Perishable Product Supply Chains in Health Care: Models, Analysis, and Computations

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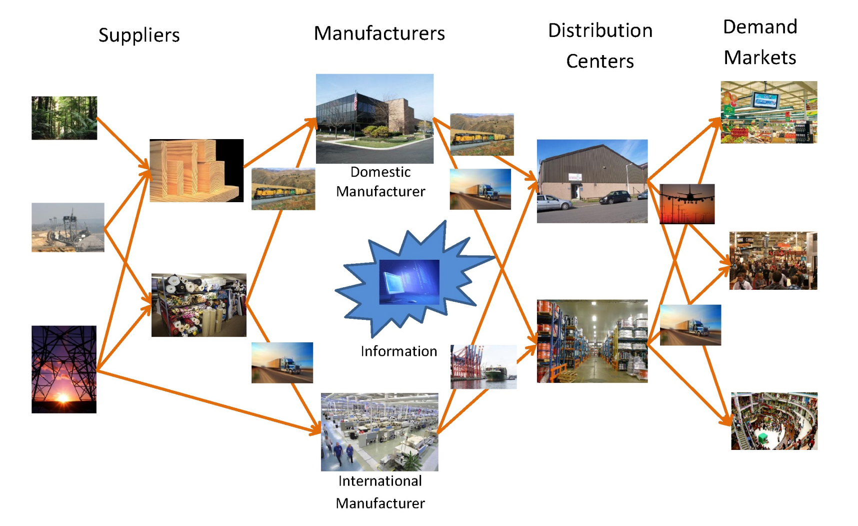
Background and Motivation

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 That We Focus on in This Talk

Healthcare Supply Chains

Humanitarian Relief

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

Supply chains are, in fact, *Supernetworks*.

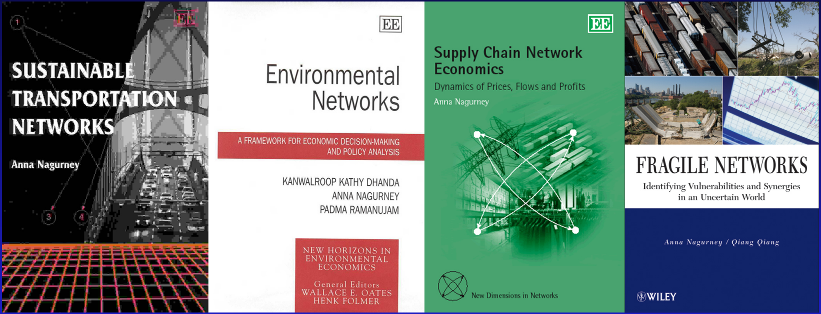
Hence, *any formalism that seeks to model supply chains and to provide quantifiable insights and measures must be a system-wide one and network-based.*

Indeed, 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.

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*.

Our Approach to Supply Chain Network Analysis and Design



The Pharmaceutical Industry and Issues

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 is expected to experience *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 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 has risen to 211 – close to an all-time record –* with only 58 in short supply in 2004.

According to the Food and Drug Administration (FDA), hospitals have reported shortages of drugs used in a wide range of applications, ranging from cancer treatment to surgery, anesthesia, and intravenous feedings.

Some Consequences of Product Shortages

The consequences of such shortages *include the postponement of surgeries and treatments, and may also result in the use of less effective or costlier substitutes*.

According to the American Hospital Association, all US hospitals have experienced drug shortages, and 82% have reported delayed care for their patients as a consequence (Szabo (2011)).

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*.

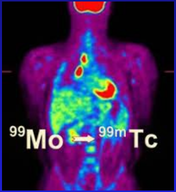
Due to the severity of this medical crisis for leukemia patients, Food and Drug Administration is exploring the possibility of importing this medical product (Larkin (2011)).

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

Medical Nuclear Product Supply Chains

Technetium, ^{99m}Tc, which is a decay product of Molybdenum, ^{99}Mo, is the most commonly used medical radioisotope, accounting for over 80% of the radioisotope injections and representing over 30 million procedures worldwide each year.

There have been shortages of this critical radioisotope due to nuclear production problems.



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.

Some Possible Causes of Shortages

Hence, the low profit margins associated with such drugs may be forcing pharmaceutical companies to make a difficult decision: whether to lose money by continuing to produce a lifesaving product or to switch to a more profitable drug.

Unfortunately, the FDA cannot force companies to continue to produce low-profit medicines even if millions of lives rely on them.

On the other hand, where competition has been lacking, shortages of some other lifesaving drugs have resulted in spikes in prices, ranging from a 100% to a 4,500% increase with an average of 650% (Schneider (2011)).

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, presently, generate more than $142 billion in sales, are expected, over the next five years, to be faced with generic competition.

In 2011, pharmaceutical products valued at more than $30 billion are losing 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*.

Waste and Environmental Impacts

Another pressure faced by pharmaceutical firms is the environmental impact of their medical waste, which includes the perished excess medicine, and inappropriate disposal on the retailer / consumer end.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

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.

Our proposed supply chain network model can be applied to similar cases of oligopolistic competition in which a finite number of firms provide perishable products.

However, proper minor modifications may have to be made in order to address differences in the supply chain network topologies in related industries.

Some Examples of Oligopolies

- airlines
- freight carriers
- automobile manufacturers
- oil companies
- beer / beverage companies
- wireless communications
- fast fashion brands
- certain food companies.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

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.

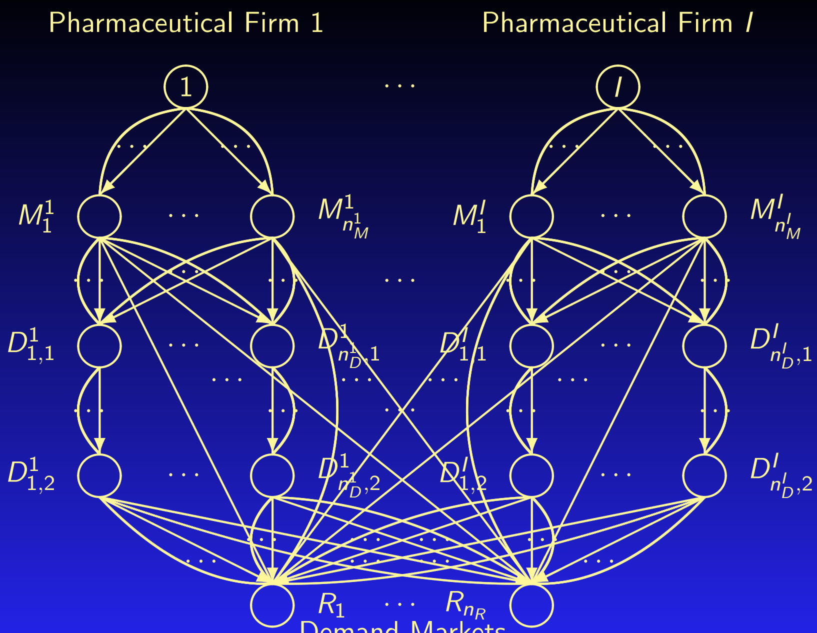


Figure: The Pharmaceutical Supply Chain Network Topology

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

Each pharmaceutical firm i; $i = 1, \ldots, I$, utilizes n^i_M manufacturing plants and n^i_D 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_is: $L \equiv \cup_{i=1,\ldots,I} L^i$.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

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.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

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 $D^i_{1,1}, \ldots, D^i_{n^i_D,1}$ 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.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

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.

A Generalized Network Oligopoly Model for Pharmaceutical Supply Chains

T here 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)).

How We Handle Perishability

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.

How We Handle Perishability

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.

How We Handle Perishability

As in Nagurney, Masoumi, and Yu (2011), 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:

$$f_a' = \alpha_a f_a, \qquad \forall a \in L. \tag{1}$$

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:

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

How We Handle Perishability

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:

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

How We Handle Perishability

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,

$$x_p \geq 0, \qquad \forall p \in P^i_k;\ i = 1, \ldots, I;\ k = 1, \ldots, n_R, \qquad (4)$$

where P^i_k is the set of all paths joining the origin node i; $i = 1, \ldots, I$ 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,

$$\mu_p \equiv \prod_{a \in p} \alpha_a, \qquad \forall p \in P^i_k;\ i = 1, \ldots, I;\ k = 1, \ldots, n_R. \qquad (5)$$

How We Handle Perishability

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:

$$\alpha_{ap} \equiv \begin{cases} \delta_{ap} \prod_{a' < a} \alpha_{a'}, & \text{if } \{a' < a\} \neq \emptyset, \\ \\ \delta_{ap}, & \text{if } \{a' < a\} = \emptyset, \end{cases} \tag{6}$$

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.

How We Handle Perishability

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

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

How We Handle Perishability

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.

How We Handle Perishability

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:

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

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 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

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

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,

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

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 firm' 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:

$$U_i = \sum_{k=1}^{n_R} \rho_{ik}(d) \sum_{p \in P_k^i} \mu_p x_p - \sum_{a \in L^i} \hat{c}_a(f) - \sum_{a \in L^i} \hat{z}_a(f_a). \qquad (11)$$

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; $i = 1, \dots, I$, with the I-dimensional vector $\hat{U}$ being the vector of the profits of all the firms:

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

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; $i = 1, \ldots, I$:

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

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

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)).

The Variational Inequality Formulation

Theorem 1

Assume that, for each pharmaceutical firm i; $i = 1, \ldots, I$, 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:

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

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.

The Variational Inequality Formulation

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

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

$$\left.\sum_{l=1}^{n_R}\frac{\partial \rho_{il}(x^*)}{\partial d_{ik}}\mu_p\sum_{p\in P_l^i}\mu_p x_p^*\right]\times[x_p-x_p^*]\geq 0,\quad \forall x\in K^1, \quad (15)$$

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

$$\frac{\partial \hat{C}_p(x)}{\partial x_p}\equiv\sum_{b\in L^i}\sum_{a\in L^i}\frac{\partial \hat{c}_b(f)}{\partial f_a}\alpha_{ap} \text{ and } \frac{\partial \hat{Z}_p(x)}{\partial x_p}\equiv\sum_{a\in L^i}\frac{\partial \hat{z}_a(f_a)}{\partial f_a}\alpha_{ap}. \quad (16)$$

The Variational Inequality Formulation

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:

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

$$+ \sum_{i=1}^{I} \sum_{k=1}^{n_R} \left[-\rho_{ik}(d^*) - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(d^*)}{\partial d_{ik}} d_{il}^* \right] \times [d_{ik} - d_{ik}^*] \geq 0, \quad \forall (f, d) \in K^2, \tag{17}$$

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

The Variational Inequality Formulation

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

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

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

$$F(X) \equiv \Big[\frac{\partial \hat{C}_p(x)}{\partial x_p} + \frac{\partial \hat{Z}_p(x)}{\partial x_p} - \rho_{ik}(x)\mu_p - \sum_{l=1}^{n_R} \frac{\partial \rho_{il}(x)}{\partial d_{ik}} \mu_p \sum_{p \in P_l^i} \mu_p x_p; \; p \in P_k^i; \;$$

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

The Variational Inequality Formulation

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

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

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

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

Relationship of the Model to Others in the Literature

Relationship of the Model to Others in the Literature

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.

Relationship of the Model to Others in the Literature

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 (2011).

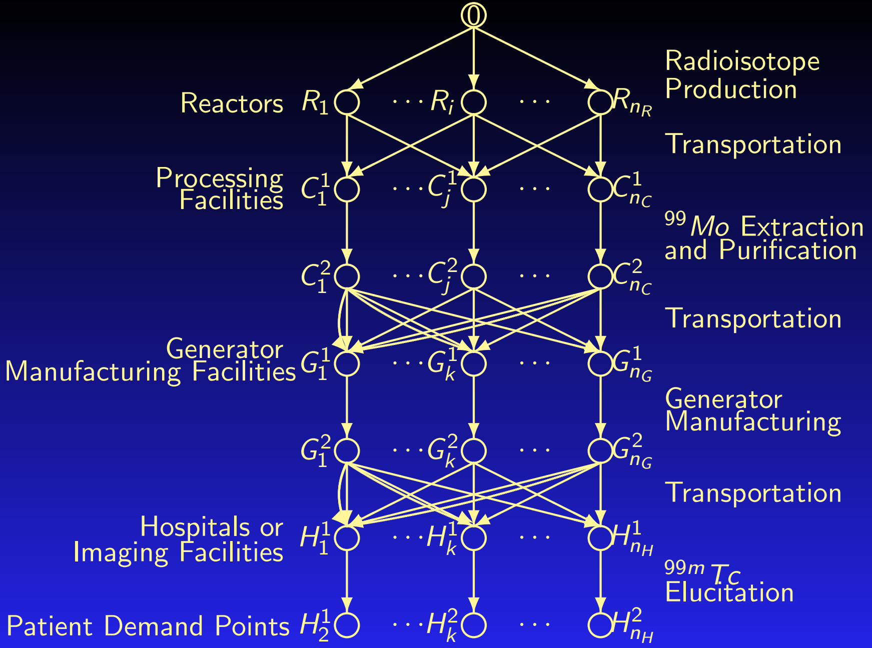


Figure: The Medical Nuclear Supply Chain Network Topology

Relationship of the Model to Others in the Literature

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), in press.

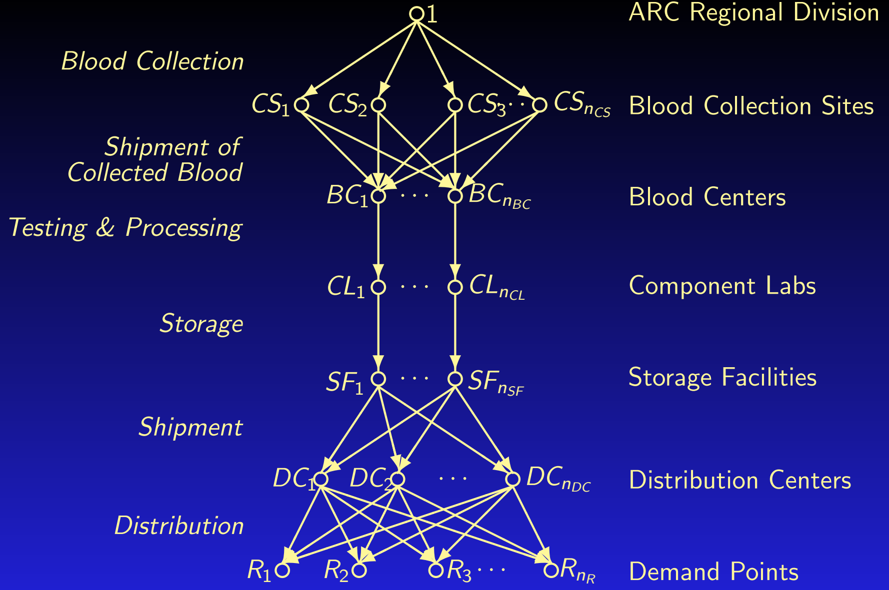


Figure: Supply Chain Network Topology for a Regionalized Blood Bank

Relationship of the Model to Others in the Literature

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

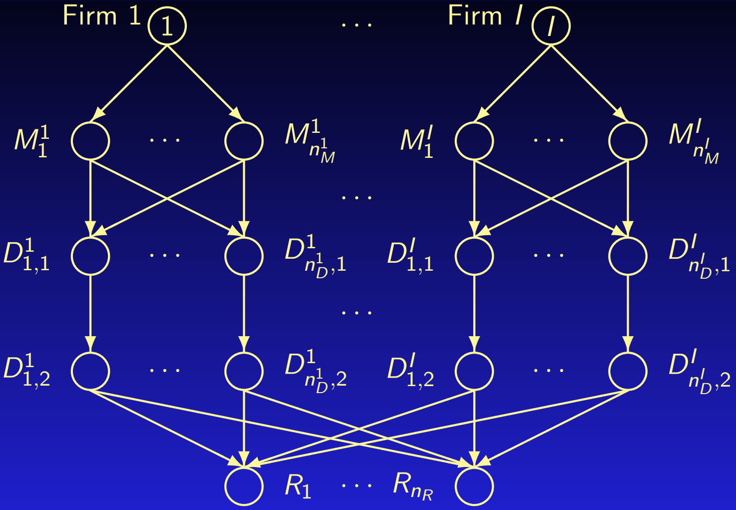


Figure: Supply Chain Network Structure of the Oligopoly Without Perishability; Nagurney, *Computational Management Science* **7**(2010), 377-401.

Mergers Through Coalition Formation

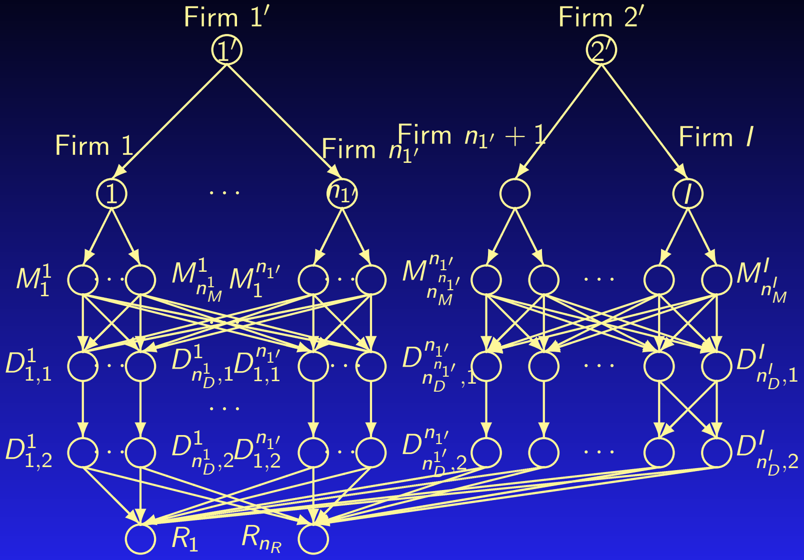


Figure: Mergers of the First $n_{1'}$ Firms and the Next $n_{2'}$ Firms

A Simple Perishable Product Numerical Example

A Simple Perishable Product Numerical Example

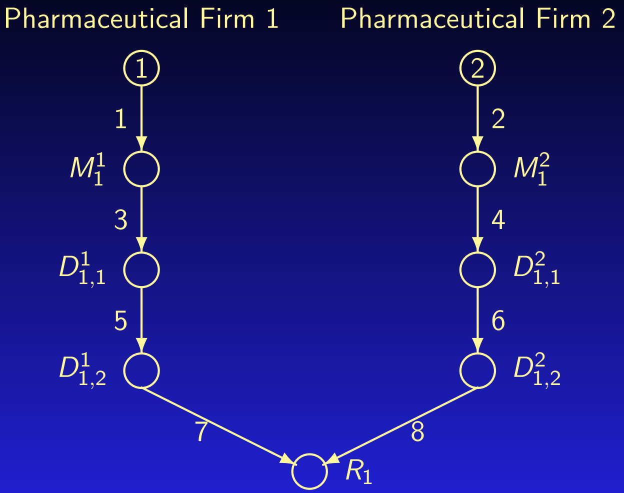


Figure: Supply Chain Network Topology for the Pharmaceutical Duopoly in the Illustrative Example

A Simple Perishable Product Numerical 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:

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

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

A Simple Perishable Product Numerical Example

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.

A Simple Perishable Product Numerical Example

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

$$\left[\frac{\partial \hat{C}_{p_1}(x^*)}{\partial x_{p_1}} + \frac{\partial \hat{Z}_{p_1}(x^*)}{\partial x_{p_1}} - \rho_{11}(x^*)\mu_{p_1} - \frac{\partial \rho_{11}(x^*)}{\partial d_{11}}\mu_{p_1} \times \mu_{p_1} x^*_{p_1}\right]$$

$$\times [x_{p_1} - x^*_{p_1}]$$

$$+ \left[\frac{\partial \hat{C}_{p_2}(x^*)}{\partial x_{p_2}} + \frac{\partial \hat{Z}_{p_2}(x^*)}{\partial x_{p_2}} - \rho_{21}(x^*)\mu_{p_2} - \frac{\partial \rho_{21}(x^*)}{\partial d_{21}}\mu_{p_2} \times \mu_{p_2} x^*_{p_2}\right]$$

$$\times [x_{p_2} - x^*_{p_2}] \geq 0, \; \forall x \in K^1.$$

A Simple Perishable Product Numerical Example

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:

$$\left[\frac{\partial \hat{C}_{p_1}(x^*)}{\partial x_{p_1}} + \frac{\partial \hat{Z}_{p_1}(x^*)}{\partial x_{p_1}} - \rho_{11}(x^*)\mu_{p_1} - \frac{\partial \rho_{11}(x^*)}{\partial d_{11}}\mu_{p_1} \times \mu_{p_1} x^*_{p_1}\right]$$

$$\times [x_{p_1} - x^*_{p_1}] = 0,$$

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.

A Simple Perishable Product Numerical Example

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:

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

A Simple Perishable Product Numerical Example

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:

$$f^*_1 = 5.21, \quad f^*_3 = 4.95, \quad f^*_5 = 4.90, \quad f^*_7 = 4.85,$$

$$f^*_2 = 6.98, \quad f^*_4 = 6.84, \quad f^*_6 = 6.84, \quad f^*_8 = 6.64.$$

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 now 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:

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

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: $\sum_{\tau=0}^{\infty} a_\tau = \infty$, $a_\tau > 0$, $a_\tau \rightarrow 0$, as $\tau \rightarrow \infty$.

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).

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. In particular, we have the following closed form expressions for all the path flows $p \in P^i_k, \forall i, k$:

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

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

Numerical Cases

Case I

This case is assumed occur 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., been producing Zocor, another cholesterol regulating brand, whose patent expired in 2006.

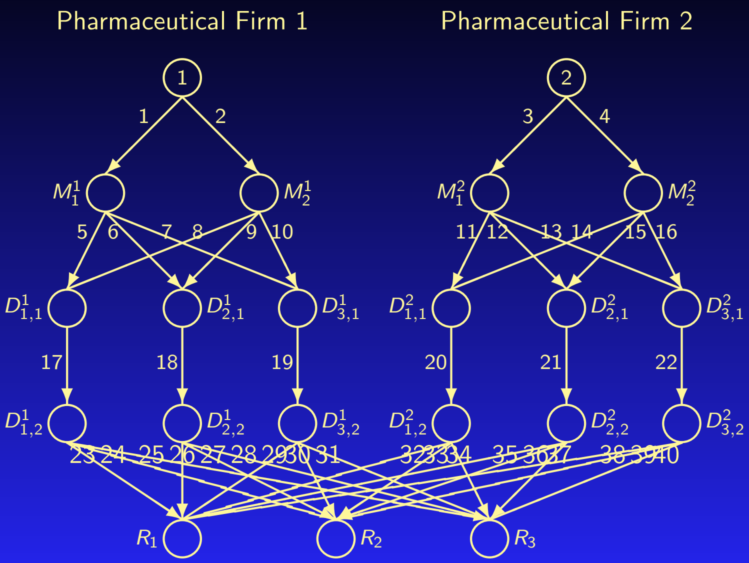


Figure: Case I Supply Chain Network

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	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	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	α_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	$.35f_{38}^2 + 2f_{38}$	$.4f_{38}^2$	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:

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

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

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

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.

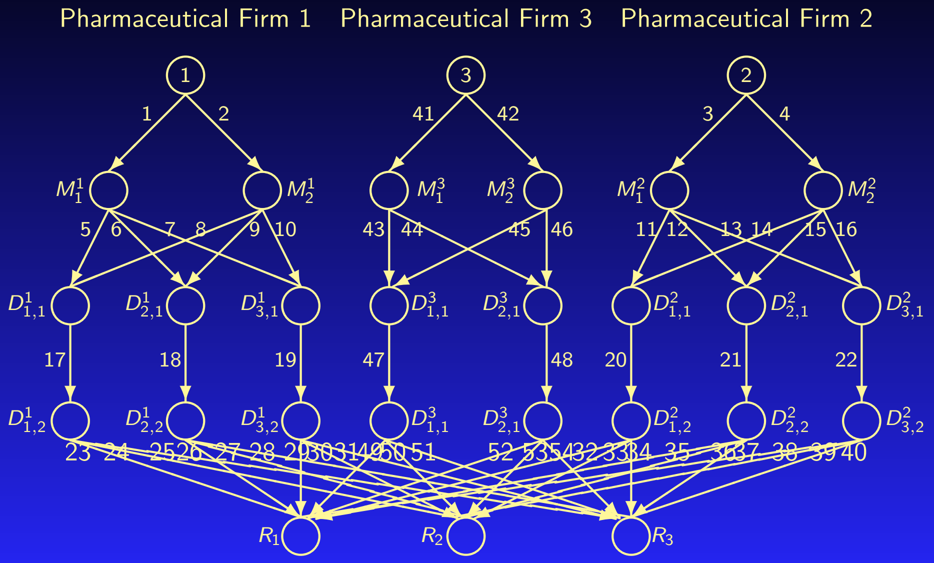
The profits of the two firms are:

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

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



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	$6.5f_3^2 + 4f_3$	$.3f_3^2$	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	$2.5f_{18}^2 + f_{18}$	$.55f_{18}^2$	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	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^2$	1.24

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

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

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

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:

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

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:

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

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

$$\rho_{31} = -0.9d_{31} - 0.6d_{11} - 0.8d_{21} + 170;$$

$$\text{Firm 2: } \rho_{12}(d) = -0.9d_{12} - 0.8d_{22} - 0.7d_{32} + 166;$$

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

$$\rho_{32}(d) = -0.8d_{32} - 0.5d_{12} - 0.6d_{22} + 153;$$

$$\text{Firm 3: } \rho_{13}(d) = -1.4d_{13} - 1.0d_{23} - 0.5d_{33} + 173;$$

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

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

Link a	α_a	$\hat{c}_a(f_a)$	$\hat{z}_a(f_a)$	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	$.7f_9^2 + 3f_9$	$.6f_9^2$	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	$.7f_{27}^2 + .8f_{27}$	$.4f_{27}^2$	1.31

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

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

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

Case III: Results

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

$$d_{11}^* = 7.18, \quad d_{21}^* = 7.96, \quad d_{31}^* = 4.70,$$

$$d_{12}^* = 4.06, \quad d_{22}^* = 0.00, \quad d_{32}^* = 6.25,$$

$$d_{13}^* = 2.93, \quad d_{23}^* = 5.60, \quad \text{and } d_{33}^* = 3.93.$$

$$\rho_{11}(d^*) = 172.24, \quad \rho_{21}(d^*) = 157.66, \quad \rho_{31}(d^*) = 155.09,$$

$$\rho_{12}(d^*) = 157.97, \quad \rho_{22}(d^*) = 138.97, \quad \rho_{32}(d^*) = 145.97,$$

$$\rho_{13}(d^*) = 161.33, \quad \rho_{23}(d^*) = 151.67, \quad \text{and } \rho_{33}(d^*) = 148.61.$$

The computed amounts of firms' profits:

$$U_1(X^*) = 1,199.87, \quad U_2(X^*) = 1,062.73, \quad \text{and } U_3(X^*) = 980.83.$$

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 1

	Path Definition	Path Flow
O/D Pair $(1, R_1)$	$p_1 = (1, 5, 17, 23)$	$x^*_{p_1} = 1.87$
	$p_2 = (1, 6, 18, 26)$	$x^*_{p_2} = 1.46$
	$p_3 = (1, 7, 19, 29)$	$x^*_{p_3} = 1.57$
	$p_4 = (2, 8, 17, 23)$	$x^*_{p_4} = 0.73$
	$p_5 = (2, 9, 18, 26)$	$x^*_{p_5} = 1.17$
	$p_6 = (2, 10, 19, 29)$	$x^*_{p_6} = 0.87$
O/D Pair $(1, R_2)$	$p_7 = (1, 5, 17, 24)$	$x^*_{p_7} = 0.89$
	$p_8 = (1, 6, 18, 27)$	$x^*_{p_8} = 0.57$
	$p_9 = (1, 7, 19, 30)$	$x^*_{p_9} = 0.66$
	$p_{10} = (2, 8, 17, 24)$	$x^*_{p_{10}} = 0.68$
	$p_{11} = (2, 9, 18, 27)$	$x^*_{p_{11}} = 0.82$
	$p_{12} = (2, 10, 19, 30)$	$x^*_{p_{12}} = 0.71$
O/D Pair $(1, R_3)$	$p_{13} = (1, 5, 17, 25)$	$x^*_{p_{13}} = 0.60$
	$p_{14} = (1, 6, 18, 28)$	$x^*_{p_{14}} = 0.16$
	$p_{15} = (1, 7, 19, 31)$	$x^*_{p_{15}} = 0.64$
	$p_{16} = (2, 8, 17, 25)$	$x^*_{p_{16}} = 0.49$
	$p_{17} = (2, 9, 18, 28)$	$x^*_{p_{17}} = 0.53$
	$p_{18} = (2, 10, 19, 31)$	$x^*_{p_{18}} = 0.72$

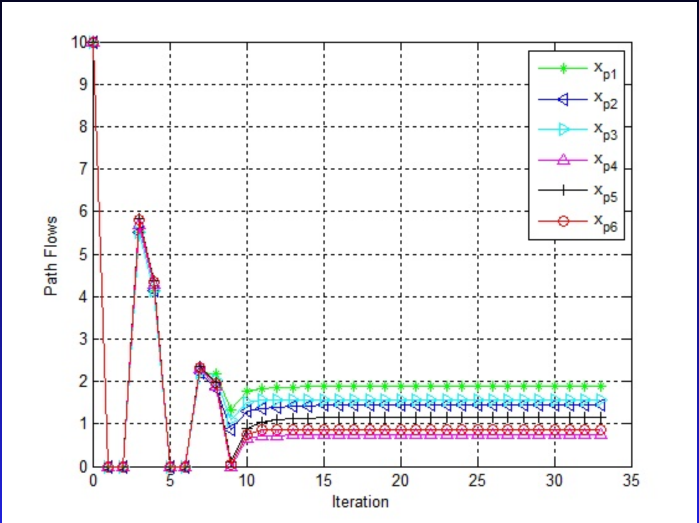
Paths Definition and Optimal Path Flow Pattern - Firm 2

	Path Definition	Path Flow
O/D Pair $(2, R_1)$	$p_{19} = (3, 11, 20, 32)$	$x^*_{p_{19}} = 1.26$
	$p_{20} = (3, 12, 21, 35)$	$x^*_{p_{20}} = 0.77$
	$p_{21} = (3, 13, 22, 38)$	$x^*_{p_{21}} = 1.51$
	$p_{22} = (4, 14, 20, 32)$	$x^*_{p_{22}} = 1.63$
	$p_{23} = (4, 15, 21, 35)$	$x^*_{p_{23}} = 1.16$
	$p_{24} = (4, 16, 22, 38)$	$x^*_{p_{24}} = 2.12$
O/D Pair $(2, R_2)$	$p_{25} = (3, 11, 20, 33)$	$x^*_{p_{25}} = 0.00$
	$p_{26} = (3, 12, 21, 36)$	$x^*_{p_{26}} = 0.00$
	$p_{27} = (3, 13, 22, 39)$	$x^*_{p_{27}} = 0.00$
	$p_{28} = (4, 14, 20, 33)$	$x^*_{p_{28}} = 0.00$
	$p_{29} = (4, 15, 21, 36)$	$x^*_{p_{29}} = 0.00$
	$p_{30} = (4, 16, 22, 39)$	$x^*_{p_{30}} = 0.00$
O/D Pair $(2, R_3)$	$p_{31} = (3, 11, 20, 34)$	$x^*_{p_{31}} = 1.26$
	$p_{32} = (3, 12, 21, 37)$	$x^*_{p_{32}} = 1.05$
	$p_{33} = (3, 13, 22, 40)$	$x^*_{p_{33}} = 0.57$
	$p_{34} = (4, 14, 20, 34)$	$x^*_{p_{34}} = 1.26$
	$p_{35} = (4, 15, 21, 37)$	$x^*_{p_{35}} = 1.29$
	$p_{36} = (4, 16, 22, 40)$	$x^*_{p_{36}} = 0.54$

Paths Definition and Optimal Path Flow Pattern - Firm 3

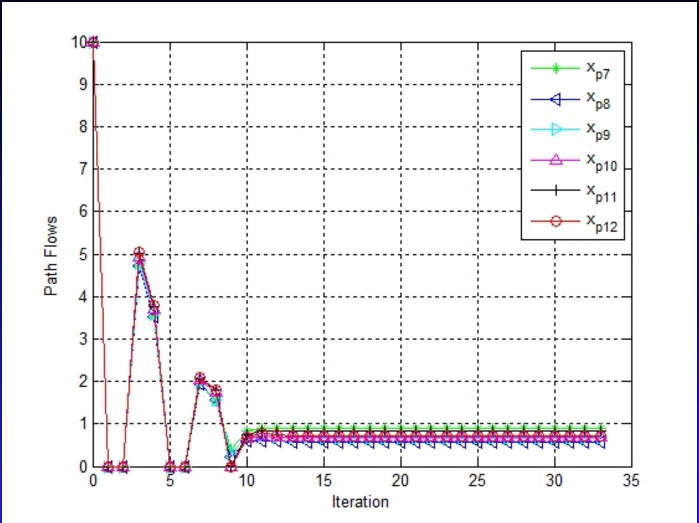
	Path Definition	Path Flow
O/D Pair $(3, R_1)$	$p_{37} = (41, 43, 47, 49)$	$x^*_{p_{37}} = 1.87$
	$p_{38} = (41, 44, 48, 52)$	$x^*_{p_{38}} = 1.78$
	$p_{39} = (42, 45, 47, 49)$	$x^*_{p_{39}} = 0.70$
	$p_{40} = (42, 46, 48, 52)$	$x^*_{p_{40}} = 0.68$
O/D Pair $(3, R_2)$	$p_{41} = (41, 43, 47, 50)$	$x^*_{p_{41}} = 1.61$
	$p_{42} = (41, 44, 48, 53)$	$x^*_{p_{42}} = 1.46$
	$p_{43} = (42, 45, 47, 50)$	$x^*_{p_{43}} = 2.07$
	$p_{44} = (42, 46, 48, 53)$	$x^*_{p_{44}} = 1.90$
O/D Pair $(3, R_3)$	$p_{45} = (41, 43, 47, 51)$	$x^*_{p_{45}} = 0.84$
	$p_{46} = (41, 44, 48, 54)$	$x^*_{p_{46}} = 0.53$
	$p_{47} = (42, 45, 47, 51)$	$x^*_{p_{47}} = 1.46$
	$p_{48} = (42, 46, 48, 54)$	$x^*_{p_{48}} = 1.33$

Path Flow Trajectories



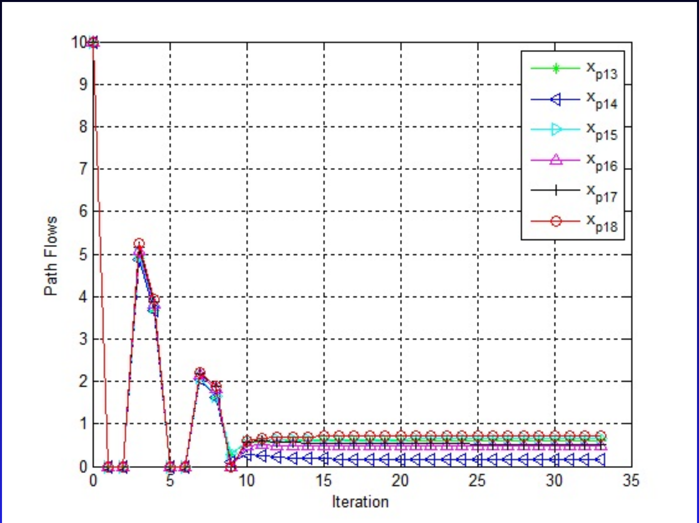
The Trajectories of Product Flows on Paths $p_1 - p_6$

Path Flow Trajectories



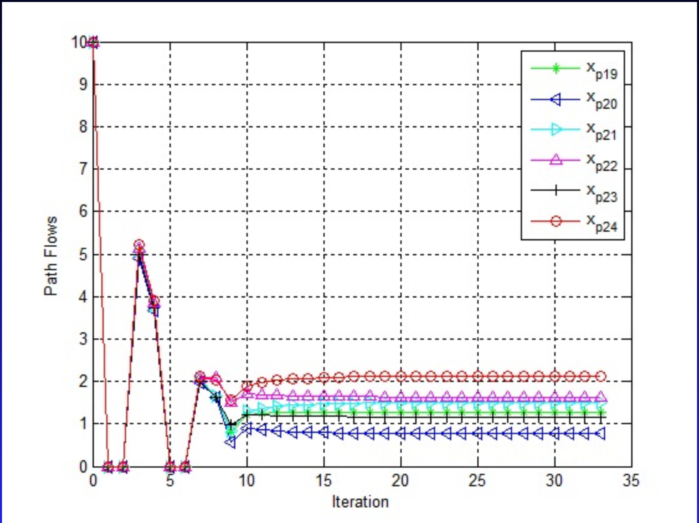
The Trajectories of Product Flows on Paths $p_7 - p_{12}$

Path Flow Trajectories



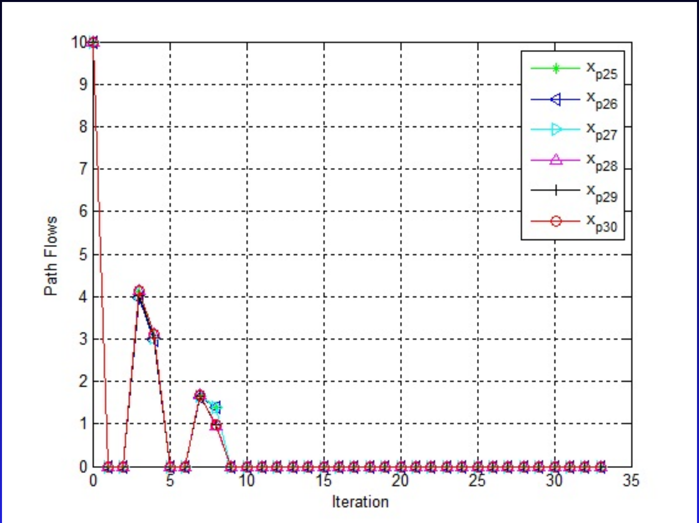
The Trajectories of Product Flows on Paths $p_{13} - p_{18}$

Path Flow Trajectories



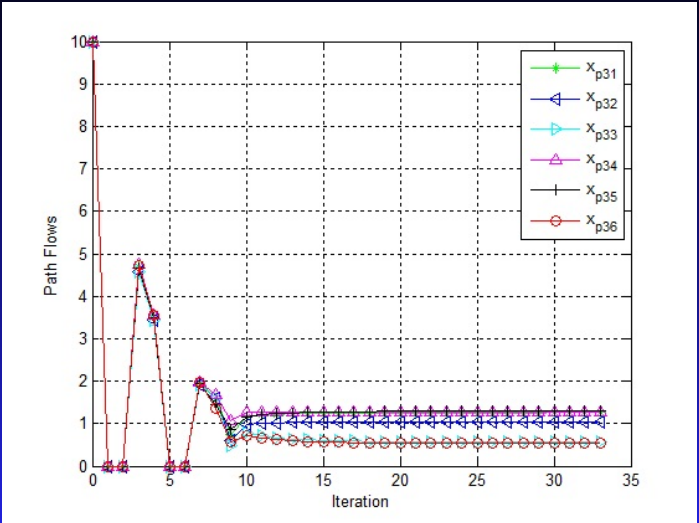
The Trajectories of Product Flows on Paths $p_{19} - p_{24}$

Path Flow Trajectories



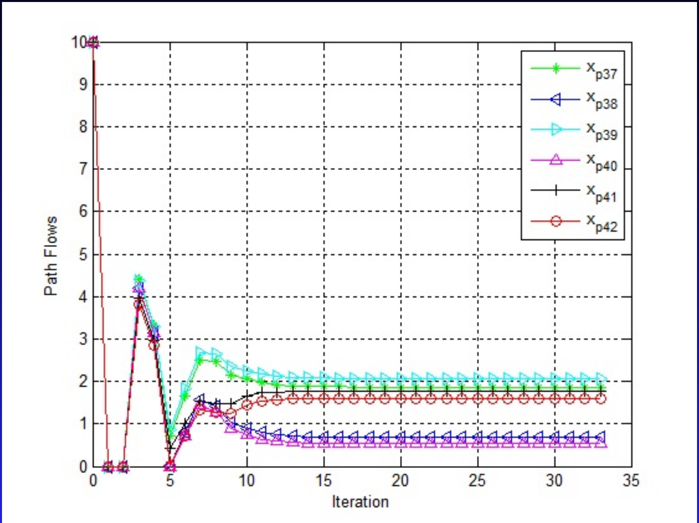
The Trajectories of Product Flows on Paths $p_{25} - p_{30}$

Path Flow Trajectories



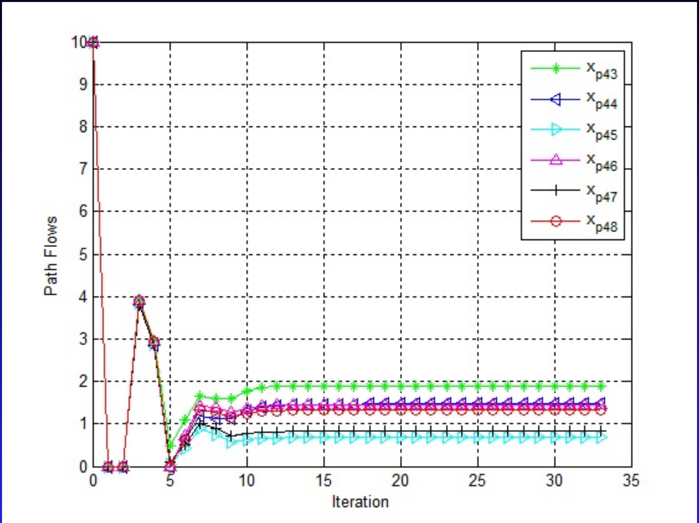
The Trajectories of Product Flows on Paths $p_{31} - p_{36}$

Path Flow Trajectories



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

Path Flow Trajectories



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

Blood Supply Chains for the Red Cross

Blood Supply Chains for the Red Cross

A. Nagurney, A. Masoumi, and M. Yu, "Supply Chain Network Operations Management of a Blood Banking System with Cost and Risk Minimization," *Computational Management Science*, (2012), in press, published online by Springer August 2011.

Blood Supply Chains for the Red Cross

- Over 39,000 donations are needed everyday in the United States, and the blood supply is frequently reported to be just 2 days away from running out (American Red Cross (2010)).
- Hospitals with as many days of surgical delays due to blood shortage as 120 a year have been observed (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)).

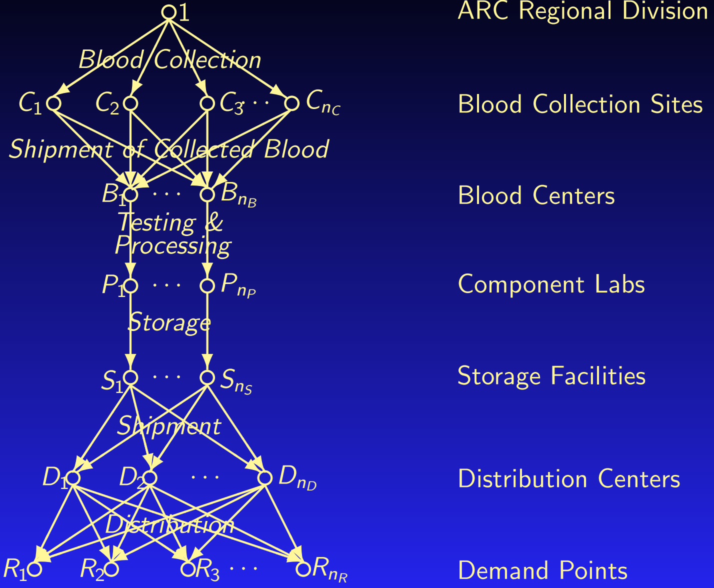
The American Red Cross is the major supplier of blood products to hospitals and medical centers satisfying over 45% of the demand for blood components nationally (Walker (2010)).

Background and Motivation

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



Blood Supply Chains for the Red Cross

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:

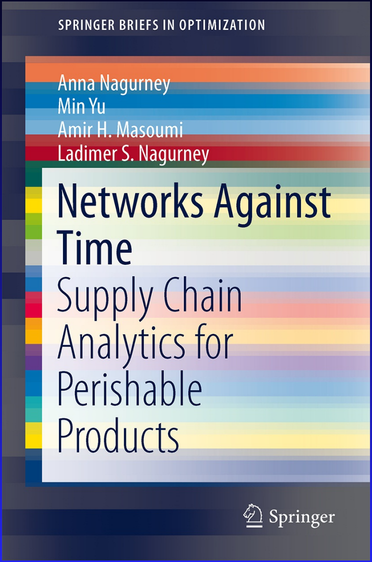
- It captures *perishability of this life-saving product* through the use of arc multipliers;
- It contains *discarding costs* associated with waste/disposal;
- It handles *uncertainty* associated with demand points;
- It assesses *costs associated with shortages/surpluses at the demand points*, and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

Blood Supply Chains for the Red Cross

The model has also been extended to supply chain network design; see, "Supply Chain Network Design of a Sustainable Blood Banking System," A. Nagurney and A. H. Masoumi, in *Sustainable Supply Chains: Models, Methods and Public Policy Implications*, T. Boone, V. Jayaraman, and R. Ganeshan, Editors, Springer, London, England, 2012, in press.

Teaming in Humanitarian Operations and Network Synergies

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



Teaming in Humanitarian Operations and Network Synergies

A successful team depends on the ability to measure the anticipated synergy of the proposed team, which can be viewed as a merger (cf. Chang (1988)).

- A. Nagurney (2009) "A System-Optimization Perspective for Supply Chain Network Integration: The Horizontal Merger Case," *Transportation Research E* **45**, 1-15.

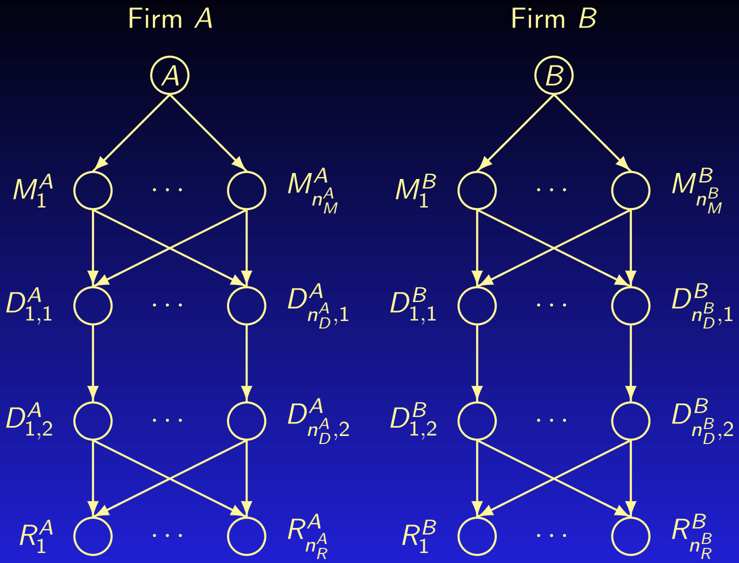


Figure: Case 0: Organizations A and B Prior to a Horizontal Merger

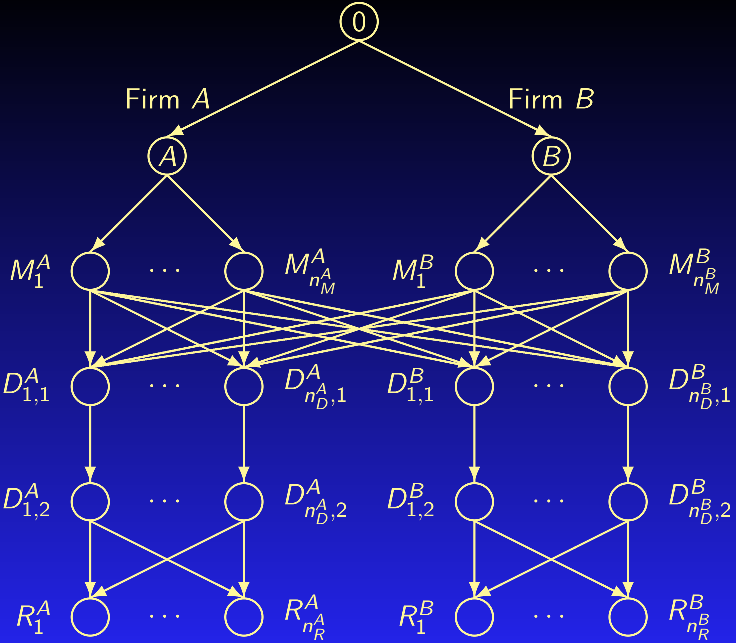


Figure: Case 1: Organizations A and B Team Up or "Merge"

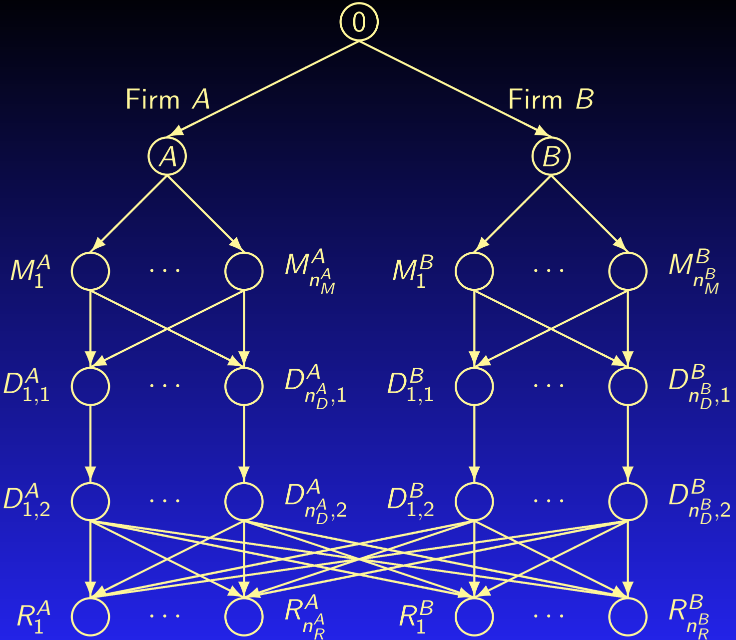


Figure: Case 2: Organizations A and B Merge

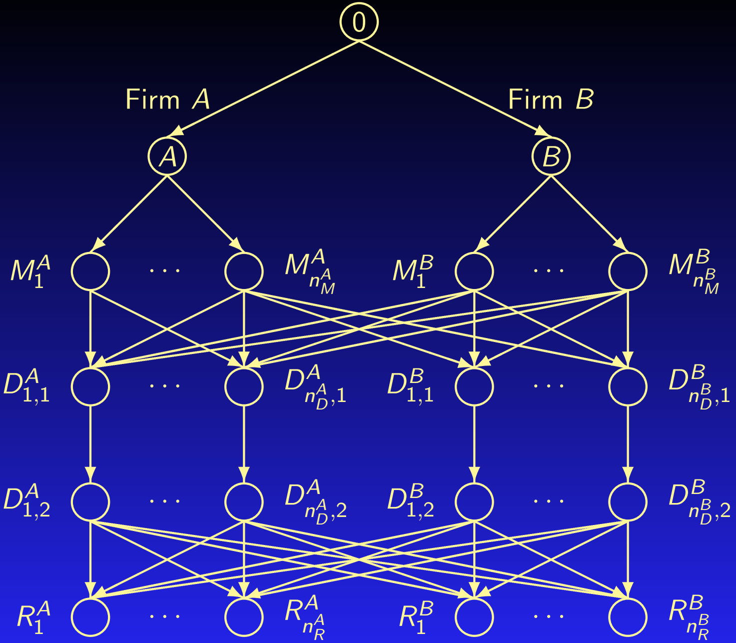


Figure: Case 3: Firms A and B Merge

Synergy Measure

The measure that we utilized in Nagurney (2009) to capture the gains, if any, associated with a horizontal merger Case i; $i = 1, 2, 3$ is as follows:

$$\mathcal{S}^i = \left[\frac{TC^0 - TC^i}{TC^0} \right] \times 100\%,$$

where TC^i is the total cost associated with the value of the objective function $\sum_{a \in L^i} \hat{c}_a(f_a)$ for $i = 0, 1, 2, 3$ evaluated at the optimal solution for Case i. Note that $\mathcal{S}^i$; $i = 1, 2, 3$ may also be interpreted as *synergy*.

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

Bellagio Conference on Humanitarian Logistics

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

Some References

- A. Nagurney, T. Woolley, and Q. Qiang (2010) "Multiproduct Supply Chain Horizontal Network Integration: Models, Theory, and Computational Results," *International Journal of Operational Research* **17**, 333-349.
- A. Nagurney (2010) "Formulation and Analysis of Horizontal Mergers Among Oligopolistic Firms with Insights into the Merger Paradox: A Supply Chain Network Perspective," *Computational Management Science* **7**, 377-401.
- A. Nagurney (2010) "Supply Chain Network Design Under Profit Maximization and Oligopolistic Competition," *Transportation Research E* **46**, 281-294.
- Z. Liu and A. Nagurney (2011) "Supply Chain Outsourcing Under Exchange Rate Risk and Competition," *Omega* **39**, 539-549.

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 products.

- In addition, we have been heaving involved in *constructing mathematical models that capture synergies in mergers and acquisitions with the inclusion of risk* as well as exchange rate risk associated with outsourcing.

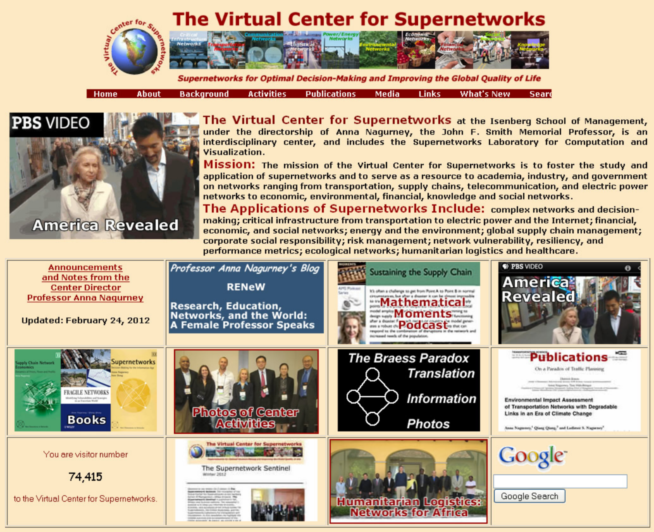
- Our research in supply chains has also led us to other time-sensitive products, such as *fast fashion*, and

- Finally, we are now working on modeling disequilibrium dynamics and equilibrium states in ecological predator-prey networks, that is, supply chains in nature.

- *We expect that future research will include design for robustness and resiliency.*

- Some recent research that we have begun in this direction: "Modeling of Supply Chain Risk Under Disruptions with Performance Measurement and Robustness Analysis," Q. Qiang, A. Nagurney, and J. Dong (2009), in *Managing Supply Chain Risk and Vulnerability: Tools and Methods for Supply Chain Decision Makers*, T. Wu and J. Blackhurst, Editors, Springer, London, England, 91-111 and
- "A Bi-Criteria Indicator to Assess Supply Chain Network Performance for Critical Needs Under Capacity and Demand Disruptions," Q. Qiang and A. Nagurney, *Transportation Research A* **46(5)** (2012), 801-812.

THANK YOU!



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