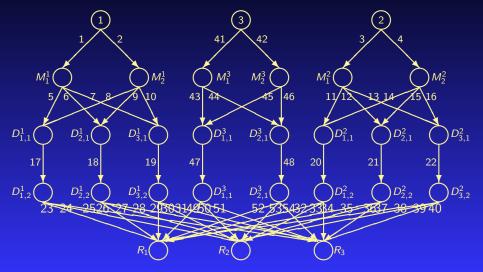
$$U_1(X^*) = 2{,}936.52$$
 and $U_2(X^*) = 1{,}675.89$.

A Case Study -Case II

In this case, we consider the scenario in which Firm 1 has just lost the exclusive patent right of its highly popular cholesterol regulator. A manufacturer of generic drugs, say, Sanofi, here denoted by Firm 3, has recently introduced a generic substitute for Lipitor by reproducing its active ingredient Atorvastatin (Smith (2011)). Firm 3 is assumed to have two manufacturing plants, two distribution centers as well as two storage facilities in order to supply the same three demand markets as in Case I (See Figure).

The Pharmaceutical Supply Chain Network Topology for Cases II and III

Pharmaceutical Firm 1 Pharmaceutical Firm 3 Pharmaceutical Firm 2



Case II

Firm 1 has just lost the exclusive patent right of its highly popular cholesterol regulator. A manufacturer of generic drugs, say, Ranbaxy Laboratories, here denoted by Firm 3, has recently introduced a generic substitute for Lipitor by reproducing its active ingredients.

The demand price functions for the products of Firm 1 and 2 will stay the same as in Case I. The demand price functions corresponding to the product of Firm 3 are as follows:

$$\rho_{31}(d) = -0.9d_{31} - 0.6d_{11} - 0.8d_{21} + 150;$$

$$\rho_{32}(d) = -0.8d_{32} - 0.5d_{12} - 0.6d_{22} + 130;$$

$$\rho_{33}(d) = -0.9d_{33} - 0.7d_{13} - 0.5d_{23} + 133.$$

Link a	α_{a}	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f _a *
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	13.73
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	10.77
3	.96	$6.5f_3^2 + 4f_3$	$.4f_2^2$ $.3f_3^2$	8.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	10.55
5	1.00	$.7f_5^2 + f_5$	$.5f_5^{2}$ $.5f_6^{2}$ $.5f_7^{2}$	5.21
6	.99	$.9f_{6}^{2}+2f_{6}$	$.5f_6^2$	3.36
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	4.47
8	.99	$f_8^2 + 2f_8$.6f ₈ ²	3.02
9	1.00	$.7f_9^2 + 3f_9$	$.6f_8^2$ $.6f_9^2$	3.92
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^2$	3.50
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	3.10
12	.99	$.8f_{12}^2 + 5f_{12}$	$.4f_{12}^{2}$	2.36
13	.98	$.9f_{13}^2 + 4f_{13}$	$.4f_{13}^2$	2.63
14	1.00	$.9f_{13}^{2} + 4f_{13}$ $.8f_{14}^{2} + 2f_{14}$	$.5f_{14}^{2}$	3.79
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	3.12
16	1.00	$1.1f_{16}^2 + 3f_{16}$ $2f_{17}^2 + 3f_{17}$	$.6f_{16}^2$	3.43
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	8.20
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	7.25
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^{2}$	7.97
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^2$	6.85
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	5.42
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	6.00
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	3.56
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.66
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	2.82
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	3.34
27	.99	$.7f_{27}^2 + .8f_{27}$.4f ₂₇	1.24

Link Multipliers, Total Cost Functions and Link Flow Solution for Case II

Link a	α_{a}	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	2.59
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	3.45
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.28
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	3.09
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.54
33	.99	$.4f_{33}^2 + 3f_{33}$	$.3f_{33}^2$	3.43
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^{2}$	0.75
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^2$	1.72
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	2.64
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^{2}$	0.95
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^2$	3.47
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^2$	2.47
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^{2}$	0.00
41	.97	$3f_{41}^2 + 12f_{41}$	$.3f_{41}^{2}$	6.17
42	.96	$2.7f_{42}^2 + 10f_{42}$	$.4f_{42}^{2}$	6.23
43	.98	$1.1f_{43}^2 + 6f_{43}$	$.45f_{43}^2$	3.23
44	.98	$.9f_{44}^2 + 5f_{44}$	$.45f_{44}^2$	2.75
45	.97	$1.3f_{45}^2 + 6f_{45}$	$.5f_{45}^2$	3.60
46	.99	$1.5f_{46}^2 + 7f_{46}$	$.55f_{46}^2$	2.38
47	.98	$1.5f_{47}^2 + 4f_{47}$	$.4f_{47}^2$	6.66
48	.98	$2.1f_{48}^2 + 6f_{48}$	$.45f_{48}^2$	5.05
49	.99	$.6f_{49}^2 + 3f_{49}$	$.55f_{49}^2$	3.79
50	1.00	$.7f_{50}^2 + 2f_{50}$	$.7f_{50}^2$	1.94
51	.98	$.6f_{51}^2 + 7f_{51}$	$.45f_{51}^2$	0.79
52	.99	$.9f_{52}^2 + 9f_{52}$	$.5f_{52}^2$	1.43
53	1.00	$.55f_{53}^2 + 6f_{53}$	$.55f_{53}^2$	1.23
54	.98	$.8f_{54}^2 + 4f_{54}$	$.5f_{54}^2$	2.28

Link Multipliers, Total Cost Functions and Solution for Case II (cont'd)

Case II: Result Analysis

The equilibrium product flows of Firms 1 and 2 on links 1 through 40 are identical to the corresponding values in Case I.

When the new product produced by Firm 3 is just introduced, the manufacturers of the two existing products will not experience an immediate impact on their respective demands of branded drugs.

The equilibrium computed demands for the products of Firms 1 and 2 at the demand markets will remain as in Case I, and the equilibrium amounts of demand for the new product of Firm 3 at each demand market is equal to:

$$d_{31}^* = 5.17$$
, $d_{32}^* = 3.18$, and $d_{33}^* = 3.01$.

Case II: Result Analysis

The equilibrium prices associated with the branded drugs 1 and 2 at the demand markets will not change, whereas the incurred equilibrium prices of generic drug 3 are as follows:

$$\rho_{31}(d^*) = 133.02, \quad \rho_{32}(d^*) = 120.30, \quad \text{and } \rho_{33}(d^*) = 123.55,$$

which is significantly lower than the respective prices of its competitors in all the demand markets.

Thus, the profit that Firm 3 derived from manufacturing and delivering the new generic substitute to these 3 markets is:

$$U_3(X^*) = 637.38,$$

while the profits of Firms 1 and 2 remain unchanged.

Case III

The generic product of Firm 3 has now been well-established, and has affected the behavior of the consumers through the demand price functions of the relatively more recognized products of Firms 1 and 2. The demand price functions associated are now given by:

Firm 1:
$$\rho_{11}(d) = -1.1d_{11} - 0.9d_{21} - 1.0d_{31} + 192;$$

$$\rho_{21}(d) = -1.2d_{21} - 0.7d_{11} - 0.8d_{31} + 176;$$

$$\rho_{31} = -0.9d_{31} - 0.6d_{11} - 0.8d_{21} + 170;$$
Firm 2: $\rho_{12}(d) = -0.9d_{12} - 0.8d_{22} - 0.7d_{32} + 166;$

$$\rho_{22}(d) = -1.0d_{22} - 0.5d_{12} - 0.8d_{32} + 146;$$

$$\rho_{32}(d) = -0.8d_{32} - 0.5d_{12} - 0.6d_{22} + 153;$$
Firm 3: $\rho_{13}(d) = -1.4d_{13} - 1.0d_{23} - 0.5d_{33} + 173;$

$$\rho_{23}(d) = -1.5d_{23} - 0.4d_{13} - 0.7d_{33} + 164;$$

$$\rho_{33}(d) = -0.9d_{33} - 0.7d_{13} - 0.5d_{23} + 157.$$

Link a	α_{a}	$\hat{c}_a(f_a)$	ŝa(fa)	f _a *
1	.95	$5f_1^2 + 8f_1$	$.5f_1^2$	8.42
2	.97	$7f_2^2 + 3f_2$	$.4f_2^2$	6.72
3	.96	$6.5f_3^2 + 4f_3$	$.3f_3^2$	6.42
4	.98	$5f_4^2 + 7f_4$	$.35f_4^2$	8.01
5	1.00	$.7f_5^2 + f_5$	$.5f_5^2$	3.20
6	.99	$.9f_6^{2} + 2f_6$	$.5f_6^2$	2.07
7	1.00	$.5f_7^2 + f_7$	$.5f_7^2$	2.73
8	.99	$f_8^2 + 2f_8$.6f ₈ ²	1.85
9	1.00	$.7f_9^2 + 3f_9$	$.6f_{q}^{2}$	2.44
10	1.00	$.6f_{10}^2 + 1.5f_{10}$	$.6f_{10}^{2}$	2.23
11	.99	$.8f_{11}^2 + 2f_{11}$	$.4f_{11}^2$	2.42
12	.99	$.8f_{12}^{2} + 5f_{12}$	$.4f_{12}^2$	1.75
13	.98	$.9f_{13}^{2} + 4f_{13}$	$.4f_{13}^2$	2.00
14	1.00	$.8f_{14}^2 + 2f_{14}$	$.5f_{14}^{2}$	2.84
15	.99	$.9f_{15}^2 + 3f_{15}$	$.5f_{15}^2$	2.40
16	1.00	$1.1f_{16}^2 + 3f_{16}$	$.6f_{16}^2$	2.60
17	.98	$2f_{17}^2 + 3f_{17}$	$.45f_{17}^2$	5.02
18	.99	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	4.49
19	.98	$2.4f_{19}^2 + 1.5f_{19}$	$.5f_{19}^2$	4.96
20	.98	$1.8f_{20}^2 + 3f_{20}$	$.3f_{20}^{2}$	5.23
21	.98	$2.1f_{21}^2 + 3f_{21}$	$.35f_{21}^2$	4.11
22	.99	$1.9f_{22}^2 + 2.5f_{22}$	$.5f_{22}^2$	4.56
23	1.00	$.5f_{23}^2 + 2f_{23}$	$.6f_{23}^2$	2.44
24	1.00	$.7f_{24}^2 + f_{24}$	$.6f_{24}^2$	1.47
25	.99	$.5f_{25}^2 + .8f_{25}$	$.6f_{25}^2$	1.02
26	.99	$.6f_{26}^2 + f_{26}$	$.45f_{26}^2$	2.48
27	.99	$.7f_{27}^2 + .8f_{27}$.4f ₂₇	1.31

Link Multipliers, Total Cost Functions and Link Flow Solution for Case III

Link a	α_{a}	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	f_a^*
28	.98	$.4f_{28}^2 + .8f_{28}$	$.45f_{28}^2$	0.66
29	1.00	$.3f_{29}^2 + 3f_{29}$	$.55f_{29}^2$	2.29
30	1.00	$.75f_{30}^2 + f_{30}$	$.55f_{30}^2$	1.29
31	1.00	$.65f_{31}^2 + f_{31}$	$.55f_{31}^2$	1.28
32	.99	$.5f_{32}^2 + 2f_{32}$	$.3f_{32}^2$	2.74
33	.99	$.4f_{33}^{2} + 3f_{33}$	$.3f_{33}^2$	0.00
34	1.00	$.5f_{34}^2 + 3.5f_{34}$	$.4f_{34}^{2}$	2.39
35	.98	$.4f_{35}^2 + 2f_{35}$	$.55f_{35}^{2}$	1.82
36	.98	$.3f_{36}^2 + 2.5f_{36}$	$.55f_{36}^2$	0.00
37	.99	$.55f_{37}^2 + 2f_{37}$	$.55f_{37}^2$	2.21
38	1.00	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^{2}$	3.46
39	1.00	$.4f_{39}^2 + 5f_{39}$	$.4f_{39}^{2}$	0.00
40	.98	$.55f_{40}^2 + 2f_{40}$	$.6f_{40}^{2}$	1.05
41	.97	$3f_{41}^2 + 12f_{41}$	$.3f_{41}^{2}$	8.08
42	.96	$2.7f_{42}^2 + 10f_{42}$	$.4f_{42}^2$	8.13
43	.98	$1.1f_{43}^2 + 6f_{43}$	$.45f_{43}^2$	4.21
44	.98	$.9f_{44}^2 + 5f_{44}$	$.45f_{44}^2$	3.63
45	.97	$1.3f_{45}^2 + 6f_{45}$	$.5f_{45}^2$	4.62
46	.99	$1.5f_{46}^2 + 7f_{46}$	$.55f_{46}^2$	3.19
47	.98	$1.5f_{47}^2 + 4f_{47}$	$.4f_{47}^{2}$	8.60
48	.98	$2.1f_{48}^2 + 6f_{48}$	$.45f_{48}^2$	6.72
49	.99	$.6f_{49}^2 + 3f_{49}$	$.55f_{49}^2$	3.63
50	1.00	$.7f_{50}^2 + 2f_{50}$	$.7f_{50}^2$	3.39
51	.98	$.6f_{51}^2 + 7f_{51}$	$.45f_{51}^2$	1.41
52	.99	$.9f_{52}^{2} + 9f_{52}$	$.5f_{52}^{2}$	1.12
53	1.00	$.55f_{53}^2 + 6f_{53}$	$.55f_{53}^2$	2.86
54	.98	$.8f_{54}^2 + 4f_{54}$	$.5f_{54}^2$	2.60

Link Multipliers, Total Cost Functions and Solution for Case III (cont'd)

Case III: Results

The computed equilibrium demands and sales prices for the products of Firms 1, 2, and 3 are as follows:

$$d_{11}^* = 7.18, \quad d_{21}^* = 7.96, \quad d_{31}^* = 4.70,$$
 $d_{12}^* = 4.06, \quad d_{22}^* = 0.00, \quad d_{32}^* = 6.25,$ $d_{13}^* = 2.93, \quad d_{23}^* = 5.60, \quad \text{and} \ d_{33}^* = 3.93.$

$$ho_{11}(d^*)=172.24, \quad
ho_{21}(d^*)=157.66, \quad
ho_{31}(d^*)=155.09, \\
ho_{12}(d^*)=157.97, \quad
ho_{22}(d^*)=138.97, \quad
ho_{32}(d^*)=145.97, \\
ho_{13}(d^*)=161.33, \quad
ho_{23}(d^*)=151.67, \quad \text{and} \quad
ho_{33}(d^*)=148.61. \\
ho_{13}(d^*)=161.33, \quad
ho_{23}(d^*)=151.67, \quad
ho_{13}(d^*)=161.83, \quad
ho_{23}(d^*)=181.61. \\
ho_{13}(d^*)=161.33, \quad
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \\
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \\
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \quad
ho_{23}(d^*)=181.61, \\
ho_{24}(d^*)=181.61, \\
ho_{24}(d^*)=181.6$$

The computed amounts of firms' profits:

$$U_1(X^*) = 1,199.87$$
, $U_2(X^*) = 1,062.73$, and $U_3(X^*) = 980.83$.

Case III: Result Analysis

As a result of the consumers' growing inclination towards the generic substitute of the previously popular Lipitor, Firm 2 has lost its entire share of market 2 to its competitors, resulting in zero flows on several links. Similarly, Firm 1 now has declining sales of its brand in demand markets 1 and 3.

As expected, the introduction of the generic substitute has also caused remarkable drops in the prices of the existing brands. Interestingly, the decrease in the price of Lipitor in demand markets 2 and 3 exceeds 35%.

Note that simultaneous declines in the amounts of demand and sales price has caused a severe reduction in the profits of Firms 1 and 2. This decline for Firm 1 is observed to be as high as 60%.

Validation of Results: Observations

As noted by Johnson (2011), the market share of a branded drug may decrease by as much as 40%-80% after the introduction of its generic rival. Thus, the model captures the observed decrease in the US market share.

Validation of Results: Observations

As noted by Johnson (2011), the market share of a branded drug may decrease by as much as 40%-80% after the introduction of its generic rival. Thus, the model captures the observed decrease in the US market share.

The reduction in demand and price due to the patent expiration has been observed in the market sales. The US sales of Lipitor have dropped over 75% (Forbes (2012) and Firecepharma (2012)).

Paths Definition and Optimal Path Flow Pattern - Firm ${\bf 1}$

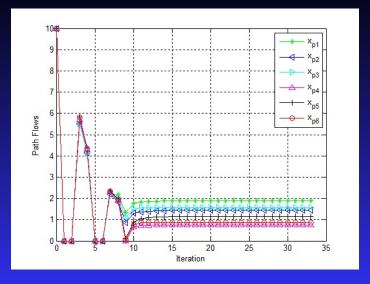
O/D Pair $(1,R_1)$	Path Definition	Path Flow
	$p_1 = (1, 5, 17, 23)$	$x_{p_1}^* = 1.87$
	$p_2 = (1, 6, 18, 26)$	$x_{p_2}^* = 1.46$
	$p_3=(1,7,19,29)$	$x_{p_3}^* = 1.57$
	$p_4 = (2, 8, 17, 23)$	$x_{p_4}^{r_3} = 0.73$
	$p_5 = (2, 9, 18, 26)$	$x_{p_5}^{p_4} = 1.17$
	$p_6 = (2, 10, 19, 29)$	$x_{p_6}^{*} = 0.87$
O/D Pair (1, <i>R</i> ₂)	$p_7 = (1, 5, 17, 24)$	$x_{p_7}^* = 0.89$
	$p_8 = (1, 6, 18, 27)$	$x_{p_8}^{*'} = 0.57$
	$p_9 = (1, 7, 19, 30)$	$x_{p_9}^{r_0} = 0.66$
	$p_{10}=(2,8,17,24)$	$x_{p_{10}}^{r_3} = 0.68$
	$p_{11} = (2, 9, 18, 27)$	$x_{p_{11}}^{*} = 0.82$
	$p_{12} = (2, 10, 19, 30)$	$x_{p_{12}}^* = 0.71$
O/D Pair (1, R ₃)	$p_{13} = (1, 5, 17, 25)$	$x_{p_{13}}^* = 0.60$
	$p_{14} = (1, 6, 18, 28)$	$x_{p_{14}}^{*} = 0.16$
	$p_{15} = (1, 7, 19, 31)$	$x_{p_{15}}^{*} = 0.64$
	$p_{16} = (2, 8, 17, 25)$	$x_{p_{16}}^{*} = 0.49$
	$p_{17} = (2, 9, 18, 28)$	$x_{p_{17}}^{*} = 0.53$
	$p_{18} = (2, 10, 19, 31)$	$x_{p_{18}}^{*} = 0.72$
		P10

Paths Definition and Optimal Path Flow Pattern - Firm 2

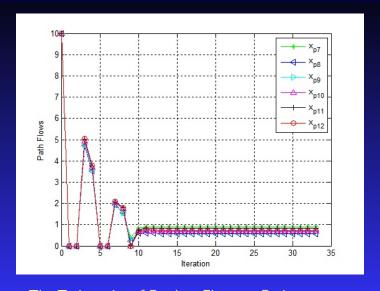
	Path Definition	Path Flow
O/D Pair (2, <i>R</i> ₁)	$p_{19} = (3, 11, 20, 32)$	$x_{p_{19}}^* = 1.26$
	$p_{20} = (3, 12, 21, 35)$	$x_{p_{20}}^{*} = 0.77$
	$p_{21} = (3, 13, 22, 38)$	$x_{p_{21}}^{*} = 1.51$
	$p_{22} = (4, 14, 20, 32)$	$x_{p_{22}}^* = 1.63$
	$p_{23} = (4, 15, 21, 35)$	$x_{p_{23}}^* = 1.16$
	$p_{24} = (4, 16, 22, 38)$	$x_{p_{24}}^* = 2.12$
O/D Pair (2, <i>R</i> ₂)	$p_{25} = (3, 11, 20, 33)$	$x_{p_{25}}^* = 0.00$
	$p_{26} = (3, 12, 21, 36)$	$x_{p_{26}}^* = 0.00$
	$p_{27} = (3, 13, 22, 39)$	$x_{p_{27}}^* = 0.00$
	$p_{28} = (4, 14, 20, 33)$	$x_{p_{28}}^* = 0.00$
	$p_{29} = (4, 15, 21, 36)$	$x_{p_{29}}^* = 0.00$
	$p_{30} = (4, 16, 22, 39)$	$x_{p_{30}}^* = 0.00$
O/D Pair (2, <i>R</i> ₃)	$p_{31} = (3, 11, 20, 34)$	$x_{p_{31}}^* = 1.26$
	$p_{32} = (3, 12, 21, 37)$	$x_{p_{32}}^* = 1.05$
	$p_{33} = (3, 13, 22, 40)$	$x_{p_{33}}^* = 0.57$
	$p_{34} = (4, 14, 20, 34)$	$x_{p_{34}}^* = 1.26$
	$p_{35} = (4, 15, 21, 37)$	$x_{p_{35}}^* = 1.29$
	$p_{36} = (4, 16, 22, 40)$	$x_{p_{36}}^* = 0.54$

Paths Definition and Optimal Path Flow Pattern - Firm 3

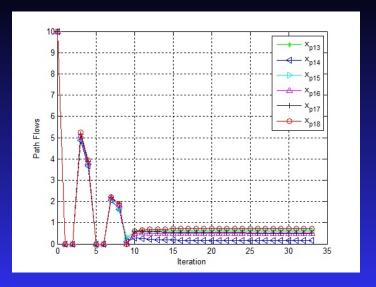
	Path Definition	Path Flow
O/D Pair (3, <i>R</i> ₁)	$p_{37} = (41, 43, 47, 49)$	$x_{p_{37}}^* = 1.87$
	$p_{38} = (41, 44, 48, 52)$	$x_{p_{38}}^* = 1.78$
	$p_{39} = (42, 45, 47, 49)$	$x_{p_{39}}^* = 0.70$
	$p_{40} = (42, 46, 48, 52)$	$x_{p_{40}}^* = 0.68$
O/D Pair (3, R ₂)	$p_{41} = (41, 43, 47, 50)$	$x_{p_{41}}^* = 1.61$
	$p_{42} = (41, 44, 48, 53)$	$x_{p_{42}}^* = 1.46$
	$p_{43} = (42, 45, 47, 50)$	$x_{p_{43}}^* = 2.07$
	$p_{44} = (42, 46, 48, 53)$	$x_{p_{44}}^* = 1.90$
O/D Pair (3, <i>R</i> ₃)	$p_{45} = (41, 43, 47, 51)$	$x_{p_{45}}^* = 0.84$
	$p_{46} = (41, 44, 48, 54)$	$x_{p_{46}}^* = 0.53$
	$p_{47} = (42, 45, 47, 51)$	$x_{p_{47}}^* = 1.46$
	$p_{48} = (42, 46, 48, 54)$	$x_{p_{48}}^* = 1.33$



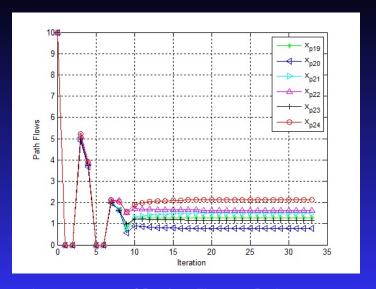
The Trajectories of Product Flows on Paths $p_1 - p_6$



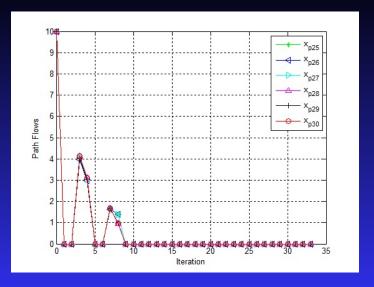
The Trajectories of Product Flows on Paths $p_7 - p_{12}$



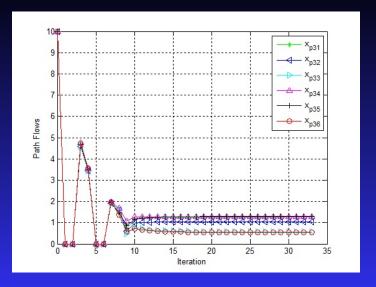
The Trajectories of Product Flows on Paths $p_{13} - p_{18}$



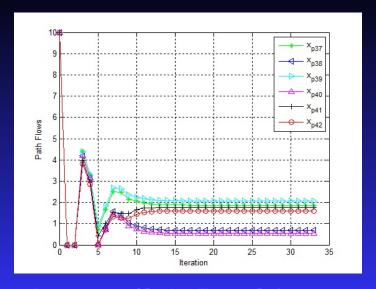
The Trajectories of Product Flows on Paths $p_{19} - p_{24}$



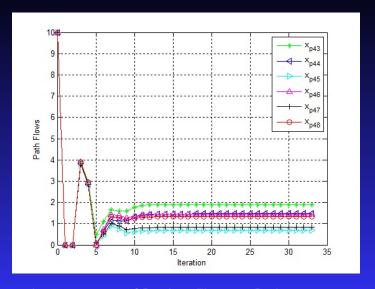
The Trajectories of Product Flows on Paths $p_{25} - p_{30}$



The Trajectories of Product Flows on Paths $p_{31} - p_{36}$



The Trajectories of Product Flows on Paths $p_{37} - p_{42}$



The Trajectories of Product Flows on Paths $p_{43} - p_{48}$

Outline – Some Other Issues that We Have Explored Using Supply Chain Network Theory

- ► Mergers & Acquisitions and Network Synergies
- ► Integration of Social Networks with Supply Chains and with Financial Networks
- Supply Chain Networks for Rescue, Recovery and Reconstruction in Disasters
- ► The Nagurney-Qiang (N-Q) Network Efficiency / Performance Measure
- ► Design of Supply Chains for Critical Needs Products
- ► Time in Disaster Relief
- ► Summary, Conclusions, and Suggestions for Future Research

Mergers & Acquisitions and Network Synergies

Mergers and Acquisitions and Network Synergies

A successful merger depends on the ability to measure the anticipated synergy of the proposed merger (cf. Chang (1988)) .

This section is based on the recent paper:

 Z. Liu and A. Nagurney (2011), "Risk Reduction and Cost Synergy in Mergers and Acquisitions via Supply Chain Network Integration," *Journal of Financial Decision Making* 7(2), 1-18.

Mergers and Acquisitions and Network Synergies

It is increasingly apparent and documented that *improving supply* chain integration is key to improving the likelihood of post-merger success!

This is understandable, since up to 80% of a firm's costs are linked to operations (Benitez and Gordon (2000)).

However, empirical studies demonstrate that *one out of two post-merger integration efforts fares poorly* (Gerds and Schewe (2009)).

In addition, in an empirical analysis of a global sample of over 45,000 data points of post-merger transactions in all significant sectors globally from services to manufacturing, *risk factors were identified to post-merger success* (see Gerds, Strottmann, and Jayaprakash (2010)).

Mergers and Acquisitions and Network Synergies

Risk in the context of supply chains may be associated with

- the production/procurement processes,
- the transportation/shipment of the goods,
- and/or the demand markets.

Such supply chain risks are directly reflected in firms' financial performances, and priced in the financial market.

Hendricks and Singhal (2010) estimated that the average stock price reaction to supply-demand mismatch announcements was approximately -6.8%. In addition, supply chain disruptions can cause firms' equity risks to increase by 13.50% on average after the disruption announcements (Hendricks and Singhal (2005)).

Illustrations of Supply Chain Risk



Mergers and Acquisitions and Network Synergies

We build upon the recent work in mergers and acquisitions that focuses on horizontal network integration (cf. Nagurney (2009), Nagurney and Woolley (2010), and Nagurney, Woolley, and Qiang (2010)).

We have developed the following significant extension: we utilize a mean-variance (MV) approach in order to capture the risk associated with supply chain activities both prior to and post the merger/acquisition under investigation. The MV approach to the measurement of risk dates to the work of the Nobel laureate Markowtiz (1952, 1959) and even today (cf. Schneeweis, Crowder, and Kazemi (2010)) remains a fundamental approach to minimizing volatility.



All firms, both prior and post the merger, minimize both their expected total costs and the risk, as captured through the variance of the total costs, with a suitable weight assigned to the latter.

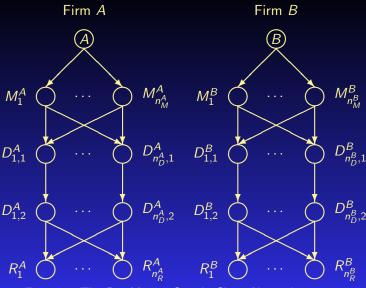


Figure 8: The Pre-Merger Supply Chain Network

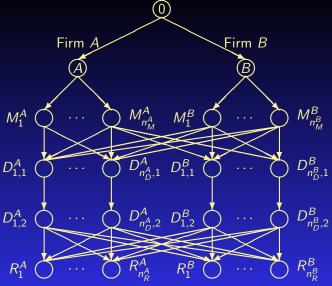
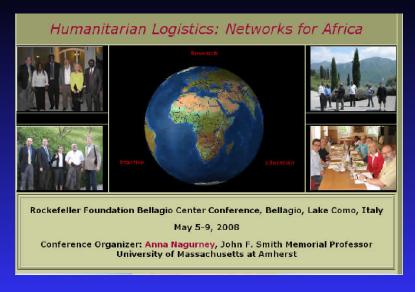


Figure 9: The Post-Merger Supply Chain Network

This model can also be applied to the teaming of organizations in the case of humanitarian operations.

Bellagio Conference on Humanitarian Logistics



See: http://hlogistics.isenberg.umass.edu/

The Supply Chain Network Oligopoly Model

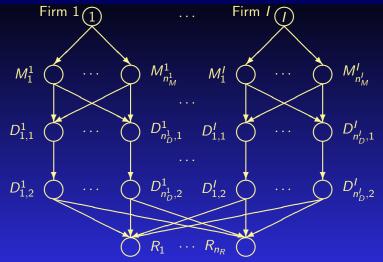


Figure 10: Supply Chain Network Structure of the Oligopoly

Nagurney Computational Management Science (2010) 7, pp 377-401.

Mergers Through Coalition Formation

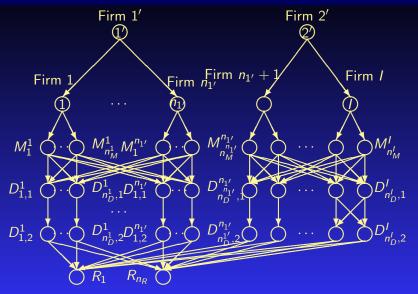


Figure 11: Mergers of the First $n_{1'}$ Firms and the Next $n_{2'}$ Firms

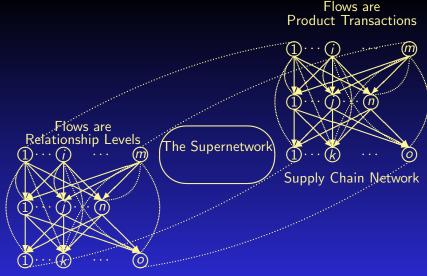
Integration of Social Networks with Supply Chains and with Financial Networks

Integration of Social Networks with Supply Chains and with Financial Networks

Two References:

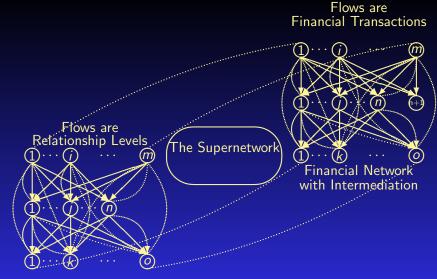
A. Nagurney, T. Wakolbinger, and L. Zhao (2006) "The Evolution and Emergence of Integrated Social and Financial Networks with Electronic Transactions: A Dynamic Supernetwork Theory for the Modeling, Analysis, and Computation of Financial Flows and Relationship Levels," *Computational Economics* **27**, pp 353-393.

J. M. Cruz, A. Nagurney, and T. Wakolbinger (2006) "Financial Engineering of the Integration of Global Supply Chain Networks and Social Networks with Risk Management," *Naval Research Logistics* **53**, pp 674-696.



Social Network

Figure 12: The Multilevel Supernetwork Structure of the Integrated Supply Chain / Social Network System



Social Network

Figure 13: The Multilevel Supernetwork Structure of the Integrated Financial Network / Social Network System

Supply Chain Networks for Rescue, Recovery and Reconstruction in Disasters

Supply chains are the *fundamental critical infrastructure* for the production and distribution of goods and services in our globalized *Network Economy*.

Supply chain networks also serve as the primary conduit for *rescue*, *recovery*, *and reconstruction in disasters*.

Recent disasters have vividly demonstrated the importance and vulnerability of our transportation and critical infrastructure systems

- The biggest blackout in North America, August 14, 2003;
- Two significant power outages in September 2003 one in the UK and the other in Italy and Switzerland;
- The Indonesian tsunami (and earthquake), December 26, 2004;
- Hurricane Katrina, August 23, 2005;
- The Minneapolis I35 Bridge collapse, August 1, 2007;
- The Sichuan earthquake on May 12, 2008;
- The Haiti earthquake that struck on January 12, 2010 and the Chilean one on February 27, 2010;
- The triple disaster in Japan on March 11, 2011;
- Superstorm Sandy, October 29, 2012.

Hurricane Katrina in 2005



Hurricane Katrina has been called an "American tragedy," in which essential services failed completely.



The Haitian and Chilean Earthquakes



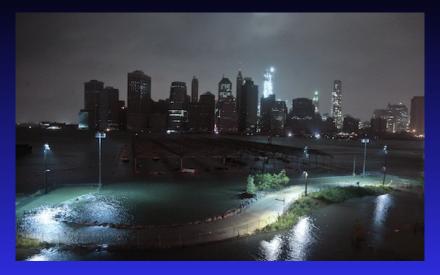
Anna Nagurney

Networks Against Time

The Triple Disaster in Japan on March 11, 2011

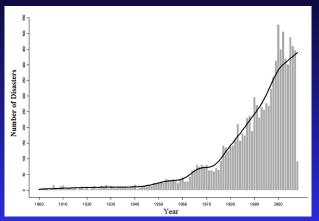


Superstorm Sandy and Power Outages



Manhattan without power October 30, 2012 as a result of the devastation wrought by Superstorm Sandy.

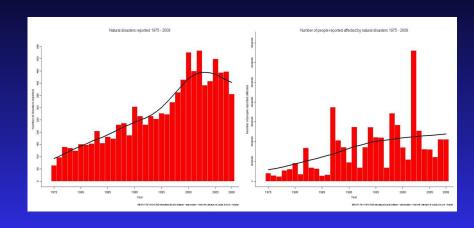
Disasters have brought an unprecedented impact on human lives in the 21st century and the number of disasters is growing. From January to October 2005, an estimated 97,490 people were killed in disasters globally; 88,117 of them because of natural disasters.



Frequency of disasters [Source: Emergency Events Database (2008)]

Disasters have a catastrophic effect on human lives and a region's or even a nation's resources.

Natural Disasters (1975–2008)



Which Nodes and Links Really Matter?

The Nagurney-Qiang (N-Q) Network Efficiency / Performance Measure

The Nagurney and Qiang (N-Q) Network Efficiency / Performance Measure

Definition: A Unified Network Performance Measure

The network performance/efficiency measure, $\mathcal{E}(\mathcal{G}, d)$, for a given network topology \mathcal{G} and the equilibrium (or fixed) demand vector d, is:

$$\mathcal{E} = \mathcal{E}(\mathcal{G}, d) = \frac{\sum_{w \in W} \frac{d_w}{\lambda_w}}{n_W},$$

where recall that n_W is the number of O/D pairs in the network, and d_w and λ_w denote, for simplicity, the equilibrium (or fixed) demand and the equilibrium disutility for O/D pair w, respectively.

The Importance of Nodes and Links

Definition: Importance of a Network Component

The importance of a network component $g \in \mathcal{G}$, I(g), is measured by the relative network efficiency drop after g is removed from the network:

$$I(g) = rac{ riangle \mathcal{E}}{\mathcal{E}} = rac{\mathcal{E}(\mathcal{G}, d) - \mathcal{E}(\mathcal{G} - g, d)}{\mathcal{E}(\mathcal{G}, d)}$$

where G - g is the resulting network after component g is removed from network G.

The Approach to Identifying the Importance of Network Components

The elimination of a link is treated in the N-Q network efficiency measure by removing that link while the removal of a node is managed by removing the links entering and exiting that node.

In the case that the removal results in no path connecting an O/D pair, we simply assign the demand for that O/D pair to an abstract path with a cost of infinity.

The N-Q measure is well-defined even in the case of disconnected networks.

The Advantages of the N-Q Network Efficiency Measure

- The measure captures *demands, flows, costs, and behavior of users*, in addition to network topology.
- The resulting importance definition of network components is applicable and *well-defined* even in the case of disconnected networks.
- It can be used to identify the *importance* (and ranking) of either nodes, or links, or both.
- It can be applied to assess the efficiency/performance of a wide range of network systems, including financial systems and supply chains under risk and uncertainty.
- It is applicable also to elastic demand networks.
- It is applicable to dynamic networks, including the Internet.

Some Applications of the N-Q Measure

The Sioux Falls Network

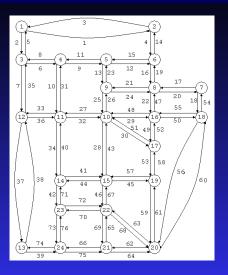


Figure 14: The Sioux Falls network with 24 nodes, 76 links, and 528 O/D pairs of nodes.

Importance of Links in the Sioux Falls Network

The computed network efficiency measure \mathcal{E} for the Sioux Falls network is $\mathcal{E}=47.6092$. Links 27, 26, 1, and 2 are the most important links, and hence special attention should be paid to protect these links accordingly, while the removal of links 13, 14, 15, and 17 would cause the least efficiency loss.

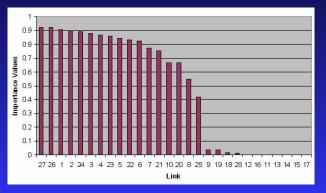


Figure 15: The Sioux Falls network link importance rankings

According to the European Environment Agency (2004), since 1990, the annual number of extreme weather and climate related events has doubled, in comparison to the previous decade. These events account for approximately 80% of all economic losses caused by catastrophic events. In the course of climate change, catastrophic events are projected to occur more frequently (see Schulz (2007)).

Schulz (2007) applied *N-Q* network efficiency measure to a German highway system in order to identify the critical road elements and found that this measure provided more reasonable results than the measure of Taylor and D'Este (2007).

The N-Q measure can also be used to assess which links should be added to improve efficiency. *This measure was used for the evaluation of the proposed North Dublin (Ireland) Metro system* (October 2009 Issue of *ERCIM News*).

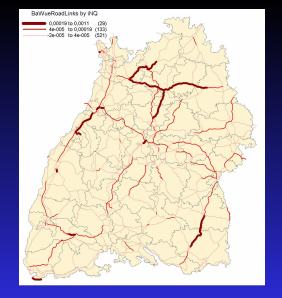


Figure 16: Comparative Importance of the links for the Baden - Wurttemberg Network – Modelling and analysis of transportation networks in earthquake prone areas via the N-Q measure, Tyagunov et al.

What About Disaster Relief?

Humanitarian Supply Chains

The supply chain is a critical component not only of corporations but also of humanitarian organizations and their logistical operations.

At least 50 cents of each dollar's worth of food aid is spent or transport, storage and administrative costs.

Vulnerability of Humanitarian Supply Chains

Extremely poor logistical infrastructures: Modes of transportation include trucks, barges, donkeys in Afghanistan, and elephants in Cambodia.

To ship the humanitarian goods to the affected area in the first 72 hours after disasters is crucial. The successful execution is not just a question of money but a difference between life and death.

Corporations' expertise with logistics could help public response efforts for nonprofit organizations.

In the humanitarian sector, organizations are 15 to 20 years behind, as compared to the commercial arena, regarding supply chain network development.



Critical Needs Products

Critical needs products are those that are essential to the survival of the population, and can include, for example, vaccines, medicine, food, water, etc., depending upon the particular application.

The demand for the product should be met as nearly as possible since otherwise there may be additional loss of life.

In times of crises, a *system-optimization* approach is mandated since the demands for critical supplies should be met (as nearly as possible) at minimal total cost.

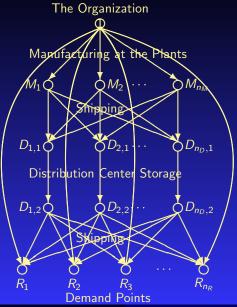
We have now developed a framework for the optimal design of critical needs product supply chains:

"Supply Chain Network Design for Critical Needs with Outsourcing,"

A. Nagurney, M. Yu, and Q. Qiang, *Papers in Regional Science* (2011), **90**, 123-142,

where additional background as well as references can be found.

Supply Chain Network Topology with Outsourcing



Applications to Vaccine Production

By applying the general theoretical model to the company's data, the firm can determine whether it needs to expand its facilities (or not), how much of the vaccine to produce where, how much to store where, and how much to have shipped to the various demand points. Also, it can determine whether it should outsource any of its vaccine production and at what level.

The firm by solving the model with its company-relevant data can then ensure that the price that it receives for its vaccine production and delivery is appropriate and that it recovers its incurred costs and obtains, if negotiated correctly, an equitable profit.

Applications to Emergencies

A company can, using the model, prepare and plan for an emergency such as a natural disaster in the form of a hurricane and identify where to store a necessary product (such as food packets, for example) so that the items can be delivered to the demand points in a timely manner and at minimal total cost.

Time in Disaster Relief

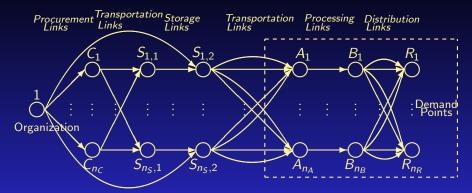


Figure 17: Network Topology of the Integrated Disaster Relief Supply Chain

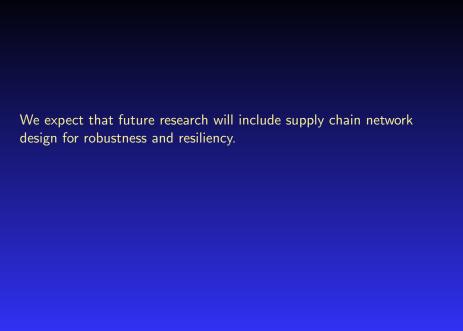
A. Nagurney, A. H. Masoumi, and M. Yu, "An Integrated Disaster Relief Supply Chain Network Model with Time Targets and Demand Uncertainty," Isenberg School of Management, UMass Summary, Conclusions,

and

Suggestions for Future Research

- ► We emphasized the *importance of capturing behavior* in supply chain modeling, analysis, and design.
- ➤ We developed an integrated framework for the modeling of competition in pharmaceutical supply chains with brand differentiation and perishability with outsourcing.
- ► The model is formulated and solved as a variational inequality problem.
- We also related the model to several others in the literatures with applications ranging from medical nuclear supply chains to blood supply chains.
- ➤ The framework can be applied in numerous situations, with some minot modifications, to capture oligopolistic competition for perishable and time-sensitive products.

- ► In addition, we have been heavily involved in constructing mathematical models for supply chain networks with quality competition.
- ➤ Our research in supply chains has also led us to other time-sensitive products, such as *fast fashion*.
- ► We have also worked on models where guaranteed time of delivery is a strategic variable.
- ➤ Finally, we have done some modeling of the disequilibrium dynamics and equilibrium states in ecological predator-prey networks, that is, supply chains in nature. This research may assist in developing frameworks for resiliency.



THANK YOU!



For more information, see: http://supernet.isenberg.umass.edu