

# Distribution of Node-to-Node Distance in a Cubic Lattice of Binding Centers

Zbigniew Domański and Norbert Sczygiol

**Abstract**—Three dimensional (3D) nanostructured substrates play an important role in a variety of biomedically-oriented nanodevices as well as in functional devices created with the use of DNA scaffolding. Spatial arrangements of binding centers influence the efficiency of these 3D substrates. We compute and analyze the distribution of distances ( $q$ ) between binding centers in the case where the centers are localized in nodes of a cubic lattice. We find that the node-to-node probability distribution is a fifth-degree polynomial in  $q$ .

**Index Terms**—distinct distances, graph theory, nanostructured substrate, polymer chain, zigzag path statistics.

## I. INTRODUCTION

**M**ACRO-MOLECULES are fundamental constituents of living organisms and plants. Among them polymers are the objects of long-term, intensive scientific works. Biologically oriented physicists are studying polymers theoretically and experimentally and they are trying to find these polymer's underlying properties which are valuable for biomedical and technological purposes [1].

From the engineering sciences point of view numerous polymer-involved approaches have been elaborated and then implemented in factory processes. One of such recent advancement in the field of nanotechnology allows 6-nm-resolution pattern of binding sites [2], [3]. This spectacular resolution is due to the so-called DNA origami technique [4], [5]. A particularly appealing feature of DNA origami comes from the precise location of the ends of DNA strand on a given substrate. In this way, functional devices created via DNA scaffolding can be sized down to reach sizes of the order of  $10^{-8}$  m or even less.

In order to achieve a few nanometer resolution the binding centers have to be accurately positioned in a given volume. Then, a functionalized polymer trapped by a pair of these centers is used as a piece of scaffolding [4]. It is worth to mention that a successful-polymer-capture takes place if the end-polymer molecules are sufficiently sensitive to the binding centers. Such an attractive interaction between the polymer ends and the binding centers creates an additional tension along the polymer backbone which in turn may result in a formation of knots or a polymer-strand entanglement. Thus, the polymer-functionalization process, i.e. the attachment of appropriate molecules to polymer's ends is a subtle process and one should take care of the resulting attractive forces between the polymer segments and the armed-polymer-ends.

Manuscript received January 27, 2014.

Zbigniew Domański is with the Czestochowa University of Technology, Dabrowskiego 69, PL-42201 Czestochowa, Poland. (e-mail: zbniew.domanski@im.pcz.pl).

Norbert Sczygiol is with the Czestochowa University of Technology, Dabrowskiego 69, PL-42201 Czestochowa, Poland. (e-mail: norbert.szczygiol@icis.pcz.pl).

A biomedical example of a three-dimensional substrate is a silicon-nanopillar array which allows one to create enhanced-local-interactions between the substrate and other macromolecules [6]. This nanostructured substrate yields a high capability to capture cancer cells detached from the solid primary tumor and thus enable one to isolate these circulating cells from the blood. In this spirit, another recently reported example of functionalized substrate, the functionalized graphene oxide nanosheets [7], clearly shows that 3D substrates can operate as valuable bio-markers for disease diagnosis.

The DNA origami technique and the medical bio-markers employ 3D functionalized substrates [6], [8]. The spacial arrangement of the binding centers of these substrates plays an important role in the capture yield. However, a considerable scientific activity is concentrated mainly on the biochemical and physical properties of adhesion process and less attention is paid to the geometry-induced characteristics of the substrate itself and to the resulting impact on the binding efficiency.

In this work we analyze how the polymer-chain-capture phenomena is influenced by the spacial arrangement of binding centers of a given substrate. For this purpose we use a simple model of the 3D substrate, i.e. we assume that the binding centers are periodically arranged in a limited volume of a three-dimensional cubic lattice. Because of the attractive force between the functionalized-polymer ends and the binding centers, the polymer feels an effective non-homogeneous electrochemical potential. This potential is modulated by the relative positions of the substrate's uptake centers and, in consequence, the polymer trajectories resemble zigzag lines. In such circumstances the Euclidean norm is not adequate to measure the distances traversed by the polymer. The lengths of zigzag-like trajectories should be measured in terms of the taxicab metric in which the distance  $q$  between points  $\mathbf{x}(x_1, x_2, x_3)$  and  $\mathbf{y}(y_1, y_2, y_3)$  is given by

$$q(\mathbf{x}, \mathbf{y}) = \sum_{i=1,2,3} |x_i - y_i|. \quad (1)$$

Below we analyze the distributions of such a distance between the functionalized-polymer-end points.

## II. DISTINCT DISTANCES IN A SIMPLE CUBIC LATTICE

Consider a set of  $(L + 1)^3$  binding centers confined in a simple cubic lattice (SC) in such a way that the binding centers are represented by the nodes of the SC and the edges of equal length ( $a = 1$ ) measure the distance between any pair of centers. In this scenario, the SC is seen as a unit distance grid graph. For a given pair of binding centers the distance between them is the length of the shortest path between the corresponding nodes, i.e. the number of edges in such path.

A polymer model can be chosen in a way related to the studied problem. For the purpose of this work we choose

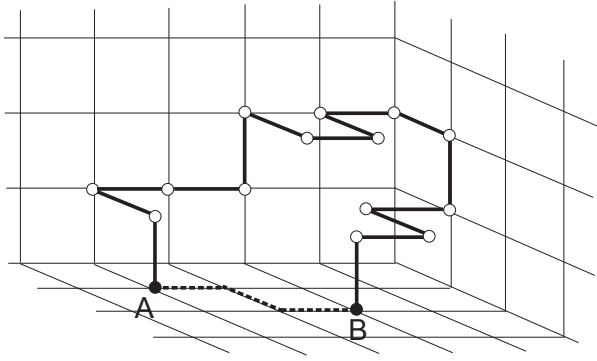


Fig. 1. Schematic illustration of the  $m$ -segment chain embedded in cubic lattice. Black-filled circles mark the chain's terminals: A, B. Here,  $m = 15$  and the end-to-end distance  $q(A, B)$  equals to 3 lattice spacing, i.e.  $q = 3$ .

a self-avoiding walk (SAW) [9]–[11] and we represent the long polymer body by the path on a lattice. Due to the excluded volume effect two monomers cannot be closer than their diameter and thus, the SAW is a path without self-intersections [11]. An example of the SAW is presented in Fig. 1. The SAW's paths have been extensively studied from the statistical physics perspective and the enumeration of these paths still is the center of interest [11]. Here, another point of view is taken into account. We are interested in the statistics of distances between nodes of the finite 3D SC lattice, under assumption that the distances are measured according to the metric (1). In the literature different wordings are used for such a distance. Here, we express it as the Manhattan distance.

In a case of the SC lattice all node-to-node Manhattan distances can be easily computed and sorted. Since the shortest path between two nodes in this lattice is at most three segments zigzag line, then a straightforward listing of all different non-ordered pairs of nodes enables one to assign the Manhattan distance to each pair of nodes and then to form an appropriate distribution. However, such an approach is justified if one deals with a primitive Bravais lattice [12], i.e. the lattice which has only one node in its unit cell. In a case of non-Bravais lattice or a decorated lattice the shape of the shortest path is not obvious and one has to either rely on the graph-theory-based tools or use some dedicated algorithms [13].

The graph-theory makes it possible to represent a lattice by the so-called adjacency matrix, also termed the connectivity matrix. For a given lattice with  $n$  nodes its adjacency matrix is the  $n \times n$  matrix  $\mathbf{A}$  with entries  $A_{ij} = 1$  only if  $i$  and  $j$  nodes share the same edge. If such an edge does not exist the corresponding entry equals to zero. A useful property of the adjacency matrix consists in a direct relation between consecutive powers  $\mathbf{A}^k$ ,  $k \in (1, 2, \dots, n)$  and the number of distinct paths in a graph. More precisely, an entry  $\mathbf{A}_{ij}^k$  is the number of paths of the length  $k$  from the node  $i$  to the node  $j$ . It is this property that we use to sum up the number of Manhattan distance in the SC lattice, i.e. (i) to each pair of nodes we assign the smallest value of  $k$  for which  $\mathbf{A}_{ij}^k \neq 0$  and then (ii) for each value of  $k$  we count the number of pairs of nodes related to this value. Since  $n < \infty$  due to (i) and (ii)

we get the required distribution of Manhattan distances [14].

This is quite a general procedure and we employ it here despite the relative simplicity of the SC lattice.

### III. RESULTS AND DISCUSSION

Using the method described in the previous section we compute the number  $N(L, q)$  of pairs of nodes separated by the distance  $1 \leq q \leq 3L$  in the SC with  $(L + 1)^3$  nodes. Note that the maximum value of the node-to-node distance  $q_{max} = 3L$  corresponds to four pairs of nodes located in the opposite corners of the cube, whereas  $q_{min} = 1$  corresponds to all cube's edges. As a result we get  $N(L, q)$ , a fifth-degree polynomial in  $q$

$$N(L, q) = \begin{cases} \sum_{n=0}^{n=5} a_n(L) q^n & ; \quad 1 \leq q \leq L + 1 \\ \sum_{n=0}^{n=5} b_n(L) q^n & ; \quad L + 2 \leq q \leq 3L \end{cases} \quad (2)$$

where, the coefficients  $a_n(L)$  and  $b_n(L)$  depend on  $L$  and they are univariate polynomials of the degree  $\leq 3$ . For example the coefficients  $a_n(L)$  read

$$\begin{aligned} a_0(L) &= (L + 1)^3 \\ a_1(L) &= -(L + 1)^2 - \frac{2}{15} \\ a_2(L) &= (L + 1) \left[ 2(L + 1)^2 - \frac{1}{2} \right] \\ a_3(L) &= -2(L + 1)^2 + \frac{1}{6} \\ a_4(L) &= \frac{1}{2}(L + 1) \\ a_5(L) &= -\frac{1}{30} \end{aligned} \quad (3)$$

Equation (2) can be written in the form of the probability distribution for  $q$ . To do this we divide (2) by a function

$$\Sigma(L) = \frac{1}{2}(L + 1)^3 [(L + 1)^3 - 1], \quad (4)$$

which is the total number of pairs of nodes in the cube. After such a normalization we obtain

$$P(L, q) = \frac{2}{(L + 1)^3 [(L + 1)^3 - 1]} N(L, q). \quad (5)$$

Figure 2 depicts the distribution (5) for values of  $L = 10, 11, 13,$  and  $14$ .

With the help of Eq. (5) we can compute the mean value  $\langle q \rangle$  of the node-to-node distance. It appears that  $\langle q \rangle$  scales with the length  $N$  of the functionalized SAW as

$$\langle q \rangle = 2/3 + (11/30)N^\alpha, \alpha = 0.98. \quad (6)$$

This power law dependence is shown in Fig. (3).

#### The large $L$ limit

When one deals with a large number of binding centers, i.e. when  $L$  grows significantly, instead of (5), a density probability function will be more suitable for characterizing the node-to-node distance distribution. Such a density formulation can be introduced in a straightforward manner. Since  $N(L, q)$ , Eq. (2), is the fifth-degree polynomial in  $q$  and the normalization function  $\Sigma(L)$ , Eq. (4), is the polynomial of the order six in  $L$ , then

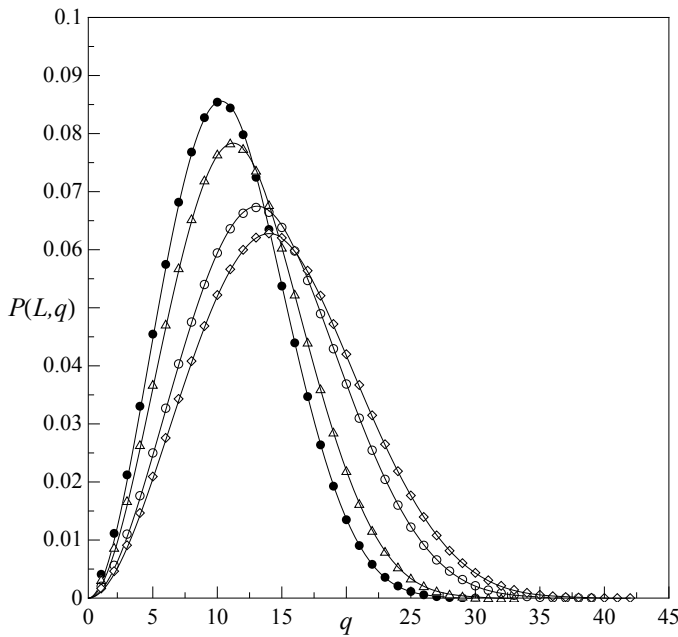


Fig. 2. Probability distribution functions p.d. of end-to-end distance  $q$  of polymer chain with ends bonded to the nodes of a simple cubic lattice with  $(L + 1)^3$  nodes:  $\bullet$ ,  $L = 10$ ;  $\triangle$ ,  $L = 11$ ;  $\circ$ ,  $L = 13$  and  $\diamond$ ,  $L = 14$ . The distance  $q$  between any pair of nodes is given by the smallest number of edges connecting these nodes. The lines are drawn using Eq. (5) and they are only visual guides.

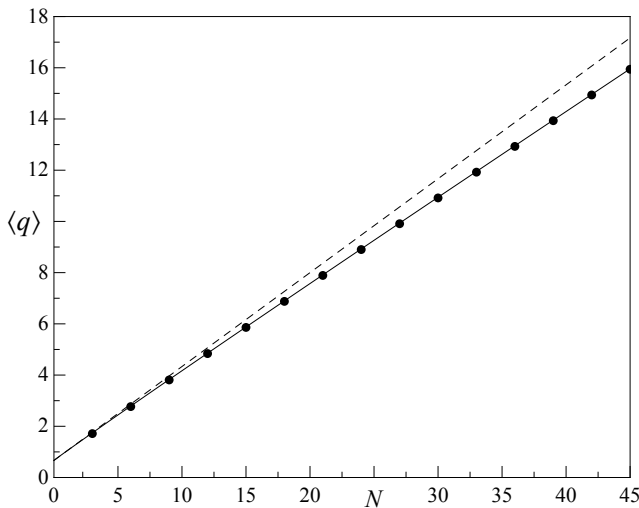


Fig. 3. The mean end-to-end distance computed with the probability distribution function  $P(L, q)$ , see Eq. (5). Solid line is the power law fit corresponding to the Eq. (6) with  $\alpha = 0.98$ . The dashed straight line is given by (6), with  $\alpha = 1$ , and it is drawn for the reference purpose only.

$$P(L, q) \rightarrow L^{-1} \tilde{P} \left( 1, x_q = \frac{q}{L} \right) \approx p(x_q) \Delta x_q, \quad (7)$$

$$x_q \in \langle 1/L, 2/L, \dots, 3 \rangle, \quad \Delta x_q = \frac{1}{L}.$$

Even though the distribution  $P(L, q)$  is exact for any  $L$ , for  $L \gg 1$  we retain only terms of the first order in  $1/L$  in the functional form of  $\tilde{P}$ . In the limit  $L \rightarrow \infty$ , the discrete set  $\langle 1/L, 2/L, \dots, 3 \rangle$  transforms in a dense subset  $\langle 0, 3 \rangle \subset \mathcal{R}$  and

$$p(x) = \lim_{L \rightarrow \infty} \lim_{x_q \rightarrow x} p(x_q). \quad (8)$$

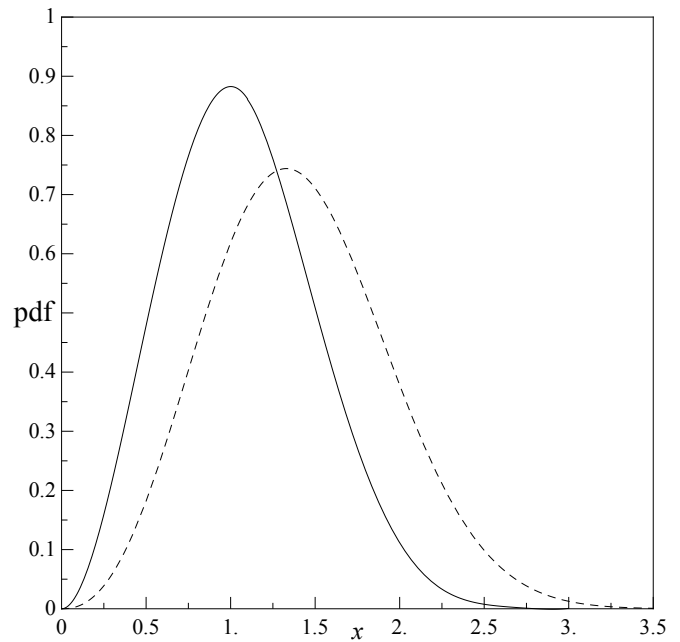


Fig. 4. The probability density function (pdf) of node-to-node distance. Equation (8) - continuous line, Eq. (9) - dashed line.

becomes the exact probability density function of the continuous variable  $0 \leq x \leq 3$ . The function  $p(x)$  is shown in Fig. 4.

When a SAW moves freely, i.e. without constraints imposed by a set of binding centers, the end-to-end distance distribution  $f$  is given by [15]

$$f(x) = ax^{d-1} x^\sigma \exp(-bx^\delta), \quad (9)$$

where in three dimensions:  $d = 3$ ,  $\sigma = 0.33$  and  $\delta = 2.43$ . Here, we take  $a = 1$ . Consequently, the value of  $b = 0.48$  results from the normalization condition for the function (9). The dashed line in Fig. (4) follows the distribution (9) and we see that this curve is shifted right compared to the solid line representing the distribution (8).

#### Final remark

The analytical approach employed in this work rests on the assumption that the taxicab metric properly characterizes trajectories traced out by the functionalized polymer-chain when it moves close to, or inside of a volume with periodically distributed binding centers. All we can say in this preliminary work is that a confined polymer sees a reduced number of accessible conformations and thus the corresponding distribution of end-to-end distance is narrower than this one related to a non-confined-polymer chain.

#### REFERENCES

- [1] R. Amin, S. Hwang, and S. H. Park, "Nanobiotechnology: an Interface Between Nanotechnology and Biotechnology", *Nano: Brief Reports and Reviews*, vol. 6, no. 2, pp. 101-111, 2011. On-line access: <http://www.worldscientific.com/doi/pdf/10.1142/S1793292011002548>
- [2] R. J. Kershner *et al.*, "Placement and orientation of individual DNA shapes on lithographically patterned surfaces," *Nature Nanotechnology*, vol. 4, no. 9, pp. 557-561, Aug. 2009.
- [3] Hh. Lin, Y. Liu, S. Rinker, and H. Yan, "DNA Tile Based Self-Assembly: Building Complex Nanoarchitectures", *ChemPhysChem*, vol. pp. 1641-1647, Aug. 2006.

- [4] S.M. Douglas, A.H. Marblestone, S. Teerapittayanon, A. Vazquez, G.M. Church, and W.M. Shih, "Rapid prototyping of 3D DNA-origami shapes with caDNAno, *Nucleic Acids Research*, vol. 37, no. 15, pp. 5001-5006, June 2009. On-line access: <http://nar.oxfordjournals.org/content/37/15/5001.full.pdf+html>
- [5] P.W.K. Rothmund, "Folding DNA to create nanoscale shapes and patterns", *Nature*, vol. 440, pp. 297-302, March 2006.
- [6] S. Wang, H. Wang, J. J. Jiao, K.-J. Chen, G. E. Owens, K. Kamei, J. Sun, D. J. Sherman, Ch. P. Behrenbruch, H. Wu, and H.-R. Tseng, "Three-Dimensional Nanostructured Substrates toward Efficient Capture of Circulating Tumor Cells", *Angewandte Chemie*, vol. 121, pp. 9132-9135, 2009.
- [7] H. J. Yoon, T. H. Kim, Z. Zhang, E. Azizi, T. M. Pham, C. Paoletti, J. Lin, N. Ramnath, M. S. Wicha, D. F. Hayes, D. M. Simeone, and S. Ngrath, "Sensitive capture of circulating tumor cells by functionalized graphene oxide nanosheets", *Nature Nanotechnology*, vol. 8, no. 10, pp. 735-741, Oct. 2013.
- [8] H. Otsuka, "Nanofabrication of Nonfouling Surfaces for Micropatterning of Cell and Microtissue", *Molecules*, vol. 15, no. 8, pp. 5525-5546, 2010. On-line access: <http://www.mdpi.com/1420-3049/15/8/5525>
- [9] I. Teraoka, *Polymer Solutions: An Introduction to Physical Properties*, John Wiley and Sons, Brooklyn NY (2002).
- [10] A. D. Sokal, "Monte Carlo Methods for the Self-Avoiding Walk", in: *Monte Carlo and Molecular Dynamics Simulations in Polymer Science*, K. Binder (ed.), pp. 47-124, Oxford University Press, New York, Oxford (1995).
- [11] G. Slade, "Self-avoiding walks", *Mathematical Intelligencer*, vol. 16, Issue 1, pp. 29-35, Winter 1994. Available: <http://www.math.ubc.ca/~slade/intelligencer.pdf>
- [12] N. Ashcroft, D. Mermin, *Solid State Physics*, Chapter 7, Brooks/Cole (Thomson Learning, Inc.) (1976).
- [13] F. F. Dragan, "Estimating all pairs shortest paths in restricted graph families: a unified approach," *Journal of Algorithms*, vol. 57, pp. 1-21, Sept. 2005.
- [14] Z. Domański, N. Sczygiol, "Distribution of the Distance Between Receptors of Ordered Micropatterned Substrates," in: *Lecture Notes in Electrical Engineering: World Congress on Engineering 2011*, H. K. Kim, S.-I. Ao, B. B. Rieger (eds.), vol. 170, pp. 297-308, Springer, Dordrecht (2013).
- [15] F. Valle, M. Favre, P. De Los Rios, A. Rosa, G. Dietler, "Scaling Exponents and Probability Distributions of DNA End-to-End Distance," *Phys. Rev. Lett.*, vol. 95, 158105, Oct. 2005. On-line access: <http://arxiv.org/pdf/cond-mat/0503577v1.pdf>