

# A simplified account of cooperative effects in molecular walker teams

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## ABSTRACT

We study the motion of random walkers with residence time bias between first and subsequent visits to a site, as a model for synthetic molecular walkers based on catalytic DNA known as molecular spiders. Even though a single one-legged walker does not exhibit directional, superdiffusive motion, we find that a team of one-legged walkers on parallel tracks, connected by a flexible tether, does enjoy a superdiffusive transient.

## CCS CONCEPTS

• **Hardware** → **Emerging architectures**;

## KEYWORDS

molecular walkers, superdiffusion

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## 1 INTRODUCTION

Many of the metabolic, signalling, and control functions in eukaryotic cells are performed by molecular walkers carrying cargo along directional filaments or microtubules [5]; e.g., kinesin walkers are highly evolved, complex protein structures that exhibit a complex coordinated gait on a directed self-assembled track, powered by a supply of ATP in the surroundings [8, 12]. Likewise, efficient guided transport of molecular cargo is an important goal in synthetic nanotechnology. Borrowing from nature, progress has been made on protein-based walkers. Designing proteins with desired function is a formidable challenge, and many groups have used DNA instead. A number of reported systems have relied on DNA strand displacement reactions to propel a walker strand along a self-assembled track, typically a directed track, and commonly built using the DNA origami technique [7]. The drive in these systems is the formation of additional Watson-Crick base pairs, and, in the directed case,

the essence of the system is a burnt-bridge mechanism—the walker cannot revisit a site.

We have been studying *molecular spider* systems [4], consisting of a streptavidin body and multiple single-stranded DNA “legs” that use catalytic DNA reactions, rather than DNA strand displacement. Each leg contains a DNase sequence, whose catalytic action is to break a phosphodiester bond and thus cleave a substrate DNA sequence. The substrates can be displayed on sites in bulk, or on a surface track, such as a DNA origami tile. A leg can rebind to an already cleaved site, but rebinding is of much shorter duration than the first binding. Here the energy source for the walker is the track itself, but the mechanism is not burnt-bridge, and there is no inherent directionality in the track. Rather, directional motion is an emergent property that arises from a combination of a kinetic effect (residence time bias between first and subsequent visits) and of kinematic constraints (the geometry of the walker body restricting the gait). Experiments in bulk have shown that molecular spiders are chemically processive: when spiders and their substrates were randomly deposited in a matrix in a 1:3800 ratio, the spiders cleaved nearly all the available substrates before dissociating from the matrix [4]. The concomitant release of products is nearly complete and happens at an essentially constant rate [11], which holds promise in biomedical applications. Experiments on DNA origami have shown that molecular spiders can follow patterned nanoscale tracks [2]. While we await experimental confirmation of the detailed motion, a number of mathematical modelling studies [1, 6, 9, 10] have characterized the spiders’ walking gaits using coarse-grained stochastic models, up to predicting their ability to do organized mechanical work against external force [3]. The foremost question in such guided transport, for its application in signalling, is whether the motion is ordinary diffusive or superdiffusive. Consider the walker’s displacement from a starting position: if the mean squared displacement scales linearly with time, the motion is *diffusive*; if it scales as a power of time greater than 1, it is *superdiffusive*; in the extreme, scaling as the square of time, it is *ballistic*. Previous models have not suggested true superdiffusive behavior in molecular spider systems, and that possibility remains an intriguing question for future work; however, they have discovered exceptionally long superdiffusive transients, which would be relevant in experiments and applications. The mechanism of the transient superdiffusion was explained via the emergence of a boundary between the new and the previously visited sites, and the tendency of the multi-legged spider to cling to this boundary, provided there is a residence time bias  $r$  between the first and the subsequent visits to a site [10]. Detailed results were obtained for a two-legged spider with hand-over-hand gait in one dimension [10]. The key insight is that the spider alternates

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between being on the visited/new boundary (and moving forward ballistically) and drifting in the sea of previously visited sites; each period this sea becomes bigger, hence the eventual breakdown of superdiffusion.

Approaches for improving the transient and perhaps asymptotic behavior of molecular spiders include modified chemistry, different walker body and leg geometry, and the use of walker teams. Walker teams are inspired by nature's molecular motor teams [13]. Rank et al. [6] provided a detailed analysis of teams of two-legged molecular spiders, on parallel one-dimensional tracks, connected by a "leash", i.e., a kinematic constraint that no two spiders can be more than a certain distance apart. They showed that teams of two, three, and four spiders successively outperform a single spider, for a range of leash lengths and chemical kinetics.

## 2 RESULTS

Here we ask: can we separate the effects of having a team of walkers from the effects of each walker having multiple legs? Our model system uses single-legged walkers, each on its own one-dimensional track, connected by a leash. Each track is prepared with fresh substrates for  $x \geq 0$ , and consumed products for  $x < 0$ ; walkers start at  $x = 0$ . With a kinetic Monte Carlo simulation we obtained 60,000 trajectories each for  $n = 1, 2, 3, 4$  walkers, setting the effective leash length to  $d = 8$  for a direct comparison with the results of [6]. As in that work, the unit of length is the lattice spacing, and the unit of time is such that the hopping rate from visited sites is 1, from new sites  $r < 1$ . In Figure 1 we see that a single single-legged walker is not directionally biased—this is to be expected, and is crucially different from the single two-legged walker in [6]. As soon as multiple walkers are leashed to form a team, the team is directionally biased in the  $+x$  direction, and at moderate times such as  $t = 10^6$  the position of the team is fairly narrowly distributed for team size 4. These results parallel those of [6]. In Figure 2, teams with more walkers exhibit more marked superdiffusive transients, which, however, decay to ordinary diffusion by time  $10^8$ .

In summary, we observe that the essential effects of a walker team are present even when each single team member is a single-legged walker rather than a two-legged spider. In addition to the numerical simulation results here, we will carry out a mathematical analysis of the team, which in turn will be simplified by having simple teammates. Furthermore, we will study such teams when placed not on separate tracks but on a shared track, modelling a microtubule. Intuitively, the geometric constraint of the leash unites the multiple walkers into a soft-bodied walker with multiple legs.

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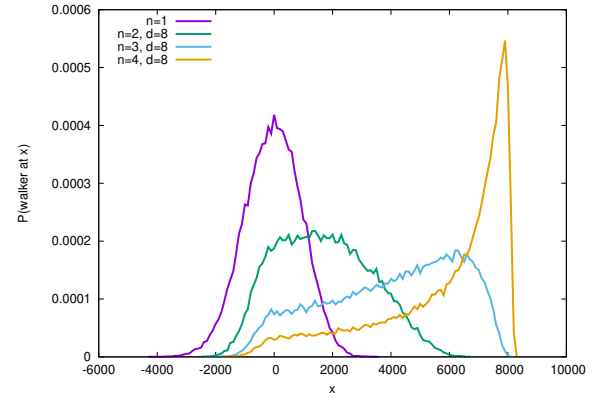


Figure 1: Position probability distribution, for residence time bias  $r = 0.01$ , at time  $t = 10^6$ .

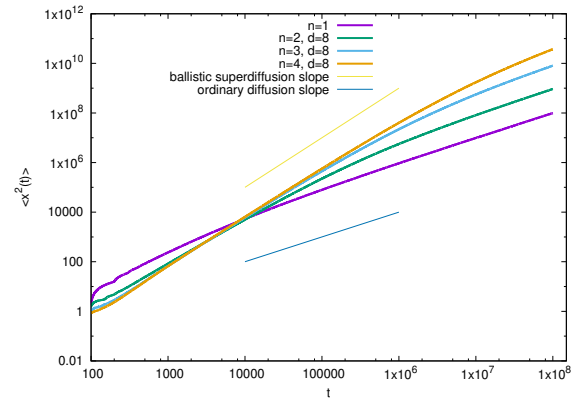


Figure 2: Mean squared displacement as a function of time, for residence time bias  $r = 0.01$ .

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