Birkbeck
UNIVERSITY OF LONDON

Studying for a PhD

At the School of Crystallography

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Institute of Structural Molecular Biology
A joint institute between Birkbeck and UCL

Studying for a PhD

at the School of Crystallography

The principal focus of the School of Crystallography at Birkbeck is on postgraduate teaching and research. Each year we take in 8-12 PhD students in the areas of Structural Molecular Biology, Bioinformatics and Industrial Materials. Our postgraduate students generally have first degrees in Biochemistry, Chemistry, Physics, Biology or other Biological or Physical Sciences.

Information about projects and supervisors for PhD studies beginning October 2007 are available in this document.

▪ PhD studentships

For the Structural Biology, Biophysics and Bioinformatics projects we have BBSRC and MRC PhD Studentships available starting October 2007 or sooner. These Research Council studentships provide both fees and a tax-free stipend of over £1,000 a month. Awards are for up to 4 years.

We have a Bloomsbury Colleges studentship for a specific project in the area of *Mycobacterium tuberculosis* open to all EU students and international students in conjunction with an ORS award.

In the area of Industrial Materials we have EPRSC studentships available to UK and EU nationals.

▪ Important information about eligibility

To be eligible for these awards you should be a European Union citizen, or have indefinite leave to remain in the UK, and have been resident in the UK for the last 3 years (this does now include for the purpose of study). Further details of eligibility can be found on the School website at www.cryst.bbk.ac.uk/studentships.html

If you are an EU citizen not resident in the UK then we have a number of schemes by which we can pay your fees, *but you will have to either fund your own living costs or find a grant body willing to fund you*. We will help you to prepare a project proposal if you can identify a suitable funding body

For non-EU nationals the college has a limited number of ORS awards which pay the difference between EU and overseas fees. If you are successful in obtaining one of these then we will normally pay the EU fees for you. However, *you will need to find other sources of money for your living costs*. We will help you with a project proposal if you can identify a suitable funding body. The deadline for application for ORS awards in March 2007, so you will need to contact us significantly before this date.

Key contacts and how to apply

at the School of Crystallography

▪ Key contacts

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▪ How to apply

Informal applications
Potential Students are asked to list up to 4 projects that interest them and to send a CV to studentships@mail.cryst.bbk.ac.uk

Formal applications
Formal applications must be made on the Birkbeck Postgraduate Application form included in this document.

The form is also available at http://www.bbk.ac.uk/about/programmes/apply

Unique advantages of studying your PhD here

at the School of Crystallography

High quality teaching and world-class research in central London - there are many unique advantages of being a student in the School of Crystallography, Birkbeck.

High quality teaching

- Because we have a large number of PhD and MRes students, we can run a formal lecture programme which includes graduate studies ('Science in the Real World'), transferable skills, modern techniques and a lecture course on structural biology especially for PhD students, which is compulsory for 1st year PhD students and recommended for all others.
- In addition, our PhD students are encouraged to sit in on any appropriate lectures from our MSc course in Bioinformatics. Also, they have access to our Web-based courses in Principles of Protein Structure, Protein Structure Determination, or Techniques in Structural Molecular Biology. We consistently get high ratings for our excellent teaching.
- Students of all ages, backgrounds and countries choose to study at Birkbeck, which makes for a dynamic learning environment.
- There are many opportunities for students to engage with researchers and other students.
- Frequent visits by top researchers and lecturers who come to present their work in seminars and symposia.

World-class research

- Researchers at the School of Crystallography are engaged in world-class research. The School of Crystallography was rated "5A" in the most recent Research Assessment Exercise 2001.
- There is a strong emphasis on collaborative research in the School of Crystallography. We are a key component of the Institute of Structural Molecular Biology (ISMB) and are part of the Bloomsbury Centre for Bioinformatics (BCB).

Wide range of support for students

- Support for current students, including Birkbeck student pages, our own course webpages, the School of Crystallography intranet, resources for PhD students and the computer support through the Crystallography Computer Support Group.
- Disability support
- Birkbeck student union, which also provides advice about welfare support.
- The Specialist Institutions' Careers Service (SICS).

Central London location

- On the same street as: the University of London Union, with bars and sports centre; the main Waterstones London academic bookshop; Royal Academy of Dramatic Arts.
- The major sights and experiences of London within easy reach: The British Museum is less than 5 minutes walk away; Tottenham Court Road and Oxford Street are less than 10 minutes away by foot; the Southbank and the Thames are less than 20 minutes walk by foot.

➲ Structural Biology

Electron microscopy projects 2007/8

Project title	*Supervisor(s)*	*Page*
▪ Kinesin motor proteins in the malaria parasite	Carolyn Moores	6
▪ Multiple structural states of S100 proteins family: a key to their functional diversity	Elena Orlova and I. Bronstein	6
▪ Analysis of the gp7 function at DNA packaging in the bacteriophage Spp1	Elena Orlova	7
▪ Analysis of the Geminin/Cdt1 complex	Elena Orlova and Andrei Okorokov	7
▪ Pore-forming cytolysins: Molecular hole punchers	Helen Saibil	8
▪ Structure and function of molecular chaperones	Helen Saibil	8

➲ Structural Biology

Protein Crystallography and Protein Biochemistry projects 2007/8

Project title	*Supervisor(s)*	*Page*
▪ Structural and functional studies of proteins involved in bacterial and eukaryotic DNA repair.	Tracey Barrett	9
Structural Biology of Neuroserpin in Dementia	Bibek Gooptu, Tracey Barrett	9
▪ Investigations into Acg and other putative nitrosoreductases, key proteins in the dormancy phase of tuberculosis. Joint Project with Prof Neil Stoker, Royal Veterinary College *This project has a Bloomsbury Colleges studentship open to all EU students and international students in conjunction with an ORS award.*	Nicholas Keep, Prof Neil Stoker, Royal Veterinary College	10
▪ Structural Studies of Ferlins	Nicholas Keep	11
▪ Structural biology of arginine-modifying enzymes	Neil McDonald	11
▪ X-ray structural studies of the toxicity of *clostridial phospholipase* Cs put with other projects list as moss and basak	David Moss and Ajit Basak	12
▪ X-ray structure analysis of *Clostridium perfringens* enterotoxin	David Moss and Ajit Basak	12
▪ Structural studies of several key proteins of *Listeria monocytogenes*	David Moss and Ajit Basak	12
▪ Structural studies several proteins of *Burkholderia pseudomallei*	David Moss and Ajit Basak	13
▪ Assembly Interactions in Small Heat Shock Proteins	Christine Slingsby	13
▪ Structure and function of bacterial ushers	Gabriel Waksman	14
▪ Structure and function of type V autotransporters	Gabriel Waksman	15
▪ Structural studies of type IV secretion machines	Gabriel Waksman	16
▪ Zinc Metalloproteases from *Myocobacterium leprae* and *Mycobacterium tuberculosis* as Targets for Rational Drug Design	Bonnie Wallace and Nora Cronin	16
▪ Molecular and Structural Biology of Sodium Channels	Bonnie Wallace and Nora Cronin	17
▪ Structural and mechanistic studies of essential enzymes of the bacterial cell wall	Mark Williams & Snezana Djordjevic	17

➲ Biophysics

Projects 2007/8

Project title	*Supervisor(s)*	*Page*
▪ Biophysical study of the Klentaq1 DNA polymerase	Gabriel Waksman	18
▪ Structure-thermodynamic studies of SH2 domains	Gabriel Waksman	19
▪ Circular Dichroism and Synchrotron Radiation Circular Dichroism Spectroscopy of Sugars and Protein/Carbohydrate Interactions	Bonnie Wallace	19
▪ Investigation of Macromolecular Complex formation by SRCD and Fluorescence Spectroscopy	Bonnie Wallace	19
▪ Spectroscopic and computational studies of hydrogen bonding in protein-ligand complexes	Mark Williams and Professor Peter Rich	20

➲ Bioinformatics

Projects 2007/8

Project title	*Supervisor(s)*	*Page*
▪ Developing a text mining service to support multi-scale simulations of the immune system	Adrian Shepherd and David Moss	21
▪ Simulating the human immune system: prediction of MHC protein-peptide binding	Adrian Shepherd and David Moss	21
▪ Mechanism of Bacteriophage SPP1 Connector at Atomic Level	Maya Topf and Elena Orlova	22
▪ Molecular modeling of pyrethroid binding to insect and mammalian sodium channels	Bonnie Wallace, with Martin Williamson, Rothamsted Research	23
▪ Bioinformatics: spectroscopic data mining and analysis of native and mutant proteins	Bonnie Wallace	23
▪ Simulating the assembly and disassembly of macromolecular complexes in a cellular context.	Mark Williams	23

➲ Industrial materials

Projects 2007/8

Project title	*Supervisor(s)*	*Page*
▪ Structure and properties of pharmaceutical (drug) polymorphs	Paul Barnes	24
▪ Exploiting low temperature powder diffraction	Paul Barnes	25
▪ Using intense synchrotron/neutron radiation to study chemical reactions or solid transformations	Paul Barnes	25
▪ Synchrotron (X-ray) Tomography of real Materials Processing in action	Paul Barnes	26
▪ Computational surface science study of metal nano-particle formation	Paul Barnes	26

➲ Structural Biology

Electron microscopy projects 2007/8

Kinesin motor proteins in the malaria parasite

Supervisor: Dr Carolyn Moores

Project overview

All eukaryotes from single-celled yeasts to humans express kinesin motor proteins that perform many microtubule-related cellular tasks. The function of these motors is relatively well conserved through evolution but some sub-classes of kinesins have organism-specific functions, while the functions of other, less common sub-classes are poorly understood. The aim of this project is to investigate the function of kinesin motor proteins from *Plasmodium falciparum*, the parasite that causes malaria. Because of its parasitic nature, *Plasmodium* exhibits unusual features that suggest the roles of the microtubule cytoskeleton may differ from the well-characterised ones seen in other eukaryotes. This project will involve cloning and expression of *Plasmodium* kinesins, and their characterisation by biochemical and structural methods. This will provide insight into their functions in *Plasmodium* and may provide information about possible drug targets for the treatment of malaria.

References

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2. Soldati, D., Foth, B.J. and Cowman, A.F. (2004). Molecular and functional aspects of parasite invasion. *Trends Parasitol*. 20, 567-574.
3. Vale, R.D. (2003). The molecular toolbox for intracellular transport. *Cell* 112, 467-480.

Multiple structural states of S100proteins family: a key to their functional diversity

Supervisor: Dr. Elena Orlova and Dr. I. Bronstein

Project overview

S100 proteins were first identified in brain and were for a long time considered to be nervous system-specific proteins. Later S100 proteins were discovered in a variety of other tissues and cells. These multifunctional proteins play a very important role in fundamental cellular functions such as cell motility, differentiation, neuroprotection, and antiparasite activity. Changes of the expression level of S100 proteins are associated with various diseases: chronic inflammation, metastasis, cardiovascular and neurodegenerative disorders.

The aim of proposed project is to investigate the structural basis of macromolecular complexes of oligomeric S100 proteins and their targets by a variety of methods including biochemical techniques, spectroscopy, electron microscopy and image analysis. The information gained by these studies will create a basis for early diagnosis of cancer, cardiovascular and neurodegenerative diseases.

References

1. Moroz OV, Dodson GG, Wilson KS, Lukanidin E, Bronstein IB. (2003) Multiple structural states of S100A12: A key to its functional diversity. *Microsc Res Tech*. 60(6):581-92.
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3. van Heel M, Gowen B, Matadeen R, Orlova EV, Finn R, Pape T, Cohen D, Stark H, Schmidt R, Schatz M, Patwardhan A. (2000) Single-particle electron cryo-microscopy: towards atomic resolution. *Q. Rev. Biophys*. 33:307-369.

Analysis of the gp7 function at DNA packaging in the bacteriophage Spp1

Supervisor: Dr. Elena Orlova

Project overview

During assembly, a number of DNA viruses, such as tailed bacteriophages and herpes viruses, load their capsids with DNA using a molecular motor embedded in one of the capsid vertices (Orlova *et al.*, 2003). Portal proteins are essential elements of the translocating machine for DNA translocation. In the bacteriophage SPP1 there is a small protein gp7 (35kDa) that is present in only two copies in the pro virion (Stiege *et al.*, 2003). Recent studies demonstrated that gp7 binds double-stranded and single-stranded DNA. The multimeric portal protein (gp6) competes for this interaction and forms gp6-gp7 complexes that do not bind DNA. Procapsids lacking gp7 are 10 times less active at DNA packaging indicating that gp7 is important for infectivity of the phages, though the mechanism is not clear. The hypothesis is that interaction of gp7 with gp6 changes connections between gp6 subunits triggering a transition between different oligomeric states. If gp7 does not bind to the portal protein the correct oligomeric state required for efficient DNA translocation will not be formed.

The aim of the project is to use electron microscopy coupled with microbiology and sequence analyses to analyse conformational changes in gp6 related to binding of the minor protein gp7. Binding of gp7 to the oligomeric portal protein changes its symmetrical properties: biochemical data demonstrated that there are 2-3 gp7 molecules per 13mer portal protein. Structural analysis of the asymmetrical complex would help to reveal changes in links between adjacent subunits caused by gp7.

References

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2. Orlova, E.V., Gowen, B., Droge, A., Stiege, A., Weise, F., Lurz, R., Van Heel, M. and Tavares. P. (2003) Structure of a viral DNA gatekeeper at 10 A resolution by cryo-electron microscopy., *EMBO J.*, 22(6): 1255-1262

Analysis of the Geminin/Cdt1 complex

Supervisors: Dr. Elena Orlova and Dr. Andrei Okorokov

Project overview

Maintenance of the human genome and the need to coordinate cellular action within the multicellular organism requires a complex system to control how and when the human genome replicates. The main function of this system is to ensure that our genomes replicate only once per cell cycle and in a co-ordinated manner each time a cell divides. This is achieved by assembling pre-replicative complexes (preRC) that are inhibited from firing by a unique small protein – Geminin (Okorokov et al., 2004). Thus, Geminin's prime function in controlling DNA replication is via its interaction with the Cdt1 protein and blocking the latter's active participation in pre-replicative complex. The chemical signal transaction(s) of licensing the DNA replication are achieved via molecular protein-protein interaction. However, despite some biochemical characterisation to date the precise molecular mechanism of this protein-protein interaction and the regulation at atomic level are yet to be elucidated.
The aim of the project is analysis of the protein-protein interaction between human Geminin and Cdt1 at molecular and atomic levels. The biochemical study of Geminin/Cdt1 complex formation and its regulation by post-translational modifications of both proteins combined with structural analysis of the complex by means of cryo-electron microscopy will allow to understanding of the mechanism of Gemini/Cdt1 interaction and how the replication licensing can be blocked.

References

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Wohlschlegel, J.A., Dwyer, B.T., Dhar, S.K., Cvetic, C., Walter, J.C. & Dutta A. (2000) Inhibition of eukaryotic DNA replication by geminin binding to Cdt1. *Science* 290: 2309-2312.
2. Okorokov, A, Orlova, EV, Kingsbury, SR, Bagneris, C, Gohlke, U, Williams, GH & Stoeber, K (2004) Molecular structure of human geminin. *Nature Struct. Mol. Biol.* 11:1021-1022.

Pore-forming cytolysins: Molecular hole punchers

Supervisor: Helen Saibil

Project overview

The cholesterol binding toxins are a highly conserved family of bacterial toxins, responsible for virulence in bacterial diseases such as pneumonia and meningitis. They are released from the bacteria as soluble monomers, but assemble into ring-shaped, membrane-bound oligomeric pores. The crystal structure is known for one member of the family, perfringolysin, and we have obtained cryo EM maps of oligomeric prepore and pore forms of another member of this family, pneumolysin. The structure of the membrane-inserted pore reveals dramatic conformational changes in pore formation. We are now carrying out studies on pore-forming cytolysins in the immune system. The protein perforin is secreted by killer cells to attack infected or transformed host cells. Like pneumolysin, perforin is also a large, multidomain protein that assembles into ring-shaped pores. The aim of the work is to understand the molecular mechanisms of pore formation.

Reference

Structural basis of pore formation by the bacterial toxin pneumolysin. Tilley, SJ, Orlova, EV, Gilbert, RJC, Andrew, PW & Saibil, HR (2005) *Cell* 121, 247-256.

Structure and function of molecular chaperones

Supervisor: Helen Saibil

Project overview

Protein folding in the cell is assisted by a range of molecular chaperones including large cage-like chaperonins and other heat shock proteins. Unfolded and misfolded proteins bind transiently to the chaperones, and are then released in folded or folding competent form. We are studying the mechanism of action of molecular chaperones using electron cryo-microscopy and image processing to determine the structure of complexes in different functional states, and with unfolded proteins. Current projects include studies on the GroE chaperonins complexed with non-native proteins, the Hsp100 class of chaperones, and small heat shock proteins.

References

1. Molecular chaperones: containers and surfaces for folding, stablilising or unfolding proteins. Saibil, HR (2000) *Current Opinion in Struct. Biol.*10, 251-258.
2. ATP-bound states of GroEL captured by cryo-electron microscopy. Ranson *et al* (2001) *Cell* 107, 869-879.
3. Allosteric signalling of ATP hydrolysis in GroEL-GroES complexes. Ranson, NA, Clare, DK, Farr, GW, Houldershaw, D, Horwich, AL & Saibil, HR (2005) *Nature Struct. Mol. Biol.*, *in press.*

Images from Helen Saibil's research projects can be found on the web page
http://www.cryst.bbk.ac.uk/~ubcg16z/

➲ Structural Biology

Protein Crystallography and Protein Biochemistry projects 2007/8

Structural and functional studies of proteins involved in bacterial and eukaryotic DNA repair.

Supervisor: Dr Tracey Barrett

Project overview

We have successfully cloned and performed preliminary expression trials on protein targets that participate in an alternative nucleotide excision repair pathway and also homologous recombination. The aim of the studentship will therefore be to establish how these proteins function within their respective mechanisms using a combination of structural and functional studies and will provide training in structural biology, biochemical/biophysical assays and molecular biology. All of the necessary expertise and equipment are available in house. Since little is currently known about alternative nucleotide excision pathways and homologous recombination in lower eukaryotes, this project should enable detailed probing of these pathways at the molecular level through the assembly and analysis of complexes involving both proteins and DNA.

Structural Biology of Neuroserpin in Dementia

Supervisors: Dr Bibek Gooptu and Dr Tracey Barrett

Project overview

The biology of neuroserpin in dementia is an exciting and growing field of research. Neuroserpin is a neurone-specific proteinase inhibitor of the serpin superfamily. Its mechanism of action involves a dramatic conformational transition from a metastable to a hyperstable state. However a variation on this sophisticated mechanism can result in severe dysfunction. Pathogenic mutations in neuroserpin cause it to undergo ordered self-assocation known as polymerisation1. Neuroserpin polymerisation both abolishes normal function and causes a gain of toxic function. We have shown that this occurs in the dementia Familial Encephalopathy with Neuroserpin Inclusion Bodies (FENIB)2. Fascinatingly, we now have evidence that wildtype neuroserpin can play a protective role in Alzheimer's disease, where it co-localises with the Alzheimer's peptide (Aβ) in amyloid plaques. Neuroserpin is able to disassemble preformed Aβ fibrils and its co-expression with Aβ is neuroprotective in cell culture and Drosophila disease models3.

This project will involve use of biochemical and biophysical techniques (FRET, H-exchange mass spectrometry) together with crystallisation of wildtype and mutant neuroserpins - both monomeric and in complex with Aβ fragments. It will characterise at high resolution the precise nature of the pathogenic conformational changes in FENIB, and the disease-modifying interactions in Alzheimer's disease models. We combine expertise in clinical and basic science, and we have ongoing collaborations with groups in San Diego and Cambridge. Thus findings from this work will integrate into in silico and in vitro screening of libraries of >1 million existing small molecules to identify lead compounds for drug design. To discuss this project further please contact b.gooptu@mail.cryst.bbk.ac.uk.

References

1 Gooptu B, et al. 2000. Inactive conformation of the serpin α1-antichymotrypsin indicates two stage insertion of the reactive loop; implications for inhibitory function and conformational disease. *Proc. Natl. Acad. Sci* (USA) 97:67-72

2 Davis, RL, et al. 1999. Familial dementia caused by polymerisation of mutant neuroserpin. *Nature*. 401:376-379

3 Kinghorn K, et al. 2006. Neuroserpin binds Aβ and is a neuroprotective component of amyloid plaques in Alzheimer's disease. *J. Biol. Chem*. 281:29268-29277

Investigations into Acg and other putative nitrosoreductases, key proteins in the dormancy phase of tuberculosis.

Supervisors: Joint Project with Dr Nicholas Keep (Birkbeck) and Prof Neil Stoker, Royal Veterinary College.

Project overview

Both Dr Keep and Prof. Stoker have been working on *M. tuberculosis* dormancy for some years, the crucial stage of its life cycle where it persists in the lungs for many years without symptoms. Dr Keep has recently published the structure of a resuscitation (from dormancy) promoting factor (1), as well as structural information on the most abundant protein in the dormant state, the α crystallin-like protein Acr1 (also called Rv2031; HspX) (2). Prof. Stoker has both biochemical and genetic expertise using M. tuberculosis and related bacteria. In particular he has studied the dosRS (for 'dormancy survival') genes that regulate expression of Acr1 in response to external stresses, as well as the effect on *M. tuberculosis* of deleting the acr1 gene (3, 4). This collaborative proposal seeks to study the gene lying next to Acr1, Acg (α-crystallin co-regulated gene; Rv2032), and its homologues (Rv3127 and Rv3131).

The aim of this project is to structurally, biochemically and genetically characterise the M. tuberculosis nitrosoreductases. In Dr Keep's laboratory the student will express, characterise and attempt to solve the atomic structure of these proteins. They will also try and identify the physiological activity use biochemical and computational approaches. Meanwhile in Prof Stoker's lab the student will knock out the homologues of these genes in the fast growing and non-pathogenic bacteria Mycobacterium smegmatis. The fast-growing relative of *M. tuberculosis*, *Mycobacterium smegmatis*, possesses some though not all of the characteristics of the pathogen. It has a DosR system, and four homologues of Acg: MSMEG3948, MSMEG3958, MSMEG3963 and MSMEG5231. These will be deleted, and the effect of the deletions on growth will be studied, particularly in the presence of NO, which is known to modulate the growth of M. smegmatis.

References

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3. Hu, Y.M., Movahedzadeh, F., Stoker, N.G. and Coates .A.R.M (2006) Deletion of the Mycobacterium tuberculosis alpha-crystallin-like hspX gene causes increased bacterial growth in vivo. *Infection and Immunity* 74, 861-868.
4. Kendall, S.L., Movahedzadeh, F., Rison, S.C.G., Wernisch, L., Parisj, T., Duncan, K., Betts, J.C. and Stoker, N.G. (2004). The Mycobacterium tuberculosis dosRS two-component system is induced by multiple stresses. *Tuberculosis* 84, 247-255

Structural Studies of Ferlins

Supervisor: Nicholas Keep

Project overview

The ferlins are a family of large proteins, whose molecular role is unclear but have been implicated in muscular dystrophy (dysferlin) and deafness (otoferlin). Dysferlin has recently shown to repair damaged membranes. The ferlins are characterised by a number of non-typical C2 domains and a region of sequence common to the family. There is also a single putative membrane spanning region at the C-terminus. The C2 domain, originally identified in protein kinase C, is widely found in eukaryotes and is thought to bind phospholipids often in a calcium dependent manner. The ferlin specific sequence region has been split into smaller regions by sequence conservation. At present it is not even possible to accurately model the C2 domains as they have very weak homology with the C2 domains, who have had their structures determined. The aim of the project is to determine the structures by X-ray crystallography or NMR of some of the constituent domains of the ferlins in order to understand how the membrane repair process works.

References

Doherty KR, McNally EM (2003) Trends in Molecular Medicine 9: 327-330 Bansal D et al., (2003) *Nature* 423:168-172.

Structural biology of arginine-modifying enzymes

Supervisors: Dr Neil McDonald

Project overview

There is an opening for a PhD student to work on the structure-function relationships of mammalian DDAH-1 and -2, enzymes that metabolise endogenous cellular inhibitors of nitric oxide synthases. These inhibitors include ADMA which is itself a known marker for predicting cardiovascular disease. The student will learn protein expression, purification and and protein crystallographic methods during the thesis work, interfacing with a larger group working towards the design of selective DDAH inhibitors (1,2). The group is a multi-disciplinary one at UCL and Birkbeck involving structural biologists, biologists, medicinal chem.ists and clinicians. The project is at an exciting stage where several lead inhibitor compounds are available for co-crystallisation to help guide the synthesis of improved chemical analogues. Although the primary aim is to develop molecules that will be of use as experimental probes, DDAH is also a validated target for therapeutic drug action in sepsis (2).

References

1. Murray-Rust, J., Leiper, J., McAlister, M., Phelan, J., Tilley,S., Santa-Maria, J., Vallance, P. & McDonald , N.Q. Structural insights into the hydrolysis of cellular nitric oxide synthase inhibitors by dimethylarginine dimethylaminohydrolase. *Nature Structural Biology* (2001) 8(8), pp 679 - 683.
2. Leiper J, Nandi M, Malaki M, Murray-Rust J, et al. & McDonald, N.Q., Vallance, P. Disruption of methylarginine metabolism impairs vascular homeostasis. *Nature Medicine* (2006) in press.

X-ray structural studies of clostridial toxins

Supervisors: Professor David Moss and Dr Ajit Basak

Project overview

The genus Clostridium is a diverse and heterogeneous group of gram-positive bacteria that are responsible for some of the most serious human and animal diseases such as botulism, enterotoxaemia and gas-gangrene. We have a research programme aimed at studying the major protein toxins involved in these diseases and are now offering two projects in this programme.

a) X-ray structural studies of the toxicity of clostridial phospholipase Cs

We have already solved the X-ray structure of phospholipase C (PLC) from *Clostridium perfringens*, which attacks cell membranes and is a major cause of gas gangrene. We now wish to determine the 3D-structures of PLCs from other clostridial species that exhibit a range of toxicities and also their molecular complexes with potential inhibitors and substrate analogues. To date, we have successfully cloned, over expressed and purified PLCs from *C. bifermentans*, *C. absonum*, *C. barati* and *C. sordellii*. These comparative X-ray studies will further our understanding of the molecular processes involved in protein-membrane interactions involved in gangrenous disease in man and enterotoxaemia in sheep and cattle.

b) X-ray structure analysis of* Clostridium perfringens *enterotoxin

C. perfringens enterotoxin (CPE), a 35kDa protein, is the primary virulence factor in type-A clostridial food poisoning that causes approximately 1 million cases of food poisoning *per annum* in the UK. We have initiated crystallographic studies of this important toxin, in collaboration with the School of Medicine at the University of Pittsburgh, USA. We have crystallised the full-length protein (proto-toxin) and collected a native X-ray dataset at a resolution of 2.7Å. Recently we have also cloned and purified the activated toxin. The research student would determine the crystal structure of the toxin in order to understand the mechanism of interaction of CPE with its receptors that have already been identified and expressed in intestinal cells. The project would appeal to students interested in structure-function studies of a very important pathogen.

Structural studies of several key proteins of *Listeria monocytogenes*

Supervisors: Professor David Moss and Dr Ajit Basak

Project overview

Listeria monocytogenes is a food-born pathogen that causes listeriosis in immunosuppressed individuals such as the very young and the elderly. This can lead to invasive syndromes such as meningitis, sepsis and stillbirth. *L. monocytogenes* is a gram-positive, non-capsulated bacterium that normally lives inside host cells. During infection it multiplies and spreads from cell to cell. The objective of this project is to determine the X-ray structure of the proteins involved in these infectious processes. We have already cloned and expressed some of these proteins and now wish to determine the 3D-structures of these key proteins. This study will help us to understand the pathogenic processes and to improve therapeutic intervention.

Structural studies several proteins of *Burkholderia pseudomallei*

Supervisors: Professor David Moss and Dr Ajit Basak

Project overview

Burkholderia pseudomallei (*B. pseudomallei*) a gram (-)ve, saprophytic bacterium present in wet soil and rice paddies in endemic areas, is a intracellular pathogen and the etological agent of melioidosis, a serious disease of man. In spite of its medical importance, very little is known about the mechanism of its pathogenicity. The majority of reported infection caused by the bacterium is in Northern Australia, S. E. Asia and other tropical areas of the world. There is no vaccine against melioidosis and although disease can be treated with antibiotics mortality rates are at least 40-45%. The full genomic sequence of *B. pseudomallei* strain K96243 has been determined. In order to understand the disease mechanisms, we have targeted several key functional proteins of this bacterium. We have already cloned, sequenced and expressed some of those proteins and wish to determine the 3D-structure of these proteins at the molecular level. The project would appeal to students interested in structure-function studies in a medically important area.

References

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Assembly Interactions in Small Heat Shock Proteins

Supervisor: Dr. C. Slingsby

Project overview

Small heat shock proteins (shsps) are polydisperse oligomers that modulate many intracellular bioprocesses by sensing normally buried or interface regions of cytoplasmic proteins and assembly systems. In this project sequence and structure analyses of our two solved "regular" shsp crystal structures will be used to engineer mondisperse versions of animal shsps. Functional analysis of their binding functions will be performed using a wide range of experimental biophysical procedures, including X-ray crystallography, electron microscopy, as well as in silico molecular simulations. The student would need to interpret their results within the scope of a vast literature on these proteins and their role in cellular networks.

Structure and function of bacterial ushers

Supervisor: Professor Gabriel Waksman

Project overview

The aim of this proposal is to study the structure of outer-membrane ushers which are involved in the pathogenesis caused by uropathogenic Escherichia coli. The infectious process requires adhesive hair-like fibers termed "pili". Pili serve as attachment devices which allow targeting of the bacteria to specific host tissues. We have used the uropathogenic E. coli as a model to provide the structural basis for pilus assembly and for bacterial adhesion. In particular, we have been interested in the type P pili, which are associated with pyelonephritis both in animals and in humans. This pilus type is encoded by the Pap gene cluster and is a polymer of 5 subunits: PapA, PapK, PapE, PapF, and PapG. All subunits are assembled at a site of assembly consisting of an hexameric pore called the usher. The usher is encoded by the PapC gene. Before assembly, each subunit requires prior association with the molecular chaperone, PapD, which prevents premature assembly of subunits in the periplasm, provides steric information for subunit folding, and targets the subunits to the usher.

We have made seminal contributions to the field of pilus biogenesis and bacterial attachment. We have crystallized the PapD/PapK and PapD/PapE binary complexes. We have crystallized and determined the structures of the PapE subunit with its cognate PapK N-terminal extension tail. We have solved the structure of a complex of the PapG receptor recognition domain with its receptor sugar on the kidney. These studies have elucidated the mechanism of pilus assembly and bacterial attachment. They have established that pilus subunit structures are Ig-folds where the 7th strand is missing. As a result, a large groove is formed at the surface of the protein which is filled by the G1 strand of the chaperone PapD. During biogenesis, the G1 strand is replaced by the N-terminal sequence (the so-called "N-terminal extension") of the subunit which is next in the assembly order. Thus, pilus biogenesis occurs though specific contacts between the groove that each subunit contains and the N-terminal extension of the subunit to be assembled next. This process is called "donor-strand exchange". The role of the usher is to facilitate the exchange process. How precisely this is done remains to be determined and will require the structure of the PapC usher. To this end, we have overproduced a PapC usher with a C-terminal His tag. Pure preparation of PapC-His can be obtained readily and we propose to crystallize this material and obtain his three dimensional structure. If the PapC usher turns out to be difficult to crystallize, we have also over-expressed successfully the SafC usher, a Salmonella enteridis usher known to assemble the SafA subunit into pili. We will also attempt to crystallise this protein. Membrane proteins are often difficult to crystallize because they are often unstable once extracted from the membrane. However, we have obtained stable preparation of the PapC and SafC ushers and thus we are optimistic that the project will yield crystals. Once crystallized, the usher structure will be determined using either MIR but preferably MAD or SAD phasing. This project will benefit tremendously from the environment in the School of Crystallography at Birkbeck which has a long history of successfully determining structures of membrane proteins. Our lab itself has an outstanding track record in the field of 3D structure determination using x-ray crystallographic methods.

This project is currently funded by a programme grant from the MRC (£1.032 million). Three postdoctoral workers are working in this area in the lab. One of them will be directly involved in the project proposed here. Thus, the student will have full support from the lab environment and personnel.

Structure and function of type V autotransporters

Supervisor: Professor Gabriel Waksman

Project overview

Haemophilus influenzae is a common cause of localized respiratory tract disease, including otitis media, sinusitis, bronchitis, and pneumonia. Less commonly, this organism causes serious systemic disease, such as meningitis, endocarditis, and septicemia. The initial step in the pathogenesis of H. influenzae disease involves colonization of the upper respiratory mucosa. A high-molecular-weight outer-membrane protein called Hia, which is present in nontypable (nonencapsulated) H. influenzae promotes attachment to the human respiratory epithelium. The Hia protein is a non-pilus adhesin and belongs to the rapidly expanding family of autotransporter proteins. Hia is synthesized as a 114 kDa precursor protein that consists of three domains: a 49 residue N-terminal signal sequence, an internal passenger domain (residues 50-779), and a C-terminal β-domain (residue 780-1098). The adhesive activity of Hia is located within the passenger domain. This activity is contained in two separate binding domains: a major domain conferring most of the adhesive activity of Hia is located between residue 541 and 714 (HiaBD1) and a secondary binding site (HiaBD2) is located at the N-terminus of the passenger domain between residue 50 and 374. Both sites bind to the same receptor as each appears to bind competitively. The identity of the host cell receptor for Hia remains unknown. Hia is an example of a variant sub-family of autotransporters characterized by an unusually small translocator domain that undergoes trimer formation. Recently we have solved the structure of the primary adhesion domain (HiaBD1) and shown that it is a highly intertwined trimer. Thus, the entire protein including the adhesion domain and the translocator domain is a trimer of estimated molecular weight over 300,000 Da.

This proposal aims at addressing two questions: 1- what is the structural basis of Hia-mediated adhesion to the respiratory epithelium, and 2- what is the structural basis of autotransport of the Hia protein. We propose to investigate these two issues by solving the structure of the full-length Hia protein. This proposal arises from the fact that we have been able recently to scale up the production of the full-length Hia protein. We cloned the full-length sequence in one of the IBA vector that allows export of the protein to the periplasm (the protein is fused behing an OmpA signal peptide) and rapid purification via a C-terminal strept-tag. We showed that the protein inserts into the outer-membrane and can be purified in large quantity from outer-membrane extracts. The protein was shown to be trimeric using gel filtration chromatography. These results indicate that full-length Hia is produced in a native state.

In this proposal, we propose to solve the structure of the Hia protein using two methods: 1- x-ray crystallography, and 2- high resolution EM. Crystallization trials will be performed. If crystals are obtained, the structure will be solved using the various phasing methods that have been developed over the years, namely, multiple isomorphous replacement (MIR), or multiwavelength anomalous dispersion (MAD), or singlewavelength anomalous diffraction (SAD). The preferred methods are MAD and SAD on the selenomethionine-substituted protein. The laboratory of Prof Gabriel Waksman has an outstanding track record in using MAD and SAD to solve structure (see CV).

However, we cannot guarantee success in the crystallization of full-length Hia and thus, we will also use high resolution EM to solve the structure. Although EM provides images of the proteins at relatively low resolution compared to x-ray crystallography, EM has the tremendous advantage that it can be implemented immediately without having to rely on the successful outcome of crystallization, and with a high probability of success. This part of the programme will be supervised by Dr. Elena Orlova, a recognized expert in the field of high-resolution EM. Dr Orlova has already obtained structures for e.g. skeletal muscle calcium release channel, ribosomal termination complex, bacteriophage portal protein and alpha-latrotoxin. Analysis will be started with electron microscopy of negatively stained samples and later should be performed in cryo-conditions.

Structural studies of type IV secretion machines

Supervisor: Gabriel Waksman

Project overview

Type IV secretion systems (T4SSs) are secretion machineries used by Gram- bacterial pathogens to export virulence factors. T4SSs are ancestrally related to bacterial conjugation systems which have significant impact on public health as they are responsible for the propagation of plasmid carrying antibiotic resistance genes. T4SSs are composed of at least 12 protein components termed VirB1-11 and VirD4 which assemble to form a secretion apparatus powered by three ATPases, VirB4, VirB11, and VirD4. Pathogens utilizing T4SSs to secrete virulence factors include Helicobacter pylori, the causative agent of gastric ulcers and MALT lymphoma, or Legionella pneumophila, the pathogen responsible for Legionnaire disease. Our aim is to derive a structural view of the type IV secretion machine but crystallizing and solving the structure of the various components of the system either alone or in complex with each other. Such work will elucidate the molecular basis of virulence factor export by this complex machinery and thus provide a handle on not only how transport occurs through the double membrane of Gram-negative pathogens but also on designing novel antibiotics targeting the machinery.

Zinc Metalloproteases from Myocobacterium leprae and Mycobacterium tuberculosis as Targets for Rational Drug Design

Supervisors: Prof. B.A. Wallace and Dr. Nora Cronin

Project overview

The zinc metalloprotease from M. leprae (the leprosy bacterium) is a 667 amino acid protein belonging to the family of highly specific zinc proteases which include the endothelin converting enzymes (ECE)and NEP. These proteases are involved in the post-secretory processing a d metabolism of vasoactive peptides such as endothelin. Endothelin was identified in 1988 as the most potent vasoconstrictor compound ever isolated and its crystal structure was solved in our lab in 1994. It has effects on both vascular and non-vascular smooth muscle. Its precursor peptide, "Big endothelin", however, has no vasoactivity, so inhibitors to the specific enzymes which cleave the precursor can effectively disable its vasoactive effects. M. leprae has 3 main targets – peripheral and neural tissues, small vessels (endothelial cells) and the monocyte-macrophage system. The bacilli survive and replicate within the Schwann cells and also within endothelial cells, from which they are released. The co-localisation of bacterial infection and proliferation with the expression of the mature peptide endothelin has led to the hypothesis of a role for the zinc metalloprotease in the pathogenesis of the disease. Hence knowledge of the 3-dimensional crystal structure of this enzyme (and in complex with inhibitors), which converts the inactive pro-peptide to the mature and active peptide, may provide a valuable basis for the design of new drugs. We have cloned, expressed, purified and crystallized this protein with an inhibitor. this project will entail crystal structure determination as well as related molecular biology, biophysics and modeling studies. We have also cloned the related enzyme (80% homology) from Mycobacterium tuberculosis, another medically-important agent of infection, and this will also be the subject of crystallographic and molecular biology studies.

Molecular and Structural Biology of Sodium Channels

Supervisor: Prof. B.A. Wallace, with Dr. N. Cronin

Project overview

Sodium channels are physiologically-important membrane proteins, which are functionally related to a variety of disease states, including epilepsy and cardiovascular diseases. This project will entail the cloning and expression, isolation, purification and characterisation and crystallization of sodium channels from a range of prokaryotic and eukaryotic sources, and their heterologous expression in bacterial systems. In addition, molecular biology constructs of chimeras and isolated domains will be made in order to produce channels with altered functional characteristics. The structures of the channel proteins produced will characterised by a number of techniques including circular dichroism spectroscopy, cryo-electron microscopy, X-ray crystallography and patch-clamp analyses. Additional goals will be to investigate the nature of their interactions with toxins and antiepileptic drugs with the ultimate goal of using rational drug design methodologies to develop new pharmaceutical agents against diseases. Thus this project will enable the student to gain experience in a large number techniques, including molecular biology, structural biology, electrophysiology, bioinformatics and molecular modelling and graphics.

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Structural and mechanistic studies of essential enzymes of the bacterial cell wall

Supervisors: Dr Mark Williams & Dr Snezana Djordjevic (UCL)

Project overview

Bacterial cells are entirely surrounded by a peptidoglycan layer (a single mega-molecule of long polysaccharide chains cross-linked by short peptides), which provides structural strength and defence against external dangers. The morphology and precise chemical composition of this layer varies between Gram-positive and Gram-negative bacteria and between species within those divisions. While the repeating disaccharide MurNAc-(β1,4)-GlucNAc is common to all bacterial peptidoglycan, there are differences in the peptide cross-links and in accessory molecules. Many enzymes are targeted to components of the peptidoglycan, because it must be continuously remodelled to allow growth and cell division and it is frequently involved in interactions between microbes and hosts. As a consequence of the peptidoglycan layer being unique to bacteria and the plethora of enzymes involved its maintenance, several important antibiotics (e.g. penicillin) act by inhibiting parts of this cell-wall machinery. We have recently being investigating the structure of the N-acetylmuramyl-L-alanine amidases (NAMLA amidases), which are responsible for cleaving the peptide crosslinks from the gylcan chain during during cell division. This project aims to extend these studies by identifying (through cross-species genome analysis), cloning, determining structures and finding inhibitors of further peptidoglycan remodelling enzymes. Structures may be solved by crystallography or NMR as appropriate.

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➲ Biophysics

Biophysical study of the Klentaq1 DNA polymerase

Supervisor: Prof Gabriel Waksman

Project overview

As DNA polymerases are vital enzymes accomplishing crucial tasks, it is important to dissect the molecular and structural mechanisms that enables DNA polymerases do rapidly and accurately replicate life's blueprints. To date, we have crystallized and determined the structure of 10 states of the DNA polymerase I enzyme Klentaq1, yielding a detailed structural description of the various steps along the kinetic pathway of nucleotide incorporation. One major contribution was to show that the fingers domain of Klentaq1 (which is also the deoxynucleoside 5' triphosphate (dNTP)-binding site) undergoes a large conformational change (from open to closed) in the enzyme:primer/template (E:p/t) complex upon addition of the correct nucleotide. This conformational change acts as a delivery mechanism for the dNTP. It was also hypothesized to be "rate-limiting", thereby providing the structural basis for a key step (the so-called "rate-limiting step") identified in kinetic studies as crucial for fidelity. Our research program recently expanded to test this hypothesis. We were able to set up a fluorescence resonance energy transfer (FRET) system capable of monitoring fingers domain motions in Klentaq1. This FRET system was instrumental in determining that the fingers domain closure is fast and not rate-limiting, a crucial contribution in the DNA polymerase field (published in Molecular cell). However, given the fundamental roles that fingers domain motions play in DNA polymerase activity, such a FRET system should also enable us to answer crucial questions touching on the fundamental mechanism of fidelity. These questions are: does fingers closure happen when the incorrect nucleotide is provided? does fingers closure require a trigger? if no trigger is required, does the fingers domain undergo continuous oscillating (closed to open and vice versa) motions? if it does, do the oscillating motions happen in the apo form? These questions are important: the fingers domains of DNA polymerases play crucial roles in delivering nucleotides to the active site and thus are potentially the gate-keepers for accurate DNA replication. Given that delivery occurs through a large conformational change in the fingers domain, it is thus important that we study the details of fingers domain motions, how they are triggered (correct versus incorrect dNTP binding), and how these motions proceed (in the apo or the E:p/t state).

To answer these questions, we propose to study fingers domain motions using single molecule FRET. We have set up a FRET system that monitors the motions of the fingers domain in an ensemble of unsynchronized Klentaq1 molecules. Although this system is appropriate to monitor fingers domain motions triggered by correct nucleotides, it is insufficient to monitor fingers domain motions triggered by incorrect nucleotides. This is because incorrect nucleotides are unable to stabilize the closed form of the enzyme. We are thus limited in what we can do by the fact that we are working with an ensemble of unsynchronized molecules. Therefore, to monitor motions taking place when incorrect nucleotides are provided, we need to be able to examine the FRET signal at a single molecule level. It is also the case that single molecule FRET is the only method that will allow us to identify a potential trigger for the conformational change as well as examining the possibility of continuous oscillating motions in the apo and E:p/t states.

Thus, the objectives of the proposal is to set up two FRET systems, one in the E:p/t state and another one in the apo state, that will permit visualization of fingers domain motion at a single molecule level.

Structure-thermodynamic studies of SH2 domains

Supervisor: Gabriel Waksman

Project overview

SH2 domains are small circa 100 amino acid domains that specifically bind tyrosine-phosphorylated sequences on receptor signalling proteins. Our research aims at understanding the structural and energetic basis by which SH2 domains bind their target. Our model system is the SH2 domain of the Src kinase, an important enzyme involved in bone metabolism. Our work consists in dissecting the entire binding interface to reveal the thermodynamic hot spots that dominate the interaction between the two binding partners. To do so, we use an array of techniques, from x-ray crystallography, isotitration calorimetry, fluorescence spectroscopy, molecular cloning, expressed and native chemical ligation, and computer modeling.

Circular Dichroism and Synchrotron Radiation Circular Dichroism Spectroscopy of Sugars and Protein/Carbohydrate Interactions

Supervisor: Professor B.A. Wallace

Project overview

Glycosylation of proteins is important for their function, assembly and targeting. Proteins are often heterogeneously glycosylated, and have very different types of sugars and linkages at different sites. In addition, protein/carbohydrate interactions are important for signaling and inter-molecular interactions. There are many diseases that arise from incorrect glycosylation.

This project will entail the use of circular dichroism spectroscopy to examine the structures of isolated sugars and glycoproteins and protein/carbohydrate complexes, to develop new methods for analyzing their structures.

It will have a significant Bioinformatics component, as well as experimental work, which will entail traveling to synchrotron sources (UK, USA, Denmark, China) for data collection.

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Investigations of Macromolecular Complex Formation by SRCD and Fluorescence Spectroscopy

Supervisor: Professor B.A, Wallace

Project overview

In collaborative studies with groups at Imperial College, and in Australia, we are examining the dynamics, conformational changes, and thermal stability changes associated with macromolecular complex formation of membrane and soluble proteins. We are developing new techniques in synchrotron radiation circular dichroism which allow us to monitor both secondary and tertiary structural changes, which can be correlated with fluorescence-detected changes for examining protein folding.

Spectroscopic and computational studies of hydrogen bonding in protein-ligand complexes

Supervisors: Dr Mark Williams & Professor Peter Rich

Project overview

Hydrogen bonds are crucial to the specificity of ligand recognition by proteins. A substantial component of the binding energy of a complex is derived from hydrogen bonds between protein and ligand and from the changes of numbers of hydrogen bonds to water and between water molecules that occur as a result of complex formation. Although, much has been learnt about hydrogen bonding over the past twenty years, many questions still remain. In particular, the basic questions; how strong are the protein-ligand hydrogen bonds and the bonds they both make to water? Both infra-red and nuclear magnetic resonance spectroscopies are able to detect the formation of hydrogen bonds. NMR can identify the atoms involved in individual hydrogen bonding through use of isotope labels and the measurement of the temperature dependence of signal frequencies or of the coupling of donor and acceptor nuclei via the correlated of motion of their valance electrons. IR difference spectroscopy can detect hydrogen bonds through measuring the change in amplitude and frequency of the vibrations of bonds of the donor or acceptor groups. Both NMR and IR effects can be related to hydrogen bond strength through ab initio quantum chemical calculations. This project seeks to combine the precise assignment of NMR spectral features and isotopic labeling strategies with the quantitative capability of IR, in order to provide the first complete description of the hydrogen bond strength changes accompanying formation of a protein – ligand complex. The investigation will complement structural studies in the group by focusing on protein-carbohydrate and glycopeptide complexes that are important in the bacterial life-cycle and in host-pathogen interaction. This study will be vital to our understanding the structural contributions to specificity of recognition in these systems.

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➲ Bioinformatics

Developing a text mining service to support multi-scale simulations of the immune system

Supervisors: Dr Adrian Shepherd and Professor David Moss

Project overview

The co-supervisors for this project are both members of the EU-funded ImmunoGrid Consortium, which is developing a multi-scale simulation of the human immune system (see http://www.immunogrid.org for more information). A key challenge is the collection of relevant information -- ranging from MHC binding data to information about T-cell and antigen concentrations over the life-time of an infection). Most of this information is not available in a well-structured form within existing data resources.

The aim of this project will be to develop services for mining the immunological literature. It will build on existing approaches developed within the Shepherd group in ways that are tailored to the specific characteristics of the vocabulary and use of language within the immunological domain. This will include: retraining the Bayesian network for combining protein named entity recognition tools at the heart of the ProSpecT service (Kabiljo and Shepherd, 2007);

identifying dependency graphs that characterise the relationships between immunological entities based on the approach discussed in (Clegg and Shepherd, 2006), which has currently been applied to the extraction of gene regulatory relationships (Clegg and Shepherd, 2007). We are particularly interested in developing approaches for assessing the accuracy of extracted information based on, for example, the complexity of the sentences from which the information was extracted.

The ultimate aim of the project will be to build a flexible, modifiable web service capable of extracting diverse immunological information from full-text papers in PDF format. The project would be particularly appropriate for a student with strong programming skill who would like to be involved with a large-scale systems biology initiative, or who has a specific interest in natural language processing.

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Simulating the human immune system: prediction of MHC protein-peptide binding

Supervisors: Dr Adrian Shepherd and Professor David Moss

Project overview

We are participants in ImmunoGrid which is a project involving eight laboratories that are collaborating to produce a computational model of the human immune system. It is funded under the EU Framework 6 STREP programme. The aim is to simulate the immune system at the organ, cellular and molecular levels. In the Bloomsbury Centre for Bioinformatics, our role is in this programme to develop a repository of data for the simulator and also to model some key interactions in the immune response to pathogens. This PhD project is focussed on the latter task.

MHC proteins bind peptides derived from both self and foreign proteins and this interaction is key to determining the T-cell response to pathogens. The experimental data on MHC protein-peptide binding is limited and is often difficult to acquire. Relevant crystal structures of these protein complexes are available and hence we wish to study the protein-peptide binding by ab initio methods, involving molecular simulation. We have shown that fairly crude simulation techniques could do as well as methods based on experimental data (Davies et al., 2003) and now wish to apply more rigorous simulation methods.

We shall use the molecular simulation package NAMD to calculate MHC-peptide dissociation constants in order to identify the peptides implicated in immune responses to disease. These calculations will use

thermodynamic integration to yield free energy values and relative binding constants. Pilot studies using this method have already been undertaken and have shown the importance of the end-point simulations. This will be further investigated during the project. These are very expensive calculations and will be carried out on our IBM Blade Cluster that currently has 67 dual Xeon 3.06GHz nodes interconnected by a 2Gb Ethernet. We are also deploying immunoinformatics calculations on a computational GRID using AHE middleware. In order to scan whole proteins for peptides that bind to MHC molecules, a GRID approach will be necessary and the thermodynamic calculations will be deployed on the GRID in order to take advantage of as many computational resources as possible.

The project will appeal to a student who is interested in developing techniques for the quantitative study of protein-ligand interactions and their application in the immune response to disease. See http://www.immunogrid.org for more information.

Reference
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Mechanism of Bacteriophage SPP1 Connector at Atomic Level

Supervisors: Dr. Maya Topf and Dr. Elena Orlova

Project overview

Tailed viruses initiate infection by releasing DNA through a tail channel into the host cell, a process that is controlled by many factors and one of them is a connector that prevents DNA release after packaging (Lurz et al., 2001). Studying the mechanism of the connector functioning as a gatekeeper of the packaged viral DNA is a crucial step towards understanding of how these viruses, as well as other DNA viruses such as Herpes viruses, infect other organisms

Bacillus subtilis SPP1 is a DNA bacteriophage with a tail. Its connector is a protein assembly composed of multiple copies of three proteins: a portal protein, gp6, and two head completion proteins, gp15 and gp16. The connector provides a link between DNA, capsid and the tail. Recently, the structures of this connector and of the portal protein alone were determined at sub-nanometer resolution at in the lab of E. Orlova at Birkbeck College using cryo-electron microscopy and images analysis (Orlova et al., 2003). Comparison of the structures shows some conformational changes that are likely to be associated with termination of DNA packaging. So far, a high-resolution structure exists only for the SPP1 portal protein in its isolated form (submitted) (and for its remote homolog from phi29 (Simpson et al., 2000)). Thus, atomic detail on the specific protein-protein interactions in the whole assembly, which could provide insights into the mechanism of the connector, is still missing.

The aim of this project is to characterize the architecture of SPP1 connector and the conformational changes that prevent DNA release at the atomic level. The student taking up this project will use bioinformatics techniques and will develop methods to combine protein structure modelling with cryoEM density fitting (Topf and Sali, 2005). The software developed as part of the project will be used to characterize the structure and assembly of other bacteriophage proteins that have been solved by cryoEM.

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Molecular modeling of pyrethroid binding to insect and mammalian sodium channels

Supervisors: Professor B.A. Wallace, with Dr. Martin Williamson, Rothamsted Research

Project overview

This project focuses on computational modelling of the interaction of insecticide pyrethroid ligands with insect and mammalian sodium channels, with *in–silico* models generated taking into account known sodium channel mutations, which have previously been shown experimentally to affect the efficacy of the pyrethroid molecules.

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Bioinformatics: spectroscopic data mining and analysis of native and mutant proteins

Supervisor: Professor B.A. Wallace

Project overview

The proposed project will entail the development of new methods for data mining, analysis and archiving of circular dichroism and other spectroscopic data based on advanced applied mathematical and statistical tools. It will enable the comparison of properties of mutant and native proteins, produce a public data bank of these characteristics, and form the basis for identification of the structural basis of disease-related mutations. It will provide training for the student at the interface of the biomedical sciences and computing/IT.

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Simulating the assembly and disassembly of macromolecular complexes in a cellular context.

Supervisor: Dr Mark Williams

Project overview

The assembly and disassembly of macromolecular complexes is fundamental to the regulation of cellular processes as diverse as signal transduction, transcription and cell motility. This computational systems biology project arises from realization that we are usually unable to use our rapidly growing knowledge of the structural, thermodynamic and kinetic properties of binary protein-protein interactions to quantitatively explain or predict to the behaviour of the multi-protein complexes found in the cell. The rates of assembly/disassembly of a multi-protein complex, depend on local concentrations of components, the structures of the proteins involved, the constituent binary interactions of protein domains, reorganization of the ionic environment in response to changes in the total electrostatic field of the complex, rates of intra-molecular conformational change and crowding effects due to surrounding non-participant proteins in the dense soup of the cytoplasm. The sizes of most of these physical effects are only predictable through detailed consideration of the time-dependent structure of the complex and its surroundings. This proposal seeks a student to build a 'computational nanoscope', which will simulate the assembly and disassembly of multi-protein complexes with nanometer and nanosecond resolution.

The student will develop software that enables stochastic simulation of the dynamic structure of multi-protein complexes on the molecular scale in a cell-like environment, i.e. as objects that are spatially extended but having limited internal detail and flexibility moving in a salty and crowded space. The computational models will be parameterized using experimental data on binary complexes as input and explicitly include the physical factors which are liable to modulate affinities and association/disassociation rates. The software developed during the project will be used to simulate the assembly and rearrangement of one or more well-characterised multi-domain/multi-protein complexes drawn from those under structural and biophysical investigation within the department. The software could become a key tool in relating molecular structure to cellular function in future models of whole cells. The project would particularly suit a graduate with a strong physical science background and/or an aptitude for computer programming.

References

1. Andrews SS & Arkin AP (2006) Simulating cell biology. *Current Biology* 16, R523.
2. Ladbury JE & Williams MA (2004). The extended interface: measuring non-local effects in biomolecular interactions. *Current Opinion Struct Biol* 14, 562.
3. Minton AP (2001). The influence of macromolecular crowding and macromolecular confinement on biochemical reactions in physiological media. *J Biol Chem* 276, 10577.

➲ Industrial Materials

Structure and properties of pharmaceutical (drug) polymorphs

Supervisors: Prof.P.Barnes, Dr.J.K.Cockcroft

Project overview

Polymorphism in drugs means that a drug compound can exist in more than one structural form. These different forms often exhibit differing properties including, most importantly, shelf life and potency; even further, different polymorphs can be subject to different patent restrictions or even lie outside existing patents. Not surprisingly then, this subject has figured in some well-publicised high court disputes. As a result X-ray diffraction has emerged as a definitive tool for identifying and distinguishing polymorphs. This project will be involved with sorting out polymorphic transformations and structures occurring in various drug systems, with the further possibility of monitoring the crystallisation of drug polymorphs inside a pharmaceutical processor using tomographic methods (see also project No.4).

References

1. Anwar, J. et al. (1989) "The Polymorphism of Sulphathiazole", *J.Pharm.Sci*. 78, 337-342.
Anwar, J. et al. (1992) "Kinetics of phase transformations in crystals of drug compounds....", *Phase Transitions* 39, 3-11.
2. Chan, F.C. et al. (1999) "Ab Initio Structure Determination of sulfathiazole polymorph...", *J. Appl. Cryst.* 32, 436-441.
3. Jacques, S.D.M. et al. (2005) ""An In-Situ Synchrotron X-ray Diffraction Tomography Study of Crystallization and Preferred Crystal Orientation in a Stirred Reactor", *Crystal Growth & Design* 5, 395-397.

Exploiting low temperature powder diffraction

Supervisors: Prof.P.Barnes, Dr.J.K.Cockcroft

Project overview

Many materials (e.g. pharmaceutical products, molecular solids, silicon clathrates) display interesting phase transitions or thermal expansion properties on cooling. The nature of such transformations (e.g. order/disorder) can be studied using low temperature powder diffraction with the bonus that the structural atomic positions become much more well defined at low temperatures. In this project the student would use low temperature (to 4 K) powder diffractometers, both newly-designed in-house versions or those at neutron/synchrotron sources. The data would be used to perform Rietveld structure refinements, in some cases combining the X-ray and neutron data when additional information can be extracted (e.g. position of hydrogen atoms; order/disorder parameters).

References

1. Vogt *et al*. (1994) "The crystal and molecular structures of rhenium heptafluoride", *Science* 263, 1265-1267.
2. Tang,X. et al. "Thermal properties of Si136: Theoretical and experimental study of the type-II clathrate polymorph of Si", *Phys. Rev*. B 74, 014109.1-10 (2006).

Using intense synchrotron/neutron radiation to study chemical reactions or solid transformations

Supervisors: Prof.P.Barnes, Dr.O.Leynaud, Dr.S.D.M.Jacques & Dr.J.K.Cockcroft

Project overview

One of the exciting trends in the last 15 years has been the ability to harness the intense radiation from synchrotron (X-rays) and neutron sources for in situ studies. What we mean by this is that we can now subject a given material to a range of environments which imitate some chemical or physical process while, at the same time, collecting X-ray or neutron diffraction patterns in real time. This in situ approach has transformed our understanding on how a whole range of chemical reactions and physical transformations take place. In this project we have the possibility, with industrial support, of choosing from a number of projects concerned with the synthesis and performance of materials:

a) the high temperature synthesis of ceramic materials
   (e.g. zirconia, novel zeolites);
b) the rapid hydration of cement compounds;
c) ion-exchange and dehydration in zeolites;
d) the performance of catalysts.

References

1. Barnes,P. et al. (1996). "Applied Crystallography Solutions..in Industrial Solid State Chemistry..ceramics, cements and zeolites", *J. Chem. Soc. Farad. Trans*. 92, 2187-2196.
2. Johnson,M. et al. (2003) "Cation-exchange, dehydration and calcination in clinoptilolite:..", *J. Phys. Chem.* B107, 942-951.
3. Lupo,F. et al. (2004) "Hydrothermal crystallisation of doped zirconia...", *Phys. Chem. Chem. Phys*. 6, 1837-1841.
4. Jacques, S.D.M. et al. "Redox Behavior of Fe-Mo-O Catalysts Studied by Ultrarapid In Situ Diffraction" *Angewandte Chemie* 45, 445 –448 (2006).

Synchrotron (X-ray) Tomography of real Materials Processing in action

Supervisors: Prof. P.Barnes, Dr.S.D.M.Jacques, Dr.J.K.Cockcroft, Prof.R.J.Cernik

Project overview

This research group has invented a novel form of tomography based on synchrotron X-ray diffraction/fluorescence and developments in novel detector systems. It has been applied to problems as diverse as watching materials being mixed in engineering processors, mapping crystallisation as it proceeds inside a seemingly "impenetrable" autoclave cell, and monitoring diffusing of dangerous species through porous environmental media. An enormous range of industrially relevant applications awaits exploitation by this technique.

References

1. Barnes,P. et al. (2001) "Tomographic...Imaging of Static and Dynamic Systems", *Nondestr. Test. & Eval*. 17, 143-167.
2. Hooper,D. et al. (2003) "An in situ study of crystallisation...of zeolites", *Phys. Chem. Chem. Phys*. 5, 4946 - 4950.
3. Betson,M. et al. (2004) "Porosity Imaging in Porous Media...", *Transport in Porous Media* 57, 203-214.

Computational surface science study of metal nano-particle formation

Supervisors: Prof.P.Barnes, Dr.Nora de Leeuw

Project overview

Computational techniques are developed and employed to investigate the formation of copper and/or cadmium nanoparticles. Experimental studies have found that the shape/size of the nano-particles are critically dependent on the surfactants present in the growth medium. This computational studentship is concerned with a) the modelling of the nucleation, growth and morphology of the Cu/Cd nanoparticles and b) the investigation of the interaction of the surfactants with the relevant Cu/Cd surfaces. The project, which is in collaboration with an experimental group at the University of Jussieu in Paris, will comprise some code development to include the capability of modelling metal/ionic interactions in existing software, as well as simulations using both classical computational methods and calculations using quantum mechanical techniques.

POSTGRADUATE APPLICATION 2007–2008

Please complete in **block capitals** and return to:

Admissions, Registry
Birkbeck, University of London
Malet Street, London WC1E 7HX

PLEASE COMPLETE ALL SECTIONS OF THE FORM

Student Number: *(Registry use only)*

Registry Use

REC'D

ACK'D

CSE

FEESTAT

APPCAT

ETH

NAT

COD

DIS

SDA

HQOE

OCC

QUALSTAT

REF1

REF2

TRANS

ELC

1 PERSONAL DETAILS

Surname/family name: _____ Title: Mr / Mrs / Miss / Ms / Dr *(please circle)*

First name(s): _____ Male / Female *(please circle)*

Former name: _____ Date of birth: _____ DD/MM/YY
(If changed since obtaining a previous degree/diploma, etc.)

Permanent address: _____ Correspondence address *(if different)*:

_____ _____

_____ _____

_____ Postcode: _____ _____ Postcode: _____

Telephone (Home): _____ Telephone (Mobile): _____

Email: _____ Telephone (Work): _____

Disability: If you have any access issues or special needs that you would like to bring to the attention of your Admissions Tutor, please state them here.

_____

Occupation: _____

Employer: _____

[*Please read Note* (i) *before completing this section.*]

Nationality: _____ Country of permanent residence: _____

Country of residence during the last three years: _____

If you are already in the UK on a visa or work permit, is there a time limit or restriction for the period in which you may remain in the UK? ☐ YES ☐ NO

If you are **NOT** an EU/EEA National but you are claiming Home/EU status on the grounds of marriage or permanent residence, please provide details. If you are applying for a **PART-TIME** place and you are **NOT** an EU/EEA National, you must provide documentary evidence that you have the right to work in the UK without restrictions. This must be **EITHER** a copy of your passport with appropriate stamp **OR** letter from the Home Office. [See Note (ii).]

Note: Failure to enclose the appropriate documentation will delay your application.

2 PROGRAMME DETAILS [*Complete either (a) or (b)* ***and*** *(c), ticking one box only in each section.*]

What programme do you intend to study?

Either (a) Taught programme: ☐ MSc ☐ MA ☐ MRes ☐ PG/Advanced Certificate ☐ PG Diploma

Title of programme: _____

Second choice, if any: _____

Or (b) Research degree: ☐ MPhil ☐ PhD

Subject area of research: _____ School: _____

Proposed start date: ☐ October 2007 ☐ January 2008 ☐ April 2008

And (c) Mode of study: ☐ Full-time ☐ Part-time ☐ Distance learning (see Postgraduate Prospectus p229)

3 CURRENT STUDIES

If you are currently completing a degree, please give title, major subject, expected completion date and the name of your university or college.

Title of degree: _____ Major subject: _____

Name of university/college: _____ Expected completion date: _____

4 YOUR EDUCATION [*Please read Note* (iii) *before completing this section.*]

Please include the following: the University/College attended and degrees already held; your subjects and grades at A-level or equivalent. Please list separately all courses that you have taken, including professional training and/or other training courses. In the case of qualifications taken outside the UK, please give the exact title of the qualification as it is known in the country where it was taken. Please do **NOT** try and describe it in terms of the UK system.

Dates (mm/yy–mm/yy)	Name of College/University/Awarding body (State country if outside UK)	Subject(s)/Course title	Full-time or part-time	Result/Grade

5 YOUR PROFESSIONAL AND/OR OTHER EXPERIENCE

Please include details of paid and voluntary work. You should also state any work-related skills relevant to your proposed studies: for example, report-writing, computer programming, work with statistics or languages, accounting procedures, etc.

Dates (mm/yy–mm/yy)	Employer	Your job title	Your responsibilities

6 SUPPORTING STATEMENT

If you are applying to do **RESEARCH**, please use this space to tell us about your research interests. Outline your research proposal in not more than 250–500 words (continue on a separate sheet if necessary). Please also list your publications/reports, if any, and tell us if you wish to work with a particular member of staff at Birkbeck.

If you are applying for a **TAUGHT COURSE**, please tell us about any relevant professional qualifications you have and your reasons for wishing to study this course. You may attach another sheet/CV if necessary.

7 YOUR ENGLISH PROFICIENCY [*Please read Note* (v) *before completing this section.*]

Is English your first language *(please tick one box only)*? ☐ YES ☐ NO

If English is not your first language, Birkbeck requires evidence of your level of ability in spoken and written English. If you do not already hold a recent acceptable qualification/test score in English (such as IELTS or TOEFL), you may be required to obtain one before you can be admitted to Birkbeck.

Please tell us about any English language qualifications you hold and enclose a copy of your certificate.

a. IELTS score [*the normal minimum requirement is 6.5 (with a minimum of 6 in the subtests)*]: _____

b. TOEFL score [*the normal minimum requirement (computer-based test) is 237 (plus 5 in the essay rating)*]: _____

c. Any other English language qualification you hold, or are about to take: _____

8 REFEREES [*Please read Note* (v) *before completing this section.*]

Give details of two referees below. Please note at least one referee must be someone who knows you in an academic context and who is qualified to comment on your suitability for your chosen area/course of study.

Name: _____

Position: _____

Name of organisation: _____

Address: _____

_____

_____

Telephone: _____ Fax: _____

Email: _____

Name: _____

Position: _____

Name of organisation: _____

Address: _____

_____

_____

Telephone: _____ Fax: _____

Email: _____

9 FINANCE

How will you finance your studies *(please tick one box only)*? ☐ Self ☐ Employer/Sponsor

If you are a sponsored student, please complete the following:

Name of organisation: _____

Name of approving manager: _____

Address: _____

_____

Fax: _____

Tel: _____

Email: _____

Web address: _____

Please give details of any scholarships or grants (for your proposed study at Birkbeck) that:

You have already obtained: _____

You have applied for: _____

Will you be able to support yourself financially during your studies if you are unable to obtain a grant? ☐ YES ☐ NO

10 DECLARATION

Applications are subject to College regulations on admissions. Any offer of admission to the College as a student of the College, whether made orally or in writing, is subject to confirmation that the applicant satisfies the relevant entry requirements and regulations for admission. Admission is conditional on the applicant undertaking to be bound by the relevant College and University regulations and to pay the prescribed fees.

Personal data

Information provided by and concerning applicants and students is held by the College in its original, electronic and other formats and is processed for the purposes of administration and management of applications, admissions, student records, student progress and support and for statistical purposes in accordance with relevant legislation, including the Data Protection Act 1998. It is a condition of the College's consideration of applications for admission and enrolment that such data will be held and processed. The declaration below must be signed in order for this application to be processed.

Declaration by applicant

1. I give my consent to the processing of my data by Birkbeck, University of London.
2. In making this application for admission to the programme named in Section 2, I acknowledge that any offer of admission I may receive is subject to the condition that I fulfil the relevant entrance requirements and that I provide, when asked to do so, original documentary evidence of holding the academic qualifications and of any other information listed above. If, having been admitted, I fail to fulfil that condition, I undertake to withdraw from the College.
3. I undertake not to engage in any course of study concurrently with that to be taken at Birkbeck, University of London.

Signature of applicant: _____ Date: _____

CHECKLIST *(Please tick as appropriate)*

I enclose:	☐ Reference 1	☐ Reference 2	☐ Degree transcript	☐ IELTS/TOEFL certificate
To follow:	☐ Reference 1	☐ Reference 2	☐ Degree transcript	☐ IELTS/TOEFL certificate

NOTES ON COMPLETING THE POSTGRADUATE APPLICATION FORM

(i) Part-time students are normally expected to be engaged in full-time employment. Your employer will not be contacted. If you are not in employment but have other commitments (e.g. domestic responsibilities, or you have retired or you have long-term health problems), please state this clearly on the form.

(ii) Applicants for PART-TIME programmes who are not EU/EEA Nationals **MUST** provide documentary evidence that confirms they have leave to remain and the right to work in the UK without restrictions. This must be **EITHER** an appropriate stamp in your passport **OR** a document from the Home Office. If you are living in London on a student or visitor's visa, you will not normally be eligible to enrol as a part-time student.

(iii) Please give the full title of the college or university where you studied, but add the name of the validating authority if different, e.g. Roehampton Institute (University of Surrey). Please also give the title of the qualification, e.g. BA, LesL, Ptychio, State Examinations.
For 'Result/Grade' obtained UK graduates should enter the class of Honours (I, IIA, IIB or III) or 'Ordinary', 'Pass' as appropriate. US graduates should give the grade point average (and any description of the award e.g. cum laude).
Other graduates should give the grade or overall mark they obtained or any description awarded e.g. bien, cum laude etc.
Please also give the year in which the degree was awarded.
Holders of professional qualifications should give the full title of their qualification, the name of the awarding body and the result obtained. Please include a note of the main subjects studied if this is not clear from the title of the qualification.
A copy of your degree transcript or professional award should be included with your application form.
Note: Original certificates are checked at enrolment.

(iv) These are the normal minimum English test scores required for entry to postgraduate programmes. Higher test scores may be required for entry to some courses e.g. management, English, humanities and law (IELTS 7.0, TOEFL 600).

(v) TWO references are normally required. One referee should be someone familiar with your academic work. If your most recent academic study was several years ago, and you feel that your professional experience is more relevant, please obtain other appropriate references. Detach the reference request forms which follow and send one to each of the referees named in Section 8.

For Registry use only

Student Number:

REGISTRAR'S NOTES TO ADMISSIONS TUTOR:

1. ☐ Eligible on the basis of degree (minimum UK Second Class Honours or overseas equivalent)
2. ☐ Eligible on the basis of approved professional or other qualification obtained by written examinations and approved by the College
3. ☐ Applicant's degree is not equivalent to UK Second Class Honours standard: any offer of a place must be subject to College approval. Please complete the enclosed Non-Standard Postgraduate Application Form.
4. ☐ Applicant's professional qualifications are not approved as equivalent to a UK Honours degree: any offer of a place must be subject to College approval. Please complete the enclosed Non-Standard Postgraduate Application Form.
5. ☐ Applicant does not have post-secondary qualifications obtained by written examination: if you wish to offer a place on the basis of his/her work experience, please submit a statement in support of this applicant and your decision.
6. Provisional upon obtaining: _____
7. Comments: _____
8. Fee liability: ☐ Home ☐ Overseas
9. Enclosed documents: ☐ Reference 1 ☐ Reference 2 ☐ IELTS/TOEFL Certificate ☐ Transcript

Please **DO NOT** remove any of the enclosed documents.

ADMISSIONS DECISION

RESEARCH PROGRAMME ☐ **MPhil** ☐ **PhD** ☐ Full-time ☐ Part-time

University Registration date: ☐ Oct 2007 ☐ Jan 2008 ☐ April 2008

Decision ☐ **Unconditional** ☐ **Conditional** ☐ **Reject** ☐ **Withdrawn** ☐ **Defer**

Conditions ☐ Degree Result: Class _____ ☐ English Language Qualification _____

☐ Other _____

Main area of research: _____ Supervisor (*please print*) _____

Minimum period of study: ☐ Three years ☐ Other _____

Head of School or authorised tutor: _____ Signature: _____ Date: _____

TAUGHT PROGRAMME ☐ **MA** ☐ **MSc** ☐ **MRes** ☐ **PgDip** ☐ **PgCert**

Title of programme: _____

Decision ☐ **Unconditional** ☐ **Conditional** ☐ **Reject** ☐ **Withdrawn** ☐ **Defer**

Conditions ☐ Degree Result: Class _____ ☐ English Language Qualification _____

☐ Other _____

Length of programme: ☐ One year full-time ☐ Two years part-time ☐ Other

Admissions tutor: _____ Signature: _____ Date: _____

QUALIFYING PROGRAMME (For 2008/2009 Entry to Programme)

Individual qualifying programme 2007/2008: ☐ Full-time ☐ Part-time

Programme to comprise (state name and number of modules/course units): _____

To enter (programme name): _____

Admissions tutor: _____ Signature: _____ Date: _____

ENGLISH LANGUAGE QUALIFICATION

☐ Please complete the enclosed English Language Check form if English is not the applicant's first language.

Please return this form to Registry. Failure to do so will delay the progress of this application and the student's enrolment.

Application for admission to postgraduate study at:
Admissions, Registry
Birkbeck, University of London
Malet Street, London WC1E 7HX

Request for confidential reference

TO THE REFEREE

The person named below has applied to this University of London College and has named you as a referee. Will you kindly let me have, as soon as possible, a confidential opinion in English on this candidate's academic and personal suitability for the proposed programme of study?

If there is a first or Master's degree examination result outstanding, I would appreciate some indication of the class of degree that you expect this candidate to obtain.

Please use the back of this letter for your reference and return it direct to the candidate, sealed in an envelope with your signature across the seal. The candidate will forward the reference with their application to my office. If you would prefer to write the reference on your own headed paper, I would be grateful if you would attach it to this letter, and use the headings given overleaf as a basis for your comments. If you wish to send the reference direct to the Registry, please let the candidate know that this is what you intend to do.

Thank you
Diana Driscoll
Deputy Registrar, Birkbeck, University of London

Reference to be returned to:
Admissions, Registry, Birkbeck, Malet Street, University of London, WC1E 7HX

TO THE CANDIDATE FOR ADMISSION

Please complete sections A, B and C below before sending out this form and a self-addressed envelope to each of the referees you have named on your application form. Please write clearly in **BLOCK CAPITALS.**

A Full name (underline family name): _____

B Proposed degree (master's or research) and programme of study: _____

C Month and year in which you intend to commence study: _____

CONFIDENTIAL STATEMENT BY REFEREE

Number of years that you have known the candidate:

In what capacity:

Academic ability of candidate and suitability for their chosen programme:

Any further relevant information:

Confirm award (if known): _____ Date of candidate's award (if known): _____

Name of referee: _____ Signature: _____

Position held: _____ Date: _____

Institution and address: _____

_____

_____

_____

Telephone: _____

Official stamp of institution

Application for admission to postgraduate study at:
Admissions, Registry
Birkbeck, University of London
Malet Street, London WC1E 7HX

Request for confidential reference

TO THE REFEREE

The person named below has applied to this University of London College and has named you as a referee. Will you kindly let me have, as soon as possible, a confidential opinion in English on this candidate's academic and personal suitability for the proposed programme of study?

If there is a first or Master's degree examination result outstanding, I would appreciate some indication of the class of degree that you expect this candidate to obtain.

Please use the back of this letter for your reference and return it direct to the candidate, sealed in an envelope with your signature across the seal. The candidate will forward the reference with their application to my office. If you would prefer to write the reference on your own headed paper, I would be grateful if you would attach it to this letter, and use the headings given overleaf as a basis for your comments. If you wish to send the reference direct to the Registry, please let the candidate know that this is what you intend to do.

Thank you
Diana Driscoll
Deputy Registrar, Birkbeck, University of London

Reference to be returned to:
Admissions, Registry, Birkbeck, Malet Street, University of London, WC1E 7HX

TO THE CANDIDATE FOR ADMISSION

Please complete sections A, B and C below before sending out this form and a self-addressed envelope to each of the referees you have named on your application form. Please write clearly in **BLOCK CAPITALS.**

A Full name (underline family name): _____

B Proposed degree (master's or research) and programme of study: _____

C Month and year in which you intend to commence study: _____

CONFIDENTIAL STATEMENT BY REFEREE

Number of years that you have known the candidate:

In what capacity:

Academic ability of candidate and suitability for their chosen programme:

Any further relevant information:

Confirm award (if known): _____ Date of candidate's award (if known): _____

Name of referee: _____ Signature: _____

Position held: _____ Date: _____

Institution and address: _____

_____

_____

_____

Telephone: _____

Official stamp of institution

STATISTICAL INFORMATION

SURNAME **FORENAMES**

Information on this page is requested for the purpose of meeting national higher education statistical requirements as defined by the Higher Education Statistics Agency (HESA) and will also be used by the College for statistical and monitoring purposes. The data will be stored in confidence by the College Registry and will not be passed on to staff in the Department(s) in consideration of your application.

NATIONALITY

COUNTRY OF PERMANENT RESIDENCE

PREVIOUS UNIVERSITY STUDY. If you have been registered as a student at any **other** university since August 1994, please enter your Higher Education Statistics Agency number (HESA number or HUSID) if known.

ETHNIC ORIGIN. Please tick the code from the list below which best describes your ethnic origin. (The codes listed are those used in the 1991 Census.) Only applicants whose permanent residence is in the UK are asked to answer this question *(please tick one code only)*.

- ☐ **11** White – British
- ☐ **12** White – Irish
- ☐ **19** Other White background
- ☐ **21** Black or Black British – Caribbean
- ☐ **22** Black or Black British – African
- ☐ **29** Other Black background
- ☐ **31** Asian or Asian British – Indian
- ☐ **32** Asian or Asian British – Pakistani
- ☐ **33** Asian or Asian British – Bangladeshi
- ☐ **34** Chinese or Other Ethnic background – Chinese
- ☐ **39** Other Asian background
- ☐ **41** Mixed – White and Black Caribbean
- ☐ **42** Mixed – White and Black African
- ☐ **43** Mixed – White and Asian
- ☐ **49** Other Mixed background
- ☐ **80** Other Ethnic background
- ☐ **90** Not known
- ☐ **98** Information refused

Disability. Please tick the code from the list of statements below that is most appropriate to you.

- ☐ **00** You do not have a disability
- ☐ **01** You have dyslexia
- ☐ **02** You are blind/are partially sighted
- ☐ **03** You are deaf/have a hearing impairment
- ☐ **04** You are a wheelchair user/ have mobility difficulties
- ☐ **05** You need personal care support
- ☐ **06** You have mental health difficulties
- ☐ **07** You have an unseen disability (e.g. diabetes, epilepsy, asthma)
- ☐ **08** You have two or more of the above disabilities/special needs
- ☐ **09** You have a disability not listed above

If you have a disability that is likely to affect your studies in any way, you should discuss the practical implications of this at your interview. You are also invited to consult the Student Disability Service Manager, Mark Pimm, on 020 7631 6315 (minicom 020 7631 6630).

FEES AND FINANCE

To help us assess Home/EU or Overseas fee liability we ask about your country of residence, both permanently and during the last three years. If you are in doubt about the rules, please contact the College Registry on 020 7631 6309.

If you have been awarded a scholarship, please give full details of the awarding body, your reference number if relevant, the duration and value of the award, and the terms and conditions of the scholarship (with a translation if appropriate). This may be most conveniently done by attaching to your application form a copy of the letter sent to you by the awarding body granting the award of the scholarship.

SUPPLEMENTARY INFORMATION FORMS

Applicants for programmes in Economics/Finance or Occupational Psychology/Organizational Behaviour or Career Management and Counselling are asked to complete special forms designed for those programmes. If you have not received such a form, please telephone the College Registry on 020 7631 6307/6390/6392/6389.

OPEN EVENINGS

Open Evenings during 2007 will be held on: 8 February, 1 May, 28 June and 6 September. For further details, please contact the Information Unit, 020 7631 6601/6692 or visit our website: www.bbk.ac.uk/openeve/

ADVICE AND INFORMATION

If you need further information or advice on completing this form, please contact the College Registry on:
Outside the UK: +44 20 7631 6307/6389/6390/6392 UK: 020 7631 6307/6389/6390/6392

CLOSING DATES AND SELECTION PROCEDURES

We aim to give equal consideration to all applications received before the end of April each year, but later applications are considered wherever possible. However, Admissions Tutors may have slightly different timetables for considering applications. Please check the description of the chosen course in the 2007 prospectus to ascertain:

- Whether a fixed closing date applies. (Note: where a fixed closing date does apply, it is sensible to send your form to the Registry a few days before the date to allow time for any queries to be resolved. The short-listing process will start shortly after the closing date, so it is important for Registry to receive your references by the closing date.)
- When interviews are to be held. (Note: some Admissions Tutors do not apply a fixed closing date, but indicate an interview period e.g. late May/early June. If this is the case try to submit your form to the College Registry at least two weeks before the earliest interview date to allow time for queries to be resolved or for samples of your written work to be called for if necessary.)
- When the programme is expected to be full. (Note: some Admissions Tutors do not apply a fixed closing date but prefer to consider applications as they are received, holding interviews each month until the programme is full. The programme description will indicate the month in which the tutor expects the programme to be full (usually June or July), but, if you are applying after the end of April, please check availability with the Admissions Tutor or with the College Registry before sending in your application.)

INTERVIEWS

Tutors will decide whether or not to invite you for interview on the basis of:

- standard and relevance of your qualifications
- information you give on your application form concerning skills, interests and experience relevant to the programme
- referees' comments on your suitability for the programme.

If international students need to be interviewed, the College will determine the most appropriate arrangements (e.g. telephone interview).

In addition, many Admissions Tutors will ask for a piece of written work to demonstrate your abilities.

OFFERS

Successful applicants will receive an official offer letter from the office of the Registrar.

SUMMARY

We aim to deal with application forms as quickly as possible. Before sending in your form please check that:

- you have included all relevant information on your application form
- your references are included with your form, if possible
- a copy of your degree transcript is included with your form (if required)
- *either* a copy of your passport with appropriate stamp *or* a letter from the Home Office (if required).

Also, if you are required to submit written work, please ensure that you submit it by the closing date.

Please detach and retain this page for information