UDC 004.45:004.942

PACKING SPHERICAL CLUSTERS FOR DESIGN OF NANOCOMPLEXES

Letuta N.V.
e-mail: nikita.letuta@nure.ua
Scientific Supervisor – Dr. Sc. (Tech.), Prof. Romanova T.Ye.
Kharkiv National University of Radio Electronics,
Department of Applied Mathematics
Kharkiv, Ukraine

Дослідження спрямоване на оптимізацію пакування на прикладі нанокомплексу Dox-C60, що потребує точного просторового розміщення компонентів для забезпечення стабільності, біодоступності та терапевтичної ефективності. Запропоновано математичну модель задачі пакування у вигляді задачі змішаного цілочислового нелінійного програмування, яка враховує геометричні та фізико-хімічні обмеження взаємодії між частинками. Для ефективного пошуку рішень розроблено стохастичний евристичний алгоритм, що поєднує випадкове вибіркове дослідження простору рішень із керованим пошуком оптимальних конфігурацій. Отримані результати свідчать про ефективність запропонованого підходу для моделювання молекулярного пакування складних наноструктур. Практична значущість дослідження полягає у можливості застосування розробленого методу для раціонального проєктування наномедичних препаратів, оптимізації процесів їх синтезу та створення ефективних систем адресної доставки лікарських засобів.

Smart systems and data-driven computational modelling have become essential tools in modern nanomedicine, offering significant potential to accelerate the design, synthesis, and clinical translation of complex nanostructures. Nanocomplexes, such as the widely studied Dox-C60 system [1], require precise spatial arrangement of molecular components to ensure stability, bioavailability, and efficacy. One of the key challenges in this domain is the problem of molecular packing – determining how multiple nanoparticles can be arranged within a confined volume while respecting both geometric and physicochemical constraints. Efficient solutions to this problem have direct implications for the production, formulation, and delivery of nanomedicines, making computational methods a critical component of nanotherapeutics research.

In this study, we address a non-standard sphere-packing problem for nanocomplex design. Each placement object is modelled as a simplified representation of the Dox-C60 nanocomplex, consisting of a spheroidal core and three identical spheroidal molecular components. These components are constrained to move along a predefined orbit around the core, reflecting realistic molecular flexibility while maintaining structural integrity. In addition, pairwise distance constraints are imposed between all nanoparticles to ensure physically feasible configurations, representing van der Waals interactions and steric limitations. The

placement objects are allowed free movement within a three-dimensional cuboidal container, representing the space available for assembly during synthesis or formulation.

The packing problem is formulated as a mixed-integer nonlinear programming (MINLP) model, which captures both discrete placement decisions and nonlinear geometric constraints. Due to the high combinatorial complexity of the problem, traditional optimization methods are computationally expensive and may become trapped in local optima. To overcome these limitations, we develop a stochastic heuristic algorithm that combines random sampling with guided search strategies. The algorithm iteratively explores the solution space, allowing for repositioning of nanocomplexes and adjustments to component orientations, thereby maximizing packing density while satisfying all distance constraints. Stochastic elements introduce variability that helps avoid premature convergence, improving the probability of identifying high-density configurations.

Computational experiments demonstrate the effectiveness of the proposed approach. Using a cuboidal container of predefined dimensions, our algorithm successfully generated configurations containing 900 and 1000 nanoclusters (rcore=0.75, rorbit=0.36, distance=0.5) in 321 and 351 seconds, respectively (see Fig. 1 and Fig 2). Visualizations of these arrangements show that the heuristic preserves inter-particle distances while maximizing occupancy, resulting in highly efficient use of available space. These results indicate that stochastic computational modelling can produce near-optimal arrangements for molecular packing in practical time frames, even for complex, multi-component nanostructures.

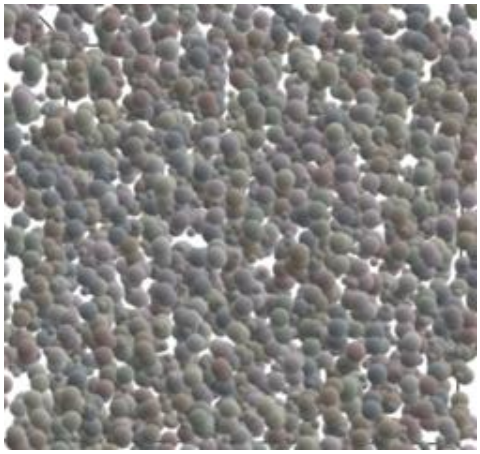

Figure 1 – Configuration of 900 clusters / 3600 nanoparticles

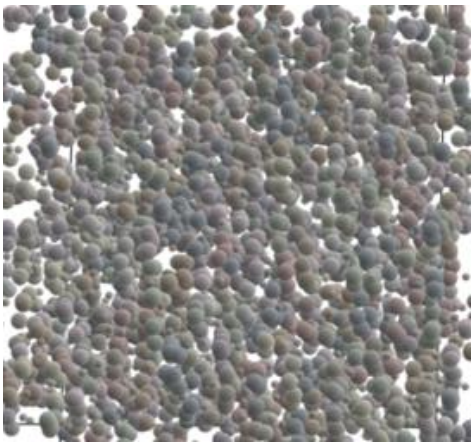

Figure 2 – Configuration of 1000 clusters/4000 nanoparticles

The implications of this work extend beyond theoretical modelling. By providing a computational approach for predicting feasible high-density configurations of nanocomplexes, our method supports rational design in synthesis and production. Pharmaceutical formulations can benefit from insights into optimal spatial arrangements, potentially improving drug stability, bioavailability, and controlled release. Furthermore, the approach is generalizable to other types of nanostructures with orbit-constrained components, making it relevant to a broad range of nanomedicine applications, including targeted drug delivery and multifunctional nanocarriers [2].

In conclusion, this study demonstrates that integrating smart computational modelling with stochastic heuristic algorithms can address complex molecular packing problems in nanomedicine. The methodology provides an efficient, flexible, and scalable approach for designing nanocomplexes with high packing density, while maintaining physical feasibility. Such tools can accelerate the translation of molecular designs from computational models to experimental synthesis and clinical application, ultimately contributing to the development of next generation nanotherapeutics. Future work may extend this approach to include dynamic simulations of molecular interactions, solvent effects, and multi-component drug systems, further bridging the gap between computational predictions and experimental realization.

References:

1. Application of C60 Fullerene-Doxorubicin Complex for Tumor Cell Treatment In Vitro and In Vivo / R. Panchuk et al. Biomed Nanotechnol. 2015. No. 11. P. 1139–1152.

2. Khudhur, Z.O.; Maad, A.H.; Ghanimi, H.A.; Abdolmaleki, A. Fullerene nanoparticle as new therapeutic agent for the nervous system disorders. Nanomed.J. 2024. No.11, 342–359. https://doi.org/10.22038/nmj.2024.78043.1903.