บันทึกข้อความ

ส่วนราชการ หน่วยสนับสนุนการวิจัยและบริการ คณะวิศวกรรมศาสตร์ มหาวิทยาลัยอุบลราชธานี โทร.3319
ที่ ศธ 0529.8.4 / 1616 **วันที่** 3 พฤศจิกายน 2560
เรื่อง ขออนุมัติเงินสนับสนุนเพื่อนำเสนอผลงานวิจัยในการประชุมวิชาการระดับนานาชาติในประเทศ

เรียน รองคณบดีฝ่ายวิจัยและบริการวิชาการ ผ่านหัวหน้าภาควิชาวิศวกรรมเครื่องกล

ตามที่ข้าพเจ้า ดร.คมสันต์ รัตนกิจสุนทร ตำแหน่งอาจารย์ประจำภาควิชาวิศวกรรมเครื่องกล ได้รับการตอบรับในการนำเสนอผลงานวิจัย เรื่อง Mass Diffusion Coefficient Measurement for Vitreous Humor Using FEM and MRI ในการประชุมวิชาการระดับนานาชาติ The 8th TSME International Conference on Mechanical Engineering ระหว่างวันที่ 12 – 15 ธันวาคม 2560 ณ ประเทศไทย นั้น

ดังนั้น เพื่อให้การนำเสนอผลงานวิจัยเป็นไปด้วยความเรียบร้อย จึงใคร่ขออนุมัติทุนสนับสนุนเพื่อนำเสนอผลงานวิจัยดังกล่าว เป็นจำนวนเงิน 15,560 บาท (หนึ่งหมื่นห้าพันห้าร้อยหกสิบบาทถ้วน) โดยมีค่าใช้จ่ายในการนำเสนอผลงานทั้งสิ้น 15,560 บาท (หนึ่งหมื่นห้าพันห้าร้อยหกสิบบาทถ้วน) ดังนี้

1.	ค่าลงทะเบียน	10,500 บาท
2.	ค่ายานพาหนะภายในประเทศ (ไป-กลับ: อุบลฯ-กรุงเทพฯ)	2,500 บาท
3.	ค่ารถโดยสารประจำทาง	1,600 บาท
4.	ค่าเบี้ยเลี้ยงภายในประเทศ (240 บาท × 4 วัน)	960 บาท

ทั้งนี้ ข้าพเจ้าขอรับรองว่าผลงานเรื่องดังกล่าว ไม่เป็นส่วนหนึ่งของผลงานระดับบัณฑิตศึกษา และขออนุมัติทุนสนับสนุนตามค่าใช้จ่ายจริงไม่เกิน ~~40,000 บาท (สี่หมื่นบาทถ้วน)~~ 15,560.- บาท (-หนึ่งหมื่นห้าพันห้าร้อยหกสิบบาทถ้วน-)

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(ชาคริต โพธิ์งาม)
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อาจารย์ประจำภาควิชาวิศวกรรมเครื่องกล

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ได้รับอนุมัติสนับสนุนทุนทำเสนอผลงาน
ประชุมวิชาการระดับนานาชาติ
จึงเห็นควรอนุมัติเงินไปประชุมเกณฑ์
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ประจำปีงบประมาณ BRD เพื่อเป็นเบิกจ่ายต่อไป

3 พ.ย. 2560

เห็นควรอนุมัติ

7 พ.ย. 60

The 8th TSME International Conference on Mechanical Engineering

12-15 December 2017, Bangkok

Early-bird Registration Form

Participant Name: Komsan Rattanakijsuntorn

Paper ID (Leave blank for non-speaker): ICOME-2017-0279

Paper Title (Leave blank for non-speaker): Mass Diffusion Coefficient Measurement for Vitreous Humor Using FEM and MRI

University/Organization: Ubon Ratchathaini University

Billing Address: Faculty of Engineering, Department of Mechanical Engineering, Ubon Ratchathani University, 85 Sathonlamark Road, Warinchamrap, Ubon Ratchathani 34190

Phone: 092-684-5885 E-mail: komsan.r@ubu.ac.th

Special Events
- ✓ I will join the banquet dinner on a cruise on 14 December 2017.
- ✓ I will join the excursion trip in the afternoon of 15 December 2017.

Attendance Category

Please select only one category:		Registration fee (THB)
☐	Speaker (General) + Regular ICOME2017 Proceedings	7,500.-
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Account name: ICOME 2017 **Swift code:** BKKBTHBK

Please also include your paper ID (ICOME-2017-XXXX) in the email title.

Komsan Rattanakijsuntorn <komsan.r@ubu.ac.th>

[icome2017] Acceptance into IOP Conference Series Proceedings

Submission TSME <icome2017@eng.kmutnb.ac.th> Fri, Oct 27, 2017 at 12:55 PM
Bcc: komsan.r@ubu.ac.th

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TSME-ICoME 2017 12-15 December 2017
Arnoma Grand Hotel, Bangkok, Thailand

12 December 2017	
Registration @ 2nd Floor Foyer	
13:00 - 18:00	Registration/Networking

13 December 2017	
Registration @ 2nd Floor Foyer	
08:00 - 08:30	Registration/Networking
Conference Opening and Keynote Speeches @ Arnoma Grand	
08:30 - 09:00	Welcome Speech by **Prof.Dr.Suwat Kuntanapreeda and Assoc.Prof.Dr.Sinchai Chinvorarat** Conference Co-Chairs Department of Mechanical and Aerospace Engineering, King Mongkut's University of Technology North Bangkok (KMUTNB) **Prof.Dr.-Ing.habil. Suchart Siengchin** President, King Mongkut's University of Technology North Bangkok (KMUTNB) **Asst.Prof.Dr.Chinda Charoenphonphanich** President, Thai Society of Mechanical Engineers (TSME) **Prof.Dr.Mari Oshima** President, The Japan Society of Mechanical Engineers (JSME)
09:00 - 09:15	Honorary Speaker: **Mr. Stefan Bienefeld** DAAD-Deutscher Akademischer Austauschdienst, German Academic Exchange Service *The role of DAAD support in fostering Mechanical Engineering Capacity for Development*
09:15 - 09:30	Honorary Speaker: **Dr. Eberhard Alles** Chancellor TU Chemnitz, Germany *Making Industry 4.0 Work: Best Practices from a University Management Perspective*
09:30-09:55	Keynote Speaker: **Univ.-Prof. Dr.-Ing. habil. Prof. E. h. Prof. Lothar Kroll** Director of Institute of Lightweight Structures, TU Chemnitz, Germany *Technology Fusion in Series Production of Lightweight Structures*

13 December 2017 (Cont.)	
09:55 - 10:20	Keynote Speaker: **Prof. Dr. Shinichi Nakasuka** Department of Aeronautics and Astronautics, University of Tokyo, Japan Micro/nano/pico-satellite Challenge for Novel Space Development and Utilization
10:20 - 10:40	Coffee Break
10:40 - 11:05	Keynote Speaker: **Prof. Dr.-Ing. Heinz Peter Berg** Chair of Combustion Engines and Flight Propulsion Brandenburg University of Technology Cottbus-Senftenberg, Germany *Microturbine- and Turbo-Fuel-Cell Technology for Highly Effective Generation of Electricity -- Example of an International Technology Transfer Supported by the DAAD*
11:05 - 11:30	Keynote Speaker: **Prof. Dr. Yasuyuki Nishioka** Department of Engineering and Design, Faculty of Engineering and Design Hosei University, Japan *Kaizen Approach to Smart Manufacturing for Connected Industries*
11:30 - 11:55	Keynote Speaker: **Prof. Dr. Suwat Kuntanapreeda** Department of Mechanical and Aerospace Engineering, Faculty of Engineering King Mongkut's University of Technology North Bangkok, Thailand *Lessons Learned from KNACKSAT Satellite*
11:55 - 13:00	Lunch

Session 1

@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
13:00 - 13:20	AMM0001	AEC0002	CST0001	DRC0002	AME0004	TSF0001
13:20 - 13:40	AMM0004	AEC0003	CST0002	DRC0003	AME0005	TSF0003
13:40 - 14:00	AMM0005	AEC0004	CST0005	DRC0006	AME0006	TSF0004
14:00 - 14:20	AMM0008	AEC0005	CST0006	DRC0008	AME0008	TSF0005
14:20 - 14:40	AMM0009		CST0007	DRC0011	AME0009	
14:40 - 15:00	Coffee Break					

Session 2

@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
15:00 - 15:20	AMM0010	AEC000A	CST0009	DRC000A	AME000A	TSF0006
15:20 - 15:40	AMM0011	AEC0006	CST0011	DRC0013	AME0001	TSF0007
15:40 - 16:00	AMM0012	AEC0007	CST0012	DRC0014	AME0010	TSF0008
16:00 - 16:20	AMM0013	AEC0009	CST0013	DRC0016	AME0011	TSF0009
16:20 - 16:40	AMM0015	AEC0010	CST0014	DRC0007	AME0012	TSF0010
16:40 - 17:00	AMM0016		CST0015	DRC0028	AME0016	TSF0011

14 December 2017						
Session 3						
@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
09:00 - 09:20	BME0001	AEC000B	CST000A	DRC0004	ETM000A	TSF000A
09:20 - 09:40	BME0002	AEC0012	CST0016	DRC0017	ETM0001	TSF0012
09:40 - 10:00	BME0009	AEC0013	CST0017	DRC0019	ETM0002	TSF0013
10:00 - 10:20	BME0010	AEC0014	CST0018	DRC0020	ETM0003	TSF0014
10:20 - 10:40	Coffee Break					
Session 4						
@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
10:40 - 11:00	AMM0017	AEC000C	BME0003	DRC0005	AME0003	TSF0015
11:00 - 11:20	AMM0018	AEC0015	BME0006	DRC0021	AME0013	TSF0017
11:20 - 11:40	AMM0019	AEC0017	BME0007	CST0020	AME0014	TSF0019
11:40 - 12:00	AMM0020	AEC0019		CST0022	AME0015	
12:00 - 13:00	Lunch					
Session 5						
@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
13:00 - 13:20	AMM0021	EDU0001	CST000B	DRC0022	ETM0005	TSF0020
13:20 - 13:40	AMM0022	EDU0002	CST0019	DRC0023	ETM0007	TSF0022
13:40 - 14:00	AMM0023	EDU0003	CST0023	DRC0024	ETM0008	TSF0023
14:00 - 14:20	AMM0024	EDU0004	CST0024	DRC0025	ETM0009	TSF0024
14:20 - 14:40	AMM0025	EDU0005	CST0025	DRC0026	ETM0010	
14:40 - 15:00	AMM0026	IEI0001	CST0026	DRC0027	ETM0012	
15:00 - 16:00	Poster Presentation (ASEAN Session)/Coffee Break					
16:30 - 18:00	Move to Pier: Buses leave from the hotel parking lot					
18:00 - 21:00	TSME Annual General Meeting & Banquet Dinner on a Cruise					

15 December 2017						
Session 6						
@	Arnoma I	Arnoma II	Arnoma III	Thip-ubol	Pathummas	Sarocha
09:00 - 09:20	AMM0002	AEC0001	CST0003	DRC0001	ETM0004	TSF0002
09:20 - 09:40	AMM0003	AEC0008	CST0004	DRC0009	ETM0006	TSF0016
09:40 - 10:00	AMM0006	AEC0011	CST0008	DRC0010	ETM0011	TSF0018
10:00 - 10:20	AMM0007	AEC0016	CST0010	DRC0012	BME0004	TSF0021
10:20 - 10:40	AMM0014	AEC0018	CST0021	DRC0015	BME0005	AME0002
10:40 - 11:00				DRC0018	BME0008	AME0007
11:00 - 11:20	Coffee Break					
Closing Ceremony @ Arnoma II						
11:20 - 12:00	Closing Remarks and Awarding Ceremony					
12:00 - 13:00	Farewell Lunch					
13:00 - 16:00	Excursion Trip (Registered Participants)					

Applied Mechanics, Materials and Manufacturing

AMM0001 Development of Solid State Bonding Technology for the Aluminum Alloy in Atmosphere by Using High Frequency Induction Heating and Ultrasonic Vibration

AMM0002 Application of grey-fuzzy approach in parametric optimization of EDM process in machining of MDN 300 steel

AMM0003 Fatigue Behavior of Resistance Spot Welded High Strength Steel Sheets with Different Nugget Sizes

AMM0005 Development and Comparison of Processing Maps of Mg-3Sn-1Ca Alloy from Data Obtained in Tension versus Compression

AMM0006 Compressive behavior of Sulcata Tortoise's carapace at high rate of deformation

AMM0007 Nanoindentation Tests of Sulcata Tortoise's Carapace

AMM0008 Evaluation of Tensile Strength and Consideration of the Rope Structure of Net for Super-Pressure Balloon.

AMM0009 Characteristics of Acoustic Emission from Corrosion in Anticorrosive Coated Steel

AMM0010 Development of the Novel Non-contact AE Sensor Using Air-coupled Ultrasonic Transducer for Plates and Cylinders

AMM0011 Development of the Evaluation Method for the Surface Condition of Spur Gears Using AE Method

AMM0012 The Method for Detecting Damages of Wire Cables using Guided Waves

AMM0013 Development of feedback-speed-control system of fixed-abrasive tool for mat-surface fabrication

AMM0014 Study of Heating and Cooling Temperature of Injection Molding to Effect on Gloss of Plastic Injection Parts

AMM0015 Dry sliding wear behavior of Fe-Cr-Mo-C steel by nickel addition

AMM0016 Use of FDM Rapid Prototyping Technology in the Production of Components and their Strength Properties

AMM0017 Study on Tool Wear Characteristics of Precision Cutting in The Ductile Iron FCD600

AMM0018 Examination of Drilling for Small-diameter Holes in Aluminum Alloys

AMM0019 Study on Ultra-Precision Cutting of Al-Mg Alloys in Multi-Facet Diamond Tools

AMM0020 Material Selection and Assembly Method of Battery Pack for Compact Electric Vehicle

AMM0021 Changes in the Hardness and Microstructures of Severely Deformed Î²-Titanium Alloys

AMM0022 Characterization of Hemp Fiber with Alkaline Surface Treatment for Polymer Matrix Composite Applications

AMM0023 Experimental Investigations of Density-Induced Segregation in Binary Granular Mixtures under Vertical Vibrations

AMM0024 A Comparison of Mechanical Properties Between Plasma Arc Welding (PAW) and Four Popular Type of Welding Process (SMAW GMAW FCAW GTAW) on Dissimilar Materials

AMM0025 Surface Roughness Determination and Comparison of Parts Printed Using Different Additive Manufacturing Techniques

AMM0026 Compressive Deformation Behavior of Meso Pillar Fabricated from Magnesium Alloy AZ 80

Biomechanics and Bioengineering

BME0001 The Evaluation of Labral Repair Affect Hip Joint by Finite Element Analysis

BME0002 Numerical Modeling of the Influence of Stromal Cells on Tumor Growth and Angiogenesis

BME0003 Numerical Simulation of the Hair Formation - Modeling of Hair Cycle -

BME0004 Particle Simulation on the Skin Formation -Melanin Transportation and Freckles Formation-

BME0005 The Development of Lab-on-a-chip Fabricated from Two Different Molds

BME0006 Kinematic analysis and trajectory of a dog-like robot

BME0007 Performance study of knee supports by electromyography (EMG) testing

BME0008 Mass Diffusion Coefficient Measurement for Vitreous Humor Using FEM and MRI

BME0009 The Strain Distribution on Varus Knee Corrected by Close Wedge High Tibial Osteotomy Supplement Distal Femoral Osteotomy

BME0010 Improved Design of a Cone-shaped Rotating Disk for Shear Force Loading in a Cell Culture Plate

TSME-ICoME 2017

The 8th Thai Society of Mechanical Engineers, International Conference on Mechanical Engineering

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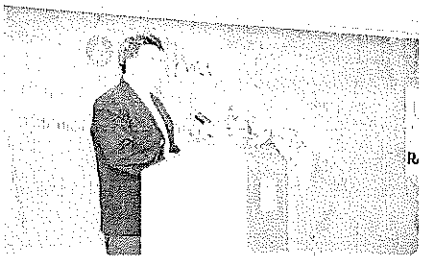
About TSME-ICoME



Since 1987, the Thai Society of Mechanical Engineers (TSME) has been holding national conferences in Mechanical Engineering yearly. These conferences are called **Mechanical Engineering Network of Thailand (ME-NETT)**. The objectives of the conferences are to encourage students, researchers, and interested persons to present their works, to create researching networks, to publish the research works for industry sectors, to find the needs of public and private organizations, to fulfill these demands to enhance the growth of country, and to be a hub in the field of Mechanical Engineering for anyone with an interest.

In 2010, with collaboration from the American Society of Mechanical Engineers (ASME), the Japan Society of Mechanical Engineers (JSME), and the United Kingdom's Institute of Mechanical Engineers (IMechE), TSME started to hold yearly international conferences under the name of the **International Conference on Mechanical Engineering (ICoME).**

In 2017, the 8th TSME-ICoME will be hosted by Department of Mechanical and Aerospace Engineering (MAE), Faculty of Engineering, King Mongkut's University of Technology North Bangkok (KMUTNB).

1st	2010	TSME at Ubonratchathani University
2nd	2011	TSME at Krabi Province
3rd	2012	King Mongkut's University of Technology Thonburi
4th	2013	Burapha University
5th	2014	King Mongkut's Institue of Technology Ladkrabang
6th	2015	Mahidol University
7th	2016	Chulalongkorn University
8th	2017	King Mongkut's University of Technology North Bangkok

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The 8th Thai Society of Mechanical Engineers, International Conference on Mechanical Engineering

General Information

Important Dates

Abstract Submission Deadline (Extended):*	~~31 May 2017~~ 14 July 2017 [Closed]
Abstract Acceptance Notification Date (Extended):	~~9 June 2017~~ 31 July 2017 [Completed]
Full Manuscript Submission Deadline (Extended):*	~~31 August 2017~~ 15 September 2017 [Closed]
Full Manuscript Acceptance Notification Date (Extended):	~~30 September 2017~~ 7 October 2017 [Completed]
Camera-Ready Manuscript Submission Deadline (Extended):	~~16 October 2017~~ 23 October 2017 [Closed]
Early-bird Registration Deadline (Extended):	~~30 October 2017~~ 3 November 2017
Conference Date:	12-15 December 2017

* submission templates can be found on the Downloads page

Conference Topics

- Alternative Energy and Combustion (AEC)
- Automotive Aerospace and Marine Engineering (AME)
- Applied Mechanics, Materials and Manufacturing (AMM)
- Biomechanics and Bioengineering (BME)
- Computation and Simulation Techniques (CST)
- Dynamic Systems, Robotics and Controls (DRC)
- Engineering Education (EDU)
- Energy Technology and Management (ETM)
- Industrial Entrepreneurship (IEI)
- Microsystem and Nanotechnology (MSN)
- Thermal System and Fluid Mechanics (TSF)

Conference Program

12 Dec 2017	Registration Open
13 Dec 2017	Opening Ceremony and Conference Presentations
14 Dec 2017	Conference Presentations and Banquet on a Cruise
15 Dec 2017	Conference Presentations, Closing Ceremony and Excursion Trip

Conference Venue

Arnoma Grand Hotel, Bangkok, Thailand (factsheet|site|map|contact)
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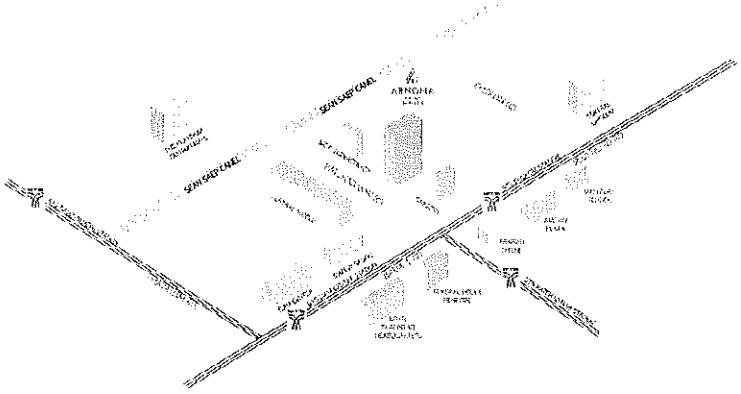

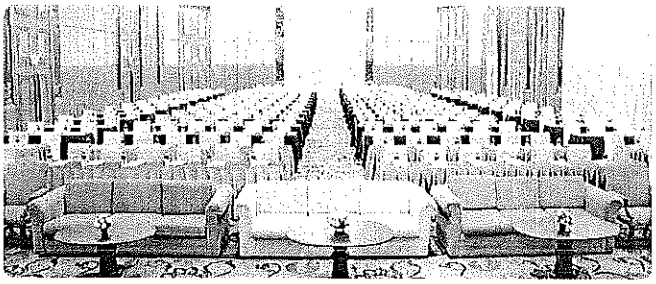

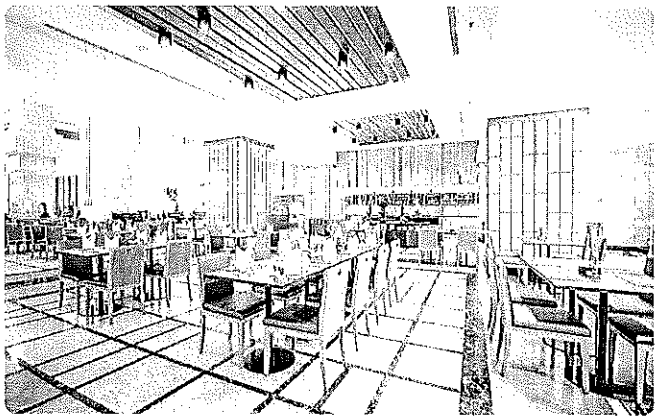

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Instruction in Thai / ขั้นตอนการลงทะเบียน

(1) กรอกแบบฟอร์มการลงทะเบียน [Word][PDF]
(2) ชำระเงินด้วยวิธีโอนผ่านตู้ ATM หรือเคาท์เตอร์ธนาคาร ตามรายละเอียดด้านล่างนี้
(3) อีเมลสำเนาการโอนเงินพร้อมแบบฟอร์มการลงทะเบียนของท่านมาที่ icome2017.register@eng.kmutnb.ac.th โดยใส่รหัสบทความ (ICOME-2017-XXXX) มาในหัวเรื่องด้วย

ธนาคาร: ธนาคารกรุงเทพ จำกัด (มหาชน)
สาขา: มหาวิทยาลัยเทคโนโลยีพระจอมเกล้าพระนครเหนือ
บัญชีออมทรัพย์เลขที่: 907-7-19742-5
ชื่อบัญชี: ICOME 2017

For registration deadlines, please refer to the information on this page.

Registration Fee (in THB)		Early-bird Registration	Regular/On-site Registration
Speakers* *(price per paper)*	General	7,500.-	9,000.-
	Student	6,500.-	8,000.-
Non-speakers	General	6,000.-	7,500.-
	Student	5,000.-	6,500.-
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Mass Diffusion Coefficient Measurement for Vitreous Humor Using FEM and MRI

Komsan Rattanakijsuntorn[1,*], Anita Penkova[2], and Satwindar S. Sadhal[2]

1Faculty of Engineering, Department of Mechanical Engineering, Ubon Ratchathani University, 85 Sathonlamark Road, Warinchamrap, Ubon Ratchathani 34190, Thailand
2Aerospace & Mechanical Engineering Department, University of Southern California, Los Angeles, CA 90089-1453, United States

* Corresponding Author: komsan.r@ubu.ac.th

Abstract. In early studies, the 'contour method' for determining the diffusion coefficient of the vitreous humor was developed. This technique relied on careful injection of an MRI contrast agent (surrogate drug) into the vitreous humor of fresh bovine eyes, and tracking the contours of the contrast agent in time. In addition, an analytical solution was developed for the theoretical contours built on point source model for the injected surrogate drug. The match between theoretical and experimental contours as a least square fit, while floating the diffusion coefficient, led to the value of the diffusion coefficient. This method had its limitation that the initial injection of the surrogate had to be spherical or ellipsoidal because of the analytical result based on the point-source model. With a new finite element model for the analysis in this study, the technique is much less restrictive and handles irregular shapes of the initial bolus. The fresh bovine eyes were used for drug diffusion study in the vitreous and three contrast agents of different molecular masses: gadolinium-diethylenetriaminepentaacetic acid (Gd-DTPA, 938 Da), non-ionic gadoteridol (Prohance, 559 Da), and bovine albumin conjugated with gadolinium (Galbumin, 74 kDa) were used as drug surrogates to visualize the diffusion process by MRI. The 3D finite element model was developed to determine the diffusion coefficients of these surrogates with the images from MRI. This method can be used for other types of bioporous media provided the concentration profile can be visualized (by methods such as MRI or fluorescence).

1. Introduction

During the past decades, many researcher have attempted to develop ocular drug delivery systems. Intravitreal drug delivery has become a popular method of treatment of many retinal diseases, commonly including AMD, Diabetic Retinopathy, and Retinal Vein Occlusions. While various drugs have been successfully developed, delivering drugs to the retina requires knowledge of the relevant fluid mechanics and transport phenomena. Low drug concentrations are insufficient to treat the retinal disease and high concentrations can carry risks of side effects [1-3]. Therefore, it is crucial to know the drug distribution within the eye following delivery by intravitreal injection.

With the help from the advanced computer software nowadays, ocular drug transport models have been developed to simulate and predict drug distribution in the eye [4-7]. These models require the values of parameters that are used in the governing equations, and one of the most common uses of

parameter is drug diffusivity. Therefore, the aim of this work is to develop a technique that delivers the values of diffusion coefficient of drugs in the vitreous from MRI images.

In early study by Penkova et al [8], the 'contour method' for determining the diffusion coefficient of the vitreous humor was developed. This technique relied on careful injection of an MRI contrast agent (surrogate drug) into the vitreous humor of fresh bovine eyes, and tracking the contours of the contrast agent in time. In addition, an analytical solution was developed for the theoretical contours built on point source model for the injected surrogate drug. The match between theoretical and experimental contours as a least square fit, while floating the diffusion coefficient, led to the value of the diffusion coefficient. This method had its limitation that the initial injection of the surrogate had to be spherical or ellipsoidal because of the analytical result based on the point-source model. With a new finite element model for the analysis in this study, the technique is much less restrictive and handles irregular shapes of the initial bolus.

2. Methods and materials

2.1. Apparatus

Whole bovine eyes were prepared for MRI visualization with the same method as described in the previous study [8]. Three gadolinium-based contrast agents: gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA, 938 Da), nonionic gadoteridol (Prohance, 559 Da), and bovine albumin conjugated with gadolinium (Galbumin, 74 kDa) were used as drug surrogates to model diffusive transport of different molecular weight drugs. Experiments were conducted by injecting 30 μL of the contrast agents in the vitreous of the whole eye. With the concentration measurement from the MRI signal at regular intervals for 2-3 hours, the concentration contours were constructed and matched with the theoretical contours from the finite element analysis. The best fit at different times gave fairly consistent values of the diffusion coefficient.

2.2. Governing equations and model development

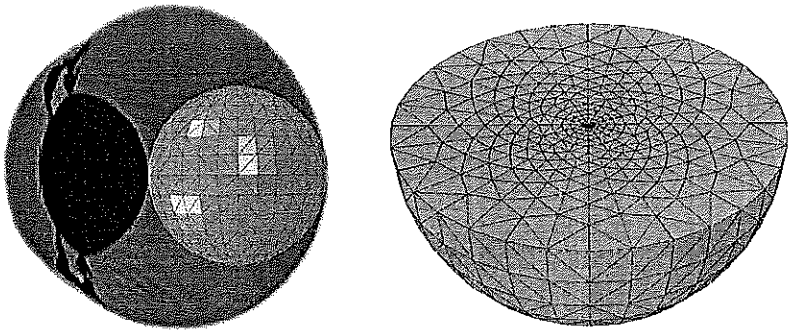
A three-dimensional finite element model of the vitreous was developed to help in analyzing MRI images and calculate diffusion coefficients by comparing simulated data to MRI experimental data. To model the drug distribution in the vitreous, the mass transport equation was applied:

$$\frac{\partial c}{\partial t} + v \cdot \nabla c - D\nabla^2 c + q = 0 \tag{1}$$

where c represents the concentration of the drug, D is the diffusion coefficient of the drug in the vitreous, v is the velocity of fluid in the vitreous, and q is the release rate of the drug. Since the experiment was conducted by excluding convection in the system, and we assumed that the drug is neither generated nor degraded within the vitreous, the terms involving with v and q were set to zero. The mass transport equation can be rewritten as:

$$\frac{\partial c}{\partial t} - D\nabla^2 c = 0 \tag{2}$$

For the purpose of modelling, the domain of interest (of the vitreous) in which drugs diffused through was simply defined as a sphere with a radius of 10 mm as illustrated in figure 1(a). The geometry created for the domain of interest, were converted into a total of 105,276 finite element tetrahedral meshes. Since the rate of change of concentration over time near the center of the domain is larger than the outer, mesh size was varied by having finer meshes near the center and coarser meshes near the outer boundary as shown in figure 1(b).



(a) (b)

Figure 1. The domain of interest and the finite element tetrahedral meshes.

2.3. Boundary and initial conditions

The vitreous humor in this study is considered to be a homogeneous substance. The lens is avascular and is considered to be impermeable to fluid flow, so we assumed that the drug surrogate does not penetrate the lens. Similarly, RPE is considered as a major barrier for the retinal delivery of hydrophilic drugs, the same assumption that we made for the lens also applied for the RPE. Since the outer boundary of the domain of interest reaches the regions of lens and RPE membrane, we simplified the boundary condition at the outer surface as zero flux condition. This kind of boundary condition would much simplify the finite element equation by eliminating the flux term as detailed in appendix A. The concentration distribution profiles of the MRI images were directly projected to the nodes in the finite element model as the initial condition for each time point. With this method, we can handle the situation that the concentration distribution profile was not symmetric.

2.4. Solution methodology

The concentration distribution in the vitreous was solved using the finite element method involving linear algebraic equations of the form,

$$[K_C]\left\{\frac{dC}{dt}\right\} + D[K_D]\{C\} = 0, \tag{3}$$

where $[K_C]$ and $[K_D]$ are the global system matrices developed from the Galerkin finite element method in appendix A. The solution employed the 3-D mesh of a total of 105,276 elements, and four nodal tetrahedral elements were used in the 3-D continuum domain. For the time discretization, we applied the well-known theta-method, which results in the equation

$$[K_C]\left\{\frac{C^{n+1} - C^n}{\Delta t}\right\} + D[K_D]\{\theta C^{n+1} + (1-\theta)C^n\} = 0 \tag{4}$$

here C^n is the concentration distribution at a specific time point, C^{n+1} is the concentration distribution at the later time point, and the parameter θ is related to the applied numerical method. It is worth emphasizing that for $\theta = 0.5$, the method yields the Crank-Nicolson implicit method which has higher accuracy and unconditional stable for the time discretization [9]. Substituting $\theta = 0.5$ in equation (4), then it can be rewritten as,

$$([K_C] + 0.5\Delta t D[K_D])\{C^{n+1}\} = ([K_C] - 0.5\Delta t D[K_D])\{C^n\} \tag{5}$$

In this equation, the concentration profile C^n was known by projecting the concentration values of a specific time point from MRI images onto the finite element domain. The unknown parameter, D, was floated in order to get the calculated C^{n+1} which represents the concentration at the later time step. The value of D between two consecutive time points can be obtained by least square fitting of C^{n+1} and the concentration profile of the later time point from MRI images.

2.5. Model validation

In order to verify the finite element diffusion model developed in the previous section, the solutions obtained from the model was compared with the exact solutions. The exact solution for a spherical bolus of radius r_0 in a spherical shell of radius R was derived in the previous study [8] and shown in equation (6).

$$c(r,t) = c_0\left[\frac{r_0^3}{R^3} + 2\sum_{n=1}^{\infty}\frac{\sin(\lambda_n r_0) - \lambda_n r_0\cos(\lambda_n r_0)}{\lambda_n R\, sin^2(\lambda_n R)}e^{-D\lambda_n^2 t}\frac{\sin(\lambda_n r)}{\lambda_n r}\right] \tag{6}$$

where c_0 is the initial concentration of the drug deposited, r is the radial distance from the point of injection, D is the diffusion coefficient, t is the time, $c(r,t)$ is the concentration, and $\lambda_n$is the set of constants satisfying the transcendental equation.

$$\lambda_n R = \tan(\lambda_n R) \tag{7}$$

For the model validation, we use the following parameters: $r_0 = 2$ mm, $R = 10$ mm, and $c_0 = 0.05$ in both finite element model and the exact solution, to compare the concentration values. Figure 2 shows the comparison of concentration distribution profiles from the developed model and the exact solution under the same initial and boundary conditions. The finite element solutions along the center line at a specific time (t=40 min) have a strong agreement with the exact solutions.

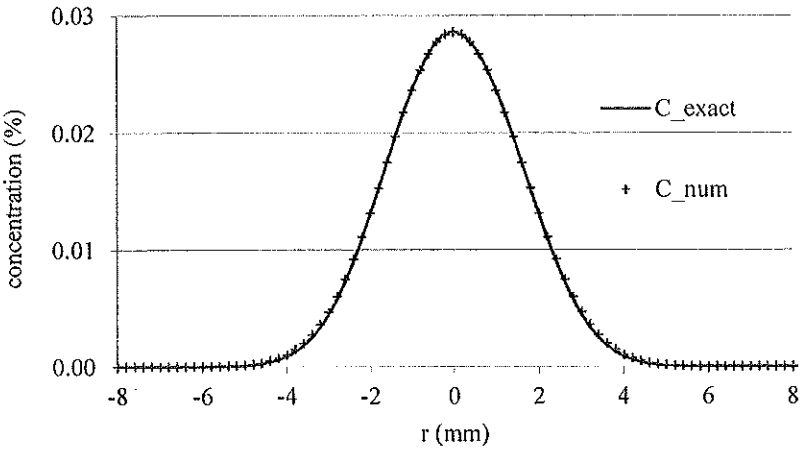


Figure 2. The comparison of concentration distribution profiles from the finite element model and the exact solution.

3. Results

Following the method of diffusion coefficient measurement by using MRI developed earlier, contours of constant concentration were established for different drug surrogates in each eye, and the comparison of these with the corresponding finite element calculation was shown in figure 3 where the (x, y, z) coordinate system in relation to the eye is shown in figure 4. While several time points for each eye were recorded and used in the analysis, only a selected example for each contrast agent is shown for illustrative purposes. The diffusion coefficients values of each drug surrogates acquired from the finite element method were presented in figure 5. We have made a comparison of previously reported D values for Gd-DTPA from the analytical method in the previous study [8] with the current method (finite element), and found that they were very consistent. The diffusion coefficient was $(3.040 \pm 0.274) \times 10^{-6}$ cm^2/s from the analytical method, and $(3.069 \pm 0.237) \times 10^{-6}$ cm^2/s from the finite element method. By comparing the diffusion coefficients between Gd-DTPA (molecular weight 938 Da), Prohance (molecular weight 559 Da), and Galbumin (molecular weight around 74k Da), we found that Galbumin had the lowest diffusivity, while Gd-DTPA had the highest diffusivity in the vitreous.

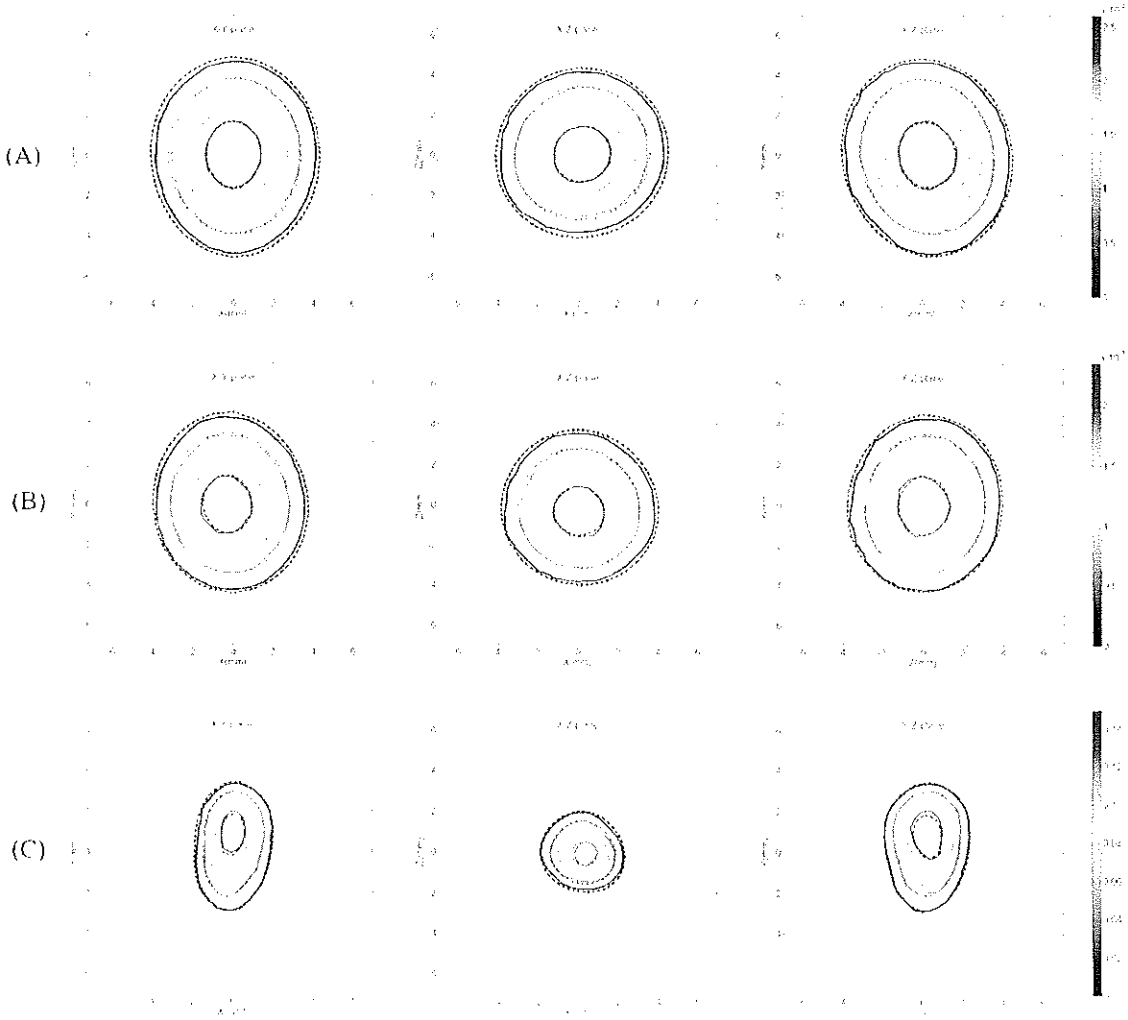


Figure 3. Contours of constant concentration in (A) Gd-DTPA at t=85 min, (B) Prohance at t=88 min, and (C) Galbumin at t=185 min (—— : measurement, ---- : finite element).

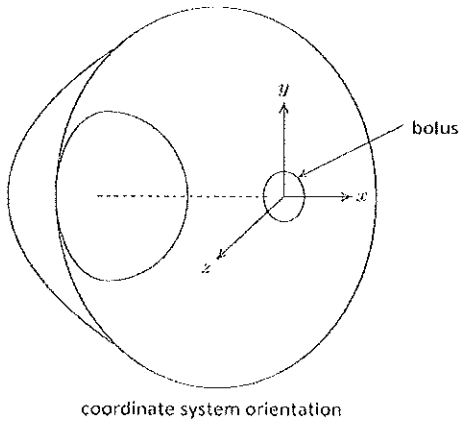


Figure 4. Coordinate system orientation with respect to the eye. The origin located at the center of the bolus.

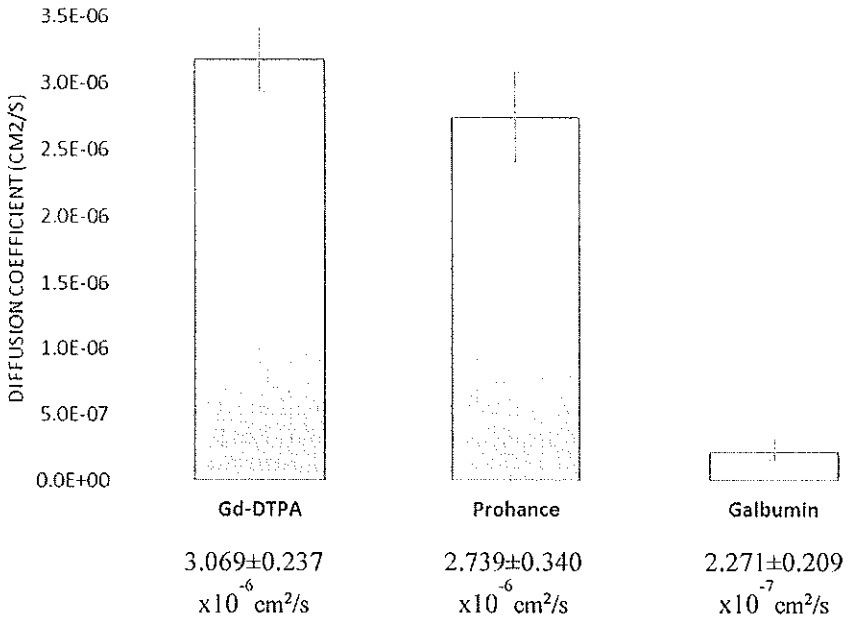


Figure 5. Diffusion coefficients of drug surrogates in bovine eyes.

4. Discussion

Early investigations of diffusion coefficients of different MRI contrast agents had been conducted by Gillis et al [10]. They measured diffusivity of a negatively charged contrast agent Gd-DTPA and the non-ionic gadoteridol, Prohance, in control cartilages using MRI. The diffusion coefficients for Gd-DTPA and Prohance were reported by Gillis et al as $(1.84 \pm 0.12) \times 10^{-6}$ cm^2/s and $(1.55 \pm 0.22) \times 10^{-6}$ cm^2/s respectively. In our study, we found that the diffusion coefficient in the vitreous of a smaller molecule, Prohance was $(2.739 \pm 0.340) \times 10^{-6}$ cm^2/s which was lower than the diffusion coefficient of

a larger molecule, Gd-DTPA. This implied that the effect of negative net charge on Gd-DTPA is likely to enhance the diffusivity in the vitreous.

Galbumin used in this experiment is a bovine albumin conjugated with gadolinium which has negative charge. Molokhia et al estimated the free aqueous diffusion coefficient of Galbumin in water at 37 °C as 8×10^{-7} cm^2/s using the diffusion coefficient of bovine serum albumin (BSA), viscosity of water, and molecular weights of Galbumin and BSA [11]. The diffusion coefficient of Galbumin in this study was found to be $(2.271 \pm 0.209) \times 10^{-7}$ cm^2/s which is in the same order as the one estimated by Molokhia. Our lower value can also be attributed to the fact that we conducted experiments at room temperature. To compare with the smaller negative charge Gd-DTPA, Galbumin has a lower diffusion coefficient as expected.

5. Conclusion

The contour method recently developed is a very useful technique for the diffusion coefficient measurement in vitreous humor. With a new finite element model for the analysis, it can handle arbitrary shapes of the concentration contours, and we are able to show a comparison of diffusion coefficients of Gd-DTPA with Prohance and Galbumin. It has been found that both molecular weight and net charge of drugs affect the diffusion process in the vitreous humor. This method does not only work for the measurement in the vitreous humor, but also can be applied for other types of tissues in which the concentration profile can be visualized by MRI or fluorescence. The fact that we can now handle irregular shapes of the contours, the technique can be opened up to measure parameters that include convective transport effects as well.

Acknowledgement

The work in this paper is supported by NIH (National Institute of Health) under award number 5R01EY026599-02.

Appendix A. Finite element equations for the intravitreal diffusion

This section provides a detailed derivation of 'weak form' of the drug diffusion equation using Galerkin method. Basic concept and application of this method can be found in literature [9]. The procedure starts by considering the suitable form of the mass transport equation which is given by equation (2),

$$\frac{\partial C}{\partial t} - D\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} + \frac{\partial^2 C}{\partial z^2}\right) = 0 \tag{A1}$$

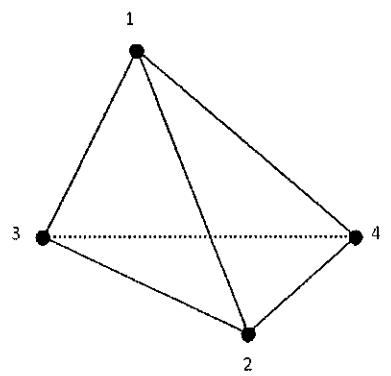


Figure A1. Linear tetrahedral element.

A domain V is divided into linear tetrahedral finite elements connected at nodes as shown in figure A1. Shape functions Ni are used for interpolation of concentration inside a finite element,

$$C = [N]\{C\}$$

where

$$[N] = [N_1 \;\; N_2 \;\; N_3 \;\; N_4]$$

$$\{C\} = \begin{Bmatrix} C_1 \\ C_2 \\ C_3 \\ C_4 \end{Bmatrix}$$

Here {C} is a vector of concentrations at nodes and [N] is a matrix of shape functions. Using the Galerkin method, we can write equation (A1) in the following form:

$$\int_V N_i \left[\frac{\partial C}{\partial t} - D\left\{\frac{\partial}{\partial x}\left(\frac{\partial C}{\partial x}\right) + \frac{\partial}{\partial y}\left(\frac{\partial C}{\partial y}\right) + \frac{\partial}{\partial z}\left(\frac{\partial C}{\partial z}\right)\right\}\right] dV = 0 \tag{A2}$$

Applying the divergence theorem to the terms in the bracket {}, we arrive at the relations:

$$\int_V N_i \frac{\partial C}{\partial t} dV + D \int_V \left[\frac{\partial N_i}{\partial x}\frac{\partial C}{\partial x} + \frac{\partial N_i}{\partial y}\frac{\partial C}{\partial y} + \frac{\partial N_i}{\partial z}\frac{\partial C}{\partial z}\right] dV$$

$$- D \int_S \left[N_i \frac{\partial C}{\partial x} n_x + N_i \frac{\partial C}{\partial y} n_y + N_i \frac{\partial C}{\partial z} n_z\right] dS = 0 \tag{A3}$$

where n_x , n_y , and n_z are outer normal components to the surface of the body. Since we applied the zero flux boundary condition at the surface of the body, the last terms in the integral of S is zero. Now the equation (A3) can be simplified as,

$$\left(\int_V \{N\}\,[N] dV\right)\left\{\frac{dC}{dt}\right\} + D\left(\int_V \left\{\frac{\partial N}{\partial x}\right\}\left[\frac{\partial N}{\partial x}\right] dV + \int_V \left\{\frac{\partial N}{\partial y}\right\}\left[\frac{\partial N}{\partial y}\right] dV + \int_V \left\{\frac{\partial N}{\partial z}\right\}\left[\frac{\partial N}{\partial z}\right] dV\right)\{C\} = 0$$

Let's denote

$$[K_C] = \int_V \{N\}\,[N] dV$$

$$[K_D] = \int_V \left\{\frac{\partial N}{\partial x}\right\}\left[\frac{\partial N}{\partial x}\right] dV + \int_V \left\{\frac{\partial N}{\partial y}\right\}\left[\frac{\partial N}{\partial y}\right] dV + \int_V \left\{\frac{\partial N}{\partial z}\right\}\left[\frac{\partial N}{\partial z}\right] dV$$

The discretized finite element equation for the mass transport equation can be rewritten as in equation (3),

$$[K_C]\left\{\frac{dC}{dt}\right\} + D[K_D]\{C\} = 0 \tag{A4}$$

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