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Agent-based Simulation of the Pharmaceutical Parallel Trade Market: A Case Study

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Abstract

The pharmaceutical parallel trade market emerged as a consequence of the European single market for pharmaceuticals, involving multiple players that partake in different types of competitions. These competitions not only affect players' profit, but also have a significant impact on European people's healthcare access and welfare. Hence, modeling the pharmaceutical parallel trade market provides a way to study the market and to offer valuable decision support to authorities, people, and players involved in the market. Agent-based modeling offers a computational methodology to study macro-level outcomes emerging from individual behaviors while offering to relax conventional assumptions of standard mathematical economic models. Here, we demonstrate a use case of an agent-based model of the European pharmaceutical parallel trade market and investigate its abilities by analyzing various market scenarios.

Keywords: Agent-based modeling and simulation, Modeling and simulation, Pharmaceutical parallel trade

1. Introduction

Agent-based modeling (ABM) is a computational modeling technique for simulating heterogeneous individuals' interactions in an environment and analyzing the bottom-up outcomes of a system. ABM enables us to go beyond the expressiveness of mathematical models by permitting relaxation of assumptions and making models more analytically tractable. ABM is commonly used to represent individuals' behavior to study social phenomena. Schelling's segregation model was one of the first efforts with ABM, which was developed to study social segregation [22, 23, 14]. The idea of an agent-based model is that a system, process, or event can be modeled by defining agents, their characteristics, an environment, and agent-agent, agent-environment interaction rules. Depending on its initial assumptions, an agent-based model can combine multi-agent systems, game theory, complex systems, and evolutionary algorithms

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concepts. An agent-based model enables us to investigate the interactions' outcomes while considering a model's stochasticity by simulating micro-interactions. The output of an ABM can be an equilibrium at the agent level or ongoing dynamics, reflecting the constant adjustment of agents' behavior.

Digital computation enables us to generate numerical solutions and relaxes oversimplifying assumptions. Since in economics, most theorems, lemmas, and formal propositions, are mostly mathematical and strict, it is frequently difficult to find an analytical model to accurately describe the different behaviors of players involved in a market-related competition. One solution for this difficulty is to build a model by specifying agents involved in a market and their interaction rules, and letting the agents interact with each other, instead of solving equations. Interaction rules produce agents' behaviors, resulting in evolution in a dynamic system which is more realistic [1]. Tesfatsion [24] discusses the potential ability to employ ABM in economics and also elucidates its challenges. By early advancement of computational solutions, Cohen [3] discussed the potential application and challenges of simulation or analyzing economic models and studying firms' behaviors. Every market can be formalized as a complex adaptive system consisting of multiple adaptive agents with interactions. These interactions cause macroeconomic emergence as regulations, protocols, and norms. In other words, microeconomic interactions are the source of macroeconomic behaviors, which has been a relevant topic for over 50 years [22, 9, 18]. The Sugarscape model [4] is another early example of using ABM to research an economic situation where the authors investigated wealth distribution. In a practical research, Kirman and Vriend [12] investigated the impact on buyer-seller loyalty in a fish market using an agent-based model. Multiple efforts have been made to use ABM to study auctions [8, 6, 7]. Moreover, ABM was employed to research industrial organizations and firm operations where ABM might relax some conventional characteristics such as rationality. However, ABM models still were able to present rational results. ABM is also employed in manufacturing control [13], marketing [20], and customer behavior [21].

On the other hand, game theory is vastly used to study business, and economics-related strategic behaviors, such as competitive bidding, settlement negotiations, bargaining, and research and development strategies [26]. In a game theory model, a situation or competition can be modeled as a game where players involved in it choose their actions based on a predefined set of rules, and their actions determine their pay-off [2].

Developing a computational model of the pharmaceutical parallel trading market could be of huge interest to economists studying the market. Parallel trade of medicines is legal and strictly regulated in Europe, enabling parallel distribution of medicine in the EU. When a new medicine is developed, the patent holder can prohibit other companies from producing it. However, the patent holder can not prevent reselling the medicine by licensed wholesalers or parallel traders. In fact, parallel traders and wholesalers can buy a medicine and move it to a destination market, repackage the medicine to comply with local legalization, and sell it at a lower price than the local price for the same identical product sold by the original manufacturer or local license holders. Parallel trade of pharmaceuticals prevents monopoly prices by the patent holder in every national market, which is good for people's health, welfare and economy.

The concept of parallel trade has been studied using game theory [19, 5, 10]. These models, however, have limitations in their assumptions. First, all parallel traders in these models are considered to be the same. However, in the real world, players involved in pharmaceutical trade markets or trade markets have different characteristics. Secondly, multiple players, such as manufacturers, parallel traders, pharmacies, hospitals, and wholesalers, are involved in the pharmaceutical trade market. It would be challenging or impossible to build a game-theoretic model that considers all of the players involved in this market and their specific characteristics. Finally, the players involved in these models are not modeled as intelligent, which is also unrealistic. Based on the game theoretic models, we developed an agent-based model of the pharmaceutical market [11]. Our agent-based model not only replicated the equilibrium results of the game theoretic models but also enabled us to investigate scenarios considering the different characteristics of players involved in the market.

In this paper, we aim to employ our initially developed agent-based model of the pharmaceutical trading market [11] and extend it toward a more accurate market representation. In the game theory model, price is highly dependent on the demand for medicine. However, in economic literature, the price of prescribed medicines is considered to be inelastic to their demand. Inelasticity means the demand for a medicine remains unchanged even when the price changes. Here we focus on the price elasticity of medicine and experiment with implementing a different pricing strategy for players involved in the market. Subsequently, we use this extended model to run new possible scenarios in the market. The rest of the paper is structured as follows: Section 2 provides information about the game theory model, our initial agent-based model, and our new extended model. In Section 3, we run multiple scenarios employing the new model.

Afterward, in Section 4, we discuss the application of the presented model while discussing the possible extension and how they can be utilized to benefit from data. Finally, in the last Section 5, we will provide the summary and outlook.

2. Model

2.1. Game theory model

Pecorino's [19] game theory model investigates the impact of the pharmaceutical parallel trading market between the US and Canada on a manufacturer's profit and social welfare. Gue et al. [5] extended Pecorino's model to study the impact of parallel traders on a manufacturer's profit. To illustrate their model, first, we need to describe what are *monopoly* and *demand function*. *Monopoly* happens when a supplier sets the price for their product or service without fear of competition [25]. *Demand function* is defined as the mathematical equation demonstrating the relationship between a product's price and its demand quantity at that price. In Pecorino's model, two countries (E and I), a manufacturer, and a number of parallel traders are involved. In the game theory model, two major steps are defined: first manufacturer and the government of country I due to regulation in the country I, negotiate the price of the medicine to come up with the price of the medicine in the country I. Second, parallel traders check the price in the country I to check if they can make a profit by purchasing the medicine in the country I and reselling it in the country E. If parallel traders can make a profit, they will participate in price competition with each other and the manufacturer in the country E's market. In the game theory model, the price of the medicine in the first step is considered to be the result of a Nash Bargaining game [17] between the government and the manufacturer considering the demand function of the medicine in the country I. Pecorino examined two demand functions for medicine in his model. In the second step of the model, if parallel traders do not participate in the market of country E, the manufacturer sets a monopoly price for the medicine in the country. However, suppose parallel traders do participate in the market of country E. In that case, the model treats the competition between manufacturers and parallel traders as a *Cournot competition*, since they are offering the same product. In this type of competition, companies offering identical products compete for market share.

2.2. Previous agent-based model

The game theory model of the pharmaceutical parallel trade market provides a broad understanding of the market, allowing us to analyze its overall effects, such as the manufacturer's profit or the medicine price, in the presence of parallel traders. However, the agent-based model of the pharmaceutical parallel trade market [10], not only allows us to study these same outcomes, but also enables us to take into account the various characteristics of the players in the market. For example, in the game theory model, parallel traders are assigned a fixed transfer cost, which represents the cost of transporting the medicine from country I to country E and repackaging it. However, the agent-based model allows us to assign different transfer costs to each parallel trader, based on their individual infrastructure. This enables us to examine the impact of changes in these attributes on the price competition in country E. Simulations using the agent-based model can be useful for companies in this market to plan for future expansion, such as improving their transfer and repackaging infrastructure or even acquiring smaller companies.

The agent-based model of the pharmaceutical trading market [11] is based on the game theory models in which also two countries were considered. In our previous research, we followed Macal and North tutorial [15] to develop their model where three components were needed to develop an agent-based model, a set of agents with their attributes and behavior rules, a set of interaction rules between agents, and a definition of environment and its attribute where agents interact with each other and environment. In our agent-based model, we considered having three types of agents: Government, which is the country I's government with only one attribute named bargaining power. The manufacturer is the second type of agent in this model with four attributes named bargaining power, Market share in E, step revenue, and total revenue. The last agent type is the parallel trader with transfer cost, market share in E, step revenue, and total revenue as attributes. The interaction rules in our model are as follows: Each step of the model starts with the price negotiation between the government and the manufacturer, where they set the price in the country I using the Nash Bargaining equilibrium equation considering their bargaining power. Then traders check the price in I to see if they can make a profit by selling the medicine in E considering their transfer cost. Transfer costs indicate a parallel trader's costs to move the medicine from I to E and repackage them. In case of no parallel trader participation, the manufacturer acts as a monopolist in the country E and sets a price to maximize their profit. On the other hand, in the case of parallel traders participation, in each step, the manufacturer and traders involved in the market E adjust their market share (sell quantity) in E, considering their revenue function and the market's current status. They can adjust their market share by a fixed rate called the "step quantity adjustment rate." After this step, the price of the medicine in the country E is calculated based on the demand function of the medicine for the country and the total sell quantities of players involved in the market. The model's environment is the whole market which has seven attributes: the number of traders, country I market size, country E market size, price in I, price in E, step total sell quantity in E, and step quantity adjustment rate. In this model number of traders, country I market size, country E market size, and step quantity adjustment rate are fixed and are given to the model, while other attributes are variable, and their value is based on interactions in each step.

2.3. Current agent-based model

In all aforementioned models, as we described, the price of the medicine in the country E is based on the result of the quantity competition among players in the market and using the considered demand function. However, logically medicines have inelastic demand. *Inelastic Demand* for a product or service means that the market's demand is not related to price fluctuations. For medicines that are prescribed for a person, we assume that their demand is not related to the price of the medicine. By considering an inelastic demand for medicine, we decided to model the competition in the market as a price competition that is not related to the demand. To get a better understanding of this, we researched the pharmaceutical market of Denmark, and in this market, the price competition over a medicine is described as follows: Every two weeks, for every medicine that needs a prescription, every company (parallel trader or manufacturer) who wants to sell the medicine in Denmark should set a retail price for the medicine without any knowledge about other companies' prices. Then, for the subsequent two weeks, players in the market have to sell their products at pharmacies with the same offered retail price. Pharmacies prioritize the product with the lowest price to the consumers. If the player with the lowest price can not deliver all or partition of the demand, then pharmacies start selling the product with the next priority (the second lowest price). Hence, using the demand function to estimate the pharmaceutical market prices is unrealistic. Instead, considering a model in which the price competition among players is not related to the demand function seems to be practical for studying the market's behavior.

We used the presented agent-based model [11] of the pharmaceutical trading market as a basis of the model that we present in this paper while changing the price competition in E. In the new model, we have the same two countries, I and E. The manufacturer sells the medicine at an agreed price with the government in I, and then parallel traders start buying the medicine from I, transfer and repackage it, and then sell it in E to make a profit. In the E, we considered having a price cap for the medicine, which indicate the maximum possible price for the medicine and it is higher than the price in I. Otherwise, parallel traders will not participate in the market. In each step of our model, players (manufacturer and parallel traders) in the market of E set their retail prices for the medicine considering their current stock and capacity. Now that we presented the new setup for pricing in market E, we will present the model in a structured way following Macal and North tutorial [15] procedure.

The first step is to define the set of agents, their attributes, and their behavior rules. Since we considered the medicine price in country I is already set over a negotiation between the government and the manufacturer, and the negotiated price is a fixed number, we eliminated the government agent from our previous agent-based model. In our model, we have two types of agents, manufacturer and parallel trader. The manufacturer has five attributes: 1) warehouse capacity indicates their warehouse capacity in the country E (fixed); 2) stock which is the number of current medicine units available in their warehouse (variable); 3) share which indicate the amount of medicine they sell in the current step which (variable); 4) revenue which is the total revenue of them in market E (variable); and 5) revenue margin which demonstrates their desired revenue margin in percentage based on the price in country I when they want to sell the medicine in country E (fixed between 0 and 1).

In each step, the manufacturer adds a fixed amount of the medicine to their warehouse, considering their warehouse capacity. Then they will set their retail price for the step, and finally, they calculate their step revenue and add it to their total revenue. Parallel traders have the same attributes plus an attribute called transfer cost, which indicates medicine transferring and repackaging costs. Parallel traders' step procedure is almost the same as the manufacturer, they buy a fixed amount of medicine from I and then repackage and transfer it to their warehouse in E and finally set a price for it to sell in the market of E.

The second step is defining interaction rules. In our model, there is price competition among players involved in the market in each step. All players set their retail price for the same medicine. They all use the same pricing strategy, defined by a simple function. In this function, every player considers four types of prices. First, the *desired price* is the medicine price in I (P_I) plus P_I times revenue margin plus transfer cost. Where transfer cost is considered to be zero for the manufacturer. The second one is the *sufficient price*, which is the same as desired price, but P_I times the revenue margin is divided by two. The third one is the *zero revenue price*, which is the P_I plus transfer cost. The last one is the *minimum price* which is the zero revenue price minus ten percent of the P_I plus transfer cost. After calculating all the prices for the market in E, players use a pricing function to come up with their retail price. The pricing function pseudocode is presented in the Algorithm 1. In our model, we considered a simple pricing strategy that is based on the occupied space of a player's warehouse. Players in this market have small knowledge about other players' behavior, and because of that, their pricing strategy is only based on the percentage of warehouse capacity occupied. Each player in the market considers an eligible pricing range based on the percentage of occupied space in their warehouse. Then the player chooses their retail price from the range randomly.

The final step is to define the model's environment and its attributes. The model's environment is the market, and its attributes are as follows: 1) the number of traders (fixed); 2) medicine's price in I (fixed); 3) medicine's price in E (variable); 4) price cap in E (fixed); and 5) demand size in E (variable). Medicine's price in E is the weighted average of selling prices in each step. The maximum price in E is the price cap in the country E, which is a fixed number. The demand size in E is a random number in each step.

Algorithm 1 Pricing function

```
function PRICING(x = stock/warehouse capacity)
    if x < 0.6 then
        Price = Random(Desired price , E max price)
    else if x < 0.75 then
        Price = Random(Sufficient price, Desired price)
    else if x < 0.9 then
        Price = Random(Zero revenue price, Sufficient price)
    else if x < 0.95 then
        Price = Zero revenue price
    else if x < 1.00 then
        Price = Random(Minimum price, Zero revenue price)
    else
        Price = Minimum price
    end if
```

3. Description of case study

3.1. Implementation detail

We implemented our model in Python using the Mesa library[16]. All initial values we used for the model are inspired by the available data we had from the Danish market. Since the data was insufficient for the model, we approximated reasonable values for all remaining parameters. In all our simulations, we considered the medicine's price in I to be 50, the price cap in E to be 75, and the number of parallel traders to be 3. Each step's demand is a randomly generated number from a normal distribution with a mean of 3000 and a standard deviation of 800. Demand is generated throughout the simulation time with the same seed for all experiments, so we have the same list of demand amounts over all simulations. The warehouse capacity of the manufacturer and parallel traders are considered 10000 and 8000, respectively. The manufacturer and parallel traders' revenue margins are set to be 0.3 and 0.2, respectively. The transfer cost for all parallel traders is considered to be 5. Since in the pharmaceutical parallel trade market, parallel traders buy medicine from different sources and countries, to simplify the model and focus on studying pricing competition, we consider that all players in the market, at each step, can import a fixed amount of medicine. Therefore, at each step of our model, all players import 750 units of the medicine.

3.2. Market scenarios

The pharmaceutical trading market can be further explored and studied by employing our model to investigate the effects of multiple variables on the market. Moreover, players involved in the market can utilize the model not only to analyze their strategies' and decisions' impact on their revenues and the market but also to predict the market's future considering the market's current status. In this section, we describe five scenarios that we are going to investigate, and in the next section, we will present the details and results of each scenario.

In the first scenario, we analyze the effect of the balance between supply and demand on player revenues by manipulating the import amount of medicine in the market. The second scenario examines the relationship between warehouse capacity and the revenue of parallel traders. The third scenario evaluates the impact of revenue margins on the total revenue of market participants. The fourth scenario explores the effect of transfer costs on the total revenue of parallel traders. In the final scenario, we simulate a market with five parallel traders, each with different attributes, to demonstrate how our model could be used as a decision-support system by players in this market.

4. Simulation Experiments

Varying values of agents' attributes, specified in the last section 3.1, we ran simulations for 1000 steps and 3000 replications to calculate 95% confidence interval for the total revenue of each player in the market. Therefore if we consider all parallel traders have the same attributes, confidence intervals for the total revenue of manufacturer and parallel traders resulted as follows: (8 706 756, 8 717 694), (5 322 776, 5 332 478), (5 326 275, 5 335 959), and (5 313 771, 5 323 395), respectively. We observed if we consider the same attributes for parallel traders, they will have almost the same total revenues after 1000 steps of simulation, and presented confidence intervals can be employed as a reference point to investigate each attribute's impact on the total revenue.

Demand supply balance: To investigate the impact of the market's supply and demand balance on the total revenues of players in the market; first, we reduced the medicine import amount for every player from 750 to 700. The resulting confidence intervals for total revenues were (13 428 185, 13 433 423), (9 906 111, 9 911 461), (9 904 821, 9 910 073), and (9 906 475, 9 911 789) referring manufacturer and parallel traders, respectively. The result demonstrates how a shortage of medicine in the market could cause less competition among players in the market, resulting in higher prices and bigger revenue for players. On the other hand, if each player in the market were able to import 800 units of medicine in each step, the confidence intervals resulted as (1 553 541, 1 564 306), (−1 623 771, −1 616 204), (−1 622 918, −1 615 446), and (−1 612 792, −1 605 253). This result demonstrates the negative impact of the excessive import of medicine specifically for parallel traders because they should also consider their transfer cost, and if they buy too much of the medicine, they might force to sell their medicines at a lower price than the net cost price just to reduce their financial loss.

Warehouse capacity: In this scenario, we investigate the impact of warehouse capacity on the total revenue for parallel traders. In this simulation, we considered the warehouse capacity of three parallel traders to be 4000, 8000, and 12 000, keeping the total warehouse capacity of the parallel traders the same. The resulting total revenue confidence intervals for parallel traders were (3 813 753, 3 824 577), (5 585 137, 5 595 783), and (6 032 326, 6 042 133) which demonstrate higher capacity resulted in higher total revenue. However, although the difference between the warehouse capacity of the first and second parallel traders is the same as the difference between the second and third, their total revenue gap is almost one-third. While in the real world, having a bigger warehouse means bigger expenses, the gap difference indicates the importance of optimizing the warehouse capacity.

Revenue margin: To investigate the impact of revenue margin on parallel traders' total revenue, we ran simulations considering different values for each parallel trader. Here we considered revenue margins to be 0.1, 0.2, and 0.3, resulting in (4 689 374, 4 698 739), (5 320 222, 5 330 003), and (5 149 624, 5 160 925), respectively. This result shows that parallel traders must optimize their revenue margin in their pricing procedure instead of increasing it, which could cause less revenue in the long run.

Transfer cost: Transfer cost in our model means general expenses to move medicine from the origin country to the destination and repackage it. To investigate the impact of the transfer cost, we set the parallel traders' transfer costs at 2, 5, and 8. As we expected, the confidence intervals for the total revenues were (7 366 025, 7 376 716), (5 710 145, 5 720 510), and (3 815 399, 3 825 239), which demonstrate the importance of investment on infrastructure for a parallel trader.

Five unique traders: In this scenario, we aim to demonstrate the practical application of our model in a pharmaceutical trading market with five different parallel traders. In this setup of our model first manufacturer has the same attributes as before. The first parallel trader is a small trader who just recently joined the market, their transfer cost is 8, their warehouse capacity is 2000, they can import 200 units of medicine in each step, and since they are new to the market, they consider 0.15 revenue margin. Parallel trader number two is a medium size company with a transfer cost of 5, warehouse capacity of 4000, and revenue margin of 0.2 while they can 350 units of medicine in each step. The third trader is also a medium size company with the same attributes as the second one except for its warehouse capacity, which is 5000. The last two traders are big companies, both of them have a transfer cost of 2, a warehouse capacity of 8000, and they can import 700 units of medicine in each step. However, the fourth parallel trader has a revenue margin of 0.2, and the fifth one has a revenue margin of 0.25. We ran the simulation for 1000 steps over 5000 replications with this setup and presented total revenue averages and 95% confidence intervals for each player involved in the market in Figure 1. In this figure, total revenues are presented in millions. 95% confidence interval for the total revenue of each player in the market resulted as follows: (7 674 389, 7 682 046), (634 622, 636 827), (2 169 566, 2 173 842), (2 348 324, 2 352 783), (6 154 620, 6 161 717), and (6 299 448, 6 306 823). The first confidence interval is for the manufacturer, and subsequent confidence intervals correspond to parallel traders in the same order that we presented them.

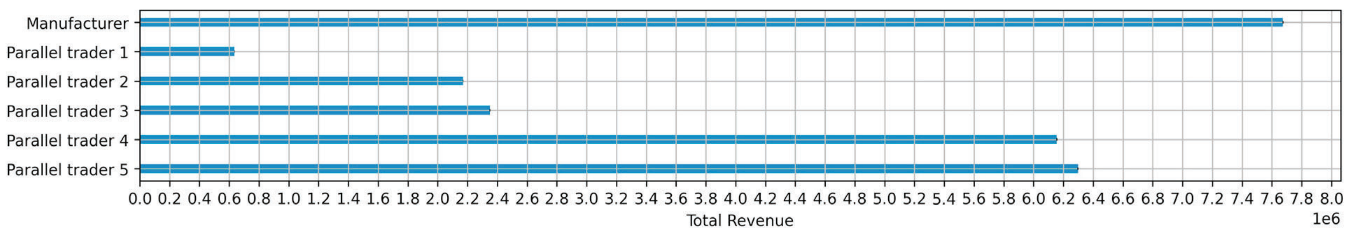

Fig. 1. A manufacturer's and five different parallel traders' total revenue averages and 95% confidence intervals after 1000 steps (1 step = each player import medicine and sets the price to sell) of simulations for 3000 replications.

Our goal is to illustrate how our model can be used by market participants to make informed decisions and optimize their revenue. For example, parallel trader one, the smallest company in this market, can investigate what would be their total revenue if they had a bigger warehouse. If we change the first parallel trader's warehouse capacity value from 2000 to 4000 and run the simulations with the same values for other players. The simulation result demonstrates that their total revenue confidence interval increases from (634 622, 636 827) to (917 158, 919 755). This means they can expect almost a 50 percent increase in their total revenue after 1000 steps of the market if they invest in their warehouse capacity.

5. Summary and outlook

The purpose of this paper is to demonstrate the capabilities of an agent-based model for simulating the pharmaceutical trading market. Through experiments with our model, we observed how it can serve as an explainer of market events, a predictor of macro outcomes based on micro changes in the market, and even an optimization tool for players to improve their revenues. The experiments presented in Section 4 only scratch the surface of the potential uses of the agent-based model for economists, authorities, and market players. While we simplified the pricing strategies of players in the pharmaceutical trading market for the purpose of these simulations, the results we obtained demonstrate the model's potential for producing rational outcomes. Another benefit of using an agent-based model is the ability to track and analyze interactions at each step, which aids in the interpretation of events within the simulation.

There are several ways in which the presented model can be improved and extended. One possibility is to utilize historical data to estimate the model's parameters, which would not only allow us to predict market behavior but also validate the model. This could lead to improvements in the underlying assumptions and interactions, resulting in a more accurate market representation. Another option is to enhance the intelligence of the agents in the model by improving their trading strategies. For example, players in the market could utilize machine learning models to predict demand at each step. By running simulations with different prediction models, we can determine which ones are most effective in this market. Another possibility is to expand the pricing strategy, such as by using complex machine learning techniques to predict other players' prices at each step and evaluating how this improves the model. Adding additional attributes could also improve the simulations, such as considering the expiry date of a medicine, which can impact pricing decisions. Finally, introducing other agents and interactions to the market, such as wholesalers, pharmacies, or hospitals, could make the model a more comprehensive representation of the pharmaceutical trading market.

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